SCALE OF URINARY COLORS, ACCORDING TO VOGEL.

I.
**Pale Yellow.**

II.
**Light Yellow.**

III.
**Yellow.**

IV.
**Reddish Yellow.**

V.
**Yellowish Red.**

VI.
**Red.**

VII.
**Brownish Red.**

VIII.
**Reddish Brown.**

IX.
**Brownish Black.**

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# MANUAL

OF

# URINARY ANALYSIS

CONTAINING

A SYSTEMATIC COURSE IN DIDACTIC AND
LABORATORY INSTRUCTION
FOR STUDENTS

TOGETHER WITH

REFERENCE TABLES AND CLINICAL DATA
FOR PRACTITIONERS

BY

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# MANUAL

OF

# URINARY ANALYSIS

MITCHELL

# PREFACE.

THE object of this book is to provide the medical student and the practitioner with a practical, accurate, and reliable method for examination of the urine. The chemical and microscopical operations described have been repeatedly verified by the author, and nothing of this kind is commended which has not stood the test of personal investigation and demonstration. The book is original in the sense that unverified quotations from the writings of others have been made but to a very limited extent, and the clinical matter it contains is, for the most part, based on the result of some three thousand examinations, made by the author, of the twenty-four hours' urine.

Complete analyses of the twenty-four hours' urine are given in many cases in which death, post-mortem examination, or surgical operation during life, confirmed the diagnosis and prognosis previously made, based upon the urinary analysis. Results, also, of a large number of analyses of the urine in various nervous diseases are given, together with tables of differential diagnosis in Bright's disease, hematuria, pyuria, diabetes, and other maladies

At the request of a number of physicians in the West, and in accordance with my own desire, I have included in this volume the notes on diagnosis by the microscope which I took, not long since, in my course with Dr. Charles Heitzmann, of New York Cuts of the slides which I obtained from him are also shown.

C. M.

70 STATE STREET, CHICAGO,
*June, 1897.*

# TABLE OF CONTENTS.

# URINARY ANALYSIS.

## CHAPTER I.

### COLLECTION OF THE TWENTY-FOUR HOURS' URINE.

Modern examination of urine requires the whole quantity for twenty-four hours, which should be collected day and night separately. By **night** urine is meant only the urine voided *after* going to bed, and including what is voided on rising in the morning. All other urine is **day** urine. Patients should void urine *before* going to stool to avoid loss. It is best to begin the collection of the twenty-four hours' urine just after breakfast. Clean, wide-mouthed bottles or glass pitchers should be used for receiving purposes. (Figs. 1 and 2). After the urine is collected, the volume of the day and that of the night should be measured separately in a graduate (Fig. 3), and the quantity of each noted down, the two figures added, and the urine mixed.

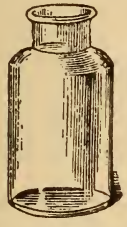

Fig. 1. Wide-mouthed quart bottle for receiving urine.

Fig. 2. Neckless glass pitcher for receiving urine.

Fig. 3. Graduate for measuring quantity of urine.

**Quantity of urine normal for twenty-four hours:—**
For healthy men, 40 to 50 fluidounces, at most; 30 to 40 for women; 10 for children under 3 years of age; 10 to 20 when from 3 to 6 or 8 years; 20 to 30 between 8 and 12. (Sixteen fluidounces make one pint, and 29.52 cubic centimeters, or approximately 30, one fluidounce).

**The normal ratio of day urine to night:—**

The healthy person voids three times as much day urine as night. If, however, he drinks freely before going to bed the quantity of night urine will be greater; so also if the sleeping hours are long. *But*, as a rule, *when the quantity of night urine persistently equals or exceeds the day, cardiac or renal disease is present* The writer has noticed this equality of day urine and night in chronic myelitis also.

**The object of collecting**

The twenty-four hours' urine is to compare day with night, to compare the total with normal average standards, to observe the physical characteristics, and to make quantitative estimates of the solids, as urea, phosphoric acid, uric acid, together with albumin and sugar, if either of the latter is present. In addition to the twenty-four hours' urine we must have a sample of urine *freshly voided*, passed, if possible, in presence of the physician, for purposes of microscopical examination. Women should take cleansing vaginal injection or tampon the vagina before passing urine for such microscopical examination. The reason of the latter precaution is that otherwise vaginal fluids may be mixed with urine, and the sediment of the urine be largely composed of matters from the vagina.

**In order to preserve** the specimen of freshly voided urine, add at once ten grains of chloral hydrate, or a few drops of a solution of chromic acid, strength one-half of one per cent. Then set it aside for at least six hours, until the sediment has settled, or settle it in the centrifuge.

Moreover, in cases where albumin in small quantities is for any reason suspected, but not found in the twenty-four hours' mixed urine, the patient's urine should be examined four times, viz.: (1) that passed on rising, (2) at noon, (3) at six o'clock p. m., and (4) as late as possible at night before going to bed. If sugar is suspected, but not found in the twenty-four hours' mixed urine, be sure to test the urine

voided at different times in the day, and especially in the afternoon.

**The apparatus** required for the collection and measurement of the twenty-four hours' urine is as follows:

Two *clean* "wide-mouthed" quart bottles with labels and *clean* corks.

One small, *clean*, say eight-ounce, wide-mouthed bottle and *clean* cork.

If wide-mouthed bottles are not to be had, get ordinary clean bottles, and a glass funnel. Let the patient urinate either directly into the funnel resting in the neck of the bottle, or else use a quart glass pitcher (suitable ones may be had at an expense of 25 to 50 cents) for receiving the voided urine.

One graduated jar, holding thirty-two fluid ounces, graduated also in pints and cubic centimeters. These can be had of the dealers in chemical apparatus at a cost of $2.25 or thereabouts.

For comparisons with normal averages see tables in APPENDIX.

[For microscopical examination of the sediment it is always well to have as concentrated a sample of urine as possible. Dark-colored urine is likely to have more sediment in it than pale, watery urine.]

### REFERENCE TABLE 1.*

#### Quantity of Urine per 24 Hours.

**A. Quantity somewhat less than 48 ounces.**—1. Not uncommon normally, and especially in women. 2. Normal in children under fifteen. 3. May be due to (*a*) vigorous perspiration; (*b*) hot weather; (*c*) rest; (*d*) abstention from fluids; (*e*) copious passages from the bowels.

**B. Quantity considerably less than 48 ounces.**—1. In all diseases except the six or seven mentioned below. 2. In acute diseases, daily diminution of the urine means increase in the intensity of the disease. 3. As dropsy increases, urine may diminish. 4. May be due to ingestion of mineral salts, as those of iron and copper; poisoning from external use of pyrogallic acid or aniline compounds; from atropine as a collyrium. 5. May be due to copious vomiting, or abundant watery stools.

**C. Urine scanty or suppressed.**—1. In all types of violent

* The REFERENCE TABLES are for advanced students and practitioners.

fever and inflammation, as scarlatinal nephritis, yellow fever, collapse of cholera. 2. In late stages of chronic nephritis. 3. Shock or collapse from internal injuries; reflex shock from catheterization; administration of chloroform and ether. 4. Poisoning by potassium chlorate, phosphorus, cantharides, arsenic, carbolic acid, ergot, iodine, mercury, opium. 5. In cirrhosis of the liver and in scurvy.

**D. Quantity more than three pints.**—1. Ingestion of large quantities of food or drink, especially beer. 2. In cold weather. 3. Due to diuretic drugs, as acetate of potassium, lithium benzoate and citrate, diuretin, spirit of nitrous ether. 4. Due to inhalation of oxygen. 5. In diabetes, interstitial nephritis, lardaceous disease of the kidneys, pure cardiac hypertrophy, some cases of chronic pyelitis; temporarily, in hysteria, and convulsions. 6. In convalescence from severe illness in which the urine has been decreased. 7. In typhus at the height of the disease, sometimes; in cerebro-spinal fever, sometimes; in some cases of rheumatism. 8. In cases of neurasthenia.

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## REFERENCE TABLE 2.

### The Quantity of Urine in Bright's Disease.

**A. Diminished:**—In acute nephritis, in chronic (diffuse) nephritis, in chronic congestions, in acute intercurrent attacks of chronic nephritis, in last stages of all forms.

**B. Increased:**—In chronic interstitial nephritis, in lardaceous diseases of the kidneys, after reduction of dropsy in chronic diffuse nephritis, in convalescence from acute scarlatinal nephritis.

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## CLINICAL NOTES.

1. **Polyuria** in neurasthenia has been observed by the author in a number of cases. Chas. L. Dana says: "Neurasthenics of middle age often pass enormous amounts of urine of low specific gravity."

2. I am of the opinion that 50 (1,500 c.c.) ounces is **above the normal average** voided by Americans. In 1,300 specimens of the twenty-four hours' urine, records of which I have recently gone over, more than 1,000 were less than 50 ounces (1,500 c.c.) in volume.

3. **Diminution** in the quantity of urine during or after an attack of urinary fever (called, also, *urethral fever*) is a bad sign and means suppression of urine and death.

4. **After surgical operations,** in general, on the urinary tract, if the volume of urine is good the great-

est danger is averted, but when not a drop is secreted for a considerable period the case is usually fatal.

5. It is said that the time of **maximum** secretion of urine is from 2 to 4 P. M., and the **minimum** from 2 to 4 A. M.

6. Dr. Howard A. Kelly, after numerous ureteral catheterizations, calculates that each kidney secretes about half a c.c. per minute, a total of 60 c.c. per hour. The urine flows into the bladder in gushes at intervals of 10 or 15 or 30 seconds.

### CHEMICAL EXERCISE 1.

1. **The student** should collect his twenty-four hours' urine, according to directions given, day and night separately, bring it to the laboratory, and measure it in the graduates. He should be required to express the results in both French and American measures, consulting *Table 1* in APPENDIX.

FOR EXAMPLE:

**Day urine,** 900 cubic centimeters, or 30 fluidounces.

**Night urine,** 300 cubic centimeters, or 10 fluidounces.

By use of *Table 1,* APPENDIX, the conversion of cubic centimeters into fluidounces is easily accomplished, the fluidounces being in the first column of figures to the left, and the cubic centimeters corresponding in the second column. Take the nearest figure. For example, if it be required to convert 900 cubic centimeters into fluidounces, run the eye down columns 2 and 5, and pick out the nearest figure to 900. It is found in column 2, namely, 885. The number of fluidounces corresponding is found in the same line in column 1, namely, 29.5, or 30 in round numbers. To convert 300 c.c. pick out 275 in column 5, and find 9.16 fluidounces corresponding, or in round numbers 10, since 275 is considerably less than 300.

[The division into separate sets of figures for male and for female patients is entirely for comparison with normal averages, and either set may be used for conversion, since 29.52 c.c. equals one fluidounce, regardless of sex.]

2. **Having measured** the quantity of *day* urine and of *night* urine, and expressed each in cubic centimeters and in fluidounces, next find the relation of the quantity of day urine to that of night, by dividing the figure representing the quantity of day urine by that of the night. In the case above 900 divided by 300 equals 3. In other words, the day urine in this case is *three times* the night urine. In scientific language this is expressed as follows: the ratio of the quantity

of day urine to night is as 3 to 1; or, briefly, day urine : night urine=3 : 1.

Next consult *Table 2*, Appendix, and ascertain whether this ratio of 3 : 1 is normal or not, and if not, in how much it differs from normal. In this table a ratio of 3 *or more* to 1 is taken as normal, so in the case above the day urine bears a normal ratio to the night urine. Suppose, however, the day urine were 500 c c. and the night urine 1,000 c.c. :—in this case 500 divided by 1,000 equals 0.5. The ratio of day urine to night is here as 0.5 : 1. Consulting *Table 2*, Appendix, and finding the nearest figure, find 0.45 to 1, which is said to be 15 per cent. of normal. That is, assuming 3 or more to 1 as the normal ratio, which we may indicate by the figure 100 (*i. e.* 100 per cent. of normal equals normal itself), 0.5 to 1 would bear the same relation to 3 : 1 as 15 to 100, hence we say 0.5 to 1 is 15 per cent. of the normal. From this we establish the following :—

**Rule 1.** *Divide the quantity of day urine by the quantity of night urine. Make a proportion thus: Day urine : night equals quotient of day divided by night :1. Find in Table 2*, Appendix, *the nearest proportion to this, and set down the per cent. figure as indicating the relation to normal in your case.*

Next add the figure representing the quantity of day urine to that representing the quantity of night to get the total volume of urine passed in twenty-four hours. In the case above 900 c.c. plus 300 c.c. equals 1,200 c.c. or 40 fluid ounces. Now ascertain by use of *Table 1*, Appendix, what relation to the average normal quantity this total bears, keeping in mind now for the first time the sex of the person. If the person is a man, find the nearest figure to 1,200 in column 2, of *Table 1.* It is 1,225. Now find on the same line in column 3, the figure 90. This means that calling normal 100, the total urine in this case may be represented by 90, or is, in other words, 90 per cent. of normal. Do not write 90 per cent. thus, *.90 per cent.* Prefixing a decimal makes it 9-10 of 1

per cent., a fact seemingly unknown to many students. Suppose now the person is a female, who passes 1,200 c.c. in 24 hours:—Looking in column 5, at the top we find the highest figure 1,100 c.c., but going down to the ascending scale in column 5, we find 1,200 there, and to the right in the same line the figure 100, or normal.

The reason of division into two scales, descending and ascending, is that normal averages vary according to nationality. The French observers, Yvon and Berlioz, think 1,100 c.c. the average normal for women, while the English make it 1,200. In other words, women void 1,100-1,200 c.c. (37 to 40 ounces), according to nationality.

My own statistics show that the French figures are nearer right in case of Americans than are the English figures. Out of 1,300 different persons where the 24 hours' urine was measured by the author, nearly 80 per cent. voided less than 48 fluidounces of urine.

4. Finally make out a report on work done as follows.

1. Name of person; 2. Sex; 3. Age; 4. Weight.
5. Day urine ..... c.c. ..... fl. oz.
6. Night urine ..... c.c. ..... fl. oz.
7. Ratio of day urine to night .....
8. What per cent. this ratio is of the normal ratio per cent. ....
9. Total volume of urine in 24 hours ..... c.c. ..... fl. oz.
10. What per cent. of the normal average per sex this volume is ..... per cent.

Mix the two samples of urine, day and night, pouring to and fro, from one graduate to the other, *down the side of the glass, thus avoiding foam*, and set the whole aside for the next exercise.

## CHAPTER II.

### SIGNIFICANCE OF THE VARIOUS PHYSICAL CHARACTERISTICS OF URINE.

The physical characteristics of urine, in addition to the twenty-four hours' quantity, include the *color*, *odor*, *specific gravity*, from which the *total solids* may be computed when the quantity of urine is known, *reaction*, *appearance*, *consistency*, and *condition of frothiness*.

**The color** of the healthy filtered urine of twenty-four hours is *straw yellow*. The color is due chiefly to coloring matters called *urochrome* and *urobilin*, the latter a derivative of hematin. See No. 3 on Vogel's Scale, *Frontispiece*.

**The odor** of freshly voided urine, contrary to the prevailing impression, is decidedly agreeable, and called *aromatic*. The odor of the twenty-four hours' urine is usually not unpleasant, though in the case of women nearly always slightly pungent from decomposition of the mucus present in that part of the urine which is oldest. The twenty-four hours' urine of men is, in health, often of an aromatic odor, though sometimes this odor is lost, and a slight indescribable pungency noticed. The *taste* is slightly alkaline or bitter.

**The specific gravity** of the twenty-four hours' urine is not, as formerly stated, 1015 to 1025, but, more commonly, 1020 to 1025 in the healthy adult.

What do we mean by the figures 1015, 1020, etc.? Urine is heavier than water, since it contains certain salt-like solid matters, derived from the blood, dissolved in it. Every one knows that a pint of water in which several ounces of salt are dissolved will weigh more than another pint in which no salt is dissolved. Now, urine contains enough salt-like matters

dissolved in it to make one pint of it weigh 1.020 to 1.025 times more than one pint of water of the same temperature. In other words, a pint of urine will weigh one and two-hundredths more than a pint of pure water. When this is the case we say the specific gravity of the urine is 1020, the decimal point being omitted by general consent.

In order to find the specific gravity of a given sample of urine we pour it into a tall glass, and let a urinometer float in it. Fresh urine should be cooled to 77° F. before the specific gravity is taken. The cooling is best accomplished by setting the fluted jar in cold water. A **urinometer** is composed of a graduated stem, a central cylinder-like portion, and a bulb at the bottom weighted with mercury, the whole so constructed that it floats upright in water or other liquids. In pure water it sinks to the very top of its graduation, and this point where it sinks in water is marked by the zero sign (0), in some instruments, and 1000 in others. It is worth while to know whether your instrument is graduated for use in liquids of a temperature of 60° or those of 77° F. The more modern American urinometers are *standardized*, as it is called, at 77°, sinking to the zero of graduation in distilled water of 77° Fahrenheit temperature. The urinometers commonly sold, while they may all sink to the zero point in pure water, nevertheless will vary among themselves considerably in liquids of a high specific gravity, 1030 or upwards.

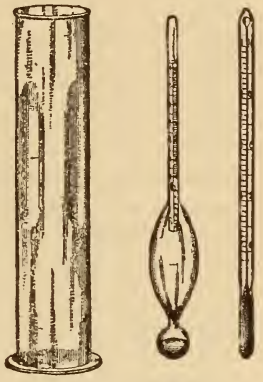

FIG 4.—Urinometer, fluted jar, chemical thermometer; for ascertaining specific gravity of urine.

**By the term total solids** in urine is meant the weight of all the normal solids dissolved in it. Abnormal constituents, as albumin, sugar, bile, blood, etc., are not included in this category.

The most important normal solids are urea, com-

mon salt, the sulphates, phosphates, urates, kreatinine, and hippuric acid, the average quantity of which per twenty-four hours is shown in the following table:

TABLE I.

| CONSTITUENT. | Average amount in 24 hours. |
|---|---|
| Water, | 40 to 50 fluid ounces, 1,200 to 1,500 c.c. |
| Urea, | 310 to 615 grains, 20.0 to 40.0 grammes. |
| Urates, | 6 " 12 " 0.4 " 0.8 " |
| Hippuric acid, | 8 " 15 " 0.5 " 1.0 " |
| Kreatinine, | 8 " 20 " 0.5 " 1.3 " |
| Chlorides, | 155 " 245 " 10.0 " 16.0 " |
| Earthy phosphates, | 15 " 23 " 1.0 " 1.5 " |
| Alkaline " | 30 " 60 " 2.0 " 4.0 " |
| Sulphates, | 45 " 60 " 3.0 " 4.0 " |

The sum total of these various solids in the urine of a healthy adult male, weighing about 150 pounds, on ordinary mixed diet, and taking ordinary exercise, may be expressed as follows:

| | |
|---|---|
| Urea, | 500 grains. |
| Common salt, | 250 " |
| Other solids, | 250 " |
| Total solids, | 1,000 " |

That is, urea represents about half the total solids and common salt about one-quarter.

In my opinion these figures are maximum ones, and much lower results may be obtained by analysis in the case of perfectly healthy persons under certain circumstances of age, diet and exercise, as will be shown further on.

**The weight of the total solids** in urine, which chemists obtain by evaporating the liquid to dryness and weighing the solid residue, may, for clinical purposes, be computed mathematically as follows:

1. Take the specific gravity of the twenty-four hours' mixed urine;

2. Multiply the last two figures of the specific gravity by 2.33 (Haeser's coëfficient);

3. Divide the product by 1,000;

4. Multiply quotient by number of c. c. of urine voided in 24 hours. Result is grammes of solid matter in the 24 hours' urine.

Now, in taking the specific gravity of the urine two precautions must be observed: First the urinometer* must be fairly accurate: second, the specific gravity must be taken at the temperature at which the urinometer is standardized.

Pour a sample of the twenty-four hours' urine into the fluted jar; set the latter in a glass of warm or cold water; take the temperature of the urine with the thermometer; when it is 77° F., remove the fluted jar from the water and take the specific gravity at once.

I have not been able to draw any deductions whatever from our former method of comparing the total solids estimated, as above, with some arbitrary normal average, as 58 grammes. When nothing is known about the patient, as is sometimes the case, we may indeed guess at the amount of "renal insufficiency" by comparing the solids computed as above with 58 grammes (900 grains). But when the age, weight, diet, and exercise of the patient are known, our ideas of the relation of solids excreted by him compared to the work his kidneys ought to do, are much better.

For example, take the following: twenty-four hours' urine, 900 cubic centimeters (30 fluid-ounces); specific gravity 1015. Total solids, 15 times 2⅔ times 900, divided by 1000, equals 31½ grammes, or 488 grains. Suppose the patient's condition be unknown. We would say, in a general way, that his kidneys were doing only half the work they ought to, since 488 is about half of 900 to 1000 grains, which we assume the normal excretion to be. But suppose the patient was above 70 years of age, or, if between 20 and 40,

*There are two kinds of urinometers, fairly accurate ones, and decidedly inaccurate ones. Those made by Squibb are recommended as being accurate. I know from experience that if thirty or forty urinometers are successively floated in the same urine at the same temperature, the readings will vary very considerably. I have known these variations in urines of high specific gravity, 1030 or upwards, to be as great as 8 or 10°. Urinometers are standardized from chemical solutions, but solutions of the same strength of different chemicals give different readings with the same urinometer. For example, 2 per cent. solutions of urea, sodium carbonate, and potassium sulphate gave the writer specific gravities of 1009, 1012, and 1017 respectively. Potassium sulphate has no water of crystallization in its formula.

weighed only 100 pounds, and was in bed on restricted diet? It is evident that in either of these cases we might be seriously at fault in assuming renal insufficiency. In order to make deductions of any definite value from the actual quantity of solids found, says Dr. Purdy, careful regard must be paid to certain conditions and features connected with each individual case, the most prominent of which are the weight, age, diet, and amount of exercise taken. Purdy's rules for making reduction or addition for weight, age, diet and exercise involve considerable figuring; so I have constructed a table, based on his rules, giving reductions or additions for weight and age at a glance.

The normal average excretion of solids for a person between 20 and 40 years of age, weighing 145 pounds, on ordinary mixed diet and taking ordinary exercise, is assumed to be 945 grains (61.14 grammes). On this assumption the following table is constructed:

TABLE II.

| WEIGHT. | NORMAL EXCRETION. | | | | |
|---|---|---|---|---|---|
| | Age 20 to 40. | Age 40 to 50. | Age 50 to 60. | Age 60 to 70. | Age above 70. |
| 145 pounds. | 61 gms., 945 grs. | 55 gms., 850 grs. | 48 gms., 756 grs. | 42 gms., 660 grs. | 30 gms., 473 grs. |
| 140 " | 912 " | 820 " | 730 " | 634 " | 456 " |
| 135 " | 878 " | 790 " | 702 " | 608 " | 439 " |
| 130 " | 845 " | 760 " | 675 " | 582 " | 423 " |
| 125 " | 812 " | 730 " | 649 " | 556 " | 406 " |
| 120 " | 780 " | 702 " | 624 " | 530 " | 390 " |
| 115 " | 748 " | 673 " | 598 " | 504 " | 374 " |
| 110 " | 715 " | 644 " | 572 " | 478 " | 357 " |
| 105 " | 682 " | 614 " | 545 " | 452 " | 341 " |
| 100 " | 650 " | 585 " | 520 " | 426 " | 325 " |
| 95 " | 618 " | 556 " | 494 " | 400 " | 309 " |
| 90 " | 585 " | 526 " | 468 " | 374 " | 293 " |
| 85 " | 552 " | 497 " | 442 " | 348 " | 276 " |
| 80 " | 520 " | 468 " | 416 " | 322 " | 260 " |
| 75 " | 488 " | 439 " | 390 " | 296 " | 244 " |
| 70 " | 456 " | 410 " | 365 " | 270 " | 228 " |
| | For weights above 145 pounds (66 kilograms). | | | | |
| 150 " | 978 " | 880 " | 782 " | 685 " | 489 " |
| 155 " | 1010 " | 910 " | 808 " | 707 " | 505 " |
| 160 " | 1042 " | 938 " | 833 " | 729 " | 521 " |
| 165 " | 1074 " | 967 " | 859 " | 751 " | 536 " |
| 170 " | 1106 " | 998 " | 885 " | 773 " | 553 " |
| 175 " | 1138 " | 1024 " | 910 " | 795 " | 569 " |
| 180 " | 1170 " | 1053 " | 936 " | 817 " | 585 " |
| 185 " | 1202 " | 1082 " | 962 " | 840 " | 601 " |
| 190 " | 1234 " | 1110 " | 988 " | 862 " | 617 " |
| 195 " | 1266 " | 1140 " | 1014 " | 884 " | 633 " |
| 200 " | 1298 " | 1168 " | 1040 " | 907 " | 649 " |
| 205 " | 1330 " | 1197 " | 1066 " | 930 " | 665 " |
| 210 " | 1362 " | 1226 " | 1092 " | 952 " | 681 " |
| 215 " | 1394 " | 1255 " | 1118 " | 973 " | 697 " |
| 220 " | 1426 " | 1284 " | 1144 " | 995 " | 713 " |
| 225 " | 1458 " | 1312 " | 1170 " | 1020 " | 729 " |

The preceding table, page 32, gives the normal averages of total solids in the urine of persons on ordinary diet, taking ordinary exercise. It represents the mean of the combined observations of eight writers.

The table gives corrections for age and weight only. From these figures deduct 33 per cent. for fasting two or more days, as in some fevers, or 12 to 16 per cent. for a sparing diet, or 10 per cent. when the person is not eating as freely as when in health.

*Furthermore*, deduct 10 per cent. if the person is in bed, or 5 per cent. if confined merely to the house.

*Examples* illustrating the above:

1. Solids computed, 530 grains in the twenty-four hours' urine.

Patient 35 years old; weight, 155 pounds; diet, ordinary; exercise, ordinary.

*Deduction.*—A person 35 years old, weighing 155 pounds, should excrete (Table II.), on ordinary diet and exercise, 1010 grains. The person in question excretes 530 grains. Therefore he or she is passing only about half what should be excreted in twenty-four hours.

2. Solids computed, 530 grains in twenty-four hours' urine. Patient 65 years old, weighs 140 pounds, eats sparingly, and is confined to the house.

*Deduction.*—A person 65 years old, weighing 140 pounds, should pass (Table II.) 634 grains of solids when on ordinary diet and exercise. But as the diet is sparing, deduct from 12 to 16 per cent. of 634, say 90 grains; 634—90 equals 544 grains. Still further, deduct 5 per cent. from the figure last obtained since the patient is confined to the house. Five per cent. of 544 is about 28 grains. Final figure, 544—28, or about 515 grains. In other words, a person under these circumstances should void about 515 grains of solids in twenty-four hours. The amount computed is 530 grains. Therefore, he or she is passing just about what would be expected under the conditions.

It goes without saying that *a faulty urinometer* will cause considerable difference in results.

*Example 3.*—Urine in twenty-four hours, 1000 c.c. (33 fl. ozs.); specific gravity by one urinometer, 1030; by another, 1022.

Patient weighs 175 pounds; age, 30; diet, hearty; exercise, vigorous. By one urinometer, the first, he is voiding 70 grammes (30 times $2\frac{1}{3}$ times 1000, divided by 1000), or 1085 grains. By the second instrument he is voiding 51 grammes, or 890 grains. A person of his age, weight, etc., should void at least 1138 grains (Table II.). If the first urinometer is correct, he is voiding only about 50 grains short of what we should expect. If the second urinometer is correct, he is voiding 250 grains less than he ought; 890 grains would represent the excretion of a person weighing 40 pounds less than the person in question.

The whole calculation, with the table and reductions, depends greatly on the *accuracy of the urinometer* used.

Lastly, if the urine contains any sugar or albumin in abundance the method of computing solids is not trustworthy, since the specific gravity of the urine is changed by the abnormal constituent present. Also in cases where there is considerable polyuria *an inaccurate urinometer* will give rise to a considerable error in results. For example, suppose the total quantity of urine in twenty-four hours be 2,800 c.c., or 93 fluid-ounces. Suppose the true specific gravity at 77° F. be 1006. In this case the total solids are 6 times 2.33 times 2,800, divided by 1,000, equals 39 grammes, or 600 grains. But a urinometer giving a reading of 1008 would indicate total solids amounting to 52 grammes, or 800 grains, the error amounting to 200 grains.

When there is no great polyuria the total solids may be computed from saccharine urine by first fermenting with yeast, then filtering, and taking specific gravity at 77° F.

PRACTICAL APPLICATIONS TO DIAGNOSIS AND TREATMENT.

1. In gynecological cases and nervous diseases Dr. N. B. Delamater has shown for fifteen years past that

deficiency in solids, with accompanying symptoms, often yields to eliminative treatment.

2. Dr. J. H. Etheridge has, independently, confirmed the statements so often made by Dr. Delamater, showing that amenorrhœas, neuralgias, pelvic peritonitis, dyspepsias, bronchitis, cutaneous eruptions, headaches, backaches, leucorrhœas, nervousness, and insomnias accompany deficient excretion of urinary solids. Women passing not to exceed 400 grains of solids daily present various degrees of nervous irritability. When less than 300 grains are passed the condition of nervousness becomes serious; bronchitis, neuralgia, perimetritis or pleurisy may then result from taking cold. A very close relation exists between renal insufficiency and pelvic disorders. Many disorders of this character are relieved by including in the treatment remedies that increase the urinary solids.

3. Deficiency in solids in the urine of men I have found to indicate unrecognized interstitial nephritis in some cases; in others, serious nervous disorders. Purdy says the same thing so far as the renal condition is concerned. In such cases collect the twenty-four hours' urine, day and night separately, determine urea and phosphoric acid, look for casts, and examine the patient's chest for cardiac lesions.

4. The differential diagnosis between diabetes insipidus and simple hydruria may be made by determining the total solids, which in the former disease are largely in excess of the normal average.

5. In fevers and acute diseases, as pneumonia and typhoid fever, the severity of the disease is indicated by increased quantity of solids in the urine; if, on the other hand, the temperature is high, but the excretion of solids in the urine is deficient, eliminative treatment should be employed, since elimination is evidently defective.

6. In diseases in which there is exudation, marked increase in the quantity of solids in the urine is a good sign, and indicates that eliminative treatment is not needed.

7. By subtracting the total urea determined in the twenty-four hours' urine from the total solids computed, an idea may be had as to the general composition of the urine in question. In cases in which the total urea is greater than three times the total salts (difference between total solids and total urea) I have observed great mortality.

## CHAPTER III.

### THE REACTION, APPEARANCE, CONSISTENCY AND ODOR OF URINE, AND THEIR SIGNIFICANCE.

The next physical characteristic to be considered is the reaction of the urine, whether acid, neutral or alkaline.

**The reaction** of the normal twenty-four hours' mixed urine is slightly acid, made so by the presence of sodium acid phosphate. Blue litmus paper is turned slightly reddish when held immersed in it some little time.

If the urine when boiled turns cloudy, and the cloudiness is dispelled by adding a few drops of 20 per cent. acetic acid, and shaking, the reaction is not sufficiently acid. Normal urine should be as clear after it is boiled as before, when not over twenty-four hours' old.

**Litmus paper** is sensitive to light and air, and should be kept in small salt-mouthed bottles, tightly corked, and covered with paper to keep out the light. I prefer soft litmus paper to stiff, for the reason that the latter in small pieces has a way of curling up and floating on the surface of urine, instead of sinking quickly, when dipped into it, hence it is less economical for use. In larger pieces the stiff paper is easily managed. Different articles of litmus paper vary in the tint of red obtained by dipping into the same sample of urine. This is because some paper is impregnated with more coloring-matter than others. Some blue litmus paper will give a fairly bright red tint with urine which when boiled becomes cloudy, the cloudiness being dissipated by addition of acid, so that deficiency in acidity should be tested for


FIG. 5. Litmus Pencil.

by this means as well as by use of litmus. Litmus pencils (*Fig. 5*) may be used instead of litmus paper and are preferable in that they do not lose their color as does litmus paper. One end of the pencil is blue the other red. Rub the sharpened ends on paper and get ready-made litmus paper of either color.

**The appearance** of normal urine when freshly voided is invariably clear. The twenty-four hours' urine is almost always slightly hazy, when looked at in a glass held *below* the window sill. Urine voided in a cold room, 40° to 35° F., may soon, though normal, become turbid. The urine of even healthy women almost always, on standing, deposits a more or less abundant whitish sediment, derived chiefly from vaginal fluids mixed with it.

**The consistency** of normal urine is that of water—easily dropping. Normal urine foams when shaken, but the foam disappears in time, not remaining permanently on top of the liquid.

Now, the chief clinical points of value to be derived from study of the physical characteristics are these:

Decrease in the twenty-four hours' urine is usually accompanied by increase in the color, odor, acidity, and specific gravity. If a patient passes a pint in twenty-four hours, the color will be darker, the odor more noticeable, the acidity greater, and the specific gravity higher, than when he passes three pints. Exceptions may be found in nephritis, and especially in atrophy of the kidney, when the specific gravity is low.

As a rule the urine voided at 10:30 A. M. should not be strongly acid. Keyes thinks this an important point in the diagnosis of the cause of pain in the back, which he thinks renal in origin, no other cause being apparent, provided the urine voided at 10:30 A. M. is noticeably acid. Physiologically the urine at this hour should be less acid than at other times, that is it should be neutral or only slightly alkaline.

In general, the urine of digestion (two hours, say, after a meal) is less acid, unless acid foods or drinks be taken. This urine is called *urina cibi*, the urine of food.

Urine voided on rising in the morning is called *urina sanguinis*, urine of the blood, because it is voided when the stomach is empty. It is deeper in color, higher in gravity, etc., than at other times of the day; in other words, its characteristics are *increased* in intensity.

Urine voided after copious draughts of fluids is called *urina potus*, the urine of drinking. Its characteristics are diminished, *i. e.*, it has less color, less acidity, etc. Its specific gravity may be very low, 1005 even.

We find, as a general rule, that *polyuria*, or voiding of increased urine in twenty-four hours, is attended by diminution in the intensity of the physical characteristics, except in diabetes mellitus, in which one characteristic, specific gravity, is greatly increased.

Unusual shade of color, as greenish, deep yellow, or deep red, may be seen when bile is in the urine, or when certain drugs containing coloring-matters have been taken, as santonin, rhubarb, etc.

In cardiac or renal diseases when a patient who has been in the habit of passing light-colored urine suddenly and without any apparent cause, begins to void urine of a bright red tint, death is apparently inevitable. I have noticed this change but twelve times, and all the patients concerned died in a few weeks or months, only one surviving as long as a year after the color changed. The particular color I have been able, after much trouble, to imitate by diluting a solution of the oxychloride of iron (*not* per-chloride). The appearance of the urine in these twelve fatal cases was like that of a diluted solution of oxychloride of iron, in that it was clear, or nearly so, when looked at through the sides of the glass, but inky when looked at from above, in this respect differing from bichromate solutions, with which I first tried to imitate the color. Such urine is usually more or less turbid from mucus or urates, seldom contains much albumin and, usually, but a few casts, yet it is one of the worst prognostic signs I have yet observed.

The chief points in regard to the **odor of urine** are as follows:

Urine which smells like *ammonia* when freshly voided is found in inflammations of the bladder, especially in the cases of old men with enlarged prostates, and with pus in their urine. Such urine is irritating to mucous surfaces. Normal urine, when old enough, *i. e.*, "stale," takes on this ammonia-like odor, but should not do so when only twenty-four hours old.

Urine which soon acquires a *putrid* odor, something like that of decayed meat, has decomposing mucus, pus, or blood in it. The urine of healthy women may become putrid from decomposing mucus soon after the twenty-four hours have passed, especially in warm weather.

Urine which is *turbid*, when freshly voided, is found chiefly in inflammations of the bladder and contains pus, usually with micro-organisms, and suspended phosphates. Sometimes, however, the turbidity of freshly voided urine is due wholly to suspended simple phosphates; if it clears up on addition of a few drops of acid, and shaking, this latter is the case, and usually nothing serious is indicated. But urine turbid when freshly voided, which does not clear on addition of acid, and especially if it have an ammonia-like odor, is indicative of disease, usually of the bladder. It is alkaline, turning the red paper blue, and called alkaline from *volatile* alkali, *i. e.*, ammonia.

Urine which turns the red paper blue, but has not the ammonia-like odor, and which, if turbid, clears on addition of acid, is said to be alkaline from *fixed* alkali, *i. e.*, the carbonates of sodium and potassium. Such urine, if clear when freshly voided, becomes turbid when boiled, but clear again when acid is further added. This does *not* signify presence of albumin, as supposed by some, but is due to a precipitate of simple phosphates, caused probably by increase in the alkalinity produced by the boiling, which drives off carbonic acid.

Urine which, on standing, soon deposits a pinkish sediment (*urates*) adhering closely to the sides of a

chamber-vessel or streaking the sides of a glass vessel, is too acid in reaction (*hyper-acid*). Such urine we see in what is rather vaguely called *lithæmia* or *uric-æmia*, a condition in which uric acid formed in the body is not sufficiently excreted or else not excreted with regularity. In such urines we often see little reddish or brownish specks, which are very heavy, and settle quickly to the bottom. These are *uric acid crystals.*

Urine which, on standing for a time, becomes cloudy, and then when heated becomes clear again, contains a sediment which is composed of *urates* (compounds of uric acid) especially noticeable in cold weather.

As to the character of the foam in urine, it may be said that even slightly albuminous urines foam abundantly, and the foam is persistent. Albuminous urines give rise to much foam in the urea instruments, as we shall learn further on. Urine containing sugar foams readily, and the foam is persistent. I have seen some cases of persistent foam in which I could find nothing unusual in the urine, except a sediment of uric acid and urates.

When the urine is of some unusual color and the foam has a faint or marked color, held in the right light, bile is present, and a slight or marked odor of ox-gall may be noticed. This is, on the whole, the easiest and simplest test for bile that we have.

Urine having a sediment which sticks to the glass contains pus, more or less mixed with mucus, and altered by the ammoniacal alkali present in such conditions. This is the easiest and quickest way of recognizing pus, since mucus alone does not stick to the glass. But all urine containing pus does not have this sticky sediment. In acid urine pus shows large flocks which rapidly settle, but do not stick to the glass. Set the bottle aside in a warm place, and in a day or two the sediment, if pus, will stick to the glass.

Patients sometimes pass urine containing gases, which are, probably, carbonic acid gas and nitrogen. The gases escape in large bubbles, and the unusual

occurrence generally causes much alarm. These gases form especially in cases when urine containing sugar is for any reason retained in the bladder where bacterial fermentation sets in, thus forming the various gases. The condition is known as *pneumaturia.* Keyes says that pneumaturia may exist without sugar being in the urine. The gases are usually odorless, but I have heard of one case in which an odor like sulphuretted hydrogen was claimed. Pneumaturia may exist without vesico-intestinal fistula. Keyes has seen it only in patients who used the catheter.

In certain cases it may be worth while to take the *temperature* of the freshly voided urine. For this purpose a clinical thermometer is useful.

# CHAPTER IV.

## CLINICAL SIGNIFICANCE OF THE COLOR OF URINE. REFERENCE TABLES FOR THE PRACTITIONER.

The following pages give in tabular form the clinical significance of the various physical characteristics of the urine, as set forth in the preceding chapters.

### REFERENCE TABLE 3.

#### Synopsis for Color.

**I. Pale urines.**—Either (A) physiological, after drinking, or (B) pathological; the latter in (*a*) polyuria, as in neurasthenia, hysteria; (*b*) in diabetes insipidus; (*c*) in interstitial nephritis; (*d*) in lardaceous disease of the kidneys; (*e*) in convalescence from many acute diseases; (*f*) poisoning by duboisin; (*g*) anæmia; (*h*) diabetes insipidus.

**II. Urines lighter than straw-yellow but not pale.**—(*a*) That of neurotic persons; (*b*) of most women; (*c*) normally in children; (*d*) sometimes in diseases of the prostate; (*e*) in cases of sexual debility: light, phosphatic sediment in the urine; (*f*) diabetes insipidus (milder cases).

**III. Lemon-yellow.**—Diabetes mellitus, when much sugar is present. Said to occur in cholera and in spinal disease.

**IV. Peculiar bright-yellow tints.**—Due to taking internally of gamboge, senna, logwood, picrotoxin, santonin, rhubarb.

**V. Darker than straw-yellow.**—Approaching red.—Diminution in volume of urine; physiologically, after perspiration, or when but little liquid is taken in the diet.

**VI. Reddish urine.**—In fevers and inflammations. Sometimes due to sediment of urates colored red by urœrythrine, a pathological coloring matter; in such case filter the urine, and the tint may be yellowish rather than reddish.

**VII. Peculiar bright-red tints.**—Due (*a*) to presence of bile, blood, or (*b*) to coloring matters from such substances taken internally as logwood, madder, bilberries, fuchsin, aloes, alizarin.

**VIII. Orange-red.**—Ingestion of santonin, chrysophanic acid.

**IX. Dark-red.**—(*a*) In severe acute febrile diseases; (*b*) blood in the urine; (*c*) external use of aniline chlorhydrate.

**X. Brownish tints.**—Brown-red, in acute febrile disorders or inflammations; brown-yellow or red-brown, due to ingestion of senna, rhubarb, chelidonium; greenish-brown, due to bile in urine; dark brown, (*a*) due to bile or blood in urine; (*b*) found in long continued intermittent fever; (*c*) due to external use of pyrogallic acid; brown to brown-black, in so-called methæmoglobinuria; in melanotic sarcoma; in wasting diseases; in this case the color is due to the presence in the urine of a black pigment called *melanin;* the urine, if not dark when voided, darkens on standing; this is not

the same coloring matter found in the urine in carbolic-acid poisoning. In carbolic-acid poisoning.

**XI. Black urine.** — Brownish-black, see preceding; (*a*) in poisoning by sulphuric acid, creosote, arseniuretted hydrogen, potassium chlorate; (*b*) ingestion of naphthalin, hydrochinon, resorcin, pyrocatechin; (*c*) inunction of tar; (*d*) melanuria (on standing). Urine containing melanin darkens on standing, and becomes intensely black when oxidized by ferric chloride or other oxidizing agents.

**XII. Green tints.**—(*a*) Greenish-yellow, greenish-brown, see above; (*b*) dirty-green or blue in cholera and typhus, when urine putrefies; (*c*) dark-green in carbolic-acid poisoning. Greenish to grass-green is said to have been seen in cystitis and in Bright's, in alkaline decomposed urine.

**XIII Blue* tints.**—(*a*) See above; (*b*) In typhoid fever, chronic affections of the spinal cord; (*c*) Presence of indigo. (See Sediments.)

**Pale urines** are deficient in urohematin, the normal coloring matter of urine. Lemon-yellow urine contains uroxanthin. The pinkish or rosy tints of urates in the sediment are due to urærythrin. The blue pigments are cyanurin (uroglaucin) and indigo. The greenish may be due to mixtures of uroxanthin with the blue pigments. (Thudichum.)

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## REFERENCE TABLE 4.

### Odor.

**Odor slightly aromatic.**—Health.

**Pronounced aromatic odor, not offensive.**—Decrease in quantity of urine, as after perspiration, in fevers, etc.

**Slightly pungent odor.**—Normal after twenty-four hours in men.

**Pungent odor.**—Common after twenty-four hours in urine of women containing much mucus.

**Putrid odor.**—Due to decomposing mucus, pus, blood.

**Odor of ammonia.**—Alkaline urine either stale or, if fresh, due to diseases of the prostate, bladder, or kidneys; usually cystitis.

**Odor of sulphuretted hydrogen.**—Decomposing mucus; common in the stale urine of diseases of the bladder and prostate, and in that of women containing leucorrhœal fluid. Also in urine containing cystin.

**Sweetish odor.** – Sugar in the urine.

**Sour milk or yeasty odor.**—Stale urine containing sugar.

**Odor of tainted meat.**—Stale urine containing albumin, pus, or blood.

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* Dr. Wesley A. Dunn tells me that that the urine may be colored blue as a result of application of methyl blue locally to the throat, as also when taken internally.

**Odor of chloroform-acetic acid.**—Acetone in the urine, as in diabetes with acetonuria.

**Odor of violets.**—Ingestion of oil of turpentine.

**Odor of sweet-briar.**—Fresh urine containing cystin.

**Odor of ox-gall.**—Bile in the urine.

**Substances** which more or less communicate their own odors to urine are:

| | | | |
|---|---|---|---|
| Asafœtida, | Castor Oil, | Cubebs, | Onions, |
| Asparagus, | Coffee, | Garlic, | Sandal wood, |
| Beef extract, | Copaiba, | Oil of tolu, | Valerian. |
| Cauliflower, | | | |

## REFERENCE TABLE 5.

### Specific Gravity.

1020 to 1025.—Usual normal range.

1013 to 1060.—Possible range when sugar is in the urine.

1002 to 1035.—Possible range when albumin is in the urine.

Above 1040.—Almost invariably diabetes mellitus; invariably, if polyuria.

1025 to 1030.—May be normal in those leading sedentary lives.

1025 to 1040.—Possibility of diabetes mellitus, acute nephritis, congestion of kidneys, oxaluria, some cases of neurasthenia, uric acid sediments, acute diseases generally. Functional albuminuria.

1020 to 1015.—May be normal in those who drink copiously. Possibility of neurasthenia, anæmia in women, chronic nephritis.

Below 1015.—Diabetes insipidus; neurasthenia; chronic nephritis; lardaceous disease of kidneys; hysteria; anæmia.

## REFERENCE TABLE 6.

### Chemical Reaction.

**Slightly acid.**—Usual normal reaction of the twenty-four hours' urine.

**Plainly acid.**—Urine diminished in twenty-four hours' quantity; in those who drink but little water; due to muscular exertion, meat diet, ingestion of saccharin; stale urine which has undergone acid fermentation. Milk diet sometimes increases acidity of urine.

**Strongly acid.**—Due to ingestion of acids, as boracic, benzoic or acid salts, as perchloride of iron, Horsford's acid phosphates, in febrile disorders; in the uric acid diathesis; in certain diseases of the liver.

**Neutral.**—Copious drinking; usual after meals.

**Alkaline.**—Three or four hours after meals; after perspiring copiously; after hot baths; due to vegetable diet; after copious vomiting; from ingestion of alkaline carbonates or salts of vegetable acids, as in mineral waters containing the above; lithia waters and tablets, lithium benzoate, citrate, etc., from fixed alkali in debility, nervous exhaustion, anæmia and chlorosis, pulmonary disorders, some acute diseases (pneumonia, typhus, enteritis, flatu-

lent dyspepsia; from volatile alkali in stale urine, or, when in freshly voided urine, cystitis or pyelitis).

CLINICAL NOTES ON REACTION.

1. Urine of highly acid reaction is irritating to the mucous membrane of the urinary tract and aggravates any existing disease, especially in women.
2. Alkaline urine (fixed alkali) is somewhat irritating.
3. Ammoniacal urine causes the greatest distress of all. The agony of a patient with prostatic abscess, who voids strongly ammoniacal urine, is extreme.

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## REFERENCE TABLE 7.

### The Quantity, Specific Gravity, and Color of Urine in Pathological Conditions.

**A. Quantity small, specific gravity low, color pale.**—Suspect chronic nephritis; uræmia.

**B. Quantity large, specific gravity high, color paler than normal.**—Suspect diabetes mellitus.

**C. Quantity large, specific gravity not above normal, color pale.**—Suspect diabetes insipidus, neurasthenia, interstitial nephritis, lardaceous disease of kidneys, reduction of dropsy, convalescence from acute diseases.

**D. Quantity small, specific gravity high, color high.**—(*a*) acute febrile diseases; (*b*) dropsy; (*c*) to a less degree, in cerebral and gastric neurasthenias, and in oxaluria; (*d*) in acute and chronic renal hyperæmia; (*e*) in certain hepatic disorders.

CLINICAL NOTE.

Urine as described in D has been observed by the author in (*a*) cases of gall-stone colic; (*b*) just preceding uræmic convulsions; (*c*) commonly in oxaluria (500–600 c.c. of urine in 24 hours); (*d*) in obscure mental diseases (insanity?) soon terminating fatally, with marked relative excess of uric acid in solution.

---

## REFERENCE TABLE 8.

### Consistency and Frothiness.

**A. Increased consistency.**—Presence of mucus and pus, especially in alkaline urine; chyle in the urine; fibrin in the urine.

**B. Diminished consistency, shown by increase in the frothiness.**—Albumin or sugar in the urine.

Frothiness is increased sometimes in urine of high specific gravity; in urine feebly acid or alkaline; in urine containing excess of mucus.

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## REFERENCE TABLE 9.

### Appearance of the Urine.

**A. The urine looks milky.**—In children, perhaps due to sediment of urates, cleared by heating; due to presence of pus, or chyle.

**B. The urine has a greenish-red "smoky" hue.**—Suspect presence of blood in it.

**C. The urine has a dusky hue.**—See remarks on brown and black color.

**D. The urine is turbid when freshly voided.**—Suspect presence of blood, bile, mucus, pus, phosphates. If light color, the last three; phosphates cleared by shaking with 50 per cent. acetic acid. Pus, blood, and mucus are not cleared by the acetic acid.

**E. The urine is clear when freshly voided, but becomes turbid on cooling.**—A sediment of urates has deposited and may be cleared by heat (150° F.)

**F. The urine is turbid, and, when shaken, the cloudiness has a wave-like motion.**—Presence of bacteria in the urine. Not affected by acetic acid. The urine never clears completely on standing.

**G. The urine filters slowly.**—Excess of mucus; presence of pus, blood.

# CHAPTER V.

## EXERCISES IN PHYSICAL CHARACTERISTICS.

The student having collected his twenty-four hours' urine, day and night separately, measured it, and mixed it, should determine the **physical characteristics** as follows:

### CHEMICAL EXERCISE II.

**A. Filter the urine:**—Obtain glass funnels (*Fig. 6*), **filter paper,** of the size represented in Fig. 7, **filter rings and stand** (*Figs. 8, 9, 10* show different kinds) and **collecting vessels**, as wide mouthed bottles or **beakers.**

Fig. 6. Glass funnel used in filtering urine.

*Fig. 11* shows a convenient apparatus for managing filtration. The receiving vessels in *Fig. 11* are beakers, which are sold in "nests" (*Fig. 12*) of different sizes.

Funnels should be of two sizes (*a*) those 3 or 4 inches in diameter across the top, and (*b*) those about two inches. The smaller ones may be set directly into test-tubes. The larger ones require either a support or a wide-mouthed bottle to rest in.

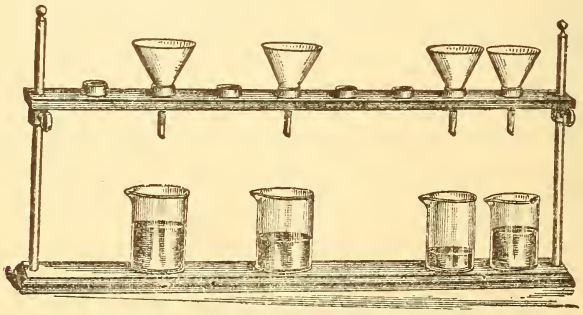

Fig. 11. Apparatus for filtration.

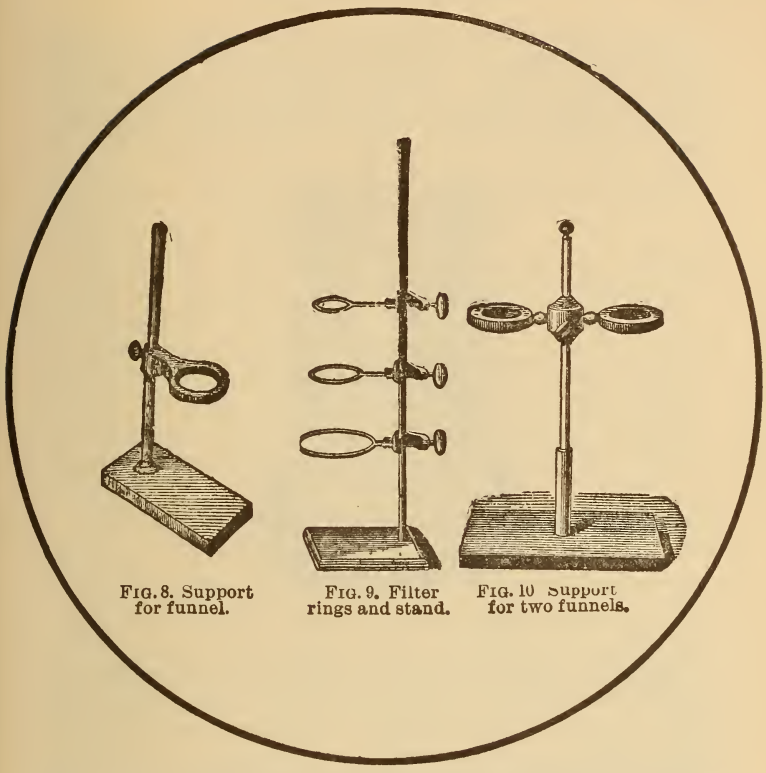

FIG. 8. Support for funnel.

FIG. 9. Filter rings and stand.

FIG. 10 Support for two funnels.

Fig. 7. This circle represents the exact size (4 inches diameter) of filter paper most convenient for use in these exercises.

Filter-paper should be bought already cut in packages of 100. For the larger funnels get paper about $7\frac{1}{2}$ inches in diameter. For the smaller funnels use the size shown in *Fig. 7*. The larger funnels and paper are useful for various quantitative filtrations, as in uric acid determinations; the smaller ones for qualitative work, especially clinical.

For the larger funnels buy what is known as **rapid filtering paper,** which is especially serviceable when it is desired to collect sediments on a filter.

For filtering urine *clear* do not use rapid filtering paper, but fold several of the smaller papers together.

In order to fold filter-paper, first fold it in *two*, then fold again in *two*, but this time at *right angles* to the first folding. A funnel shape is thus given to it, and it may be fitted into a funnel and is ready for use.

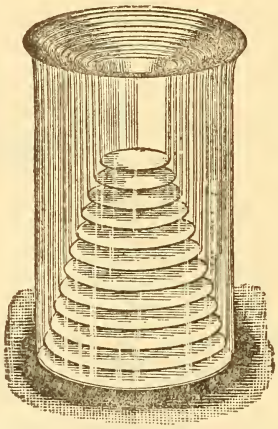

Fig. 12. "Nest" of beakers.

Filter the urine into a thin glass jar or beaker at least 3 or 4 inches in diameter, and for observing color always use the same beaker. Observe whether the urine filters slowly or rapidly. If it filters slowly, it indicates the presence of mucus in excess.

Note whether the color is normal (straw-yellow), pale, or high. More precisely, compare the shade with Vogel's Color Scale, and report the color as No. 1, 2, or 3, etc., on this scale. Note any unusual color as red, green, brown, or black.

Vogel's Color Scale divides the urinary colors into the following:—(see *Frontispiece*).

1. Pale-yellow;—2. Light-yellow;—3. Straw-yellow;—4. Red-yellow;—5. Yellow-red;—6. Red;—7. Brown-red;—8. Red-brown;—9. Brownish-black.

These colors, as given us, seldom match closely with the color of the filtered urine. Between yellow-red and red, as pictured in the books, a number of urine shades occur. Moreover the colors in the color-scale

fade on exposure, so as to show in time but little difference in the first three shades. As yet, however, nothing superior to this scale has been devised. The author has been able to imitate closely several of the urine tints by solutions of certain chemicals, as, for example, a peculiar dark inky-red by diluting oxychloride of iron solution.

**B.** Smell of the urine and note whether the **odor** is slightly (*a*) *aromatic*, not at all unpleasant, sometimes agreeable; (*b*) *strongly aromatic*, still not disagreeable, as in fevers; (*c*) *pungent*, slightly disagreeable, as in case of urine twenty-four to forty-eight hours old; (*d*) *fetid*, decidedly unpleasant, suggesting decomposition; or (*e*) *ammoniacal*, having distinct odor of ammonia. (Students are usually at fault regarding the odor of urine.)

Note whether there is any odor of ox-gall (bile), or of any drug, such as cubebs, sandalwood, creasote, etc.

**C.** Take the **specific gravity** of filtered urine in the beaker, pouring it carefully, to avoid foam, into the fluted jar which comes with Squibb's urinometer, removing foam with filter paper. When the urinometer is floating in the liquid, touch the top of the stem lightly so that it sinks and rises a few seconds, *then wait until it settles down to quietude.* Read off the scale when on a level with the eye, and note the figure on the level of the liquid. For accurate work use a chemical thermometer, and warm or cool the urine to 77° F. (25° C.), by setting the jar in hot or cold water.

**D.** Compute **the total solids** by multiplying the number of cubic centimeters of urine in twenty-four hours by the last two figures of the specific gravity, that product by 2.33, and divide last product by 1,000. The result is grammes of total solids for twenty-four hours. Convert to grains by *Table 3*, APPENDIX. Compare the number of grains found with what the student ought to excrete for his age and weight, using *Table 3* in APPENDIX.

**E.** Work out the following problems in total solids:

(*a*) Urine in twenty-four hours, 850 c.c.; specific gravity, 1012; age 55, weight 160, fasting, in bed. How does the excretion computed compare with the theoretical excretion based on 945 grains (61 grammes) minus the deductions for age, etc.

(*b*) Urine in twenty-four hours, 400 c.c.; specific gravity, 1020; age, 70; weight, 155; appetite and diet normal; exercise, normal.

(*c*) Urine in twenty-four hours, 1500 c.c.; specific gravity, 1025; age, 30; weight, 140; otherwise normal.

F. Take the **reaction** of the urine with litmus paper, holding two slips, red and blue, in the urine until saturated, or placing a drop of urine in the center of each of the slips. If the blue paper is turned red and no change has taken place in the red paper, the urine is *acid*. Notice whether the reddened litmus is only slightly red, or a bright brick-red, *i. e.*, feebly acid or strongly acid. If neither paper is affected in color, the urine is *neutral*. If the red paper is turned blue and no change takes place in the blue paper, the urine is *alkaline*. Let the paper, which has been turned blue, dry; notice whether it remains blue (fixed alkali) or turns red again (volatile alkali).

If both the blue paper is turned red and the red paper blue, the urine is what is called *amphoteric* in reaction, which is without known significance.

Acid urine on standing sometimes becomes more acid than normal, due to action of mucus as a ferment producing a lactic fermentation, darkens in color, and deposits a sediment (uric acid and urates), calcium oxalate, penicillium glaucum (fungi) and bacteria, so that the reaction should be taken as soon as possible after the twenty-four hours are up. Again, in the course of three or four days, usually, or sooner in hot weather, the urine grows turbid from the presence of micro-organisms, becomes alkaline from decomposition of the urea, which is converted into ammonium carbonate by action of the micro-organisms, and a whitish phosphatic sediment is deposited.

NOTE.—Despite the assertions of some authors it is possible to have a sediment of uric acid and triple phosphate in the same sample of stale urine. The writer has seen it occur several times. As the urine becomes hyper-acid uric acid crystals are deposited, and these may not be entirely dissolved after the alkaline change has caused deposit of triple phosphate.

**G.** Note the **appearance** of the *unfiltered* urine, whether clear or turbid. If turbid, set a few ounces aside and, after a time, a *sediment* or deposit will be noticed. Students sometimes incorrectly report "no sediment" in urine which they have previously described as "turbid". Note whether the turbidity is slight, slowly settling, as in case of almost all normal urine twenty-four hours old, or whether the urine is so turbid as to deposit an abundant sediment within half an hour or so.

When the urine of women is examined, a whitish sediment of mucus is almost always noticed.

**H.** Note the **consistency** of the urine, whether it flows easily, or is thick and ropy from presence of muco-pus; or creamy, forming a jelly-like mass on standing, due to chyle or fibrin.

**I.** Shake some of the urine in a bottle, and notice whether **the foam** subsides quickly, or whether it is wholly permanent.

**J.** Make out a report filling in the following blanks:

1. The urine filters ..... (Specify whether slowly or rapidly.)
2. Color of the filtered urine .....
3. Odor ....., suggesting .....
4. Specific gravity at 77° F. (25° C.) .....
5. Total solids by Hæser's coefficient ..... grammes; ..... grains.
6. Corrections for age, weight, diet, and exercise leave a total of ..... grammes; ..... grains of sclids.
7. The patient should void by *Table 3*, APPENDIX, and corrections ..... grammes; ..... grains of solids.
8. Therefore this patient is voiding ..... compared with what he or she ought to void.
9. Reaction .....
10. Appearance .....
11. Consistency .....
12. Frothiness .....

---

**Apparatus used in Chemical Exercise 2.**

1. Glass funnels, some 2 inches, others 3 or 4 inches in diameter across the top. 2. Slips of blue and of red litmus paper or litmus pencils. 3. A filter ring and stand. 4. Filter papers, ordinary and for rapid filtering. 5. Glass beakers. 6. Vogel's color scale. 7. Squibb's urinometer and fluted jar. 8. A chemical thermometer.

# CHAPTER VI.

## NORMAL CONSTITUENTS OF URINE: UREA.

The normal constituents of urine of clinical interest are the following:

A. Organic, { Urea; Uric acid and urates.

B. Inorganic, { Phosphates; Chlorides; Sulphates.

In addition to these there are numerous other substances of less clinical importance which will be described with less detail than in case of the above.

### UREA.

**Pronunciation:** *U'rea.*

**Synonyms:** German, *Harnstoff;* French, *Urée.*,

**Chemical constitution:** $CH_4N_2O$, or $CO\begin{cases} NH_2 \\ NH_2 \end{cases}$ *carbamide*, an amide of carbonic acid; an organic substance, containing over 45 per cent. of nitrogen.

**Occurrence:** Always in solution in urine of any reaction. Never in the sediment of urine. Urine is a solution of urea in strength about 2 per cent.

**Form:** Crystalline; quadratic prisms.

**Color and appearance:** Pure urea occurs in commerce in colorless crystals, of taste like saltpetre.

**Solubility:** 1. Readily soluble in water and alcohol. 2. Insoluble in ether and chloroform.

**Reaction:** Solutions of urea are neutral in reaction.

**Preparation:** (*a*) From the urine by evaporating the latter to syrupy consistence, adding gradually and with constant stirring pure nitric acid in excess; nitrate of urea crystallizes out, from which, when separated, urea may be obtained by decomposition with

barium carbonate. (*b*) Synthetically by heating ammonium cyanate to 100° C. (212° F), (Wöhler, 1828); (*c*) By the action of ammonia on carbonyl chloride.

NOTE: The equations in the two processes in (*b*) are as follows:

1. $CNONH_4 = CO\left\{\begin{matrix}NH_2\\NH_2\end{matrix}\right.$ by molecular rearrangement.

2. $COCl_2+4NH_3=CO(NH_2)_2+2NH_4Cl$.

**Miscellaneous properties:** The crystals of urea contain no water of crystallization; they are permanent in the air. The commercial article in time gives off an odor of ammonia, due to change into ammonium carbonate, which occurs by taking up water, as under the influence of a ferment, as follows:

$CH_4N_2O+2H_2O=(NH_4)_2CO_3$.
(Urea.) (Water.) (Ammonium carbonate.)

This change may take place in the bladder under the influence of bacteria, the *micrococcus ureæ*, to be explained further on.

*The ammoniacal odor of decomposed urine is due to this change into ammonium carbonate.*

**Combinations:** (*a*) With nitric acid, forming urea nitrate; (*b*) with oxalic acid, forming urea oxalate —$2.CO(NH_2)_2.H_2C_2O_4$. Also, combinations with mercuric nitrate in variable proportions, one of which

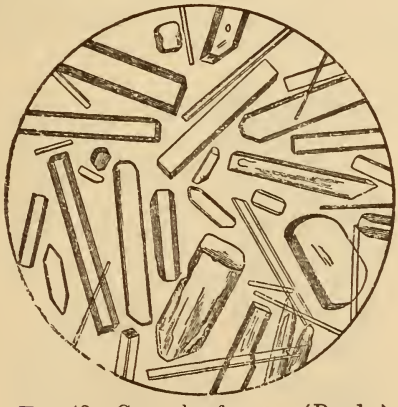

FIG. 13. Crystals of urea. (*Purdy.*)

serves as a basis for Liebig's titration method, and with various salts, as sodium chloride, and chlorides

of the heavy metals, forming combinations, for the most part crystallizable.

**Microscopical appearances:** *Urea itself:* Silky, four-sided prisms with oblique ends, or (rapidly crystallized) in delicate white needles (*Fig. 13*). *Nitrate of urea:* Thin rhombic or hexagonal crystals, overlapping tiles, colorless plates, whose point has an angle of 82° (*Fig. 14*). Larger and thicker rhombic pillars

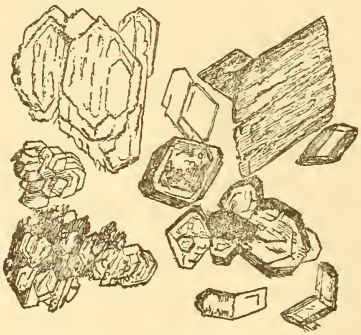

FIG. 14. Crystals of urea-nitrate.
(*Krukenberg.*)

or plates are obtained on slowly crystallizing. *Oxalate of urea:* Rhombic or six-sided prisms or plates more regular than the nitrate. (*Fig. 15.*)

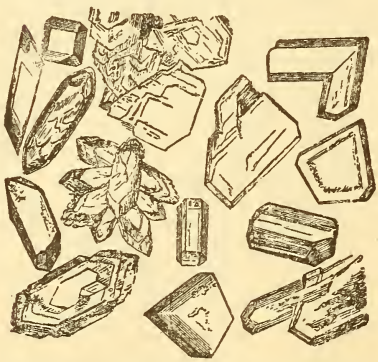

FIG. 15. Crystals of urea-oxalate.
(*Krukenberg.*)

MICRO-CHEMICAL TESTS.

1. To a drop of urine, preferably of high specific gravity, on a glass slide, add a drop of nitric acid; warm it gently and cautiously over an alcohol lamp until it is slowly evaporated. Characteristic crystals of urea nitrate may be seen under the microscope even with a low power, 150 diameters. (*Fig. 14.*)

2. Again, place a drop of urine, preferably of a high specific gravity, on the slide, add a thread and cover-glass, and allow a drop of nitric acid to enter by capillarity. Crystals of the nitrate of urea will form along the thread.

CHEMICAL TESTS.

**A. Qualitative.**

**1. The biuret reaction:** Heat crystals of urea in a test tube; the crystals melt, decompose, give off an odor of ammonia, leave a whitish residue which, dissolved in water, to which a couple of drops of sodium hydroxide solution (caustic soda) and a drop of a *dilute* solution of copper sulphate being added, a violet or rose-red color is produced.

**2. The furfurol test:** Treat a crystal of urea with a drop of a nearly saturated solution of furfurol in water, and immediately with a drop of hydrochloric acid (sp. gr. 1.1); a color-change occurs, passing from yellow through green, blue, and violet to purple-red.

3. Decomposition with solutions of **alkaline hypobromites** or hypochlorites.

**B. Quantitative.**

**Determination of urea (theoretical).** The principle on which our clinical* quantitative determinations are founded is that urea is decomposed by hypobromites, with formation of carbon dioxide and nitrogen. In practice we use an alkaline hypobromite, as sodium hypobromite, since carbon dioxide (carbonic acid gas) is soluble in alkalies, while nitrogen is insoluble. The urine is introduced into a graduated tube, filled with the chemical solutions, and the nitrogen

*The Liebig method is described in the APPENDIX.

gas evolved collects at the top of the tube and displaces the solution.

The equation is as follows:

$$CH_4N_2O+3NaBrO.=N_2+CO_2+2H_2O+3NaBr.$$

In other words, urea plus sodic hypobromite, equals nitrogen plus carbonic dioxide, plus water, plus sodic bromide. From this it may be calculated that 60 parts of urea by weight (the sum of the atomic weights of the atoms in the molecule $CH_4N_2O$) yield 28 parts of nitrogen by weight. One gramme of urea, then, would yield 28-60 gramme of nitrogen, which is known to occupy a volume of about 371½ cubic centimeters. If, then, 371½ c.c. of nitrogen gas indicates the presence of one gramme of urea in a given quantity of urine, then one c.c. of nitrogen gas would indicate the presence of one divided by 371½ which equals 0.00269 gramme of urea. Every c.c, of nitrogen gas obtained in the process at ordinary temperature and pressure signifies that 0.00269 gramme of urea is present in the amount of urine used, and on this principle the graduation of the instruments is made. In some American instruments the French measures are not used but American grains per ounce instead. Grammes per liter may be converted into grains per ounce by dividing by 2⅓.

The clinical instruments for determination of urea which are most commonly used are those of Bartley, Doremus and Squibb. The method by which we determine the quantity of urea in the urine is given in full in the next Chemical Exercise, where the three instruments are described.

# CHAPTER VII.

## PROPERTIES AND REACTIONS OF UREA.

### CHEMICAL EXERCISE III.

*A. Properties and Reactions of Urea.*
*B. Quantitative Determination of Urea.*
*C. Calculation of Results.*

### Properties and Reactions of Urea.

1. Examine **crystals of urea**. Note color, taste, solubility in water and alcohol; action of hot alcohol; of ether, and of chloroform.

2. Take the **chemical reaction** with litmus paper of an aqueous solution of urea. What is it?

3. Perform the **biuret test**, as follows:—

Fuse about 0.3 gm. (5 grains) of urea in a test-tube, shown in *Fig. 16*. Now boil the liquefied crystals till a white residue appears; next add about 10 c.c. (2 to 3 fluidrachms) of distilled water, shake thoroughly and add several cubic centimeters (1 to 2 fluidrachms) of a strong solution of sodium hydrate (10 gm. in 25 c.c. water, or 155 grains to the fluidounce).

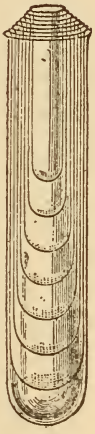

FIG. 16. Test Tubes.

Set the tube aside for the present. Now make a solution of cupric sulphate in distilled water, strength 0.5 gramme (3 grains) to 100 c.c. (3½ fluidounces.) Add several drops of this copper solution, drop by drop, to the alkaline solution above made, and a beautiful red-violet color appears at the top. Too much or too strong copper solution gives a blue color with the alkali, which can be seen by adding a large number of drops of the copper solution.

In this test urea is converted into biuret, or allophanamide, a derivative of urea.

4. Perform **the furfurol test** as follows: Shake up one c.c. of furfurol with about 15 c.c. of water. To a crystal or two of urea on a porcelain surface add a drop of the furfurol solution and immediately a drop of strong hydrochloric acid, and observe the color change, in which a purplish tint is prominent. Furfurol is an expensive article, and waste should be avoided.

**Quantitative Determination of Urea (Practical).**

1. The student having collected, mixed, and measured his twenty-four hours' urine, should proceed to determine the quantity of urea by use of Bartley's ureometer, and Leslie Beebe's clamp (*Fig 17.*)

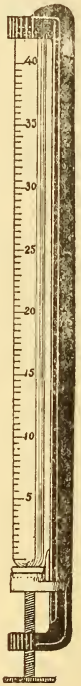

FIG. 17. Leslie Beebe's clamp.

Bartley's ureometer consists of a somewhat long, graduated tube, called by chemists a "gas tube," and a 1 c.c. pipette, about twice the length of a medicine-dropper, with a rubber nipple on one end of it. That is the entire apparatus. To estimate urea with this instrument it is only necessary to proceed as follows:

1. Fill the long graduated tube up to the mark five with a twenty per cent. solution of C.P. potassium bromide (bromide of potash).

2. Next, pour in a solution of Squibb's chlorinated soda up to the eighteenth mark, or anywhere between the eighteenth and twentieth mark on the tube. [In buying the chlorinated soda solution, get Squibb's 2 per cent. U. S. P., put up in sealed bottles containing 250 grammes. The solution does not keep long after the bottle is opened, hence it is better to get six 250 gramme bottles, rather than one large one.]

3. Let water trickle slowly down the side of the tube till the latter is filled to the twenty-fifth mark.

4. Now take up urine with the pipette exactly to the

single mark on this little instrument. Some practice is necessary in order to do this well. See that the rubber nipple is not cracked. It is well to buy a few dozen pure gum rubber nipples, but care must be taken that they fit tightly to the large orifice of the pipette.

In order to take up urine in the pipette exactly to the mark on the pipette, dip the latter below the level of the urine, squeeze the rubber nipple, then gradually relax pressure and the urine will rise in the tube. Keep the tip end of the pipette below the level of the urine always so that no air bubbles shall rise, and keep trying till finally you have the urine exactly to the mark. Relax all pressure on the nipple when this has been obtained—but it is best to relax gradually so that by the time all pressure is relaxed the urine has risen to the mark.

NOTE.—By use of a soft rubber nipple 1 c.c. of urine can be easily obtained as follows: Draw up *more* than one c.c. into the pipette and then work the nipple down. The urine flows out as the nipple is worked downward, and no air-bubbles enter from below. Work the nipple down until the level of the urine is exactly that of the 1 c.c. mark, then take the pipette by the glass portion, avoiding pressure on the nipple, and introduce it into the Bartley tube.

5. Now hold the long tube well inclined in the left hand and with the right cause the urine in the pipette to trickle slowly down into the liquids in the long tube, squeezing the rubber very gently. When all the urine has been squeezed out of the pipette, gradually raise the inclined long tube to the perpendicular and put Beebe's clamp over the mouth of the tube. Invert the long tube several times. Inside the tube the urine mixes with the chemicals and a lively effervescence takes place. *Nitrogen gas* has been set free by the action of the chemicals on the urea and is trying to escape from the tube. Now bring the tube to the perpendicular position, and wait for the effervescence to cease. This may take several minutes. Read what mark on the tube is even with the level of the liquid in the tube after the foam has settled. You will see the figure 15 without difficulty somewhere near the level of the liquid in the tube. The next *long* mark not lettered is 16, the next 17, the short marks

between the long ones representing quarters. If, then, the level of the liquid is one long mark plus two short ones *below* 15, then the level is at sixteen and a half. Having made the reading accurately, carry the instrument to the nearest jar (*Fig. 18.*) filled with water, and plunge the instrument below the level of the water. When once below the water's edge, remove the clamp and notice that instantly the level of the liquid in the tube sinks. This is because the pressure of the clamp being relaxed the nitrogen gas is able to expand to its proper bulk, which it does, driving out the liquid as it does so. Now see that the level of the liquid inside the tube is the same as the water outside, raising or lowering the tube as necessary, but always keeping its mouth under water. Wait three minutes for diffusion to take place. Then take a second reading. The level of the liquid will now be down anywhere from the twentieth to the twenty-fifth mark, in exceptional cases from the nineteenth to the thirtieth. Subtract the first reading before the clamp was removed from the second reading, after the clamp was removed, and the difference represents grains of urea in one fluidounce of the urine under examination. For example, if, after the effervescence has ceased, and the clamp is still over the mouth of the tube held perpendicularly, mouth down, the level of the liquid inside is at the sixteen-and-a-half mark, and if, after you have plunged the instrument under water and taken away the clamp the level of the liquid is now at the twenty-six-and-a-half mark, then twenty-six-and-a-half minus sixteen-and-a-half equals ten, that is, ten grains of urea in every fluidounce of the urine.

FIG. 18. Jar for use in Bartley's process.

If you are working with the twenty-four hours' urine, as you ought to be, then multiply the ten, or whatever figure you get, by the number of fluidounces of the urine in twenty-four hours; that is, if there are fifty fluidounces of urine in twenty-four hours, and ten grains in every fluidounce, then you have 500 grains

of urea in twenty-four hours. If you have, say forty fluidounces, and the difference in the readings is seven, then seven times forty, or 280 grains, in twenty-four hours. [To convert grains per ounce to grammes per liter, see *Table 4*, APPENDIX. Grains total to grammes, *Table 5*.]

The whole operation is simple, and takes less time to perform than to describe. I recently distributed Bartley's ureometers to a class of fifty or sixty students who had never before used them, and the results of the first trial in ninety per cent. of the cases were sufficiently near my own to be "clinically accurate." After three or four trials there were but one or two who did not obtain the correct results. The only precautions of importance are:—

1. To see that the urine is taken up exactly to the mark on the pipette;

2. That the clamp is not removed until the orifice of the instrument is under water.

The advantages of Bartley's instrument when provided with Leslie Beebe's clamp are the following:

1. Bromine is not used.
2. The instrument is not easily broken, and can be hung up on a peg or nail.
3. The decomposition of the urea within the tube takes care of itself, does not need to be watched nor helped.
4. The urine, if of high specific gravity, does not need to be diluted.
5. Rubber tubing is dispensed with.

The advantages of the Leslie Beebe clamp are:

1. The instrument, thus closed, may be hung up on a nail, and the physician attend to other business while the decomposition is going on.
2. A tall narrow glass cylinder full of water may be used, and the reading easily taken when the clamp is removed.

# CHAPTER VIII.

## THE DETERMINATION OF UREA BY OTHER CLINICAL METHODS.

One of the most popular clinical instruments for determination of urea is that of Dr. Doremus, of New York. No modern book on clinical urinary analysis is complete without a description of this apparatus.

**Doremus' instrument.** (*Fig. 19.*) One hundred grammes (1.543 troy grains) of caustic soda dissolved in 250 c.c. (8.5 fluidounces) of distilled water. Of this solution take 10 c.c. (2.7 fluidrachms) and add 1 c.c. (16 minims) of bromine. Shake the mixture well, until the bromine is dissolved and the whole becomes yellow in color. Dilute with 10 c.c. of water. Pour the whole into the cup of Doremus' ureometer and carefully fill the limb with it by tipping backward. Then by means of the curved pipette introduce 1 c.c. of urine into the soda solution. Effervescence takes place and the soda solution is displaced by the gas formed.

The instruments are graduated either in grains per ounce or in grammes per liter. In the latter case the figures 0.01, 0.02 and 0.03 signify 10 gm., 20 gm. and 30 gm. per liter, respectively. See *Table 4*, APPENDIX, for conversion to grains per ounce.

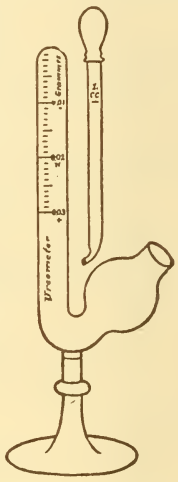

FIG. 19. Doremus' ureometer, etc., with foot.

### Manipulation.

1. Get Larkin & Scheffer's bromine, as the bottles are easier to open. Use great care in opening the bottles.

2. Use the 1 c.c. pipette in adding bromine to the caustic soda solution.

3. Dilute all urines of specific gravity 1025 or upwards with equal parts of water and multiply result obtained by 2.

CLINICAL NOTE.

The writer has made several thousand determinations of urea with the Doremus instrument, and can commend it for simplicity. It is not as durable as the Bartley, but does not involve the use of rubber tubing.

The principal objections to it are the use of bromine, and the necessity for diluting the urine in cases where the specific gravity is above 1025, since the gas, when in excess, drives the hypobromite solution below the graduation. Again, unless the instrument is provided with a foot, it is without support and, when it is made with a foot, it is easily broken. After the foot is broken insert the broken end into paraffin, melted in a tin box or other receptacle and allowed to solidify.

The great advantage of the Doremus instrument, to the author's mind, consists in the use of hypobromite, which may be freshly made for each determination. But few will agree with him from a practical standpoint, since use of bromine is exceedingly unpleasant to the majority. An important practical point in the use of bromine is the fact that Larkin & Scheffer put up bromine in such a way that it is possible to get the glass stopper out of the bottle with comparatively little difficulty. Novices who break bottles of bromine with dangerously unpleasant results will do well to note the above.

Too large quantities of hypobromite should not be made, as it deteriorates on keeping, though not in a week's time, as I have often observed. How much longer it will keep I do not know. Again, some samples of bromine combine with the sodium hydroxide solution with more energy than others. The writer once shook up 10 c.c. of bromine with 100 c.c. of caustic soda solution, with result that the bottle burst and was broken to atoms, either from the heat generated or for other reasons. It is safer in making 100 c.c. to make 10 lots of 10 c.c. caustic soda solution containing 1 c.c. of bromine each.

**The Squibb apparatus** (*Fig. 20*) consists of three bottles connected during the determination by rubber tubing. Into one of the bottles standing upright a short test tube, *F*, containing a measured volume of the urine is dropped by means of a small forceps. A bent glass tube and a rubber tube connect this with the other bottle, *B*, which, at the beginning of the test, is quite filled with water. Another glass tube connects *B* with the bottle *D*, empty at the beginning of the test

To make the test, pour into the first bottle 20 c.c. of strong hy-

pobromite solution, or 40 c.c. of the hypochlorite. Measure accurately 4 or 5 c.c. of urine into the tube, drop this into the bottle and insert the stopper. Fill *B* quite full of water, and insert its stopper which drives out a little water through the short tube into *D*. Allow the whole apparatus to stand ten minutes to take the temperature of the air, then empty *D* and replace it. Now tip the first bottle so as to mix the contents of *F* with the reagent and shake gently. Bubbles of gas escape and passing over into *B* drive out a corresponding volume of water. Repeat the shaking of the reagent bottle several times. In a few minutes the reaction

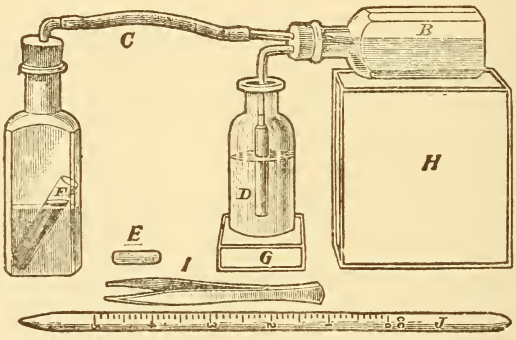


FIG. 20. Squibb's apparatus for determination of urea.

is complete, but the apparatus must be allowed to stand to cool down to the air temperature. A part of the water in *D* may be drawn back into *B*. Finally measure the volume of water left in *D*, and take this as the volume of gas liberated. Make the calculation as before on the assumption that each c.c. of gas corresponds to .0027 Gm. of urea.

The results obtained are said to be more accurate than those where but 1 c.c. of urine is used.

CLINICAL NOTE.

The Squibb apparatus is unpopular with most students and physicians, who prefer a more ready method, even if the results obtained are not so accurate.

The principal objection, in the writer's mind, to Squibb's apparatus is the use of small rubber tubing which, in time, wears out and must be replaced. The instrument is, however, certainly to be commended to those who have time and opportunity for more careful clinical determinations.

**Error of the clinical instruments:**

It must not be assumed that the clinical instruments are chemically accurate in the results shown. When

the quantity of urea in the urine is small, two to four grains per ounce (1 to 2 gm. per liter), the error is small, but when the percentage of urea is high, 10 to 15 grains per ounce, the error is considerable. Drs. Bader, Holloway, Leslie Beebe, and the writer have conducted numerous experiments for information on this point. The results have been as follows:

**Bartley gas tube:**

Solution of urea 9½ grains per ounce; five determinations with the Bartley instrument and Leslie Beebe clamp gave 10 grains, 10¼, 10¼, 10¼, 10½ respectively. Error, one-half grain to a grain per ounce, too high.

Solution of urea 4¾ grains per ounce: Bartley gave 5⅜ grains. Error about two-thirds grain per ounce too high. Another determination, 5 1-5 grains, about a half grain too high.

Solution of urea 15⅜ grains per ounce: Bartley gave 14 grains per ounce, or one and two-thirds grains too low.

**Doremus' instrument:**

Solution of urea 4.7 grains per ounce: Doremus' instrument 4 grains per ounce, or about three-quarters of a grain too low.

Solution of urea 15⅜ grains per ounce: Doremus' instrument, 11½ grains per ounce, or about 4 grains per ounce too low.

Now, while these errors, from a chemist's viewpoint, are great, clinically we have not much cause to complain, for the following reasons:

1. In cases in which urea is low in grains per ounce the error is usually but a fraction of a grain. Suppose it be a whole grain. If the patient passes 50 ounces of urine, the total error is at most 50 grains in, say, 200 to 300 grains total of urea per 24 hours. In cases where the patient voids 80 or 100 fluidounces of urine, the total error is not correspondingly increased since the quantity of urea in grains per ounce will be less, and the error less per ounce.

2. In cases where the urine is concentrated and the error 2 to 4 grains per ounce, the total error is likely

to be no greater, if as great as above, because the quantity of urine per 24 hours will be small. Moreover, by diluting the urine in these cases with equal parts water, as is of necessity done when the Doremus instrument is used, the error is not as great.

I conclude, therefore, that the clinical methods enable us to determine the total quantity of urea present within 25 or 50 grains at most, which in anything above 100 grains is of no great importance. In general, any quantity of urea below 200 grains in 24 hours is small, and above 450, large, unless in the latter case the patient be a large, heavy person. If the patient is passing less than 300 grains, it should attract our attention. The clinical instruments certainly enable us to determine these points, and also to judge in a general way whether the elimination of urea is increasing or decreasing to a marked extent.

### C. Calculation of results:

BARTLEY INSTRUMENT.

1. Subtract the reading made before immersing in water from that made after the Beebe clamp is removed under water. The difference is grains of urea in fluidounces of urine. Convert into grammes per liter by *Table 4*, APPENDIX, and find out also by this table what per cent. of the normal average it is.

2. Multiply the grains of urea per ounce by the number of fluidounces of urine in 24 hours. Product represents the total grains of urea in the 24 hours' urine. Convert into grammes per 24 hours by *Table 5*, APPENDIX, and find out also by this table what per cent. of the normal average it is.

3. Determine what per cent. of the weight of the twenty-four hours' urine the urea for twenty-four hours is, (so-called percentage of urea in the urine; *carefully distinguish from per cent. of normal average.*) To do this divide the grammes per liter found in 1 by 10. The result is approximate only, since the specific gravity of the urine is disregarded.

**Examples:**

1. Male patient passes 40 fluidounces of urine in 24 hours:

Reading before immersion, 16; after, 25. (40 fl. oz. equals about 1200 c.c.).

**Answers:**

(*a*) 25 minus 16 equals *9 grains per ounce;*
(*b*) 9 grains per ounce by *Table 4* equals *19.35 grammes per liter;*
(*c*) 9 grains per ounce or 19.35 gm. per liter in a **male** (*Table 4*) equals *90 per cent. of the normal average;*
(*d*) 9 times 40 equals *360 grains urea in 24 hours;*
(*e*) 360 grains by *Table 5*, APPENDIX, equals *about 23 grammes;*
(*f*) 360 grains, or 23 gm. in a *male* equals by *Table 5*, *90 per cent. of the normal average;*
(*g*) 19.35 gm. per liter (*b*) divided by 10 equals *1.93 per cent. of urea in the 24 hours' urine.*

2. Female patient voids 66 fluidounces of urine in twenty-four hours: the reading before immersion is 15¼, after immersion it is 19.

(*a*) 19 minus 15¾ equals *3 1–4 grains urea per ounce urine;*
(*b*) By *Table 4*, APPENDIX, 3¼ grains per ounce equals about *6.4 gm. per liter;*
(*c*) By *Table 4*, APPENDIX, 3¼ grains per ounce or 6.4 gm. per liter, equals about *35 per cent. of the normal average in case of females;*
(*d*) 3¼ times 66 equals *215 grains urea in 24 hours;*
(*e*) By *Table 5*, 215 grains equals *about 14 grammes;*
(*f*) By *Table 5*, 215 grains or 14 gm. *in females equals 70 per cent. of the normal average;*
(*g*) 6.4 gm. per liter (*b*) divided by 10 equals 0.64 per cent. (SIXTY-FOUR HUNDREDTHS of one per cent.) of urea in the urine.

REPORT.

Make out a report as follows:

Urine per 24 hours, c.c..... fl. oz.....
What per cent. of normal for sex.....
Urea, grains per ounce.....
grammes per liter .....
What per cent. of normal for sex.....
Urea, grains per 24 hours.....
grammes per 24 hours.....
What per cent. of normal for sex.....

---

**Chemicals and Apparatus Used in Chemical Exercise III.**

An ounce of urea crystals.
Distilled water.—Alcohol.—Ether.—Chloroform.
Litmus paper.
Solution of sodium hydroxide, 100 grammes in 250 c.c. of water.
Solution of cupric sulphate, one-half of one per cent.
Solution of furfurol, nearly saturated.
Hydrochloric acid, c.p., U. S. P.
Nitric acid, c.p., U. S. P.
Strong solution of oxalic acid.
One dozen five-inch test-tubes, with test-tube, rack, (*Fig. 21.*)
Bartley's urea instruments.
Leslie Beebe's clamps.
Tall narrow jars, preferably 10 or 12 inches high and 2 or 3 inches in diameter; in default of these any container of this size or larger.
Test-tube cleaner.

FIG. 21. Test-tube cleaner.

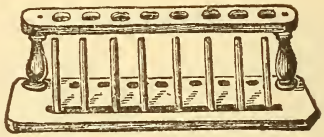

FIG. 22.—Test-tube rack.

Alcohol lamp (*Fig. 23*), or Bunsen burner. (*Fig. 24.*)

FIG. 23, Alcohol Lamp.

FIG. 24. Bunsen Burner.

Glass slides.

Solution of potassium bromide, c.p., freshly made, 20 per cent.

Squibbs' solution of chlorinated soda, in amber bottles, with rubber stoppers, containing 250 grammes.

[Standard methods for determining urea, and total nitrogen, are given in the APPENDIX.]

MICROSCOPICAL EXERCISE I.

1. (*a*) Dissolve some crystals of urea in water, warm a few drops of the solution on a glass slide, and examine with a low power (150 diameters) and subsequently with a high power (500). Make a drawing in a note-book, of the crystals seen. (*b*) Dissolve some crystals in alcohol, let it evaporate spontaneously, and examine. See *Fig. 13*.

2. Perform the micro-chemical tests in which urea nitrate crystals are found, making a drawing of the crystals obtained as above. See *Fig. 14*.

3. Add a strong solution of oxalic acid to a solution of urea, warm slowly, gently and cautiously a few drops of the mixture on the slide, and compare the crystals obtained with those of oxalic acid and of urea respectively. See *Fig. 15*.

REQUIREMENTS.

Microscope with half-inch and one-fifth-inch objectives. (Bausch & Lomb's BB stand is recommended.) Glass slides, cover-glasses, pipettes, alcohol lamp, nitric acid, oxalic acid, alcohol.

# CHAPTER IX.

## UREA: PHYSIOLOGY, PATHOLOGY, AND CLINICAL SIGNIFICANCE.

### A. PHYSIOLOGY.

**Regularity of excretion.**—Urea is the chief vehicle by which the nitrogenous food leaves the body. About ninety per cent. of the nitrogen taken in the food is excreted as urea. Contrary to the statements of various authors I find the total amount of urea passed in a day not exceedingly variable. In the urine of a person of regular habits the daily excretion of urea is sometimes remarkably regular: one patient, for example, whose urine I examined once a week for seven weeks voided a total of 13, 12, 14½, 13½, 13, 12, 13½ grammes respectively. Moreover, the amount of urea voided by the same person may not vary greatly in a term of years. Thus in a case in which I examined the urine eight times in five years the urea ranged from 14 to 24 grammes, five of the analyses showing quantities from 20 to 24 grammes inclusive.

It would seem that the quantity of urea passed by an individual fluctuates within a not very great range, and that, if the average for any ten days be compared with that of any other ten days, the difference is not great.

In one case the *average* excretion for a period of ten days was to a grain (0.6 gm.) the same as that for another period of the same length.

**Quantity per twenty-four hours.**—The figures given by English observers as the average in twenty-four hours, 26 to 33 grammes (412 to 515 grains), I regard as being too high. Out of 200 Americans whose urine contained neither albumin nor sugar I found only 11 to contain as much as 30 gm.

(465 grains) in twenty-four hours. Two-thirds voided less than 20 gm. (310 grains) in twenty-four hours. But inasmuch as nearly all these persons were not typically healthy, and in fact many were ill enough to consult a physician, I can not take their average as the normal one. But the urine of such healthy Americans as I have examined has scarcely ever contained as much as 500 grains of urea. I would assume the quantity to be about 26½ gm. (410 grains) in men, and 20½ gm., or 315 grains, in women. These are the figures of the French observers, Yvon-Berlioz, and I regard them as approaching more closely our American average than the English figures do.

The excretion of urea per hour is said to be 0.015 to 0.035 gramme for every kilogram of weight; that is, 0.231 to 0.54 of a grain for every 2¼ pounds. For adults I would regard the smaller figure rather than the larger as correct.

Children are said to void 0.131 gm. a day for every kilogram of weight when weighing from 18 to 36 kilogrammes (4½ grains for every pound when weighing from 40 to 80 pounds), and 0.122 gm. when weighing from 28 to 56 kilograms (4 grains per pound from 60 to 120 pounds.) At this rate we would expect a child weighing 40 pounds to pass 180 grains of urea in twenty-four hours.

I have examined the urine of a number of children. The urea figures are given at the end of this chapter. Men pass 17 to 21 grammes per liter (8 to 10 grains per ounce), and women 16 to 19 (7½ to 9).

**Formation in the body.**—Part of the urea excreted may possibly be formed in the liver from ammonium carbonate. The reasoning that points to the liver as the chief seat of urea formation is as follows:

1. In diabetes, where we know the metabolism of hepatic cells is greatly increased, urea is increased

2. In degenerative changes in the liver, urea formation is decreased.

Unfortunately, however, the first of these premises is vulnerable. Out of 45 typical diabetics, in whose

twenty-four hours' urine the author determined the urea, half voided from 20 to 40 grammes, (310 to 620 grains) which is not an excessive amount considering the polyuria, and 15 patients voided less than 465 grains (30 grammes), which is less than the normal average of the English. A comparatively low excretion of urea is possible even in severe cases of diabetes; for example, one of the writer's patients passed only 265 grains of urea in the twenty-four hours' urine, containing five-and-a-half per cent. of sugar, or nearly 1,250 grains.

Moreover, in diseases not attended by degenerative changes in the liver a low excretion of urea may be found: as, for example, in the case referred to the writer by Dr. Thomas E. Roberts, in which in 825 c.c. (27 fl. oz.) of urine there was less than 1 gm. (15 grains) of urea. Women often void as little as 6 grammes (93 grains) in a day and recover.

In view of such facts I am inclined to agree with Dr. Long, who says, "how or where the conversion of nitrogen into urea takes place is not known."

**Effect of diet and exercise.**—Urea is increased by animal diet, and mental and physical activity; decreased by non-nitrogenous diet and quietude. Hence, more urea is voided during the day than during the night. In thirty-one instances in which the writer has examined the day urine and night urine of twenty-three patients separately the day urea was found to be greater than the night urea in twenty-nine out of the thirty-one samples examined. In only six of the twenty-nine was the day urea as much as twice the night urea, and in but two instances, three times. The amount by which the day urea exceeded the night varied from 0.3 gm. (5 grains) to 1 5 gm. (225 grains); the average excess of day over night was about 2.5 grammes (40 grains). One of the two cases in which the night urea exceeded the day was that of acute chorea following diphtheria; in the other the diagnosis is unknown.

**Effect of milk diet.**—Milk is said to increase urea in urine. One of my patients voided 46 gm. (715 grains) of urea on strict milk diet, but, unfortunately,

what his excretion was prior to the diet is not known. In another case no increase at all was noticed in a considerable period of time. Both were cases of slight albuminuria without casts.

B. PATHOLOGY.

**Relative urea and absolute urea.**—Much confusion has been caused in the past by not distinguishing a *relative* increase in urea from an *absolute* increase. By *relative* increase in urea we mean an increase in urea as compared with some other constituent of the urine, notably water. In this book when speaking of relative increase of urea I shall mean an increase compared with the water of the urine, *i. e.*, *an increase of urea in grains per ounce* (grammes per liter).

Thus, if the urine of a certain patient contain 15 grains of urea to the ounce of water, urea in this case is *relatively* increased, since 8 to 10 grains per ounce is normal.

By *absolute* increase in urea we mean increase in the total urea for twenty-four hours as compared with the normal average quantity for that period: thus, a patient who passes 750 grains of urea in twenty-four hours, voids urea which is absolutely increased in quantity.

**Relative increase and absolute deficiency.**—Something which puzzles beginners is the fact that a patient may pass urine in which urea is relatively increased but absolutely deficient. Thus, suppose a patient voids 10 ounces of urine in twenty-four hours containing 15 grains of urea to the ounce. Urea is *increased relatively*, since 15 grains to the ounce is one-and-a-half times the normal average of 10 grains to the ounce; but urea is *decreased absolutely*, since the total product is 10 times 15, or 150 grains total, about one-third the normal quantity for twenty-four hours.

**Relative deficiency and absolute increase.**—Again, in the same urine urea may be relatively deficient and absolutely increased: thus, if a patient voids 100 ounces of urine containing 6 grains to the ounce, urea is deficient *relatively*, since 6 grains per ounce is less

than 6 to 10, the normal range. On the other hand urea is increased *absolutely*, since 600 grains the total quantity, is in excess of the normal range, 400 to 500 grains at most.

DISEASES IN WHICH UREA IS DECREASED IN GRAINS PER OUNCE (RELATIVE DEFICIENCY OF UREA).

Urea is decreased relatively from physiological causes, after copious ingestion of fluids. Pathologically relative decrease takes place in the following diseases:

1. Chronic nephritis, except when dropsy is excessive.
2. Diabetes insipidus.
3. Hysteria (after paroxysm).
4. Anæmia.
5. Some cases of neurasthenia.

EXAMPLES.

In eighteen cases of **chronic nephritis** in which the twenty-four hours' urine contained large percentage of albumin, urea was relatively deficient in all but four. In one case but 2 gm. per liter of urea (1 grain per ounce) was found. Nine grammes per liter (4 grains per ounce) is quite commonly observed in **chronic interstitial nephritis.** In one case of *hysteria with anæmia* urea was as low as 1 gramme per liter (one-half grain to the ounce.) The patient recovered and afterwards voided normal urine. In some cases of *neurasthenia* the writer has noticed urea 9 to 13 grammes per liter ($4\frac{1}{2}$ to 6 grains per ounce), but this is not invariable.

DISEASES IN WHICH UREA IS INCREASED IN GRAINS PER OUNCE (RELATIVE INCREASE).

Urea is relatively increased physiologically by abstinence from liquids or other causes which diminish the volume of urine. Pathologically it is increased relatively in the following diseases:

1. Febrile disorders, especially acute rheumatism.
2. Acute or chronic nephritis, where the urine is concentrated and high-colored from dropsy.

3. Congestion of the kidneys.
4. Certain hepatic disorders.
5. Some cases of diabetes mellitus.
6. Certain nervous diseases.
7. *Before* the convulsions of pregnancy.

EXAMPLES FROM THE AUTHOR'S CASES.

In all these cases the twenty-four hours' urine is understood as specified.

CHRONIC NEPHRITIS.—In the case of a dropsical woman 31 gm. gm. per liter (15 grains per ounce) and subsequently 25 gm. and 21 (12 grains and 10 grains). In the case of a woman who passed but 40 c.c. (1 fl. oz.) of urine in twenty-four hours, urea was 49 gm. per liter (23 grains per ounce).

GALL-STONE COLIC.—In one case 41 gm. per liter, 20 grains per ounce.

DIABETES MELLITUS.—The greatest quantity of urea ever found by the writer in diabetes was 35 grammes per liter (16 grains per ounce). The lowest, 5 gm. per liter (2½ grains per ounce). In the majority of cases 10 to 21 gm. per liter (5 to 10 grains per ounce).

NERVOUS DISEASES:

Epilepsy, in a boy of twelve years.

Chronic meningitis.

Oxaluria.

CANCER.—In one case of cancer of the intestines the writer noticed relative increase of urea in the urine. Absolutely it was diminished.

CONVULSIONS OF PREGNANCY.—In two cases of puerperal nephritis the writer has observed a high percentage of urea, 12 and 16 grains per ounce (25 and 33 gm. per liter), respectively. In one case the patient died of convulsions in less than a day; in the other there was vomiting, diarrhœa, and urine loaded with albumin.

The second case was that of a woman who had a history of puerperal convulsions at the same date in a previous pregnancy. Her urine was carefully and fully examined by me from time to time during the early months of pregnancy and found to be abundant, pale, of poor quality, urea about 4 grains per ounce (9 gm. per liter), albumin small, two per cent. *bulk.* Suddenly, without warning, the urine became scanty, concentrated, highly acid, urea increased to 16 grains

per ounce, and albumin to the enormous figure of 50 per cent. bulk, or about one per cent. weight. At the same time she was seized with violent vomiting and purging.

It is evident that in these cases urea is not decreased relatively, as in the uræmia of interstitial nephritis, but is decidedly increased.

### CHEMICAL EXERCISE IV.

Repeat the determination of urea, this time comparing the Bartley clinical instrument with the Doremus in various ways.

## CHAPTER X.

### PATHOLOGY AND CLINICAL SIGNIFICANCE OF UREA, (CONTINUED.)

**Diseases in which urea is decreased in total quantity for the twenty-four hours.**

Urea is *decreased* in total quantity per twenty-four hours (absolute decrease) in the following:

1. Chronic Diseases. Especially *many nervous ones;* in chlorosis, paralysis, ovarian tumor, uterine cancer, *chronic nephritis;*
2. In diseases of the liver, notably acute yellow atrophy;
3. Preceding and during *uræmic attacks.*
4. Before paroxysms of gout and asthma.
5. In yellow-fever and in cholera.

EXAMPLES FROM THE AUTHOR'S CASES.

Internal Cancer.—In two cases the urea was absolutely diminished. In one of these two relatively and absolutely diminished. Eleven grammes (170 grains) total in each case. The diagnosis was verified.

Uterine Fibroid.—In two cases 15 and 14 gm. (225 and 210 grains) total.

Chronic Cystitis in an Anæmic Woman.—Eight analyses gave an average of only 8.5 gm. (130 grains). The patient had an uræmic attack, but recovered and is alive today.

Chronic Nephritis.—In one case a dropsical woman averaged 10.5 gm. (165 grains) in nine analyses made during the last month of life.

In twenty-eight fatal cases of chronic nephritis in which during life albumin together with granular, fatty or waxy casts were found the average total urea excretion was 14 gm. (210 grains). When albumin was very abundant urea was below the normal in fourteen out of 18 cases, and never above normal.

In one case a female patient several days before death voided only 1.5 gm. (22 grains of urea) in twenty-four hours.

Occasionally urea is not greatly diminished until shortly before death. One patient, male, aged 55, dropsical from head to foot, passing urine loaded with albumin, several weeks before death, voided 20 gm. of urea (300 grains). A few days before death urea decreased materially.

Acute Chorea.—In one case, a child, urea was relatively and

absolutely decreased, 10.5 gm. (160 grains) total, and night urea exceeded day.

CHRONIC RHEUMATISM. — Patient, male, unable to move, averaged 13 grammes (200 grains) in seven analyses covering a period of seven weeks, and lived several years afterward.

CHRONIC ALBUMINURIA.—A man, aged 45, averaged 21 grammes (325 grains) during scattered analyses extending over a period of five years. There was absence of other symptoms.

CHRONIC PROSTATITIS.—A man, aged 70, averaged 19 grammes (300 grains) in ten analyses made one each week for ten consecutive weeks. He was invariably worse whenever urea fell below 20 grammes daily; better when it was higher.

PSOAS ABSCESS.—A child of 12 years; urea 7 grammes (110 grains). The case resulted fatally.

NERVOUS DISEASES.—In the case of one hundred patients with various nervous diseases the urea per twenty-four hours in the majority of cases was from 14 to 30 grammes (210 to 465 grains). In about one-quarter of the cases it was less than 14 grammes, but in only about 5 per cent. of the cases above 30 grammes. The diseases in which urea was greatly decreased, below 14 gm. (210 grains), were as follows:

*Great relative and absolute decrease.*—Epilepsy; neurasthenia; reflex nervous headaches from uterine diseases; acute chorea following diphtheria; locomotor-ataxia.

*Great absolute decrease only* —Irregular cerebral development; spinal irritation, with chronic meningitis; epilepsy; cerebral hemorrhage and hemiplegia; aphasia, with paralysis. In the last two cases, 11.5 gm. (178 grains) and 7 gm. (110 grains) respectively.

*Moderate decrease.*—Diseases in which the deficiency of urea was moderate, 14 to 17 grammes (220 to 265 grains) in twenty-four hours were as follows: writer's cramp; oxaluria with mental and nervous symptoms; epilepsy in a young girl; hysteria in a neurotic woman; neuritis; cerebral tumor; insanity (reflex from uterine disease); posterior spinal sclerosis; paralysis agitans; paralysis from softening of the brain; nervous symptoms reflex from uterine disease (two cases); neurasthenia; neurasthenia with tremor.

*Urea nearly normal.*—Diseases in which the excretion of urea was nearly normal, 18 to 25 gm. (280 to 390 grains), were the following: Chronic cerebral meningitis and facial paralysis; brain symptoms following sun-stroke; neurasthenia (three cases); epilepsy in a child of 11; nervous symptoms reflex from uterine disorder; epilepsy in a boy of 12; localized chorea; melancholia followed by suicide; congenital neurasthenia; cephalalgia following pneumonia; sexual neurasthenia; hypochondria; nervous symptoms reflex from disease of the eye; hysteria in several male patients; chorea; reflex epilepsy; epilepsy; melancholia.

*Urea normal.*—Diseases in which urea was full normal were the following: Nervous symptoms, from worry and abuse of tobacco; epileptoid convulsions; melancholia; nervous symptoms reflex from uterine disease, and from rectal diseases; torticollis in a neuropath; epilepsy in a boy.

DISEASES IN WHICH UREA IS INCREASED IN TOTAL QUANTITY FOR TWENTY-FOUR HOURS (ABSOLUTE INCREASE).

Urea is *increased* in absolute quantity (total per twenty-four hours) in—

1. Acute febrile diseases with emaciation, as typhoid fever; pneumonia; the exanthematous diseases; typhus; to some extent in remittent fevers; intermittents *before* the chill;
2. Pyæmia;
3. Some cases of diabetes;
4. Atrophy from dyspepsia in children (Parrot-Robin);
5. Phosphorus poisoning;
6. Some nervous diseases, as progressive muscular atrophy;
7. Sometimes in diffuse bronchial catarrh without fever.

EXAMPLES FROM AUTHOR'S CASES.

PNEUMONIA.—In one case the patient, male, on the second day and before the diagnosis was established with certainty passed 48½ gm. (750 grains). Convalescing passed but 30 gm. (465 grains.)
DIABETES.—In one case a male patient passed 81 grammes (1250 grains). Six out of 42 patients voided more than 50 gm. (775 grains).

C. CLINICAL NOTES.

1. A high figure of *relative* urea (grammes per liter, grains per ounce) is not necessarily a favorable sign in acute or chronic nephritis, for it may mean merely scanty urine, which is usually an unfavorable sign.
2. A *low* figure of urea, *relative and absolute*, is almost always observed in chronic nephritis.
3. Patients with chronic nephritis seldom show increase in absolute urea (grammes per twenty-four hours, grains per twenty-four hours) proportionately to increase in urine voided.
4. In one case under the influence of diuretin the amount of *absolute* urea was diminished one-half, although the quantity of urine was increased six-fold.
5. A patient on the same diet may pass more urea

both *absolutely and relatively* in 1,000 c.c. of urine (33 fl. oz.) than in 2,000 (66 fl. oz.)

6. In diabetes the safest excretion of absolute urea appears to be from 20 to 30 grammes (310 to 465 grains) in twenty-four hours. The mortality in cases where more than 60 grammes (930 grains) are voided is high.

7. It is possible for a pregnant woman with a history of convulsions in a previous pregnancy to be confined without convulsions when 20 days before confinement urea is but 8 gm. per liter (4 grains per oz.) and 7 gm. per twenty-four hours (125 grains), albumin and casts being absent.

8. It is possible for a pregnant woman with the urine and urea of chronic nephritis to be delivered safely and to have no convulsions after delivery.

9. On the other hand, it is possible for a pregnant woman to die of uræmic convulsions when twenty-four hours before death urea was 25 gm. per liter (12 grains per ounce), albumin and casts, granular and waxy, being present.

10. It is possible for a pregnant woman to die of convulsions when a week before death urea is normal both relatively and absolutely, albumin being a plain trace, but no casts present.

11. It is possible for a pregnant woman to have numerous convulsions at term and survive, who passed 20 gm. (310 grains) of urea in twenty-four hours a few days before confinement, albumin being between first and second mark on Esbach tube, casts, a few hyaline.

12. Drugs which are said to diminish urea are alcohol, digitalis, mercury, tea, valerian, lead, all drugs which interfere with the functions of the liver; phosphorus to increase urea temporarily; quinine to diminish urea at first; potassium bromide to decrease urea while the bromide is being eliminated; arsenic to increase it at first.

The author has noticed a diminution of urea in certain cases in which diuretin was given, but cannot say positively that it is a characteristic of this drug.

13. The drugs which are said to increase urea are the mineral acids, excess of alkaline chlorides, iron "tonics," squill, juniper, potassium chlorate, pepsin, maltin, euonymin, mercuric chloride, salicylic acid, benzoic acid, lithium benzoate, colchicum, and drugs which stimulate the liver.

The author has verified repeatedly this statement in regard to lithium benzoate, which will often increase both urine and urea per twenty-four hours, and sometimes increase relative urea.

14. In certain cases where there are obscure nervous symptoms, reasoning by exclusion leads us to suppose that retention of urea in the body is the cause of the trouble. Fifteen analyses made by the author in the case of a chronic invalid, from the year 1891 to death in 1896, showed usually about 10 gm. (155 grains) or less of urea, never more than 13 gm. (200 grains), and once or twice less than 7 gm. (105 grains). To such cases Dr. Delamater has given the name *uræmia chronica*. Less than 13 grammes (200 grains) of urea occurred in other cases quite frequently.

15. Of interest in confirming the writer's observations is the following: Lucas-Championniére has found in 800 determinations that the quantity of urea on the average does not, as is generally believed, vary between 375 and 450 grains, but really between 225 and 300 grains. Diminution of urea is most marked in ovarian cancer where, before surgical interference, effort should be made to increase the amount of urea by rest, milk diet, and relief of pain (anodynes). In mild ovarian disease urea may fall below 100 grains in twenty-four hours, to rise rapidly above it on milk diet. Pain reduces excretion of urea, and the patient's vitality may be thus so lowered as to influence materially the success of operation. Success of operation is inversely proportional to the quantity of urea before the operation. The second or third day after major

operations the proportion of urea increases; thus, after removal of the appendages of both sides urea may rise from 60 or 75 grains to 375 grains.

## UREA IN THE URINE OF CHILDREN.

GIRLS.—Six analyses of the twenty-four hours' urine of a girl *five* years of age, showed an average of 12 to 13 gm. per liter (6 grains per ounce), and an average total of 8 grammes (132 grains). Albumin in small quantity was constantly present, but no casts.

In a girl of *six* years, urea was 8½ gm. per liter (4 grains per ounce); total 11 gm. (170 grains).

A girl of *eight* years voided 12 gm. per liter (5½ grains per ounce); total 10½ grammes or 160 grains.

A girl of *ten* years voided 21 gm. per liter (10 grains per ounce); total 14¾ grammes (230 grains).

A girl of *twelve* years voided 21 gm. per liter (10 grains per ounce) and 19 gm. total (300 grains).

Two other girls, ages unknown, voided 10 gm. (155 grains) and 11 grammes (175 grains), respectively in twenty-four hours.

From these cases it appears that female children between 5 and 15 years old void from 8 to 19 grammes, 130 to 300 grains.

BOYS.—A boy of *twelve* years, weight 82 pounds, voided on an average 18 gm. per liter, 8 grains per ounce; total 11 gm., 175 grains.

A boy of *twelve* years, weighing 84 pounds, voided 17 gm. per liter, 8 grains per ounce; 13 gm. total or 200 grains.

A *feeble-minded boy of ten* years voided 19 gm. per liter (9 grains per ounce); total 8 grammes, 125 grains.

A boy of *twelve* years, with subacute diffuse nephritis, voided 200 grains total of urea on ten separate occasions (13 grammes per twenty-four hours).

An *infant* barely one year old, male, slowly dying of an obscure disorder in which the urine contained albumin and at times traces of blood, but no casts, voided but 2 gm. urea per liter (1 grain per ounce), and never over 2 grammes total or 30 grains during six weeks of fatal illness.

A *diabetic* boy of *ten* years, averaged 18 gm. per liter (8 1-2 grains per ounce); total averaged 24 grammes, about 400 grains. Case terminated fatally in a few years.

A *diabetic* girl of *twelve* years, passed 23 gm. per liter (11 grains per ounce) and 43 grammes total or 665 grains. This case soon terminated fatally.

EPILEPTIC CHILDREN.—A girl of *eight* years (epileptoid) voided 24½ gm. per liter (11 grains per ounce); total 13¾ gm. (210 grains).

A boy of *ten* years voided 26 gm. per liter. 12½ grains per ounce; total 19 gm. or 195 grains.

A boy of *eleven* years voided 12 gm. per liter, 5½ grains per ounce; total 18½ gm. (285 grains).

Another epileptic boy, C. T., age unknown, voided on an average 32 gm. per liter, 16 grains per ounce; total averaged 27 gm or 425 grains.

In other words, there seems to be a tendency in the majority of epileptic cases in children toward *relative* increase in the excretion of urea, and in some cases *absolute* as well.

## CHEMICAL EXERCISE IV.

Compare the three clinical instruments, Bartley, Doremus, and Squibb, using—(*a*) a known solution of urea, and (*b*) the same sample of urine.

For the Liebig process for urea and the Kjeldahl method of determining total nitrogen, see APPENDIX.

# CHAPTER XI.

## THE CHEMISTRY OF URIC ACID.

URIC ACID occurs uncombined in normal urine in but minute quantity. Combined it forms salts called urates, which occur in solution in the urine in considerable quantity. It is the custom among physicians, however, to use the term "uric acid" rather than urates, in referring to various clinical conditions in which these substances are thought to play a part. It must be distinctly understood that the urates may be found both dissolved in the urine, and undissolved in the sediment of urine. The following table will make the matter clear:

URIC ACID AND URATES.

Uric acid.—In solution, normally, in small quantity. In *the sediment*, abnormally in comparative abundance.

Urates.—Normally in solution in comparative abundance. Abnormally in sediment in comparative abundance.

The most convenient method to determine the quantity of urates in urine is to convert them into uric acid; or, more scientifically stated, to set free the uric acid which they contain, and determine the quantity of that. Hence the chemist speaks of the amount of uric acid the urine contains, rather than the amount of urates. It should be understood also, before proceeding further, that uric acid is a weak acid, and but loosely combined with the various bases, so that on addition of stronger acids, as hydrochloric, to urates, the stronger acid drives away the uric acid from its combination, or "sets it free," as chemists say. Moreover, uric acid differs from the familiar mineral acids, nitric, sulphuric, and the like, in being a *crystalline solid*, instead of a liquid, and in being difficultly soluble in water.

Normal urine, then, contains in solution uric acid combined with sodium, potassium, etc., forming urates

of sodium, potassium, etc. Under abnormal circumstances, to be described later, these urates may be thrown out of solution and appear as a sediment; and, still further, uric acid, itself, may be set free, and appear, itself, in the sediment. All normal urine contains urates dissolved in it. Some abnormal urine may contain urates as a sediment, some abnormal urine may contain uric acid as a sediment, some abnormal urine may contain both urates and uric acid as a sediment. In the author's experience as a teacher much confusion results in the minds of students unless these facts just stated are thoroughly understood.

URIC ACID (FORMING URATES) IN SOLUTION.

**Synonyms:**

**Uric acid.** GERMAN, *Harnsaüre*, FRENCH, *Acide Urique.*

**Urates.** GERMAN, *Harnsaüre Salzen*, *Uraten;* FRENCH, *les urates.*

**Chemical constitution.**—*Uric acid:*—$C_5H_4N_4O_3$ an organic substance containing 33 per cent. of nitrogen; a dibasic acid, $H_2(C_5H_2N_4O_3)$, that is contains two atoms of hydrogen replaceable by two of a monad metal.

The structural formula is said to be $CO<\begin{matrix}NH.C.NH\\ \quad\quad\bar{C}NH\\ NH.CO\end{matrix}>CO$, hence a derivate of acrylic acid or acrylic acid diureid. The diureids are compounds formed from two molecules of urea. Acrylic acid is $C_3H_4O_2$.

**Urates.**—Compounds of uric acid in which one or two atoms of hydrogen of the acid have been replaced by an equivalent of a metal, thus, sodium urate, $Na_2(C_5H_2N_4O_3)$. Two kinds of urates are recognized, namely, **acid urates** and **neutral urates.** Acid urates (biurates) are those in which but one atom of hydrogen has been replaced by the metal, as $Na(C_5H_3N_4O_3)$, acid sodium urate. Neutral (normal) urates are those in which both replaceable hydrogen atoms have been set free, as in the case of sodium urate above.

The formation of the two different kinds of urates is shown by

the following equations, according as uric acid combines with potassium, sodium, or ammonium carbonate or hydrate:

$C_5H_4N_4O_3+2NaOH=Na_2(C_5H_2N_4O_3)+2H_2O.$

$C_5H_4N_4O_3+Na_2CO_3=NaH(C_5H_2N_4O_3)+NaHCO_3.$

The following table shows the different urates, letting *U* represent the unchangeable bracket $C_5H_2N_4O_3$:

| Urates.* | Formula. | Solubility in water. |
|---|---|---|
| Acid ammonium | $NH_4HU$ | 1 in 1600 |
| Acid sodium | $NaHU$ | 1 in 1200 |
| Acid potassium | $KHU$ | 1 in 800 |
| Acid calcium | $CaH_2U_2$ | 1 in 600 |
| Neutral sodium | $Na_2U$ | 1 in 77 |
| Neutral potassium | $K_2U$ | 1 in 44 |
| Neutral calcium | $CaU$ | 1 in 1500 |

**Occurrence.** *Uric acid:*—In solution in all normal urine of human beings in the form of urates. In the sediment under abnormal conditions as free uric acid or as urates. More abundantly in the urine of birds and scaly amphibians; in large quantities in "chalk-stones," calculi, and in guano.

**Form.** Uric acid in sediments is crystalline. Urates in sediments may be either crystalline or amorphous. (See Sediments.)

**Solubility:**

**A.** Uric Acid:

1. Soluble with difficulty in water: 1 in 15000 cold water; 1 in 1900 boiling water.
2. Insoluble in alcohol and ether; soluble in boiling glycerine.
3. Soluble in sulphuric acid without decomposition.
4. Soluble in nitric acid with decomposition.
5. Soluble in solutions of caustic alkalies, as caustic soda and caustic potash, less so in ammonia.
6. Soluble in alkaline solutions of the lactates, phosphates, as sodium phosphate; carbonates, as lithium carbonate; acetates and borates, forming neutral salts. According to Haig salicylate of sodium is a powerful solvent.

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* According to Bence Jones the salts of uric acid are really *quadrurates*, composed of a molecule of acid urate and a molecule uric acid, thus potassium quadrurate $C_5H_3KN_4O_3.C_5H_4NO_3$ or $KHUH_2U$. The water of the urine breaks these up into free uric acid and acid urates.

7. In solutions of piperazine, lycetol, lysidin, tartarlithine, tetra ethyl-ammonium hydroxide.*
8. According to Klemperer, solutions of pure urea exercise solvent action on uric acid; according to Rudel, a liter of a 2 per cent. solution of urea dissolves 0.529 gm. of uric acid.
9. In the body, sodium chloride by forming sodium carbonate, contributes to the solubility of uric acid in the blood.
10. According to Posner urine best dissolves uric acid when of low specific gravity, and not intense reaction of either kind.

**B.** NEUTRAL URATES:

1. Lithium urate most soluble in water; potassium and sodium next, calcium least.
2. Readily soluble in hot water.

(See SEDIMENTS for individual solubilities.)

**C.** ACID URATES:

1. Sparingly soluble in cold water, especially ammonium urate.
2. Readily soluble in hot water.

(See SEDIMENTS for individual solubilities.)

NOTE:—Hence most urinary sediments of urates are *acid* urates. Owing to the feeble solubility of the acid urates in cold water, these substances are deposited as the urine cools. On the other hand urine highly charged with *neutral* urates may remain clear but, on addition of a strong mineral acid, as nitric acid, a whitish opacity is occasioned owing to formation and separation of acid urates, which, however, may be dissolved by heat.

**State:** Pure uric acid is a white, odorless, tasteless powder consisting of very small rhombic prisms or plates. As obtained from urine it is colored pinkish by urinary pigments.

**Preparation:**

**A.** Synthetically in several ways:

1. By fusing urea and glycocoll (amido-acetic acid) the latter in one-tenth the weight of the former (hydantoin and biuret are intermediate products), thus:

$$C_2H_5NO_2+3CH_4N_2O=C_5H_4N_4O_3+3NH_3+H_2O.$$

Glycocoll. Urea. Uric acid.

2. By heating trichlor-lactic acid-amide (cyanuric acid, carbon-dioxide, and other by-products not considered) with excess of urea: $C_3Cl_3H_4O_2N+2CH_4N_2O=C_5H_4N_4O_3+H_2O+NH_4Cl+2HCl$.

*See author's *Chemistry*, 4th ed., p. 338.

3. From isobarbituric acid, a ureide of oxypyruvic acid.

**B.** From the excrement of serpents, guano, or urine as follows:

1. From serpent excrement by boiling with dilute solution of caustic potash and filtering hot; the hot filtrate contains the neutral potassium urate. On passing carbonic acid gas into it one-half the potassium is displaced, and the acid potassium urate precipitated according to the equation—

$$2C_5H_2K_2N_4O_3+CO_2+H_2O=K_2CO_3+2C_5H_3KN_4O_3$$

Neutral potassium urate — Acid potassium urate

The acid urate being washed is decomposed by hydrochloric acid and yields uric acid.

2. From guano by boiling with a solution of one part borax in 20 parts water; acidulate the solution and a brown, impure precipitate of uric acid is obtained, which, being washed and decomposed with hydrochloric acid, yields a purer uric acid.

3. From urine by adding to it one-fifth its volume of hydrochloric acid to decompose the urates, allowing to stand in a cool place for several days, decanting, and dissolving the separated crystals (adhering to the sides of the vessel) in sulphuric acid, and precipitating with water.

**Relationships.** 1. Uric acid strongly heated decomposes with formation of urea, hydrocyanic acid, cyanuric acid, and ammonia.

2. Heated with concentrated hydrochloric acid in sealed tubes to 170° C., uric acid splits into *glycocoll*, carbon dioxide, and ammonia.

3. Oxidizing agents cause splitting, and oxidation takes place, either a mono-ureid or di-ureid being formed. Oxidation of uric acid with lead peroxide produces carbon dioxide, oxalic acid, urea, and *allantoin* (glyoxyl diureid). Oxidation with nitric acid, in the cold, produces urea and *alloxan*, (mesoxalyl urea, a monoureid). Warming uric acid with nitric acid produces alloxan, carbon dioxide, *parabanic* acid (oxalyl urea, $C_3H_2N_2O_3$). Parabanic acid on addition of water passes into *oxaluric acid* $C_3H_4N_2O_4$, traces of which occur in the urine, and which easily splits into *oxalic acid* and urea.

4 Reduction of uric acid with sodium amalgam produces *xanthin* and then *hypoxanthin* (sarcin).

5. Uric acid may be made synthetically from *isobarbituric acid*, a ureide of oxypyruvic acid or of *alpha-beta* dioxyacrylic acid, which when oxidized is transformed into an isomer of *dialuric acid*. This last, heated to 100°C. (212° F.), with one molecule of urea and seven times its weight of sulphuric acid, produces uric acid which in every way resembles ordinary uric acid.

6. Uric acid is nearly related also to the following other substances: Hydantoin, guanin, hippuric acid, inosic (inosinic) acid, the bile-acids, theobromine, caffein, and thein.

## Chemical Reactions:

**A.** The Murexide Test: This test is *characteristic* of uric acid and urates, Treat a few crystals of uric acid with a few drops of nitric acid, which dissolves the former with a strong development of gas (nitrogen and carbonic acid), and, after *thoroughly drying* on the water-bath (*Fig. 26*) and *cooling*, a beautiful red resi-

due (urea and alloxan) is obtained which turns *purple-red* (murexide or purpurate of ammonia, $C_8H_4(NH_4)N_5O_6$) on addition of a little ammonia; or, after cooling, on addition of a little caustic soda solution a *bluish-violet*, the latter disappearing quickly on warming (differentiation from guanin, etc.)

FIG. 26. Water bath.

NOTE.—The test as above described is not so uniformly successful as the author's modification of it, as follows: Add one cubic centimeter of nitric acid to ten c.c. of water, mix thoroughly, pour into a test-tube, add uric acid crystals to the amount, say of 20 or 30 milligrams (about half a grain), boil thoroughly over a spirit-lamp till the uric acid is all dissolved and effervescence ceases. Evaporate to dryness over the water-bath, let cool, touch with a rod which has been dipped into ammonia and a brilliant purple-red at once appears, changed to bluish-violet on addition of caustic soda solution. If the uric acid solution in dilute nitric acid is evaporated on a flat porcelain surface, the student may trace his initials on the residue, using a glass rod which has been dipped into ammonia. The letters stand out in brilliant purple red, as compared with the yellowish residue which has not been moistened with the ammonia.

**B.** SCHIFF'S TEST: Dissolve a little uric acid in as small a quantity of sodic carbonate solution as possible; a piece of filtering paper being moistened with some solution of silver nitrate, a drop of the uric acid solution in the sodic carbonate, carried on a glass rod, is made to touch the paper, when a greyish stain of metallic silver appears. The stain is black, if the uric acid is in amount 0.001 per cent. or more.

**C.** REDUCTION OF CUPRIC SOLUTIONS:

Boil a little Fehling's solution (*see Sugar*) with a solution of uric acid, and a reddish precipitate of cuprous oxide forms. An alkaline solution of bismuth is not similarly reduced.

**Quantitative determination of uric acid.**

All urates are decomposed by dilute hydrochloric acid, with liberation of uric acid, according to the equation: $\underset{\text{sodium urate}}{Na_2(C_5H_2N_4O_3)} + 2HCl + \underset{\text{uric acid}}{C_5H_4N_4O_3}$. On this fact is based a method for determining the quantity of uric acid, which is done by adding to a given volume urine one-tenth its volume of hydrochloric acid, collecting the crystals of uric acid which separate, drying

and weighing. Full details of this process are given in Chemical Exercise V. (For the Ludwig-Salkowski, Haycraft, Hopkins, and other methods, see APPENDIX.)

CHEMICAL EXERCISE V.

1. The student having obtained some urine of specific gravity not less than 1020 should measure off 200 c.c. (7 fl. oz.) into a porcelain evaporating dish (*Fig. 27*), add 10 c.c. (3 fluidrachms) of chemically pure hydrochloric acid, stir with a glass rod, and set aside in a cool, dark place for 24 to 48 hours. At the end of that time crystals will be observed adhering to the dish. Decant the urine, rub off the crystals, by means of a glass rod having a bit of rubber tubing on the end, and pour the whole into a tapering glass vessel of any kind, using wash-bottle (*Fig. 28*) if necessary. Let settle, decant supernatant fluid, add more water, let settle again, and the crystals remaining at the bottom will now be in condition for the *murexide test*, which try.

FIG. 27. Evaporating Dish.

FIG. 28. Wash-bottle.

NOTE —The wash-bottle enables the operator to blow a fine stream of water with considerable force into the dish, thus removing crystals which otherwise cannot be poured off with the rest.

2. Procure some urine of specific gravity not less than 1025, or concentrate any urine by boiling until of that specific gravity, and set aside in a *cold* (40° F.) place. It becomes cloudy from deposition of *acid urates*, which are less soluble in cold water than in warm. Now remove to a warm room, or set the glass in hot water, and the urine becomes clear again, owing to the ready solubility of these urates in hot water.

### MICROSCOPICAL EXERCISE II.

Into the sediment of uric acid crystals obtained in Chemical Exercise III. dip a camel's-hair brush, and remove the crystals adhering to it to a glass slide. Examine with a power of 150 diameters or upward, and note a large number of crystals of *various forms*, but all of *yellowish-red color*, which latter is characteristic. (Study of the forms will be taken up under the head of *Uric Acid Sediments.*)

# CHAPTER XII.

## PHYSIOLOGY OF URIC ACID.

**History.**—Scheele discovered uric acid in 1776 and thought it solely a constituent of urinary calculi, hence named it *lithic acid*, from the Greek *lithos*, signifying *a stone*. In 1797 Wollaston showed that gouty concretions were composed of sodium urate. In 1848 Garrod claimed that an excess of uric acid existed in the blood prior to an attack of true gout and at the period of it. In 1884 to 1892 Alexander Haig has found that the excretion of uric acid can be made to vary at any time and in any direction. In 1892 Sir William Roberts made the announcement that the amorphous urates are quadrurates normally, and that any departure from this condition must be regarded as pathological. Horbaczewski has shown that uric acid originates from nuclein, and Kuehnau that the leucocytes are the principal, if not the exclusive source of the formative materials of uric acid.

**Difficulties.**—Almost insurmountable difficulties lie in the way of reconciling the theories of different observers as to the formation, source, and quantity of uric acid. For example Haig, using Haycraft's process, speaks of large quantities of uric acid in abnormal conditions, sometimes producing a ratio of urea to uric acid as low as 14 or 12 to 1. Herter, on the other hand, asserts that a ratio of urea to uric acid lower than 20 to 1 is impossible. The trouble is due to the different chemical processes used for determination of uric acid, which in the same sample of urine will show widely different results.

The following is a résumé of the different theories which comprise our knowledge to date.

**Formation in the body.**—Since uric acid is regarded as a diureid of acrylic acid, *i. e.*, by oxidation, splits

up into two molecules of urea and one of a non-nitrogenous acid, it has been assumed that, when the process of oxidation is imperfectly performed within the body, free uric acid will be found in excess in the urine. But although uric acid is indeed a less oxidized substance than urea, the latter is probably derived from a different source, at least in greater part. Minkowski finds, so far as birds go, that ammonia and lactic acids have to do with the formation of uric acid, and that the liver is the chief seat of formation. Geese with their livers extirpated show a very significant decrease in elimination of uric acid, while elimination of ammonia is increased, and considerable amounts of lactic acid occur in the urine. The remnant of uric acid in the urine after extirpation of the liver originates from xanthin or similar products.

Ebstein's theory is that uric acid is a by-product from insufficient oxidation of the nitrogenous waste into urea. Jaksch tends to uphold this theory, having recently concluded that the "uric acid diathesis" is due to disorders of the red blood-corpuscles, the vehicle by which oxygen is carried.

Horbaczewski and his pupils think that uric acid originates from nuclein, probably through the intermediary of adenin, which is related to xanthin and hypoxanthin. Uric acid is, according to this view, formed in the spleen, and is not notably influenced by alimentation.

Kuehnau concludes that the leucocytes are the principal, if not the exclusive, source of the formative materials of uric acid.

**Quantity.**—The average amount of uric acid excreted in twenty-four hours is said to be 0.7 gm. ($10\frac{3}{4}$ grains), with a possible range of from 0.4 to 0.8 gm. ($6\frac{1}{4}$ to $12\frac{1}{2}$ grains).

The ratio of urea to uric acid is differently stated. Haig calls it 33 to 1; Parkes, 45 to 1; Meyer, 50 to 1; Herter, 50 to 1; Yvon-Berlioz, 40 to 1; Hammarsten, from 50 to 1 up to 70 to 1. The statement of Haig that the formation of uric acid is always in relation to the urea formed, and as 1 is to 33, is said to be entirely

disproved by the fact shown recently that the ratio varies normally at different periods of the day.

The author's observations tend to show that assumption of a fixed urea-uric acid ratio for that of health is entirely out of the question. The ratio of urea to uric acid fluctuates, but in all probability within more or less definite limits in the same individual. E. E. Smith has, independently, arrived at the same conclusion and thinks the range to be from 45 to 1 to 60 to 1. The author is in the habit of regarding any ratio below 30 to 1 as certainly indicating very large excess of uric acid, and is skeptical about the ratios below 20 to 1 reported by some observers. With uric acid determinations carefully conducted I have never seen a ratio below 20 to 1, though by means of the older processes, and perhaps one or two of the more modern ones, whose value is yet doubtful, ratios below 20 to 1 have often been found by me. It is said that in infants the ratio may be as low as 14 to 1, but in a child two years old I recently found the ratio 45 to 1.

### EFFECT ON URIC ACID OF DIET AND REGIMEN.

The only point, says Roberts, which is really clear about diet, is that the excretion of uric acid is heightened by increasing the albuminoid ingredients of the food. Sugar, fat, and fruit are not proved to have the slightest direct influence on the production and excretion of uric acid. I hold, on the contrary, that it is a clinical fact, which has been verified time and again, that abstinence from sweets improves the general condition of uricæmic patients, at least those subject to *uric acid deposits.*

It is said that on an abundant meat diet uric acid may amount to 2 gms. (31 grains) in 24 hours. The author has, however, eaten heartily of butcher's meat, three times daily for the last five years, but has not found more than 1 gm. of uric acid at most in his urine. Things which *increase* uric acid according to various authors are milk, beef-tea and beef-extracts, alcoholic drinks, especially champagne, muscular fatigue, hot rooms, weather in which there are warm

southwest winds. Uric acid is said to be *decreased* by vegetable diet, moderate exercise, such as bicycle riding in moderation, copious draughts of water.

According to Haig the excretion of uric acid is relatively large during the three or four hours after breakfast, *i. e.*, during the period of "alkaline tide."

**Action of drugs.**—The drugs which are said to *increase* uric acid in the urine are the following:

| | | |
|---|---|---|
| Euonymin, | Quinine (in small doses), | Salicylates. |
| Mercuric chloride, | Phosphate of sodium, | Colchicum, |
| | Alkalies generally. | |

Those which *decrease* it in the urine are, according to Haig:

| | | |
|---|---|---|
| Acids, | Lead, | Acid phosphate of sodium, |
| Iron, | Manganese | Various sulphates, |
| Lithia, | Calcium chloride, | Various chlorides; |

also,

| | | |
|---|---|---|
| Opium, | Antipyrin, | Hyposulphites, |
| Cocaine, | Caffeine, | Strychnine. |
| Mercury, | The nitrites, | |

Haig's View of Uric Acid. Haig's observations are that uric acid is not influenced by dietary or medication in its formation, that being regarded as constant and uniform with the production of urea in the ratio of 1 to 33. As a substance insoluble in acid media, uric acid, when the blood and fluids of the tissues decrease in alkalinity, is no longer held in solution by these liquids and thus carried through the renal system, but is deposited in the organism, largely in the liver and spleen. If, for any reason, this decreased alkalinity be overcome, and a wave of increased alkalinity induced, as by administration of alkalies, these deposits are redissolved and carried in the current, producing an excess in actual circulation.

The Lithia Question.—Haig admits that compounds of lithium will dissolve uric acid in the test-tube, but insists that in the body the lithium salts never have a chance to affect uric acid, since lithium forms, according to Rose, a nearly insoluble triple phosphate with the phosphate of sodium or with the triple phosphates of ammonium and sodium, salts generally present in animal fluids. Again sodium phosphate is a good solvent of uric acid, and the lithium, by uniting with it, robs the blood of one of the natural solvents of uric acid. Moreover, Haig found, taking lithia himself, that uric acid was decreased in his urine, and accounted for it as above.

Chemists doubt the value of lithium salts as uric acid solvents in the body. Clinical testimony, however, as to the diuretic action of certain lithium compounds, (benzoate and citrate) is certainly great, and also as to the benefit derived from their action on patients supposedly suffering from uric acid complaints. Dr. Mary Putnam Jacobi, in objecting to Haig's theories, speaks of a typical lithæmic patient whom mild diet with lithia and vichy greatly relieved. Discussion of this subject properly belongs to a work on therapeutics and will not be continued here.

Opponents of Haig's Views: Many observers fail to agree with Haig, some attacking him on one side, others on another. Clinically his dietary and regimen are of undoubted benefit in some cases, though not in others. The profession, however, is under obligations to him for his brilliant and earnest research work. His position has been strengthened by the observation recently made, that in 1,000 consecutive determinations of the urea-uric acid ratio in an individual the ratio of urea to uric acid was found to be 35 to 1.

## CHAPTER XIII.

### PATHOLOGY OF URIC ACID.

In considering the increase of uric acid in the urine, the increase in the total quantity for twenty-four hours is meant.

It is probable that a sediment of amorphous urates, especially if occurring in urine of specific gravity less than 1025, is fairly reliable evidence that uric acid is in excess in that urine, but the latter may be in excess and yet no sediment betray it, hence quantitative determination of the whole uric acid in twenty-four hours should be made.

On the other hand, a sediment of uric acid itself gives no indication of an excess of the total uric acid, signifying merely some change in the saline constituents, coloring-matters, or acidity, hence again quantitative determination is needed.

In general it is held that uric acid is increased whenever either an increased formation of leucocytes, rich in nuclein, takes place in the blood or an increased destruction of leucocytes occurs. In general, then, *an excess of uric acid is an indication of some nutritional disturbance.*

#### DISEASES IN WHICH URIC ACID IS INCREASED IN THE URINE.

I. Fevers.

II. Leukæmia.

III. Diseases of the spleen.

IV. Acute articular rheumatism, in which increase of uric acid is an unfavorable sign, and decrease a favorable one.

V. Diseases of the lungs and heart, in which respiration is hindered (dyspnœa); also in ascites; large abdominal tumors.

VI. Whooping-cough.

VII. Poisoning by carbonic oxide gas; after alcoholic excesses.

VIII. Inanition.

IX. Cachexias in which there is great destruction of the corpuscle tissues.

X. Extensive burns.

XI. Some skin diseases, as lepra and eczema.

XII. Chorea.

DISEASES IN WHICH URIC ACID IS DECREASED IN THE URINE.

In general those in which but little leucocyte formation takes place, and where but slight destruction of them occurs:

I. Chlorosis and anæmia.

II. Osteomalacia.

III. Disturbances of nutrition; chronic lead-poisoning.

IV. After use of quinine and atropine.

V. In chronic gout when the urates are deposited in the joints.

VI. In arthritis, especially the gouty form.

VII. In hydruria and urina spastica.

VIII. In chronic diseases of the spinal cord.

CLINICAL NOTES.

1. In *diabetes mellitus* uric acid is more often diminished than increased.

2. In the beginning of *cirrhosis of the liver* uric acid is increased; in the stage of *atrophy* decreased.

3. In *interstitial nephritis* uric acid is significantly decreased; in *chronic parenchymatous nephritis* uric acid is much increased.

4. Dr. J. W. Hunter, of Texas, reports a number of cases of *asthma* caused by uric acid, and cured by appropriate treatment.

5. According to Drs. C. N. Pierce and E. C. Kirk, the morbific element in *pyorrhœa alveolaris* is uric acid.

6. Haig speaks of a characteristic uric acid *headache*, which may be produced at will, and which is accompanied by a very large excretion of uric acid. The

headache, he holds, is due to increase of vascular tension caused by excess of uric acid in the circulation.

7. Sutherland thinks that uric acid produces trouble in children with two classes of symptoms,* those due to presence of uric acid in the system, and those due to excretion of it. In the former case catarrhal disorders are prominent, in the latter abdominal pains.

8. According to Jaksch uric acid is not responsible for the acid intoxication of fever.

9. Krauss, Pryor, Herter, and others believe that the pathogenic rôle of uric acid has been greatly exaggerated.

10. Levison regards it as proved that a simple excess of uric acid is not enough to cause lasting excess in the blood, but that there must also be a faulty elimination by the kidneys.

11. Haig in his latest work (1896) thinks uric acid a factor in the cause of high arterial tension, headache, epilepsy, mental depression, paroxysmal hemoglobinuria, and anæmia, Bright's disease, diabetes, gout, and rheumatism. Raynaud's disease and hysteria are added to this list by others.

12. E. E. Smith thinks that if the ratio of the urea and uric acid is expressed by a number above 45, the uric acid excretion is probably normal; while if it is expressed by a number below 40 there is good ground to believe that the excretion is in excess.

### CHEMICAL EXERCISE VI.

**Quantitative determination of uric acid.**—The student having collected and measured his twenty-four hours' urine should determine the quantity of uric acid in it, using the method of Heintz, the simplest *clinical* method, as follows:

Measure off 200 c.c. (7 fluidounces) of the twenty-four hours' urine, add to it 10 c.c. (one-third of a fluidounce) of hydrochloric acid. Let stand twenty-four to forty-eight hours in a cool, dark room. Collect the precipitated uric acid crystals on a previously weighed

* See author's article in Tooker's "Diseases of Children," p. 464.

small filter, wash with cold distilled water, dry in drying oven, (*Fig. 29*) and weigh. The difference in the weight of the filter before and after filtering represents the weight of uric acid in 200 c.c. of urineal. If albumin is present, the urine should be acidulated with a few drops of acetic acid, boiled, and filtered, the filtered urine being used for the uric acid determination.

**Technique.**—The above directions, given in several of our books, seem simple and easy to carry out, but there is a chance for various errors unless the following precautions are observed:

1. *Before weighing or filtering* first *dry the filter* which should be done in the drying oven at a temperature of 100° C. (212° F.).

2. After it ceases to lose weight, for which will be required about an hour's drying, record the weight. Use preferably *milligram weights* (*Fig. 30*). The small filters weigh from 550 to 750 milligrams when dry.

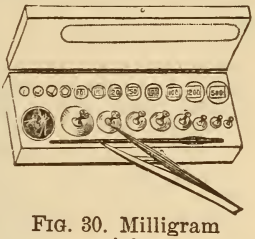


FIG. 30. Milligram weights.

3. Fold the filter, insert into the funnel, and filter the urine through it, being careful to *save the filtered urine.*

4. Rub off the crystals of *uric acid adhering to the dish* by use of a glass rod, tipped with rubber tubing, and wash them into the filter, using filtered urine for washing purposes.

5. Let *the urine run completely* through, then fill up the filter about two-thirds full with distilled water, using the wash bottle, and washing as thoroughly as possible with the amount of water used. This should not exceed 30 to 40 c.c. (about one fluidounce).

6. After the water has run through, remove filter from the funnel with small pincers, being careful not to tear it, set it in a porcelain dish in the drying oven and dry it for several hours, if necessary, until it ceases to lose weight.

7. Measure the amount of filtered urine plus wash-water, which will usually be 250 c.c., multiply the

number of c.c. obtained by 48, and point off three places. The result is usually *12 milligrams.* (Correction of 4.8 milligrams for every 100 c.c. of urine, adopted by chemists on account of the solubility of uric acid in water).

8. When the filter is dry, weigh it; subtract the weight obtained before filtering from the weight now obtained, and add 12 milligrams (or the result obtained in 7). The final result is in milligrams, the amount of uric acid in 200 c.c. of urine. Multiply by 5 to ascertain grammes per liter, pointing off three places; and multiply this product by the number of liters of the twenty-four hours' urine to get grammes of uric acid per twenty-four hours.

NOTES:—(1) According to Schwanert the uric acid crystals should be washed on the filter until a solution of silver nitrate gives no precipitate with the filtered wash-water. The writer has found that this precaution makes the results lower by about 4 milligrams than when only 30–40 c.c. of water are used as above, that is, when the correction is made as in 7. Thorough washing with say 100 to 125 c.c. of water will take off 10 milligrams from the weight, but the correction, as in 7, will bring up the total.

(2) Urine cloudy with urates should first be warmed before the hydrochloric acid is added.

(3) Urines less than 1020 in specific gravity should be concentrated over the water-bath until the specific gravity rises to that figure.

**Calculation of results:** Suppose weight of dried filter before filtering is 750 milligrams. Suppose after drying again it is 820 milligrams. Suppose the filtered urine and wash-water amount to 250 c.c. Then we have the following: 820 minus 750 is 70 milligrams; 250 times 48 divided by 1.000 equals 12 milligrams; 70 plus 12 equals 82 milligrams of uric acid in 200 c.c. of urine. Then 82 × 5 equals 410 milligrams of uric acid in a liter (1000 c.c.) of urine or 0.4 gm. Suppose total urine in 24 hours is 850 c.c.; 0.4 gm. times 0.850 is 0.34 gm of uric acid in 24 hours. Turn now to *Tables 6* and 7. We find 0.4 gm. per liter is just about normal, but 0.34 gm. in 24 hours is about two-thirds the usual normal average. Reduce to American measures by the Tables. Suppose total urea is 13.6 gm.; 13.6 divided by 0.34 equals 40. *Ratio of urea to uric acid* is 40 to 1 in this case. See *Table 11.*

NOTE —Inasmuch as the term *relative* uric acid, *relative* phosphoric acid, etc., are used by some German writers to mean the *total quantity of uric acid*, phosphoric acid, etc., compared with *the total quantity of nitrogen*, care must be taken to notice that the author uses this term always with reference to the quantity of water of the urine. When used in the sense the Germans use it, full explanation will be given.

### Apparatus Required.

1. Small filters, 5-6 centimeters (about two inches) in diameter.
2. Chemical balance (*Fig. 31.*)

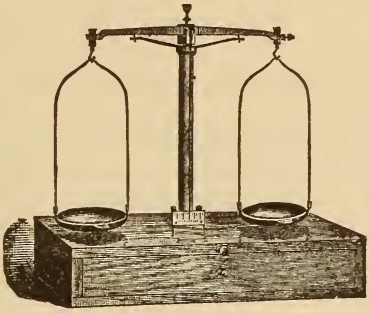


FIG. 31. Chemical balance.

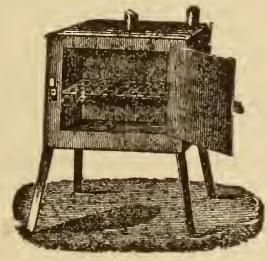


FIG. 29. Drying oven.

3. A drying oven, (*Fig. 29.*)
4. A glass rod tipped with rubber tubing.
5. An evaporating dish holding 200 c.c. (half-a-pint) of urine. (*Fig. 27.*)

NOTE:—Unless what is called rapid filtering paper is used, the operation according to Schwanert's directions is a very slow one requiring several hours unless a filter-pump is at hand.

# CHAPTER XIV.

## SUBSTANCES RELATED TO URIC ACID.

The substances of minor clinical importance related to uric acid are, in alphabetical order, as follows:

Allantoin; Kreatin; Kreatinin; Xanthin, and allied substances.

These substances all contain *nitrogen*, and together with urea and uric acid, are the means by which this important element is excreted in the urine.

**Allantoin**, or glyoxyldiureid, $C_4H_6N_4O_3$, an *organic* substance, occurs in the urine of children within the first eight days after birth. In small amounts in the urine of grown persons; rather abundantly in that of pregnant women.

*Related to uric acid.* Formed by oxidizing uric acid with lead peroxide. Colorless prisms soluble in hot water, slightly in cold, insoluble in alcohol and ether. Precipitated by mercuric salts.

*Detection:* Precipitate urine with baryta water, filter, remove baryta with sulphuric acid, filter, precipitate the allantoin with mercuric chloride in alkaline solution, decompose precipitate with sulphuretted hydrogen, concentrate strongly, purify the crystals by recrystallization.

**Kreatin.**—This *organic* substance, $C_4H_9N_3O$, one of the *nitrogenous* substances of urine, occurs normally in alkaline urine in greater quantity. In acid urine kreatinin appears in greater quantity. Kreatin is easily transformed into kreatinin, which see. Also converted by certain germs into *methylguanidin*, which causes symptoms resembling uræmia.

**Kreatinin.**—Important because of the *nitrogen* it contains.

*Chemical constitution*, $C_4H_7N_3O$, or $NH{=}C{<}^{NH-CO}_{N(CH_3)}{>}CH_2$, an anhydride of kreatin, one of the strongest bases in the body.

*Form.*—Crystallizes in large colorless prisms. (See *Sediments.*)

*Occurrence.*—Constantly in solution in the urine.

*Solubility.*—Easily soluble in water, hence rarely in the sediment. Less soluble in alcohol. Insoluble in ether.

*Properties.*—Alkaline in reaction, converted by bases into kreatin. Combines with both acids and salts. A characteristic compound of the latter class is

*kreatinin-chloride of zinc* $(C_4H_7N_3O)_2ZnCl_2$, difficultly soluble in water.

Kreatinin has strong *reducing properties*, as on Trommer's and Fehling's test-liquids, but not on alkaline bismuth solutions.

*Tests.*—(1) Add to the urine a few drops of freshly prepared very dilute solution of nitroprusside of sodium and, afterward, a few drops of dilute sodium hydroxide solution, when a red color appears which changes to yellow on standing. Now add acetic acid in excess, and heat, when a greenish, then blue color appears, and finally a precipitate of Berlin blue.

(2) Add to the urine a little picric acid solution and a few drops of dilute sodium hydroxide solution, when a red coloration appears, which lasts for an hour, and changes to yellow on addition of acid (glucose gives this red color on warming). (For quantitative determination, see APPENDIX.)

PHYSIOLOGY. Kreatinin has its origin in the muscles, being formed from the kreatin of them. The change probably takes place in the muscle. Bunge thinks muscle kreatinin ultimately converted into urea and urine kreatinin derived from the food. The average quantity in the urine per twenty-four hours is 0.6 to 1.3 gramme, the most on an exclusive meat diet. It is diminished by fasting.

PATHOLOGY. *Increased* in acute diseases, especially in pneumonia, typhoid, and intermittents; also in some cases of diabetes mellitus. *Diminished* in convalescence from acute diseases, in advanced Bright's, and in tetanus; also in diseases characterized by muscular wasting. (See also *Sediments.*)

**Xanthin bodies.**—These are xanthin, hypoxanthin, carnin, adenin, paraxanthin, and heteroxanthin. *Organic, related to uric acid.* Thus, uric acid $C_5H_4N_4O_3$, xanthin $C_5H_4N_4O_2$. Xanthin occurs in very small quantity in human urine, according to Neubauer, 1 gramme in 300 liters. The xanthin bodies are almost insoluble in water, unite with bases, acids, and salts, are precipitated by ammoniacal silver solutions like uric acid, and give at red-heat, like uric acid, the odor

of hydrocyanic acid. Xanthin is insoluble in alcohol and ether, readily soluble in alkalies, and also in dilute nitric and hydrochloric acids. It sometimes occurs as a deposit (see *Sediments*), and is a constituent of a rare form of calculus, found always in case of young persons.

*Detection.*—Remove albumin from the urine by boiling and filtering, and treat the urine intermittently with phospho-tungstic acid, and hydrochloric acid, until no more precipitate takes place. The precipitate is allowed to settle for twenty-four hours, then washed with dilute sulphuric acid (5 :100) by decantation till free from chlorine, filtered and treated with excess of barmin hydroxide and application of heat to remove uric acid. The filtrate is precipitated with ammoniacal solution of silver, and the precipitate which contains the xanthin bases is washed. Dissolved in dilute hydrochloric acid hexagonal crystals of xanthin separate on evaporation. Evaporated to dryness with nitric acid a yellow residue remains, which turns red with caustic potash solution, and reddish violet when heated. (For quantitative determination see APPENDIX).

PATHOLOGY: The pathology of xanthin, paraxanthin, etc., has been experimentally investigated by B. K. Rachford (*Medical Record*, 1895). He calls these bodies *uric acid leucomaïns*, and asserts that paraxanthin and xanthin are etiologically related to a group of nervous disorders which are manifestations of leucomaïn poisoning. The three clinical forms of the auto-intoxication are as follows: 1, A true migraine or leucomaïn headache; 2, a migrainous epilepsy, or leucomaïn epilepsy; 3, a migrainous gastric neurosis, or leucomaïn gastric neurosis. Paraxanthin is by far the most poisonous of all leucomaïns, xanthin is much less poisonous. His conclusions are as follows:

"1. Paraxanthin and xanthin are poisonous leucomaïns of the uric-acid group, capable of producing the most profound nervous symptoms. They are readily soluble in water, urine, and blood.

"2. Paraxanthin is found in normal urine in such small quantities that its poisonous properties are lost in dilution. Salomon found only 1.2 gm. in 1,200 liters of urine. This quantity is so minute that its presence cannot be satisfactorily demonstrated in such quantities of normal urine as can conveniently be obtained from patients. In a recent personal communication Salomon says: 'Nine liters of urine is a very small quantity to prove the presence of paraxanthin, if one has not previously worked with larger quantities so as to master the details of the work, and very much harder would it be to prove the presence of paraxanthin in four liters of normal urine, as I know from experience. . . . I would advise that not less than ten liters of normal urine be used to demonstrate the presence of paraxanthin.' My own experience is in accord with Salomon's. In previous papers I have recorded my failure to demonstrate the presence of paraxanthin when working with as little as four liters of normal urine; and since these papers were written I have made a large number of examinations of normal and other urines, and I have always failed to demonstrate the presence of paraxanthin in four liters of normal urine. Upon this evidence I have concluded that paraxanthin is present in abnormally large quantities when I can find it in less than four liters of urine. Xanthin also, as a rule, requires more than four liters of urine to demonstrate its presence, but I have frequently found small quantities of xanthin where I could not find paraxanthin in working with four liters of urine.

"3 Paraxanthin and xanthin are not formed in the kidney. They are excreted from the blood by the kidneys. The presence, therefore, of large or small quantities of xanthin bodies in the urine means that these bodies were present in large or small quantities in solution in the blood previous to their elimination by the kidneys." (*Rachford.*)

4. In certain cases of migraine paraxanthin and xanthin are excreted in great excess during the attacks, but not in the intervals.

5. In the study of a case of migrainous epilepsy the following was ascertained by him: During the attack the patient excreted a quantity of paraxanthin and xanthin enormously in excess of normal, but during the interval between the attacks not enough paraxanthin was excreted to be detected in three liters of urine. The paraxanthin excreted in such large quantities just following these attacks must have been in solution in the blood during the paroxysms.

6. In a case of migrainous gastric neurosis the quantities of xanthin and paraxanthin in the urine during the attacks, were enormously increased, two liters of urine being enough to allow separation of both bodies Two minims of "final fluid," 3 c.c. in volume, thrown into the muscles in the back of a mouse produced death in from 15 to 30 minutes. In four liters of urine between the attacks no paraxanthin was found and the final fluid was not poisonous to mice.

See APPENDIX for the process of isolation and detection.

# CHAPTER XV.

## AROMATIC COMPOUNDS IN THE URINE.

The aromatic compounds in urine may be classified as follows:

I. Aromatic compounds of glycocin, as *hippuric acid.*

II. *Glycuronic acid* combinations with aromatics.

III. *Uncombined aromatic substances.*—As cumarin, hydroparacumaric acid, etc.

IV. *Ethereal sulphates* as phenol-sulphuric acid, indoxyl-sulphuric acid, etc.

**Hippuric acid,** $C_9H_9NO_3$, $H(C_9H_8NO_3)$, a monobasic organic acid occurs in small amounts, 0.7 gramme daily in normal urine. By diet rich in fruits and vegetables as cranberries, prunes, plums, etc., it may be increased to two grammes (31 grains).

*Chemical constitution.*—Chemically hippuric acid is *benzoyl glycocoll,*

$$\begin{matrix} CH_2.NH(C_6H_5CO) \\ | \\ COOH, \end{matrix}$$

and is *a derivative of benzoic acid,* from which it may be formed within the body by oxidation, when benzoic acid, or a number of other substances, is taken internally.

*Origin.* Not definitely ascertained.

Phenyl-propionic acid produced in the body during the process of intestinal putrefaction is absorbed into the blood and thought to be transformed there into benzoic acid (phenyl-formic acid). Benzoic acid coming into contact with glycocoll, a substance probably produced during intestinal putrefaction, probably forms hippuric acid according to the equation

$$\begin{matrix} C_6H_5 \\ | \\ COOH \end{matrix} + \begin{matrix} CH_2NH_2 \\ | \\ COOH \end{matrix} = \begin{matrix} CH_2NH(C_6H_5CO) \\ | \\ COOH \end{matrix} + H_2O$$

Benzoic acid Glycocoll Hippuric acid.

*Solubility.* It is soluble in 600 parts of cold water, easily soluble in hot water, readily so in hot alcohol and ether, insoluble in petroleum-ether, and benzene; soluble in ammonia water, insoluble in hydrochloric acid.

*Occurrence.* In solution in all normal urine and occasionally in the sediment. (See *Sediments*).

*Physical characteristics.* Colorless, odorless, of slightly bitter taste.

*Form.* When obtained from urine or made synthetically, it forms fine needles or vertical rhomboid prisms. According to Heitzmann the prisms in urine often show **indentations.** (See *Sediments*).

*Detection.* Evaporate the urine with nitric acid, heat residue dry in a test tube, and an odor like oil of bitter almonds indicates presence of hippuric acid. More conclusive is the following: Make the urine alkaline with sodium carbonate, concentrate by evaporation as much as possible, and extract the residue with absolute alcohol. The alcohol is evaporated, the remaining mass dissolved in water, the solution made acid with sulphuric acid and extracted with five fresh portions of acetic ether by shaking repeatedly. The ethereal extract is several times washed with water, then freed from the latter and evaporated at moderate temperature. The hippuric acid is now freed from benzoic acid, fat, and the like by washing with petroleum-ether, dissolved in a little warm water, and the solution evaporated at about 50° C. (122° F.) to crystallization. The crystals are then collected and weighed.

*Micro-chemical detection.* If the urine contain excess of hippuric acid, the latter may be detected by evaporating slightly, and feebly acidulating with hydrochloric acid. On standing a few hours hippuric acid crystallizes out and may be recognized by the microscope. (See *Sediments*).

Physiology: Hippuric acid in the organism owes its origin to the oxidation of albumin, and its quantity depends on the degree of albumin decomposition in the intestine. It is present in comparatively large amount in the urine of herbivora, much less in that of omnivora, and absent in the urine of carnivora. It is increased by vegetable diet and by such fruits as cranberries, etc., already mentioned. It is also increased by administration of benzoic acid, oil of bitter almonds, toluol, cinnamic acid, benzylamin, phenylpropionic, and kinic acid. It is decreased by an animal diet but remains in small quantities even on an exclusive meat diet.

Pathology: Increased in acute febrile processes, diseases of the liver, chorea, diabetes mellitus. (See *Sediments*).

Decreased in amyloid degeneration of the kidneys.

In acute and chronic parenchymatous nephritis administration of benzoic acid does not result in elimination of hippuric acid.

**Glycuronic Acid Combinations:**—Small quantities of this **organic** substance in combination with aromatics occur in the urine. Normally it occurs in very slight traces, hence will not be considered here. See *Abnormal Constituents.*

**Cumarin:**—An *organic aromatic substance* said to occur in urine.

**Hydroparacumaric acid:**—One of the uncombined *aromatic substances*, $C_6H_4.(OH)CH_2.CH_2.COOH$, produced by the decay of tyrosine. *Organic.*

**Oxyphenylacetic acid** is another one of the uncombined aromatic substances occurring in urine.

**Ethereal sulphates.**—The ethereal sulphates in urine are combinations of sulphuric acid with phenol, parakresol, pyrocatechin, indoxyl, and skatoxyl. They contain the radical $HSO_3$ and are incorrectly called *sulphonates.* Also called *sulpho-conjugated acids*, or *conjugate sulphates*, sometimes also *aromatic sulphates.*

They are derived in small part from aromatic substances in the food, being chiefly due to putrefactive changes in the intestine. They serve as a guide to us of the amount of putrefaction in progress within the body, and are also of diagnostic importance when we wish to determine whether febrile diseases, exanthems, etc., depend on intestinal processes, or whether melancholia is a sequence of intestinal disturbance.

*Increase* of ethereal sulphates takes place in deficient absorption of normal products of digestion, as in peritonitis and intestinal tuberculosis; in fermentative diseases of the stomach; in putrefactive processes outside the alimentary canal, as in putrid cystitis, abscesses, peritonitis, etc. Discharge of putrid matter diminishes the quantity. As no simple clinical method is known for quantitative determination of them, see Appendix for complete process.

**Test.**—To test for the conjugate sulphates 25 c.c. of urine are treated with about the same volume of an alkaline barium chloride mixture (2 volumes of a solution of barium hydrate and 1 volume of a solution of barium chloride both saturated at ordinary temperatures) and filtered after a few minutes, the mineral (preformed) sulphates as well as the phosphates being thus removed. The filtrate is then strongly acidified with hydrochloric acid and boiled, when the occurrence of a precipitate will be referable to conjugate sulphates.

In the quantitative method (see Appendix), the same procedure is followed and the precipitate being filtered off is washed, dried, and weighed.

**Significance.**—The normal ratio of the mineral (preformed) sulphates to the ethereal sulphates is 10 to 1. This ratio may be enormously decreased in

coprostasis, the result of carcinoma, as low as 2 to 1 having been observed. C. E. Simon has seen the ratio 1.5 to 1 in a case of volvulus of ten days' standing.

*The degree of intestinal putrefaction may be measured directly by the elimination of the ethereal sulphates:*—Increased degree of intestinal putrefaction accompanies diminution of secretion of hydrochloric acid by the stomach, and vice versa.

In obstructive jaundice Simon has noticed an increase of the ethereal sulphates, while in non-obstructive jaundice the *total* sulphates (mineral and ethereal) were decreased.

In diarrhœa the total sulphates were diminished, likewise the ethereal sulphates, while the ratio of the mineral to the ethereal increased. Terpenes and camphor cause a decrease in the excretion of the ethereal sulphates. Carlsbad and Marienbad waters at first cause an increase but subsequently a decrease of the ethereal sulphates. Kefir, in doses of from 1 to 1.5 liters a day, has proved an excellent remedy for checking intestinal putrefaction.

John A. Wesener of Chicago deserves mention for original work in connection with the ethereal sulphates and, in view of the rather scanty space in text-books which is accorded most investigators on this side of the water, we insert his paper almost in full:

The literature of the aromatic sulphates has been summed up by Wesener as follows: Baumann noticed in a patient with a fistula in the upper part of the small intestine, that urine during the time in which the intestinal contents did not pass out by the natural means, showed a considerable diminution of aromatic sulphates, containing only traces of phenol and indol. When this fistula was closed and the intestines restored to their normal function, it was noticed that the elimination of the aromatic sulphates was increased very much. An exactly similar case was reported by Ewald. These observations go to show that in the jejunum a certain number of aromatic combinations are produced by the action of micro-organisms and the intestinal juices on the food Baumann and Wasliff found a decrease of aromatic sulphates in the urine of starving dogs, and an entire absence of the same after the intestine had been disinfected by large doses of calomel given several consecutive days. It might be well to mention here the researches of Ortwiler, who ascertained that in febrile diseases not involving the intestinal tract, which are accompanied by

destructive tissue changes, there is no increase of indican in the urine.

If these aromatic combinations are not products of intestinal decay, then why do we not find them in the muscles and healthy organs? All investigations have failed to show their presence there, while on the other hand the intestinal discharges of starving animals always show the presence of considerable indol; furthermore, it has been proved by Kühne and Nencke that indol is exclusively a product resulting from the action of bacteria on albuminoids. If we consider that micro-organisms do not occur in the tissues of healthy organs, as has been conclusively proved by Meisner, Zahn, and Henser, we must necessarily come to the conclusion that the formation of aromatic combinations in the organs outside of the intestinal tract is, under physiological conditions, out of the question.

Salkowski has shown that there is an increase of indol and phenol in the urine of patients who suffer from ileitis and peritonitis. Brieger has shown that in chronic anæmia and in cachexia there is much indoxyl and little phenol in the urine, whereas in diseases of the stomach there is an increase of phenol, leading one to infer that free HCl is a large factor in lessening putrefaction.

He found an increase of phenol in tuberculosis of the peritonæum, acute peritonitis with constipation, empyema of the lungs, septic and puerperal fevers, diphtheria, erysipelas, etc. He concludes from this that phenol shows either increased decomposition of the contents of the intestine or the presence of a putrid area in the body.

Jaffé found an increase of indoxyl in diseases of the small intestines; a decrease in dysentery, pathological conditions of the large intestine, stomach, and duodenum.

Senator reports an increase of indol in chronic wasting diseases —such as malignant lymphoma, chronic peritonitis, and cancer of the stomach.

The writer of this paper (Wesener) has found the aromatic combinations greatly increased in one case of pernicious anæmia and in a number of chlorotics. It may be said here, before administering iron to these cases, it is absolutely necessary to disinfect the intestinal canal.

Heninge says that a large amount of indoxyl is present in the urine of pernicious anæmia, typhus, cholera, chronic suppuration, progressive atrophy of muscles, and Addison's disease. He attributes it in part to the increased separation of the constituent of the albuminoids and in part to an increase in the amount of pancreatic juice.

Hoppe-Seyler, as a result of exact clinical investigation, has come to the conclusion that in general the excretion of these bodies goes hand and hand with an increase of those processes which impair the digestion in the small intestine. The investigations of Hirschler, T. R. Müller, Helden and others show that the aromatics are diminished in the urine when the albuminoids are excluded from the food and a large amount of carbohydrates is used instead. As a result of these observations we can see that the derivatives of the aromatic series appear in the urine under physiological conditions as the result of the putrefaction of substances containing water.

Ortwiler found that bismuth subnitrate in large doses had no effect on intestinal putrefaction; large doses of castor oil produced an increase of the aromatic sulphates. Kast ascertained that neutralizing the stomach with large doses of alkaline carbonates had a very decided and lasting effect in the increase of aromatic sulphates; in hyperacidity of the stomach the aromatic sulphates were diminished.

Morax, in his experiments performed upon animals, found that calomel and iodoform diminished the aromatic sulphates, whereas ordinary doses of calomel given to human beings did not act as an intestinal disinfectant.

Rovighi found that large doses of the terebene group and camphor given to animals diminished the putrefaction to a considerable extent; these compounds administered to healthy persons had very little effect.

Biernecky found that on an exclusive milk diet the aromatic sulphates diminished one-half in twenty-four hours.

Winternitz, by his experiments, has proved that albuminous putrefaction is greatly lessened in the presence of milk sugar, glycerine, and lactic acid. He found that on adding a large quantity of milk to beef extract, albuminous putrefaction was greatly diminished.

In experiments performed with dogs, who were first fed on meat, then on a milk diet, it was found that in the former the aromatic sulphates were three times and a half as high as when the latter was given.

According to Carl Schmit, milk sugar is the compound in milk which prevents intestinal putrefaction. He fed dogs on meat and milk sugar, and the aromatic sulphates were greatly lessened.

The writer (Wesener), in order to determine whether casein or milk sugar is the compound which disinfects the small intestine, undertook the following experiment: Casein was precipitated from milk and then washed with hot alcohol until all milk sugar was removed. This diet was given for three days, the total twenty-four hours' urine being saved; the aromatic sulphates were not diminished. When albuminoids are removed from the food and carbohydrates substituted, the putrefaction is diminished largely; this result is brought about in all probability by the starvation of those bacteria which live upon proteids. It is very probable that in the course of intestinal putrefaction there are, besides the aromatic compounds, other unknown chemical combinations which are, perhaps even more poisonous than the former. Observations have shown that more aromatic sulphates are excreted during the day than during the night. If the subject for experiment receives no water, and we examine the urine, we find the aromatics lessened. It appears from this that drinking causes an increase of the aromatic sulphates, and **it is therefore necessary in ascertaining the amount of aromatics excreted to figure on the total amount of the urine that has been passed during twenty-four hours.**

Wesener's conclusions are as follows:

1. Saline cathartics at first increase the aromatic sulphates, then decrease them.

2. Calomel in large doses for two or three days slightly diminishes them.

3. Oil of eucalyptus given for three to four days diminishes them.

4. Kumyss reduces putrefaction to a minimum, diminishing the aromatic sulphates 85 to 100 per cent.

Chas. E. Simon, of Baltimore, in his excellent work on "Clinical Diagnosis" summarizes in regard to the ethereal (conjugate) sulphates as follows:

1. An increase in the conjugate sulphates in a general way points to increased intestinal putrefaction, the direct cause for which must, according to our present knowledge, be sought in a total anachlorhydry, or at least a hypochlorhydry of the gastric juice, associated with intense bacterial fermentation, provided that lactic acid and butyric acid are not present in large amounts; an obstruction to the flow of bile and intestinal obstruction may, however, produce the same result.

2. A diminution in the quantity of conjugate sulphates, on the other hand, may be referable to hyperchlorhydry associated with torular fermentation, ulcer of the stomach forming an exception, in which, notwithstanding the fact that conjugate sulphates are frequently eliminated in increased amount, hyperchlorhydry usually exists.

3. In cases of diarrhœa the absolute as well as the relative quantity of total sulphates and of conjugate sulphates is diminished, while the ratio of the mineral sulphates to the conjugate becomes greater.

# CHAPTER XVI.

## THE AROMATIC COMPOUNDS—CONCLUDED.

The remaining aromatic compounds to be considered are:

INDOXYL-SULPHURIC ACID (INDICAN), PHENOL-SULPHURIC ACID, ETC.

### INDOXYL-SULPHURIC ACID.

**Nomenclature:**—This substance is usually, though incorrectly, called *indican*, being thought to be identical with vegetable indican, which is a glucoside. The substance occurring in the urine is, however, an ethereal (conjugate) sulphate.

**Synonyms:**—GERMAN, *Indoxyl-schwefelsäure*, *Harnindican;* FRENCH, *indican.*

**Clinical constitution:**—Potassium indoxyl-sulphate, $C_8H_6NO.KSO_3$ or $SO_2<^{C_8H_6NO}_{OK}$ a conjugated sulpho-acid salt of potassium.

**Origin in the body:**—Indol formed during the process of intestinal putrefaction is oxidized to indoxyl in the blood, thus:

$$\underset{\text{Indol}}{C_8H_7N} + O = \underset{\text{Indoxyl.}}{C_8H_7NO}$$

Indoxyl combining with sulphuric acid forms indoxyl-sulphate according to the equation

$$\underset{\text{Indoxyl}}{C_8H_7NO} + \underset{\text{Sulphuric acid}}{SO_2<^{OH}_{OH}} = \underset{\text{Indoxyl sulphate}}{SO_2<^{C_8H_6NO}_{OH}} + \underset{\text{Water.}}{H_2O}$$

Indoxyl-sulphate and dipotassic hydrophosphate are eliminated in the urine as indoxyl-potassium sulphate and potassium dihydrophosphate as follows:

$$K_2HPO_4 + SO_2<^{C_8H_6NO}_{OH} = KH_2PO_4 + SO_2<^{C_8H_6NO}_{OK}$$

**Occurrence:**—In solution in the urine.

**Form:**—When isolated as potassium indoxyl-sulphate, it occurs in white tablets and plates. Obtained from urine it is a clear, brown syrup.

**Solubility:**—Soluble in water, sparingly in alcohol.

**Effect of oxidation:**—By oxidation of indoxyl-potassium sulphate indigo-blue is formed and the blue, green, and some red tints of urine in disease are probably derived from different stages of oxidation of this substance. A bluish-red pellicle may often be seen in decomposing urine consisting of microscopic crystals of indigo-blue and red, formed from decomposition of the substance. (See SEDIMENTS).

Ord has described a calculus composed of indigo.

**Tests:**—1. The most convenient test is Stokvis's modification of Jaffé's well-known test: Mix a few c.c. of the whole 24 hours' mixed urine with an equal volume of concentrated pure hydrochloric acid. Add 2 or 3 drops of a strong solution of sodium hypochlorite, calcium hypochlorite, or common saltpeter, and 1 or 2 c.c. of chloroform. Shake the mixture thoroughly, and set aside. The chloroform is colored blue by the indigo set free from the indican, and the intensity of the color compared with a 24 hours' normal specimen shows the degree of increase of indican.

NOTE:—Since methods for the **quantitative** determination of indican, except by the spectroscope, are inaccurate, lengthy, and complicated, they will not be described here The method given above, if used systematically, on the same quantity of urine in each case and with the same quantity of reagents each time, enables the physician to judge of the **degree of increase** fairly accurately.

In performing the above test bile-pigment, if present, must be removed by careful addition of a solution of subacetate of lead (avoiding excess) and filtration. Very dark urines should be treated in the same way. Urine to be tested for indican should not contain potassium iodide, as the iodine set free on addition of acid will color the chloroform. Albumin does **not** interfere with the test.

**2. Keilmann's test:**—Equal parts of urine and strong hydrochloric acid are shaken together and a little chloroform added. In presence of indican the chloroform becomes blue and falls to the bottom of the tube. Add, drop by drop, a 5 per cent solution of calcium hypochlorite, and judge of the amount of indican present by the number of drops of hypochlorite necessary to decolorize it. Three or four drops may be enough, but in some cases 50 to 80 are required.

**3. Marten's test:**—Warm the urine and add yellow nitric acid, when a dark brown color appears becoming black on further addition of acid.

**4. The spectroscopic method of McMunn:**—Equal parts of urine and hydrochloric acid with a few drops of nitric acid are boiled together, cooled and shaken with chloroform. The latter is colored violet, and shows an absorption band before D, due to indigo-blue, and another after D, due to indigo-red.

**Physiology:**—The chemistry of its origin in the body has already been considered. Indol is a specific product of albuminous putrefaction in the presence of organized ferments. Indican being derived from indol, micro-organisms are always concerned in the production of indican and, in health, *the large intestine* is its only source.

The quantity eliminated normally in the urine varies with the kind of diet, 6.6 milligrams per liter being the average of eight observations of Jaffé. Red meats increase it, milk or kumyss decrease it. The urine of new-born children does not contain it. Starvation increases it, since secretions rich in albumin putrefy in the intestine.

**Pathology:**—Indican is increased in the urine in the following:—

1. Whenever there is an *increase of intestinal putrefaction* as in anachlorhydry, hypochlorhydry; in *carcinoma* of the stomach; in acute, subacute, and chronic gastritis; also in ulcer of the stomach, although hyperchlorhydry may simultaneously occur.

NOTE:—Hypochlorhydry the secretion of a deficient amount of free hydrochloric acid, less than 0.1 per cent; anachlorhydry, absence of hydrochloric acid; hyperchlorhydry, excessive secretion, more than 0.2 per cent

2. In conditions in which the peristaltic movements of the *small* intestines have become impeded: *ileus*, acute and chronic peritonitis, no matter what the state of the gastric juice is.

3. In diseases in which, in general, abundant albuminous putrefaction is progressing in some part of the body, as pleurisy with abundant unhealthy exudation, peritonitis with formation of putrid pus, fetid bronchitis, multiple lymphoma, empyema, gangrene of the lungs. In such cases phenol-sulphuric acid may be more abundant relatively in the urine than indican.

4. In a number of diseases as Addison's, cholera, cancer of the liver, chronic phthisis, central and peripheral diseases of the nervous system, typhoid fever, dysenerty, diabetes mellitus, trichiniasis, paraplegia, long standing suppurations. In the majority of these C. E. Simon holds that the indicanuria is merely an index of the condition of the gastric juice.

5. After use of certain drugs as turpentine, oil of bitter almonds, nux vomica, and creosote.

CLINICAL NOTES.

1. Dr. C. E. Simon, of Baltimore, has studied the relation between indican (indoxyl-sulphuric acid) and the acidity of the gastric juice. His conclusions are as follows:

1. The gastric juice possesses antiseptic and germicidal properties.
2. These properties are referable to the presence of free hydrochloric acid.
3. A subnormal amount of free hydrochloric acid will call forth an increased degree of intestinal putrefaction.
4. The conjugate sulphates form an index of the degree of intestinal putrefaction.
5. The increased intestinal putrefaction in cases of subacidity and anacidity of the gastric juice is largely referable to an increased formation of indol.
6 The elimination of indican in the urine may be regarded as an index of the amount of free hydrochloric acid present.
7. A normal acidity of the gastric juice is never associated with increased indicanuria.
8. Cases of ulcer of the stomach apparently form an exception to this rule, an increased indicanuria being usually associated with hyperchlorhydry.
9. In other cases of hyperchlorhydry a subnormal or normal amount of indican is eliminated.
10. Simple constipation is rarely accompanied by an increased elimination of indican.
11. Diarrhœa referable to a catarrhal condition of the colon, often following a previously existing coprostasis, as well as

diseases of the colon in general, is not associated with an increased indicanuria.

12. In the differential diagnosis between ileus and coprostasis, a small amount of indican excludes the former condition.

13. In cases of an achlorhydry with much lactic acid, the indican is not necessarily increased.

14. No indican, or but little indican, with delayed Günzburg potassium-iodide reaction, indicates the absence of free hydrochloric acid, with much lactic acid. (The Günzburg test is for free HCl in the stomach.)

15. Much indican, with a normal or anticipating Günzburg reaction, is suggestive of ulcer.

16. In cases in which the use of the gastric tube is impracticable or contra-indicated, or in cases of a mere superficial examination, the indican reaction will furnish a valuable index of the condition of the patient's digestive powers

17. By means of the indican reaction we are enabled to follow very closely the results of treatment instituted in cases of gastro-intestinal disease.

Given as premises:

1. That a resorption of decomposing pus is not taking place anywhere in the body, as such a process itself is capable of producing an increased elimination of indican.

2. That there does not exist a stenosis of the small intestine.

3. A normal mixed diet containing no excessive amounts of red meats.

NOTE:—Simon finds that a large quantity of indican may be of decided value in differential diagnosis of **ileus**, since diseases of the large intestine alone are never associated with an increase in the amount of indican.

2. Suppuration may be suspected as taking place in the body if, after administration of intestinal disinfectants (naphthol, bismuth), indicanuria still persists.

3. Fahn finds indican increased in tuberculosis.

4. Herter finds indicanuria (1) in chronic intestinal dyspepsia with clay-colored stools and mental depression, (2) in neurasthenia from sexual excess, (3) in chronic constipation, (4) in chronic epilepsy, especially after the attacks.

Marten out of 6 cases of indicanuria found in all but one some intestinal trouble or other. The exception was a drunkard subject to fits.

6. According to C. E. Simon, examination of the urine for indican is at least as important as that for albumin and sugar

**Skatoxyl-Sulphuric acid:**—Formula, $C_9H_8N.O.SO_2.OH$, an aromatic substance, *ethereal* (*conjugate*) *sulphate*, found in normal urine. It resembles indican in that it is an organic product of the decomposition of albumin.

*Test:*—Jaffé's test for indican, when performed on urine rich in skatoxyl, shows a dark-red to velvet color on addition of hydrochloric acid. If nitric acid be used, a cherry-red color is developed; if hydrochloric acid, ferric chloride, and heat are used a red color occurs, which can be removed from the fluid by ether or acetic ether, while on heating with zinc dust skatol is liberated.

*Significance:*—It is found in very small quantities in normal urine and its significance is said to be much the same as that of indican, so far as increase goes. Urines rich in skatoxyl darken on exposure to the air, as in carboluria, while at the same time they take on from the surface a reddish or velvet color, often almost black.

**Phenol-Sulphuric Acid:**—Formula, $C_6H_5O.SO_2.OH$, an organic aromatic substance, ethereal or conjugate sulphate, found in very small quantity in the urine. The phenol is a product of intestinal fermentation, and some of the sulphate is derived from tyrosine.

*Detection:*—Acidulate the urine with sulphuric acid and distill. Add (a) bromine-water to distillate and a deep-yellow precipitate of tribromphenol appears, if phenol is present. Or (b) warm the distillate with Millon's reagent, and a cherry-red color appears.

NOTE:—Millon's reagent is made by dissolving 10 grammes of mercury in 20 grammes of nitric acid (sp. gr. 1.42) and diluting with 20 c.c. of water.

A third test (*c*) may be tried by adding ferric chloride solution to the distillate, when a deep violet color appears.

*Significance:*—Phenol-sulphuric acid is *increased* by internal or external use of phenol (carbolic acid), also in certain diseases as tuberculous enteritis, pyæmia, intestinal obstructions, etc.

**Carboluria** is the name given to the voiding of dark urine, the result of excessive use of carbolic acid which splits up in the urine into pyrocatechin and hydroquinone, which substances, on exposure to the air, become dark-brown in alkaline urine.

Phenol has been found in the urine of patients taking guaiacol carbonate in large doses.

**Other conjugate sulphates:** — Several other conjugate sulphates occur in urine: they are **paracresol-sulphuric acid** $C_7H_7.O.SO_2.OH$, forming paracresol-potassium sulphate, **pyrocatechin,** and **hydroquinone.** Hydroquinone is recognized by the development of a quinone-like odor, when heated with ferric chloride.

# CHAPTER XVII.

## NORMAL URINARY COLORING MATTERS AND CHROMOGENS.

Urinary pigments are of two classes (*a*) those already formed and (*b*) those appearing only on addition of certain reagents.

**Preformed coloring matters:**—These are *urochrome* and *uroerythrin*. Urochrome is the substance to which the normal yellow color of urine is due to a certain extent. It is probably identical with the *normal urobilin* of MacMunn, is derived from *bilirubin*, and results from oxidation of the latter in the intestinal tract. Bilirubin, as is known, has its origin in the hæmatin and hæmoglobin of the blood. Urochrome may also originate directly from blood-pigments. It is *increased* in cases in which resorption of large extravasations of blood is taking place, *i. e.*, whenever an increased destruction of red corpuscles is noted, and *decreased* in conditions associated with deficient formation of red corpuscles, as in anæmia, Bright's disease, diabetes, diseases of the bone marrow, etc. It is closely related, chemically, to a coloring matter known as urobilin, or better, *pathological urobilin*, from which, however, it may be readily distinguished by the spectroscope. [See *Abnormal Coloring Matters* and do not confound notes on "urobilinuria" in books and journals with the voiding of urine containing normal urobilin or urochrome. Much confusion exists in regard to these substances].

Urochrome or normal urobilin of MacMunn may be obtained from normal urine by acidulating with 1 to 2 grammes of dilute sulphuric acid for each liter of urine, filtering, and saturating with ammonium sulphate; the flakes which are found in an excess of the ammonium sulphate are dried, treated with warm, slightly ammoniacal absolute alcohol, and the pigment obtained on evaporation of the alcohol.

An alcoholic solution of the pigment thus obtained exhibits a beautiful greenish fluorescence when treated with ammonia and a few drops of solution of zinc chloride, in this respect resembling pathological urobilin, but it differs from the latter spectroscopically in that its acidulated alcoholic solutions present a broad band of absorption at "F" extending more to the left than to the right of this line, while the remainder of the spectrum at the same time is absorbed to the right end from a point somewhat to the left of "G."

**Uroerythrin** is the pigment to which the red color of urate sediments and uric acid crystals is due. It is related chemically to hæmoglobin, hæmatoidin, and bilirubin. When abundantly present in urine, it gives a salmon-red color to urinary sediments. Its quantity may be judged by the following test: Add solution of barium chloride or of neutral lead acetate to the urine and let the precipitate settle, waiting ten or fifteen minutes; a milky-white precipitate indicates absence of uroerythrin, a pale rose-colored one presence of uroerythrin in appreciable amounts, and a more pronounced rose-color large quantities.

Uroerythrin is, when present in notable quantities, indicative of *hepatic insufficiency*, in which the liver, owing to a greatly increased destruction of red corpuscles, is either unable to transform all the blood pigment carried to it into bile pigment or else an absolute insufficiency on part of the hepatic cells exists, so that the organ is not even able to bring about transformation of a normal quantity of hæmoglobin. The diseases in which uroerythrin is found in large quantities in the urine are hepatic cirrhosis, carcinoma of the liver, pneumonia, malarial fever, erysipelas, spinal curvature, etc.

According to recent writers normal urine contains two other pigments, namely *urospectrin* and *hæmatoporphyrin*. Urospectrin is extracted from urine by shaking the latter with acetic-ether which removes about two-ninths of the coloring matter. The residue left upon evaporation of the acetic-ether extract is soluble in ether. The ether extract contains the chromogen of urobilin and urospectrin. Upon exposure to light the urobilin chromogen is decomposed and the urobilin may be removed by

shaking with water. Solutions of urospectrin in ether and alkalies give four absorption bands; acid solutions give two bands.

Hæmatoporphyrin may be extracted from urine by adding 20 c.c. of a ten per cent solution of sodium hydroxide to every 100 c.c. of urine; the precipitated phosphates are collected and washed with water. The precipitate is dissolved in rectified spirit and acidified with hydrochloric acid; the solution shows the bands of acid hæmatoporphyrin. Ammonia is then added to precipitate the phosphates and acetic acid to redissolve them; chloroform then extracts the pigment completely and shows the bands of the alkaline pigments.

**Normal chromogens:**—Chromogens are substances which when treated with certain reagents yield pigments. The chromogens of normal urine are indican, urohæmatin, and an unknown chromogen which yields urorosein, when treated with mineral acids, hence called urorosein ogen. *Indican* has already been considered under the heading of conjugate sulphates. *Urohæmatin* appears to be the chromogen of the red pigment found in urine and called by various names, as the red pigment of Scherer, indigo-purpurin of Bayer, urrhodin of Heller, indigo-red, etc. It is probably an indoxyl derivative; when present in increased amount, it is conveniently detected by the *reaction of Rosenbach*, as follows: Boil the urine and add to it, while boiling, nitric acid, drop by drop. In presence of large amounts of the red pigment the urine will assume a dark Burgundy color, which sometimes takes on a bluish tinge, if held to the light; the mixture becomes cloudy, and the foam assumes a blue color. In some cases addition of from 10–20 drops of acid will suddenly change the color from red to yellow, while in others the Burgundy color is not changed.

Rosenbach's reaction is an important one and its significance is the same as the well-marked indican reaction, namely, *greatly increased intestinal putrefaction*, as in extensive disease of the small intestine, in carcinoma of the stomach, acute and chronic peritonitis. The reaction has been found to be absent in carcinoma of the colon, occlusion of the *large* intestine, stricture of the œsophagus, and chronic diarrhœa. If constant and continued in spite of medical or

surgical measures, Rosenbach's reaction is of *bad prognostic significance.*

**Uroroseinogen** is the chromogen which yields a rose-red pigment, *urorosein*, apparently identical with Heller's urophain. It is not a conjugate sulphate, but otherwise little or nothing is known of its chemical nature. It occurs normally only in traces but appreciable amounts are found pathologically and may be detected as follows:—Treat 5 or 10 c.c. of urine with an equal amount of concentrated hydrochloric acid and 1 or 2 drops of a concentrated solution of bleaching powder. If much indican is present the mixture first assumes a dark greenish, blackish, or dark-blue color, owing to formation of indigo. When the mixture is shaken with chloroform, the supernatant fluid will exhibit a beautiful rose-color due to urorosein. This may then be extracted with amyl alcohol, and separated from any other pigment present at the same time, by shaking with sodium hydrate, by means of which the solution is decolorized. On the addition of a drop or two of hydrochloric acid to the alcoholic extract the rose-color will reappear.

A rose-red ring due to this pigment may be noticed in pathological urines when Heller's cold nitric acid test is used for detection of albumin.

Appreciable amounts of this pigment are met with in pathological conditions associated with grave disturbances of nutrition, as nephritis, diabetes, carcinoma of the stomach and dilatation, pernicious anæmia, typhoid fever, phthisis, and at times in profound chlorosis. It is also apparently increased by vegetable diet.

## CHEMICAL EXERCISE VII.

The student having collected his twenty-four hours' urine should test it for the following:

1. *Indican:*—Chapter XVI, Stokvis-Jaffé test.
2. *Skatoxyl:*—Chapter XVI, Jaffé's test.
3. Obtain *urochrome* by the process outlined in chapter XVII.
4. Test for *uroerythrin* with neutral lead acetate solution: Chapter XVII.
5. Try *Rosenbach's reaction:* Chapter XVII.
6. Test for *urorosein:* Chapter XVII.
7. Compare the Stokvis-Jaffé test for indican with *Richardson's test*, as follows: Take equal quantities of urine and hydrochloric acid, add a few drops of a solution of *hydrogen dioxide*, and then chloroform as in Jaffé's test.

# CHAPTER XVIII.

## THE NON-NITROGENOUS ORGANIC ACIDS OF NORMAL URINE.

The non-nitrogenous organic acids occurring normally in urine may be classified as follows:

1. **Oxalic acid** combined with calcium forming **calcium oxalate.**
2. **Succinic** and **lactic** acids.
3. Acids of the **fatty acid** group: Formic, acetic, butyric, propionic.
4. **Glycero-phosphoric acid.**

**Oxalic acid:**—In combination forming calcium oxalate $CaC_2O_4$ held in solution by the sodium dihydric phosphate of the urine. *Sediments* therefore contain calcium oxalate when the urine is diminished in acidity or on standing exposed to the air. The occurrence of calcium oxalate in the sediment does not then necessarily indicate excess of it in the urine. For the quantitative determination of the oxalic acid in urine no simple process is known. See APPENDIX for complete process, and SEDIMENTS for other information, pathology, etc.

Oxalic acid is related to uric acid as is also another acid found in normal urine known as *oxaluric acid*, which occurs in traces in the urine as ammonium oxalurate.

**Succinic acid** has occasionally been found in urine after ingestion of asparagus and asparagin. It is a third acid of the oxalic series. The relationship of the acids of the oxalic series may be seen by the formulas, as follows:

Oxalic acid, $H_2C_2O_4$ or COOH.COOH.

Oxaluric acid, $(CON_2H_3).CO.COOH$.

Succinic acid, $COOH.C_2H_4.COOH$.

**Lactic acid** probably does not occur in urine, but sarco-lactic is said to occur after severe muscular labor and physiological disturbances. It is, however, chiefly met with in pathologic states and should be considered among the constituents of abnormal urine. There are no tests for it available for clinical purposes. It has been found in trichinosis, acute yellow atrophy of the liver, phosphorus poisoning, rickets, leukæmia, osteomalacia, cirrhosis of the liver.

**The Fatty acids** occur in traces under normal conditions and are probably formed in the lower segment of the small intestine. They are formic, acetic, butyric, and propionic, and occur apparently in the free state. They are *increased* slightly in (*a*) febrile disorders and greatly in (*b*) hepatic diseases affecting the structure

proper of the liver; they are also increased (*c*) in diabetes. The condition when they are present in increased amount is known as *lipaciduria*.

There is no simple method of detection; the usual *method of detection* is to distill the urine with phosphoric acid, neutralize the distillate carefully with sodium carbonate, evaporate to dryness on the water bath, extract the residue with boiling alcohol, filter, evaporate again, dissolve in water, and test as follows:—

1. Treat solution with sulphuric acid and alcohol. Odor of acetic ether shows presence of *acetic acid*.

2. To another portion add ferric chloride solution: a red tint appears which disappears on boiling leaving a rusty precipitate.

3. Addition of silver nitrate solution causes a white precipitate which rapidly blackens if *formic acid* is present.

**Glycero-phosphoric acid,** $C_3H_9PO_6$, occurs in small traces in normal urine, resulting as a decomposition product of *lecithin*, which is a combination of choline and glycero-phosphoric acid, occurring in the bile, brain, yolk of egg, etc.

The normal quantity of glycero-phosphoric acid in urine is said to be about 15 milligrams per liter. It is *increased* in chyluria, pernicious anæmia, dementia, lesions of the brain substance, diabetes mellitus, and after chloroform narcosis.

Inasmuch as in the writer's experience the phosphoric acid of the urine (oxidized phosphorus) is certainly *diminished* in conditions of nerve waste, it is reasonable to suppose that the glycero-phosphoric acid (unoxidized phosphorus) is *increased* at the same time. The experience of Robin would appear to confirm this view, hence the use clinically of the glycero-phosphates, phospho-albumins, etc.

Unfortunately it is a difficult matter to determine the glycero-phosphoric acid in urine hence see APPENDIX for processes.

# CHAPTER XIX.

## CARBOHYDRATES NORMALLY PRESENT IN URINE.

THE carbohydrates normally present in urine may be classified as follows:

I. Glucose.
II. Glucosazone.
III. A substance allied to dextrine.
IV. A carbohydrate in combination with benzoyl.
V. Animal gum.
VI. Inosite.
VII. Lactose.

The total amount of carbohydrates with reducing properties eliminated daily in normal urine, has been shown by Baisch to be from 0.12 to 0.32 gm. (about 2 to 5 grains), of which *glucose* itself amounts to from 0.08 to 0.18 gm. or about 1¼ to 2½ grains. Among the other carbohydrates are glucosazone, a substance allied to dextrine, and a carbohydrate in combination with benzoyl.

**Animal gum** is a mucin product. It is precipitated by alcohol but does not reduce alkaline solutions of cupric salts.

**Inosite,** a *sugar* found in small quantities in normal urine. $C_6H_{12}O_6.2H_2O$, muscle-sugar. It is usually found in normal urine only after use of large quantities of water.

*Form:*—Crystalline, when obtained pure, forming large, fine, clinorhombic or monoclinic tables. Impure it crystallizes in cauliflower-like masses.

*Solubility:*—Soluble in 16 parts water at 10° C., insoluble in absolute alcohol and ether.

*Properties:*—Sweetish taste, does not rotate plane of polarization, does not ferment. In alkaline solution it does not reduce hydrated cupric oxide. It yields sarco-lactic acid when fermented with putrefying albumin.

**Tests:** (1) *Scherer's test:*—On evaporating a solution containing inosit on the water bath nearly to dryness in a porcelain dish, having added a few drops of common nitric acid, and then treating the nearly dry residue with some drops of a freshly-prepared, not too dilute, watery solution of ammonia and calcium chloride solution, a rose-red mass remains, which, after some time, becomes changed in color.

(2) *Gallois's test:*—An aqueous solution treated in a porcelain dish with a little mercuric nitrate Hg $(NO_3)_2$ in solution—a drop will suffice—gives a yellowish precipitate. If this is spread out on the edge of the dish quickly, and heated carefully, it becomes

dark red. The color disappears on cooling to reappear on heating. Albumin, sugar, and tyrosin interfere with the reaction.

**Preparation from urine:**—A large quantity of urine (several liters) is feebly acidified, precipitated completely with neutral acetate of lead, filtered, and the warmed filtrate treated with basic acetate of lead, as long as a precipitate forms. After standing for forty-eight hours this precipitate is filtered off, washed, suspended in water, and treated with a stream of sulphuretted hydrogen. From the filtrate, after some hours, uric acid separates, from which the fluid is poured off. The solution is then evaporated to a syrup on the water bath, and precipitated with absolute alcohol. The precipitate is dissolved in hot water and three or four times as much alcohol of 90 per cent as water added. The alcohol is then treated with ether until the clouding is permanent, when the inosit crystallizes out. The watery solution can be used for Scherer's reaction directly (Salkowski and Leube).

PATHOLOGY:—Inosite is found in the urine in *increased* quantity in diabetes, mellitus and insipidus; also in Bright's disease.

**Lactose,** milk-sugar, an *organic* substance, *carbohydrate* $C_{12}H_{22}O_{11}.H_2O$, is found in the urine of nursing-mothers and in lesions of the mammary glands. Positive detection of it is difficult because of its resemblance to glucose in answering to tests. The writer has found, however, that it reduces Haines's test-liquid more slowly than glucose. (See writer's Chemistry, 4th edition, p. 525.) Its presence may be inferred if a positive result is obtained with Trommer's and Nylander's tests for glucose (see Chap. on Sugar), while the phenylhydrazin and fermentation tests give negative results. It is said that persistent and copious elimination of lactose in the urine is a sign of a good wet-nurse. The most certain means for its detection is to isolate it according to the method of F. Hofmeister. Precipitate the urine with sugar of lead, filter, wash with water, unite the filtrate and wash-water, and precipitate with ammonia. The liquid filtered from the precipitate is again precipitated by sugar of lead and ammonia, until the last filtrate is optically inactive. The several precipitates, with the exception of the first, which contains no sugar, are united and washed with water. The washed precipitate is decomposed in the cold with sulphuretted hydrogen and filtered. The excess of sulphuretted hydrogen is driven off by a current of air; the acids set free are removed by shaking with silver oxide. Now filter, remove the dissolved silver by sulphuretted hydrogen, treat with barium carbonate to unite with any free acetic acid present, and concentrate. Before the evaporated residue is syrupy it is treated with 90 per cent alcohol until a flocculent precipitate is formed, which settles quickly. The filtrate from this when placed in a desiccator deposits crystals of milk-sugar, which are purified by re-crystallization, decolorizing with animal charcoal and boiling with 60-70 per cent alcohol.

THE MUCOUS CLOUD (NUBECULA) IN URINE. ENZYMES. PTOMAINES

Normal urine, on standing, deposits a slight cloud in the case of men, but a bulky one in the case of women. If this "cloud" be removed by means of a pipette and sedimented in the centrifuge the microscope shows it to consist of a few mucous corpuscles and pavement epithelia in the case of men, but in women a great mass of epithelia may be seen, of vaginal origin. Traces only of mucin or a mucin-like substance or even none at all are to be found in the urine of healthy men, while in women admixture of vaginal fluids causes a mucin-reaction in almost every sample of urine examined. See *Mucinuria* in Chapter on "Albumin."

The enzymes found in urine are the following:

*Diastase:*—Minute quantities of ptyalin or a similar diastatic *ferment* have been obtained from urine.

*Pepsin*, an organic ferment, has been isolated from normal urine and is found most abundant in the morning. Small pieces of fibrin soaked in urine absorb the pepsin from it and, on being removed to 0.1 per cent hydrochloric acid solution, they are then rapidly digested.

*Rennet:*—Traces of a ferment which curdles milk have been found in urine.

Ptomaines:—These organic substances, and *leucomaines*, poisonous substances of an unknown kind, which are often called *alkaloidal* substances, occur in normal urine according to Bouchard and others. (See *Toxicity of Urine.*)

# CHAPTER XX.

## INORGANIC NORMAL CONSTITUENTS OF URINE.

The inorganic normal constituents of urine will be considered under the following

**Classification.**

I. Compounds of the negative elements phosphorus, chlorine, and sulphur, forming *phosphates*, *chlorides*, and *sulphates*, occurring in considerable quantity in the urine.

II. Compounds of other elements occurring in small quantity or in traces in the urine—nitrates, nitrites, carbonates.

III. Free gases.

### THE PHOSPHATES.

**Introductory:**—Phosphoric acid, $H_3PO_4$, occurs in the urine entirely in combination with bases, forming *phosphates*.

There are several kinds of phosphates in urine, and this is why the beginner meets with difficulty. Let it be remembered, first, that all urine normally contains phosphates dissolved in it, and, second, that under certain circumstances some of these phosphates appear in the urinary sediment. But all the phosphates in urine are not found in the sediment under any circumstances. The phosphates which are always in solution and never in the sediment are the phosphates of sodium and potassium, and are called *alkaline phosphates*. The phosphates which are sometimes in solution and sometimes in the sediment are the phosphates of calcium and magnesium, the so-called *earthy phosphates*.

The question now arises, When does the urine contain phosphates in the sediment? The answer is, when the reaction is feebly acid, neutral, or *alkaline*. The phosphates of calcium and magnesium are dis-

solved by acid urine, but when the urine, for any reason, loses its acidity these phosphates separate, and form a dirty-white flocculent sediment. The other phosphates, those of sodium and potassium, however, are not affected by any change in the reaction, but remain always in solution. We have, then, the following:—

*Acid urine:*—Phosphates of sodium and potassium in solution, $H_2NaPO_4$ and $H\,KPO_4$. Phosphates of calcium and magnesium, in solution, $Ca_3(PO_4)_2$ and $MgHPO_4.7H_2O$.

*Alkaline urine:*—Phosphates of sodium and potassium in solution. Phosphates of calcium and magnesium in the sediment.

*Ammoniacal urine:*—Same as alkaline urine plus triple phosphate, $NH_4MgPO_4.6H_2O$ (ammonio-magnesium phosphate), in the sediment.

I hope that this table makes matters sufficiently clear. Nearly every year my students are disconcerted by the fact that the alkaline phosphates do not appear in the sediment, whilst the earthy phosphates may.

*Solubility:*—When feebly acid or alkaline urine is boiled, it becomes cloudy from precipitation of phosphates. These phosphates thus precipitated are always the earthy phosphates, those of calcium and magnesium, never the alkaline phosphates, those of sodium and potassium. *The alkaline phosphates are always in solution* in the urine, whether it be acid or alkaline in reaction, or hot or cold in temperature.

Now, inasmuch as albumin, if present in the urine, is coagulated by boiling, the earthy phosphates, when urine is feebly acid or alkaline, may be, and, to my knowledge, frequently are, mistaken for albumin. Addition of acetic acid, however, dissolves the phosphatic cloud but does not affect the albuminous coagulum, if such it be. So then, not only do the earthy phosphates form a sediment or deposit in alkaline urine, but if either feebly acid or alkaline urine is boiled, they are thrown out of solution. In other words, the phosphates of calcium and magnesium possess the remarkable property of being *less*

soluble in hot than in cold water. The alkaline phosphates, those of sodium and potassium, are not affected by boiling the urine, and cause no trouble.

Again, when urine is tested for sugar, either by liquor potassæ, by Haines' liquid, Trommer's or Fehling's test, a complication ensues from presence of phosphates. Inasmuch as these tests all involve addition of strong alkalies to the urine, and boiling, it follows, from what is said above, that the earthy phosphates will be precipitated whether or not sugar is present. Hence, when sugar is absent, a dirty white precipitate of earthy phosphates will always be seen, sometimes more conspicuous, sometimes less. *Whenever urine is boiled with an alkali or with a blue sugar-test liquid* (which contains alkali) *flocks of precipitated earthy phosphates will be seen.* These phosphates are the phosphates of calcium and magnesium, not of potassium and sodium. We have then the following:

**Summary:** — Phosphoric acid, $H_3PO_4$, combined with bases, is found in all urine, forming phosphates.

1. *Alkaline phosphates:*—Phosphates of sodium and potassium, present in *solution* in every sample of urine, never in the sediment, not affected by boiling, nor by addition of alkali. Do not complicate the albumin tests nor the sugar tests.

2. *Earthy phosphates:*—Phosphates of calcium and magnesium. Present in solution in every sample of urine and also in the sediment of every alkaline urine. Precipitated from solution in feebly acid, neutral, or alkaline urine when the latter is boiled. Precipitated whenever an alkali like liquor potassæ is added to the urine, as in the various tests for sugar. Re-dissolved when any acid is added to the precipitate, or to the sediment.

The composition of the phosphates may vary somewhat with the reaction of the urine. Thus in acid urine we may have acid phosphates, $NaH_2PO_4$ and $CaH_4(PO_4)_2$; in neutral urine, neutral phosphates, $Na_2HPO_4$, $CaHPO_4$, $MgHPO_4$; in alkaline urine, basic phosphates $Na_3PO_4$, etc.

3. *Triple phosphate:*—In addition to the phosphates already mentioned there is still another phosphate, known as ammonio-magnesium phosphate, or "triple" phosphate. (It is called triple phosphate, $NH_4Mg.PO_4.6H_2O$, because of the water of crystallization forming the third part of its formula.) This phosphate is naturally not found in normal urine but, if for any reason, through disease (septic inflammation of the urinary passage), retention of urine takes place, either in the kidney-pelvis or in the bladder, and there is decomposition of urea, ammonium carbonate being formed, some of the ammonium unites with the magnesium phosphate of the urine to form the double salt, ammonio-magnesium phosphate, which, however, owing to the presence of six molecules of water in its formula, has received the name of "triple" rather than "double." So, then, triple phosphate is found in *the sediment of ammoniacal* urine. It is also sometimes found in slightly acid urine (acidity probably due to some salt which reddens litmus) and in alkaline urine without odor of ammonia.

Urine which turns red litmus paper permanently blue is said to be alkaline from fixed alkali (carbonates of sodium and potassium). Urine which turns red litmus paper blue, the latter fading on exposure to air, and which has odor of ammonia, is said to be alkaline from volatile alkali. It is in urine alkaline from volatile alkali that we find the triple phosphate. Such urine is always, *when freshly voided*, significant of disease. Care must be taken to note the words 'when freshly voided."

*Chemical tests:*—From what has already been said it is easy to see that a simple test for earthy phosphates is to add to any sample of urine sufficient liquor potassæ to render it alkaline, and then boil. Flocks of phosphates at once appear. They are usually dirty white, but may be reddish or brownish. To detect the alkaline phosphates, filter the sample and add to the clear filtered urine one-third its bulk of magnesian fluid, when a snow-white deposit takes place.

Magnesian fluid is made by dissolving 10 grams (155 grains) of pure magnesium sulphate and a like amount of pure ammonium chloride in 10 c.c. of strong aqua ammoniæ and 80 c.c. of distilled water.

How may the *quantity* of phosphates in the urine be determined? Accurate analyses are made with difficulty for the general practitioner, so that the volumetric determination of the total phosphoric acid is the best method to be followed. It is given in CHEMICAL EXERCISE (?).

### PHYSIOLOGY OF THE PHOSPHATES.

**Quantity:**—Different observers make from 2 to 4 grams of *phosphoric acid* normal per twenty-four hours. The author inclines to the opinion that for Americans 2 to 2.5 grams (31 to 38 grains), is not too small.* Of this quantity about one-third is bound to the earthy phosphates, and two-thirds to the alkaline. The total quantity of *phosphates* is variously reckoned at from 3 to 5.5 grams per twenty-four hours (45 to 85 grains). Of this the earthy phosphates form 1 to 1.5 grams (15 to 22 grains), and the alkaline 2 to 4 grams (30 to 60 grains). These figures are altogether to high in case of Americans, so far as my experience goes. The proportion of calcium phosphate to magnesium phosphate is given by Tyson as 33 to 67. The potassium phosphate is the smallest in amount of all the phosphates.

**Source:**—Phosphoric acid in the urine comes largely from the blood, but also partly from the decomposition of lecithin (a phosphorized fatty body, $C_{42}H_{84}NPO_9$, occurring in brain and nerve tissue), and nuclein (an albuminoid substance occurring in the nuclei of corpuscles, in spermatozoids, brain, milk, etc.), which also contains phosphorus. Nerve tissue yields relatively more phosphorus than muscle tissue.

*Formation:*—In the blood phosphoric acid is found combined with bases forming phosphates: *neutral*

* Ten medical students in health, whose urine was examined by the writer, averaged 2 grams (31 grains).

sodium and *neutral* potassium phosphates in the blood appear in the urine as *acid* salts, for the reason that by the act of secretion the bicarbonates and neutral phosphates in the blood become carbonates and acid phosphates, according to the equation:

$$\underset{\text{sodium bicarbonate,}}{HNaCO_3} + \underset{\text{neutral sodium phosphate,}}{HNa_2PO_4} = \underset{\text{sodium carbonate,}}{Na_2CO_3} + \underset{\text{sodium acid phosphate.}}{H_2NaPO_4}$$

The acid salts pass out in the urine, obeying the law of diffusion, but the carbonates remain in the blood.

**Excretion:**—The maximum excretion is in the evening, the minimum about mid-day. The excretion varies somewhat with the amount of food taken, being increased by meat diet, since this tends to increase formation of alkaline phosphates. According to Dr. Long the phosphates in urine have decreased since changes in milling processes have made material reductions in the percentage of phosphates in flour. Phosphatic beverages are said to increase the phosphates in the urine, but in the writer's experience no great excess has been found in *any considerable number* of cases from any cause whatever, the general tendency being toward figures considerably lower than those of the European observers. The phosphates are said to be increased by drinking freely, but increased elimination is followed by a certain degree of retention.

**Ratio of urea to phosphoric acid in health:**—Like all other ratios this is given differently by different observers. From 8 to 1 to 10 to 1 is adopted by some. E. E. Smith thinks it to vary between 12 and 15 to 1. In my own experience out of 36 cases recently examined in which this ratio was determined, in persons in whose urine no abnormal constituents could be found, and who were, so far as I know, healthy, the following was the result:

| | |
|---|---|
| Ratios less than 10 to 1 | 9, |
| 10 to 1 | 3, |
| 11 to 1 | 10, |
| 12 to 1 | 5, |
| 13 to 1 | 3, |
| 14 to 1 | 4, |
| 16 to 1 | 2. |

In other words, *27 out of 36 were not over 12 to 1*, so that ratios above 12 to 1 must be regarded as infrequent. I incline to the opinion that the ratio varies between 8 to 1 and 12 to 1, when the clinical urea instruments are used.

It must be borne in mind, however, that the clinical process for determining urea is not accurate, chemically speaking, while the volumetric determination of $P_2O_5$ by uranium nitrate is in most cases accurate. In all research work the ratio of total nitrogen to phosphoric acid is to be preferred. See Appendix for Kjeldahl-Gunning method.

## CHEMICAL EXERCISE VIII.

### DETECTION AND ESTIMATION OF PHOSPHATES IN THE URINE.

THE presence of phosphates in the urine is very readily shown by means of certain simple tests. Moreover in testing for albumin and for sugar these substances are often precipitated since all urine contains them in greater or less amount.

*A. Detection of earthy phosphates:*—To half a test tube full of urine add a few drops of ammonia or other alkaline solution, shake well, and boil; whitish flocks appear, indicating presence of *earthy phosphates*. If blood is present, the flocks are blood red; if bile, yellow-brown; if vegetable colors (as rhubarb, senna) rosy-red.

*B. Detection of alkaline phosphates:*—Filter the mixture obtained in A and to the filtrate add one-third its volume of magnesian fluid. A snow-white precipitate, crystalline *ammonio-magnesium phosphate*, mixed with amorphous calcium phosphate, occurs. (The crystals thus rapidly formed have a fern-leaf shape (Fig. 31), not prismatic, nor coffin-lid, as in spontaneous deposits. See Sediments).

NOTE:—The student should bear in mind the difference in results obtained by tests A and B, and understand the reason for it. The earthy phosphates in test A are actually seen, being thrown out of solution on addition of alkali. The alkaline phosphates (of sodium and potassium) on the other hand do not thus appear in test B. Owing to the ready solubility in water of compounds of sodium and potassium, it is difficult to precipitate them unchanged from solution. We must have recourse to another method, *i. e.*, that of splitting them up by double decomposition

as it is termed and obtaining a precipitate of *a new and insoluble compound.* The phosphates of sodium and potassium are split up by the magnesian fluid, the phosphate radical uniting with the ammonium and magnesium to form a new and insoluble compound, ammonio-magnesium phosphate. By insoluble understand in the fluids used.

*C. Precipitation of phosphates by heat:*—Obtain some urine which is feebly-acid, as after a hearty meal or at time of "alkaline tide" (10:30 a. m.), filter clear, through three thicknesses of filter paper, into a tall, narrow test-tube. Fill it about three-quarters full. Hold tube by closed end between thumb and fore finger, and boil *upper third* of the liquid over a spirit lamp. A cloud appears owing to precipitation of earthy phosphates. Add ten drops of 20 per cent acetic acid, and shake; the cloud disappears, the phosphates being dissolved by the acid.

*D. Approximate determination of earthy phosphates:*—A test-tube, 16 centimeters (6.2992 inches) long and 2 centimeters (.787 inch) wide, is filled *one-third* with clear or filtered urine, to which a few drops of caustic ammonia or caustic potash solution are added, and warmed gently over a spirit lamp until the earthy phosphates begin to separate in flakes. It is then placed aside for ten or fifteen minutes for them to subside. If the layer of sediment is one centimeter (.3937 inch) high, the earthy phosphates are present in normal amount; if they occupy two to three centimeters (.787 to 1.181 inch), they are increased; if, on the other hand, only a few flakes are visible, the earthy phosphates are diminished.

*E. Approximate determination of alkaline phosphates:*—To a suitable quantity of urine placed in a beaker-glass about *one-third* as much of the magnesian fluid is added. *All* of the phosphates are thrown down in the shape of a snow-white deposit. If the entire fluid present a *milk like cloudy appearance*, the alkaline phosphates may be considered present in normal amount; if it is denser, more cream-like, there is an increase. If, on the other hand, the fluid is but slightly cloudy, transmitting light distinctly, the phosphates are diminished.*

APPARATUS REQUIRED.

Test-tube rack and test-tubes.
Bunsen burners or alcohol lamps.
Aqua ammoniæ or liquor potassæ.
Funnels and filters.
Magnesian fluid.
Test-tubes, 6½ inches long and ¾-inch in diameter.

* In the writer's teaching experience, students cannot be depended on to decide by this test whether the phosphates are normal or increased. Whenever possible the volumetric determination of phosphoric acid should be made.

MICROSCOPICAL EXERCISE.

A. Let the precipitate of earthy phosphates settle, or obtain some already deposited in urine, and examine a drop of the sediment with both low and high power (150 and 500 diameters). Note that the sediment is amorphous, and consists of minute, pale granules in irregular patches. (See Sediments of Phosphates for figures).

B. Let the precipitate with magnesian fluid settle, and examine a drop. In addition to the granular patches will be seen amongst others the so-called "*fern-leaf*" *crystals* of triple phosphate which is the

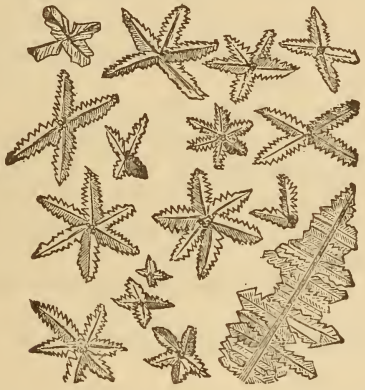


FIG. 32. Fern-leaf crystals of triple phosphate.

form the latter assumes when rapidly developed. (See Sediments of Phosphates for figures). No "coffin-lid" crystals are seen, but several other forms.

# CHAPTER XXI.

## PATHOLOGY AND CLINICAL SIGNIFICANCE OF THE PHOSPHATES IN URINE.

After making several thousand volumetric determinations of phosphoric acid in the 24 hours' urine the writer has come to the conclusion that *decrease* of phosphoric acid is far more common in disease than increase. In fact decrease of phosphoric acid is one of the commonest accompaniments of disease.

*A. Diseases in which the total* phosphates may be increased in the urine:*

1. Some cases of diabetes mellitus.
2. In the condition known as phosphatic diabetes (Tessier, Ralfe, and others).
3. Earthy phosphates increased in diffuse diseases of the bones, and in diffuse periostitis; in diseases of the nerve centers.

According to Zuelzer and others, phosphoric acid is also *increased* in:

4. Convalescence from febrile diseases.
5. Epileptic attacks.
6. Small-pox.
7. Cerebro-spinal meningitis.
8. Cholera infantum.
9. Leukæmia, just before death.
10. Pseudo-leukæmia.

According to Robin an increased elimination of phosphoric acid during the fastigium of typhoid fever is an unfavorable omen, while a decrease during defervescence is favorable.

### EXAMPLES FROM THE WRITER'S CASES.

In 25 cases of diabetes mellitus with polyuria, the greatest amount of phosphoric acid found in 24 hours' urine was 5.8 gm. (90 grains). From 4 to 5 gm. were voided by four patients, and

* The 24 hours' quantity is meant.

from 3 to 4 grams by ten patients. Nineteen patients voided at one time or other from 3 grams down. In 18 collections of 24 hours' urine of diabetics the quantity of phosphoric acid exceeded 3 grams, and in 32 collections it fell below that. So that not even in diabetes mellitus is excess of phosphates in 24 hours more common than deficiency, taking 3 grams (46 grains) as average normal.

The highest relative excretion was 2.25 gm. per liter, about one grain per ounce. It is said that in diabetes mellitus the quantity of $P_2O_5$ rises and falls in inverse ratio to that of sugar.

*B. Diseases in which phosphoric acid is especially deficient.**

1. *Chronic Bright's disease*, especially the interstitial form.
2. *Addison's disease.*
3. *Many nervous diseases.*
4. *Pyuria.*
5. Exophthalmic goitre.
6. Tuberculosis.
7. Cancer.
8. *Diseases of the uterus.*

According to Zuelzer, phosphoric acid is also diminished in:

9. Acute infectious diseases.
10. In pneumonia, typhus, scarlet fever, paroxysms of intermittent fever, febrile phthisis.
11. Acute nephritis.
12. Arthritis, acute and chronic articular rheumatism, osteomalacia.
13. Chronic anæmia.
14. Chronic diseases of the brain and chronic mania.
15. Hysterical attacks, in proportion to the intensity.
16. Chronic lead poisoning.
17. Acute yellow atrophy of liver (absence possible).
18. Cirrhosis of liver.

Zuelzer mentions decrease of phosphoric acid in Addison's disease, in which the writer also has noted marked decrease.

In some of these diseases the phosphates set free may possibly be utilized in the building up of new leucocytes, hence the deficiency in the urine.

* According to the writer's experience.

*Ratio of nitrogen to phosphoric acid:*—According to Zuelzer, the ratio of nitrogen to phosphoric acid in normal urine is 5 to 1. He finds this ratio increased wherever there is notable elimination of pus corpuscles through other channels; in febrile diseases during the febrile period (pneumonia especially), in rachitis, anæmia, in all conditions of excitation of the brain, in diabetes mellitus, in scurvy, empyema, and in Addison's disease. The ratio is diminished in re-convalescence from febrile diseases, in all conditions of depression of the brain, in tumors of the brain, in meningitis, tabes, myositis ossificans, arthritis deformans, and progressive pernicious anæmia.

NOTE:—The term "relative phosphoric acid" is used by the Germans to indicate the ratio of nitrogen to phosphoric acid. Thus Zuelzer says the "relative phosphoric acid" is *diminished* when the proportion of nitrogen to phosphoric acid is *increased* above 5 to 1. This term must not be confused with phosphoric acid relative to water (grams per liter, grains per ounce), as used by the writer. The term *relative value* of phosphoric acid is used by some writers to indicate the relation which exists between the elimination of nitrogen and phosphoric acid. This value supposes the absolute amount or value of phosphoric acid to vary between 2 and 3 grams a day, and is found according to the following:

$$N : P_2O_5 = 100 : x, \text{ and } x = \frac{100\ P_2O_5}{N}$$

In which N indicates the amount of nitrogen actually observed, $P_2O_5$ the amount of phosphoric acid in the same urine, and x the amount of phosphoric acid corresponding to 100 gm. of N. Normally the relative value of $P_2O_5$ in urine is from 17 to 20, an *increase* in this value has been noted in apoplexy (as high as 34.3), brain-tumors, tabes, arthritis deformans (30), pernicious anæmia (23.8 to 28). The value is *decreased* in anæmia, cerebral excitations, and especially preceding an attack of epilepsy, in chronic cerebral affections, delirium tremens, and acute hydrocephalus. In progressive paralysis following syphilis the value is low, but rises greatly after administration of potassium iodide. In the excitement of mania the value decreases; in the stage of depression and in melancholia the alkaline phosphates are diminished and the earthy increased.

The method of determining the total nitrogen of the urine is not ready enough for clinical purposes and is hence described in the Appendix. For ordinary clinical purposes we consider the ratio of urea to phosphoric acid.

*The ratio of urea to phosphoric acid:*—The ratio of urea (determined by the clinical instruments) to phos-

phoric acid is likely to be specially increased (above 14 to 1) in the following diseases in Americans:

1. Pyuria.
2. Chronic interstitial nephritis.
3. Addison's disease.

It is not likely to be greatly increased in cases of Bright's with dropsy and abundantly albuminous urine.

Zuelzer finds the ratio of nitrogen to phosphoric acid increased in diabetes mellitus. So far as the writer's experience goes in 25 cases recently examined, the ratio of urea (determined by clinical instruments) to phosphoric acid was as follows: Less than 10 to 1 in 7 cases; 10 to 1 in 8 cases; 12 to 1 to 14 to 1, inclusive, in 7 cases (of which 3 were 12 to 1, 2 13 to 1, 2 14 to 1); 16 to 1 in 3 cases.

EXAMPLES FROM THE WRITER'S CASES.

*Bright's Disease:—*

1. In the majority of 53 fatal cases of Bright's* disease the total quantity of phosphoric acid per 24 hours was found to be less than 25 grains (1.5 grammes).
2. The average for the whole of the fatal cases was only 18 grains (1.14 grammes) in 24 hours.
3. Less than 15 grains (1 gram) was found in about 33 per cent of the analyses.
4. More than 23 grains (1.5 gm.) occurred in about 33 per cent of the cases.
5. More than 30 grains (2 gm.) occurred in only about 12 per cent.
6. In no cases were more than 35 grains (2.2 gm.) found.
7. Phosphoric acid seems to be decreased compared with urea in cases where pus is abundant in the urine.
8. Phosphoric acid seems, as a rule, not to be decreased more than urea in cases where albumin is abundant in the urine.
9. Phosphoric acid is sometimes decreased far more than urea in cases in which but little albumin is found.

In Bright's disease there seems to be an actual insufficiency on the part of the kidneys in the elimination of phosphates.

In the case of 67 patients, in whose urine albumin together with numerous granular, fatty, or waxy casts were found, and who are still living, the excretion of phosphoric acid was as follows:

The majority of patients voided 1 to 2 gm. in 24 hours or 15 to 30 grains; seventeen voided more and five less. The greatest quantity voided was 5.94 gm. (90 grains) and the least 0.3 gm. (about 5 grains). The average excretion was 1.8 gm., 28 grains

The comparison between the excretion of phosphoric acid by those who died and by those who lived may be made as follows:

*Granular, fatty, or waxy casts in the urine of *all* these patients, together with albumin.

| | THE DEAD. | THE LIVING. |
|---|---|---|
| Above 2 gm. | 13 per cent of the patients | 24 per cent. |
| Above 1.5 gm. | 34 " " " | 57 " |
| Above 1.0 gm. | 71 " " " | 88 " |
| Below 1.0 gm. | 31 " " " | 10 " |
| Greatest quantity per 24 hours | 2.2 gm. | 5.94 gm. |
| Average excretion | 1.14 gm. | 1.8 gm. |

In other words the percentage of those who passed more than 1 gm. (15 grains) in 24 hours of both the living and the dead is not so very unlike, namely, 71 per cent of the dead and 88 per cent of the living, the excretion being nevertheless in favor of the living; but when it comes to a question of voiding from 1.5 gm. up, the percentage is greatly in favor of the living. *Twice as many people lived as died of those having albuminuria with granular, or fatty, or waxy casts when at the same time they voided more than 1.5 gm. (23 grains) of phosphoric acid in 24 hours. On the other hand, now, three times as many people died as lived when in addition to albuminuria with granular, or fatty, or waxy casts they voided less than 1 gm. (15 grains) of phosphoric acid in 24 hours.*

Those who thus far are alive voided on an average 1.8 gm. (28 grains) of phosphoric acid, whilst those who are dead voided but 1.14 gm. or about 18 grains.

It would appear from the above that, when albumin together with granular, fatty, or waxy casts is found in the urine of a patient, estimation of phosphoric acid is of value as a factor in the prognosis.

*Addison's disease:*—In the case of a well-known Chicagoan who died recently of Addison's disease, repeated determinations of phosphoric acid, made by the writer, showed marked deficiency, and a high urea-phosphoric acid ratio. The total phosphoric acid in the last year of life averaged about 1 gram (15 grains) and the ratio of urea to phosphoric acid ranged from 17 to 1 up to more than 20 to 1. So far as I know, no one, except Zuelzer, has called attention to a high urea-phosphoric acid ratio in this disease.

*Nervous diseases:*—Less than 1.5 gm. (22 grains) in 24 hours has been found by me in the following nervous diseases: Various nervous disorders in women, reflex from uterine disease, 10 cases out of a total of 13 recorded; neurasthenia, 5 cases; uræmia chronica, 3 cases; neurasthenia with tumor, 2 cases; epileptic children, 3 cases; hysteria, 3 cases, one in a male patient; in one case each of cerebral hemorrhage, paralysis from softening of the brain, hypochondria, hemiplegia, oxaluria with mental and nervous symptoms, neuritis, feeble-minded state, nervous symptoms reflex from genito-urinary disease in a man.

The smallest excretion was 0.46 grammes, 7 grains, in 24 hours, in the case of the man whose nervous symptoms were apparently reflex from genito-urinary disease. Small excretions, 0.6 gm. each, were noticed in the case of a feeble-minded woman and a woman subject to fits.

Moderate decrease, 1.5 to 2 gm. (22 to 31 grains), was noticed in the following: Localized chorea, neurasthenia (3 or 4 cases), paralysis agitans, uricæmia and anæmia, rheumatism, neuritis in a neuropath, in an epileptic child, cerebral hemorrhage and hemiplegia, brain symptoms following sunstroke, cephalalgia following

pneumonia, two cases of nervous disorder reflex from uterus, chronic cerebral meningitis and facial paralysis.

Above 2 gm., 30 grains, in the following: Melancholia followed by suicide (38 to 50 grains), cerebral tumor (32 grains), nervous symptoms, reflex from rectal disease (44 grains), torticollis in a neuropath, pregnancy (49 grains), epilepsy (42 grains), nervous symptoms from worry and abuse of tobacco (43 grains), melancholia (36 grains), nervous symptoms reflex from uterus (33 grains).

## MISCELLANEOUS.

*Exophthalmic goitre:*—One patient with this disease voided 1.4 gm., about 20 grains.

*Uterine fibroid*:—One woman with a fibroid voided less than one gram, 14 grains.

*Cancer*:—A woman who died of a cancerous growth voided less than one gram, 14 grains.

*Tuberculosis:*—A man who died of tuberculosis voided but 0.6 gm., 10 grains nearly.

*Phosphoric acid in the urine of children:*—In view of the dearth of information regarding the elimination of phosphoric acid by children the following may be of interest:

Boys:—Infant, 1 year old, slowly sinking from albuminuria, hematuria, and uræmia, 2.5 grains in 24 hours (0.15 gramme) Boy of 4 years, 10 grains (0.65 gramme). Boy of 6 years, weight 45 pounds, poorly nourished, 12.5 grains (0.8 gramme). Boy of 9 years with slight persistent albuminuria without casts, 20 grains (1.3 gramme). Feeble-minded boy, 10 years old, 10 grains (0.65 gm.). Boy weighing 84 pounds, 25 grains (1.6 gm.). Epileptic boy of 10, 24 grains (1.6 gm.). Epileptic boy of 11, 19 grains (1.2 gm.). Epileptic boy of 12, weight 50 pounds, 40, 32, 27, 27 grains (2.6 gm., 2 gm.. 1.76 gm.). Boy with chronic diffuse nephritis, 11, 14 grains (0.7, 0.9 gm.). Boy of 10, with diabetes mellitus, 40, 32, 28, 25 grains (2.6, 2, 1.82, 1.6 gm.). Boy of 15, with nocturnal enuresis, 21 grains (1.3 gm.).

Erom this it will be seen (*a*) that boys with *epilepsy* or *diabetes mellitus* may void as much phosphoric acid as grown people; (*b*). that boys 10 years old or less may not void more than 10 or 12 grains of phosphoric acid; (*c*), that a boy of 4 may void as much under certain conditions as a boy of 10 under other conditions.

Girls:—A healthy female child, 2 years old, voided 16 grains (1 gm.) in 24 hours; a girl of 5, with persistent albuminuria (without casts), voided 6, 7, 10, 13, 14, 15 grains (0.39, 0.4, 0.65, 0.8, 0.9, 0.95 gm.); a girl of 6 voided 12 grains (0.78 gm.); a girl of 8 voided 19 grains (1.2 gm.); a girl of 10 voided 17 grains (1.04 gm.); a girl of 10 voided 16 grains (1 gm.): a girl of 10, with inflammatory rheumatism, voided 20 grains (1.3 gm.); a girl of 12, with diabetes mellitus, voided 28 grains (1.52 gm.); a girl, age unknown, voided 35 grains (2.2 gm.); a girl of 15 voided 28 grains (1.82 gm.).

### ACTION OF DRUGS ON ELIMINATION OF PHOSPHORIC ACID.

Potassium bromide, cocaine, and quinine are said to diminish phosphoric acid. Salicylic acid and the glycero-phosphates increase it.

Cerebral excitants increase the ratio of nitrogen to phosphoric acid, cerebral depressants decrease it. Among the cerebral excitants are strychnine, small doses of alcohol, phosphorus, valerian, cold baths, and salt water baths. Among the cerebral depressants are chloroform, morphine, chloral, large doses of alcohol, potassium bromide, mineral and vegetable acids, prolonged cold baths, Turkish baths, and low temperature.

### CHEMICAL EXERCISE IX.

1. The student having collected and measured his twenty-four hours' urine should proceed to determine the total quantity of phosphoric acid in it:

#### APPARATUS NEEDED FOR VOLUMETRIC DETERMINATION OF PHOSPHORIC ACID IN URINE.

Two burettes of fifty cubic centimeters capacity, preferably those provided with a blue stripe on a white background, and with *glass stop-cocks.* (Fig. 33.)

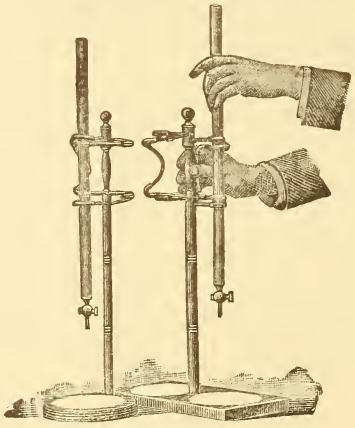


FIG. 33. Burettes.

One burette support (Chaddock) for two burettes provided with two milk-glass plates. (Fig. 33.)

FIG. 34.
Bunsen burner.

One short Bunsen burner with top for water-bath, (Fig. 34) and rubber tubing.

One copper water-bath, capacity of a pint.

Three lipped beakers, capacity four or five fluid ounces, of size so that they may fit quite closely but not too tightly into one of the rings of the water-bath.

Six stirring-rods of the lightest possible weight.

One 5 c.c. graduate. One 50 c.c. flask. (Fig. 35.)


FIG. 35.
50 c.c.
Flask.

One pound bottle, each, of the standard solutions as follows: Uranium nitrate, sodic acetate, potassic ferrocyanide. (To describe how these standard solutions are made would here take up too much space.* They may be had ready made, but care must be taken to specify that they are wanted for the phosphoric acid analysis in urine.)

METHOD OF DETERMINATION.

When the twenty-four hours' urine has been collected and measured, and the result in c.c. noted down, fill one of the two burettes with urine and measure off exactly fifty cubic centimeters of it into one of the lipped glass beakers.

Add to it just five cubic centimeters of the standard sodic acetate solution, using the five c. c. graduate as a measure. Stir well with a glass rod. Fill the water-bath not quite full of water, set it on the support over the Bunsen burner, light the gas, and raise the water in the bath to boiling. As soon as it begins to simmer, set the beaker containing urine and sodic acetate in the water, supported by the ring. The beaker should not be fitted tightly into the ring, for fear of breaking it, and about one fourth of it should be above water. In this way the boiling water constantly surrounds the liquid in the beaker. While the water in the water-bath is being heated, place ten or

*See appendix for complete instructions.

twenty drops of the standard potassic ferrocyanide solution on one of the clean, *dry*, milk-glass plates forming the foot of the burette stand. The drops should be placed *singly*, and be separate from one another on the plate.

As soon as the water in the water-bath has begun to boil, fill the second burette up to the 0 mark exactly with the standard uranium nitrate solution. Set the burette of uranium solution over the middle of the beaker which is on the water-bath, turn the stopcock, and let five c.c. of uranium solution run into the liquid in the beaker. Stir well with a glass rod and transfer a drop of the mixture, by means of the rod to one of the drops of the standard potassic ferrocyanide solution. If a slight reddish color appears the operation is over, if not, run in another five c.c. of the uranium solution and transfer a drop from the beaker again to another drop of ferrocyanide on the plate. If no color yet appears, add say another five c.c. of uranium solution and try again. If no color even yet, then proceed more cautiously adding only two c.c. of the uranium solution at a time, stirring well, and transferring a drop as before. Finally, if when twenty c.c. of uranium solution have been added there is still no color obtained on transferring a drop to the ferrocyanide drops, then run in only one c.c. of uranium solution until, at last, transference of the drop shows the reddish color.

In urines below 1015 in specific gravity not more than fifteen c.c. of uranium solution are, as a rule, necessary, and often much less. In the case of urines above 1020 in specific gravity, from fifteen c.c. upwards of uranium may be required.

To calculate the amount of phosphoric acid in the urine, divide by ten, the number of cubic centimeters of uranium nitrate solution, necessary to be added until transference of a drop of the mixture in the beaker gives a slight but perceptible reddish color with the potassic ferrocyanide drop on the plate. The quotient equals grammes of phosphoric acid per liter of urine. Convert this to grains per fluid ounce by

dividing by 2.125, or simply by consulting table in appendix.

Thus, suppose the urine in twenty-four hours amounts to fifty-six fluid ounces (1680 c.c.). Suppose the amount of uranium solution used was twenty-two cubic centimeters: Twenty-two divided by 10 equals 2.2 grammes of phosphoric acid in every liter of urine, and 2.2 divided by 2.125 equals 1.03. Then this urine contains 1.03 grains of phosphoric acid in every fluid ounce. If there are fifty-six fluid ounces of urine then 1.03 times 56 equals 57.68 grains of phosphoric acid in the twenty-four hours, or about 3.7 grammes.

EXAMPLES FOR PRACTICE.

1 Urine in 24 hours, 30 fluid ounces; number of c. c. of uranium used, 17. Required grains per fluid ounce of phosphoric acid and also grains per 24 hours. *Answers:* 0.8 and 24. Convert to grammes per liter and per 24 hours.

2. Urine, 33⅓ fl. oz.; uranium, 11½ c.c. *Answers:* 0.5 and 18.

3. Urine, 13 fl. oz.; uranium, 21 c.c. *Answers:* 1 and 12½.

4. Urine, 38 fl. oz.; uranium, 11½ c.c. *Answers:* 0.53 and 20.

5. Urine, 18⅓ fl. oz.; uranium, 23 c.c. *Answers:* 1 and 20.

Comparisons with normal averages may be made by remembering, that in health adults pass about one grain per fluid ounce of phosphoric acid, or forty to fifty grains at most in 24 hours. The tables in the APPENDIX are convenient for reference, giving, as they do, at a glance the comparison with normal.

It is my opinion that the English and French observers place the normal excretion too high. Sixteen estimations of the phosphoric acid in the writer's urine showed the average quantity to be *two-thirds of a grain per ounce* and *33 grains per 24 hours.*

6. Urine, 1200 c.c.; uranium, 14 c.c. Sex, male. What per cent of the normal averages, both relatively and absolutely?

7. Urine, 800 c.c.; uranium, 25 c.c. Sex, female. What per cent of the normal averages, both relatively and absolutely?

**Notes on Manipulation:—**

*1. Cochineal as Indicator:*—Instead of using potassium ferrocyanide as an indicator, tincture of cochineal may be substituted as follows: A few grammes of cochineal granules are digested with 250 c.c. of a mixture of 3 volumes of water and 1 volume of 94 per cent alcohol in the cold. The solution is then decanted and a few drops of it added to the 50 c.c. of urine plus 5 c.c. of the acetate mixture used. The mixture being heated to the boiling point uranium solution is run in until a trace of greenish color is noted in the precipitate, which does not disappear on stirring.

*2. Separate determination of the earthy and alkaline phosphates:*—200 c.c. of filtered urine are made strongly alkaline with ammonium hydroxide and set aside, in a covered dish, for several hours, until the earthy phosphates precipitated have settled. The supernatant liquid is carefully drained off and the balance poured upon a filter, washed with dilute ammonia (1 part ammonia water to 3 of water) and then transferred to a beaker with the aid of a little water containing a few drops of acetic acid, a small hole being made in the filter. The precipitate is then dissolved in as little acetic acid as possible, diluted to 50 c.c. with distilled water and titrated with uranium solution. *The difference between the total amount of $P_2O_5$ and the amount now obtained is the quantity of phosphoric acid combined with the alkaline earths.*

# CHAPTER XXII.

## CHLORIDES IN THE URINE.

Next to urea the most abundant constituent of the urine is *common salt*, chloride of sodium, which, together with potassium chloride, forms nearly one-quarter by weight of the total solids eliminated by the urine. In clinical interest, however, the chlorides are inferior to the phosphates.

**Synonyms:**—Chlorides; Chloride of sodium, common salt: German, *Chlornatrium*, *Kochsaltz;* French, *chlorure de soude*, *sel commun*.

**Occurrence:**—Chiefly as sodium chloride with a small amount of potassium, magnesium, and ammonium chloride. In solution in the urine. Never in the sediment.

**Chemical constitution:**—Sodium chloride, NaCl, common salt. Potassium chloride, KCl, ammonium chloride, $NH_4Cl$, magnesium chloride, $MgCl_2$, chlorine in combination with the bases sodium, potassium, and ammonium.

**Chemical test:**—To show the presence of chlorides in the urine add ten or fifteen drops of nitric acid to 10 c.c. (one-third of a fluidounce) of urine, and then a few drops of silver nitrate. A white, curdy precipitate takes place. Let it settle, pour off supernatant urine, add ammonia-water freely, shake well, and the precipitate is dissolved.

Note:—This test depends upon the fact that the chlorine in the chlorides unites with the silver in the silver nitrate to form silver chloride, according to the equation

$$AgNO_3 + NaCl = AgCl + NaNO_3.$$

Silver chloride is soluble in ammonia-water.

The object of adding nitric acid first is to prevent precipitation of phosphates.

**Determination of quantity of chlorides:** — The above test may be utilized for determining in a rough way whether the chlorides are in excess or greatly diminished. The method as proposed by Ultzmann is faulty in that more nitric acid than a few drops is required to prevent precipitation of phosphates, etc. The author's method is as follows: Fill a percentage tube (Fig. 35), such as is used in centrifugal analysis, to the 10 c.c. mark with urine. Add *not less than 15 to 30 drops of nitric acid*, and then fill up to the 15 c.c. mark with standard solution of silver nitrate, 1 to 8 (one drachm of the crystals to eight drachms of distilled water). Mix thoroughly, let settle, or better, settle in the centrifugal machine.* (See Centrifugal Machine). If the bulk of the precipitated chlorides is not greater than the fifth or sixth mark on the tube, chlorides are considerably diminished; if normal, the bulk of the precipitate should reach the tenth to twelfth mark. Results may be expressed in bulk percentage figures, 5 per cent, 6 per cent, etc. Inasmuch as for clinical purposes all that is wanted is knowledge of a marked diminution in the chlorides, or increase after such diminution, the above method answers full well.

FIG. 36. Percentage tube.

[For volumetric quantitative methods (Mohr's, Volhard's, etc.) see APPENDIX].

**Physiology:**—The chlorides are derived from the food and their daily quantity varies from 10 to 16 grammes (155 to 250 grains) or a total of from 6 to 10 gm. (93 to 155 grains) of chlorine. The chlorides are, then, next in quantity to urea. Twelve grammes (185 grains) may be taken as a common average per 24 hours but those who are fond of salt may pass double this quantity.

*Decrease* in chlorides follows deficient nourishment and in starvation traces only from the bodily fluids are

* Use a speed of 1000 revolutions per minute for three minutes.

found. If at this stage salt food be taken, a portion of the salt will be retained in the body until the equilibrium is restored; so also after ingestion of large quantities of water. Rest diminishes the excretion. Beer is said to diminish it also.

*Increase* of chlorides will follow any increase in the amount of circulating albumin, for on account of the great affinity between albumins and salt the latter is previously retained by the albuminous bodies. Active exercise and copious draughts of water increase the elimination, but this increase is likely to be followed by retention on account of the albuminous metabolism.

The chlorides increase and decrease with the volume of urine. Common salt is contained in all the tissues and secretions of the body, and by its presence metabolism is increased, secretion stimulated, and it is needed for the preparation of some of the secretions, as the gastric juice.

**Pathology:—**

*A. Diminution of Chlorides:*—The chlorides are *diminished* in the following diseases:—

1. Many acute febrile disorders as pneumonia, pleurisy, typhus, scarlatina, roseola, variola, recurrens, acute yellow atrophy where the diminution runs parallel to the height of the fever.

2. Diarrhœa and Asiatic cholera.

3. Acute and chronic diseases of the kidneys with albuminuria and dropsy.

4. In chronic diseases generally; a significant decrease occurs in anæmia, marasmus, rickets, leukæmia, chlorosis, also in melancholia and idiocy; in dementia, chorea, and pseudo-hypertrophic paralysis (less marked decrease); chronic hyper-secretion of gastric juice, in dilatation of the stomach, in carcinoma of the stomach, in ulcer of the stomach; also in impetigo, pemphigus foliaceus; in chronic lead poisoning.

NOTE:—In inflammations with exudation, salt is found in the exudation. In croupous pneumonia at the crisis there may be but one-hundredth of the normal quantity of salt in the urine. In diarrhœal diseases the bulk of the chlorides is found in the dejections. In dropsies the salt is stored up in the dropsical fluid.

Intermittent fever is an exception to the rule of diminution of salt in fevers; during the paroxysms more chlorides are excreted than during the apyrexial period. In acute febrile diseases in general there is (*a*) less salt ingested (*b*) retention in the blood due probably to increase in the amount of circulating albumin, (*c*) diminished renal secretion of water, (*d*) possible elimination elsewhere as in diarrhœas, formation of serous exudates, etc.

*B. Increase of chlorides:*—Chlorides may be *increased* in the later stages of those diseases in which they were greatly diminished at first. After the resolution of exudates and dropsies; also in diabetes insipidus (29 gm. in 24 hours); in paralytics in the first stage (due to increase of food); in polyuria after epileptic attacks; in prurigo (29.6 gm.); and after chloroform inhalations.

**Clinical notes:**—1. An increase of chlorides in acute febrile conditions and especially in pneumonia is regarded as a favorable sign. A decrease to 0.05 gramme in 24 hours is a grave condition.

2. Potassium salts, notably neutral potassium phosphate ($K_2HPO_4$), some diuretics, and chloroform increase the chlorides. Salicylic acid is said to increase them temporarily

3. An elimination of from 10 to 15 grammes daily indicates a fair condition of appetite and digestion.

4. An increase in cases of œdema when associated with serous exudates is a good sign.

5. A continued elimination of more than 15 to 20 grammes is usually significant of diabetes insipidus.

EXAMPLES FROM THE WRITER'S CASES.

In a case of *asthma and bronchitis* the writer found the chlorides about one quarter normal. In *chronic nephritis*, several cases, including one of puerperal nephritis (without convulsions) the same low figure was found. Women quite frequently pass comparatively small amounts of chlorides, half to two thirds the normal for men, without discoverable serious disorder. One of the smallest total quantities of chlorides (about one-quarter normal) was passed by a man weighing 125 pounds, seemingly in good health. In 50 or 60 determinations recently made by the chemical method described above, but four were above 12 per cent in bulk percentage.

Both large percentage and total quantity, once and a quarter normal for a man, were found in the urine of a *diabetic woman*. In a case of hematuria no increase occurred. The largest percentage ever seen, 18 per cent bulk, occurred in a case of *uræmia chronica* not long before death.

## CHEMICAL EXERCISE X.

The student having collected and measured his urine for 24 hours can determine the quantity of chlorides in it roughly as follows:

1. Compare quantity of urine in 24 hours with the normal average, and express in per cent of normal.

2. Determine bulk percentage of chlorides by author's method already given, and compare with 10 per cent—the normal average.

3. Multiply the figure obtained in 1 by that obtained in 2 and compare with 100 as normal. For example, suppose the volume of urine in 24 hours is 80 per cent of the normal average, and that the bulk percentage of chlorides is 5, the latter is about 50 per cent of normal. Hence in urine which is about 80 per cent of normal volume, we have chlorides about 50 per cent of normal percentage, therefore 50 per cent of 80, or 40, represents the total of chlorides compared with 100, which may be assumed to represent the normal excretion. In other words the individual is passing less than half the normal amount of chlorides. This method is only roughly approximate, but serves to give an idea as to whether a marked increase or deficiency exists.

4. Observe the difference in bulk of the chloride precipitate in the percentage tube when only 5 drops of nitric acid are used, and when 15 to 30 drops are used to prevent precipitation of phosphates.

5. See whether addition of 15 drops and of 30 drops, respectively, of nitric acid makes any difference.

(For work of this kind Purdy's electric centrifuge is useful).

For research work in chlorides see APPENDIX.

### APPARATUS REQUIRED.

Purdy's percentage tubes. Solution of silver nitrate, 1 in 8, say 20 grammes in 160 c.c. of distilled water (310 grains in 5 fl. oz.). C. P. nitric acid.

## MICROSCOPICAL EXERCISE III.

Let a drop of urine dry on the slide and notice the dagger-shaped crystals of common salt combined with urea. (Fig. 37.)


**A.** Chloride of sodium, in combination with urea, and evaporated quickly from urine.

**B.** Chloride of sodium, crystallized from distilled water, and resembling oxalate of lime; never exists in urine, and is soluble in water, while the oxalate is not.

**C.** Chloride of sodium crystallized slowly from urine, also resembles oxalate of lime, but differs in being soluble in water.

**D.** Chloride of sodium resembling crystals of cystine

FIG. 37. Chloride of Sodium Crystals. (John King.)

The author has noticed in giving microscopical exercises to classes that students are oftener puzzled by the drying of the drop on the slide, and the appearance of these crystals than by almost anything else in the course.

# CHAPTER XXIII.

## INORGANIC SULPHATES IN THE URINE.

**Introductory:**—There are three kinds of sulphates in the urine as follows:

1. Ordinary sulphates of potassium and sodium, called "preformed" sulphates.
2. Incompletely oxidized sulphates, whose composition is unknown.
3. Ethereal or aromatic sulphates, called "combined sulphates" organic compounds of sulphuric acid with indol, phenol, skatol, etc., containing the radical $HSO_3$. Already considered.

The above mentioned sulphates are always in solution, never in the sediment. Calcium sulphate and magnesium sulphate occasionally occur in the urine, in which case they may be found in the sediment. (See Sediments.)

### THE PREFORMED SULPHATES.

**Synonyms:**—Sulphates: GERMAN, *Sulfate;* FRENCH, *les sulfates.* Preformed sulphates: GERMAN, *Sulphatschwefelsäure, präformirte Schwefelsäure;* FRENCH, *les sulfates préformés.*

**Occurrence:**—The preformed sulphates are found in solution in all normal urine. Of the total sulphates the preformed constitute about eight-tenths, the incompletely oxidized one-tenth, and the ethereal one-tenth.

**Chemical constitution:**—The preformed sulphates are the ordinary sulphates of sodium and potassium, $Na_2SO_4.10H_2O$, and $K_2SO_4$.

**Solubility:**—Freely soluble in water, hence never occurring in the sediment.

**Chemical test and estimation:**—To 10 c.c. of urine (3 fluidrachms) add a few drops of *chemically pure* hydrochloric acid, and then barium chloride solution,

in quantity about one half that of the urine. A white, milky precipitate, barium sulphate, is formed according to the equation.

$$Na_2SO_4 + BaCl_2 = BaSO_4 + 2NaCl.$$

Pour the whole into a percentage tube such as used for chlorides, let settle, or better, settle in the centrifuge (speed 1000 revolutions per minute, time 3 minutes), and if the sediment is much below the first mark on the tube (1 per cent bulk) sulphates are decreased, if much above, increased; if just a little below, about normal.

Note:—For routine work make up a solution of the barium chloride together with the hydrochloric acid in water as follows:

Chemically pure hydrochloric acid, 8 c. c. (10 gm.)
Chemically pure barium chloride, 40 grammes.
Distilled water, 160 c. c.

Fill the percentage tube with urine up to the 10 c. c. mark and the balance with the barium solution up to the 15 c. c. mark. Mix.

In case a percentage tube is not to be had, try the following:—To 10 c. c. of urine in a test-tube add one-third its volume of the acidulated barium chloride solution; if the turbidity resulting is *milky*, the sulphates are normal; if *creamy*, excessive; if merely light and *translucent*, diminished. In the writer's experience, three or more students trying this test will report two or three different results so that the percentage tube and centrifugal machine are preferable for chemical work. For the quantitative analysis of sulphates both preformed and conjugated see APPENDIX.

**Physiology:**—The mean of the *daily quantity* of *sulphuric acid* in the urine is *2.5 grammes* (38 grains), of which that united to form the preformed sulphates would be about 2 grammes or 30 grains. The quantity of preformed sulphates, as such, would then be about 3 to 4 grammes (45 to 60 grains). Sodium sulphate exceeds in quantity potassium sulphate. *The sulphuric acid is derived chiefly from the decomposition of proteids*, by oxidation of the sulphur to sulphuric acid. The sulphates are formed by neutralization of

the sulphuric acid by alkalies (neutral phosphates transformed into acid phosphates and sodium sulphate). The excretion of sulphates, as a general rule, runs parallel to that of urea. The ratio of the total sulphuric acid to total nitrogen is 1 to 5; to urea, 1 to 12. Foods or drinks rich in sulphates or oxidizable sulphur compounds, nitrogenous diet, and active exercise *increase* the sulphates in the urine. Fasting and vegetable diet *diminish* them.

**Pathology:**—The sulphates are *increased* in febrile diseases, especially pneumonia, meningitis, encephalitis, and rheumatism; in acute myelitis, eczema, diabetes mellitus, and leukæmia. They are *diminished* in chronic diseases of the kidneys.

PREFORMED SULPHATES AND CONJUGATE SULPHATES.

1. The ratio of preformed sulphates to conjugate sulphates is 10 to 1 (See chapter on Ethereal Sulphates).

2. The excretion of total sulphates is increased by animal diet.

3. In starvation the preformed sulphates are diminished, but the conjugate may be increased.

4. The total sulphates may average 2.46 grammes in leukæmia, as compared with 1.51 grammes passed by a healthy individual on the same kind of food taken in the same amount; 5.8 gm. total may be passed before death from acute leukæmia.

5. In both forms of diabetes, carcinoma of œsophagus, progressive muscular atrophy, pseudo-hypertrophic paralysis, and eczema, the total sulphates are increased.

EXAMPLES FROM THE AUTHOR'S CASES.

In the case of a woman with moderate *diabetes mellitus* without marked polyuria and with but 2 per cent of sugar the sulphates were relatively and absolutely about half the normal quantity. In a case of *inflammation of the neck of the bladder* in a man they were about one-third normal; so also in *chronic nephritis* in several cases. The smallest amount found was in the case of a woman already several times mentioned, as having *urœmia chronica*. Not long before death in this case the sulphates were only about one-sixth the normal total. The highest percentage by bulk of sulphates seen was in the case of a woman, who died of

uræmia from *diffuse nephritis*, about 48 hours before death; the quantity was 5 per cent bulk, due doubtless in part to internal medication.

In a severe case of *diabetes mellitus* in a man the sulphates were once and a quarter the normal average bulk; but in an equally severe one in a woman they were only one-third normal total. I have noticed that when patients with acute or chronic nephritis are being *flushed out with mineral water* that the sulphates in the urine are in relative excess compared with other constituents. In the case of a man weighing 260 pounds the sulphates were barely the normal average both relatively and absolutely.

In an *epileptic* boy the sulphates were diminished compared with other constituents, being only half normal in total.

In the case of a man who died, about a month after the analysis, from *chronic nephritis* the sulphates were only one-sixth normal.

**Clinical notes.**

1. It is said that inhalations of oxygen increase the sulphates.

2. The clinical significance of the preformed sulphates and of the incompletely oxidized sulphates is slight compared to that of the ethereal sulphates.

3. Changes in the ratio of the preformed sulphates to the ethereal sulphates are of considerable significance. Thus, a urine rich in indigo, contains but little of the preformed sulphates, and in carbolic acid poisoning it is said they may disappear altogether. (Jaksch).

4. In two cases in which the author found very small quantities of preformed sulphates—one-sixth the usual average for 24 hours—death took place in a month or two. These two were the only ones of 100 individuals in whose urine the sulphates were less than one quarter the usual normal average for 24 hours.

### CHEMICAL EXERCISE XI.

Determine the quantity of sulphates approximately according to the method described under *chemical test and estimation*. Apparatus required: Purdy's percentage tubes and acidulated solution of barium chloride as described.

See APPENDIX for more accurate quantitative analysis of preformed and ethereal sulphates.

MISCELLANEOUS INORGANIC CONSTITUENTS.

**Ammonia:**—Free ammonia occurs in the urine in traces, which are greatly increased by the putrefactive changes.

**Calcium** occurs in the urine for the most part as phosphates. (See Phosphates).

**Carbon** occurs in combination in the urine, forming *carbonates. Carbonates* and *bicarbonates* of sodium, ammonium, calcium, and magnesium are present in minute quantities in fresh urine of alkaline reaction, derived from fruit and vegetable acids. Form deposits on standing. Calcium carbonate is a rare constituent of calculus. Detection: Add an acid to the urine and pass the gas given off into lime-water, which becomes turbid. (See Sediments).

**Carbonic acid,** as a gas, occurs in normal urine in the proportion of from 4 to 9 volumes of free gas; 2 to 5 combined.

**Fluorine,** in small quantity, is said to be present in urine.

**Iron** occurs in normal urine in small quantities, but in what form is yet unknown.

**Nitric acid:**—This *inorganic* substance in combination forming *nitrates* occurs in small quantities in the urine, probably originating from the drinking-water and the food. Meat diet diminishes and vegetable increases. The average amount is about 42.5 milligrammes per liter. In decomposing urine *nitrites* may be found. Schäffer's test (potassium ferrocyanide and acetic acid) is sufficient for qualitative research; Trommsdorf colorimetric method for quantitative.

**Nitrogen:**—The *free gases* of the urine are chiefly carbonic acid, oxygen, and nitrogen, which are in small proportion and may be withdrawn by the air-pump. *Nitrogen in combination* is found in urea, uric acid, kreatinin, hippuric acid, etc.

**Oxygen** may occur free, in small quantities, in urine, from which it may be withdrawn by the air-pump.

**Peroxide of Hydrogen,** $H_2O_2$, inorganic, has been found in traces in fresh urine, disappearing as decomposition sets in. Tincture of indigo and dilute solution of ferrous sulphate serve as a test, the color of the indigo being discharged by the peroxide.

# CHAPTER XXIV.

## ABNORMAL CONSTITUENTS OF URINE; PROTEIDS.

The proteids found in urine are the following:

Serum-albumin;
Serum-globulin (paraglobulin);
Albumoses [peptones];
Fibrin;
Hæmoglobin;
Histon;
Nucleo-albumin (mucin);

In addition to these, egg-albumin may be found after diet rich in eggs.

### SERUM-ALBUMIN.

**Synonyms.** German, *Albumin*, *Eiweissstoff*; French, *Albumine.*

**Chemical Constitution:** The formula is not known. It belongs to the true albuminoid substances which do not contain phosphorus except as calcium phosphate. It contains carbon, hydrogen, nitrogen, and oxygen. Rich in sulphur.

**Occurrence:** It occurs in the urine only in solution, never in the sediment. Probably does not occur at all in normal urine except in mere traces.

**Form:** It belongs to the colloids, uncrystallizable, and does not penetrate animal membranes under normal conditions.

**Properties:**—Serum-albumin is soluble in water, dilute acids, and alkalies. Solutions of serum-albumin have a specific rotatory power of —56°, and are coagulable at temperatures of from 50° to 90° C., (122° to 144° F.) according to the solvent. Solutions of serum-albumin are precipitated by the addition of large quantities of mineral acids or by metallic salts, as silver nitrate, mercuric chloride, etc. Also by alcohol but not by sodium chloride or sodium carbonate.

Serum-albumin resembles closely egg-albumin differing, however, in two respects (*a*) it is not coagulated by ether (*b*) when coagulated by heat it is more readily soluble in excess of nitric acid than is egg-albumin. Albumin is converted into *alkali-albumin* by the action of alkalies, as sodium or potassium hydroxides, and into *acid-albumin* by the action of acids, as hydrochloric and acetic.

**Reactions:**

1. Alcohol precipitates serum-albumin from urine containing it.

2. Nitric acid added drop at a time precipitates albumin, but the precipitate disappears on shaking after addition of each drop, until a certain amount of acid has been added, after which the precipitate is not dissolved by shaking; but when great excess of acid has been added the precipitate is dissolved.

3. Boiling the urine coagulates albumin in it, if the urine be acid, *not if alkaline.*

4. Acetic acid, citric acid, and vegetable acids generally do *not* precipitate albumin.

5. Boiling the urine previously acidified with acetic acid will coagulate the albumin, *provided the acetic acid is not in excess.*

6. Boiling the urine, previously acidulated with acetic acid, and to which strong solution of common salt or sulphates of sodium or magnesium have been added, will coagulate the albumin.

7. Albumin is precipitated from urine containing it, without heating, on addition of potassium ferrocyanide solution and strong acidulation with acetic acid.

8. Albumin is precipitated from urine containing it by a great number of solutions, as for example, those of chromic acid, picric acid, potassio-mercuric iodide, sodium tungstate, trichloracetic acid, metaphosphoric acid, silver nitrate, etc.

Inasmuch as many of the substances mentioned above *precipitate other substances*, besides albumin, from the urine, much depends on the *method of application* of the tests, which will be described in full further on.

## CHAPTER XXV.

### A CLINICAL TEST FOR SERUM-ALBUMIN.

Too much stress cannot be laid on the importance of technique in albumin testing, especially when the physician is unfamiliar with microscopical work. I endeavor to drill my classes so that they can detect even a trace of albumin in the urine. This cannot be done by everyone readily and easily, and some few men can never be depended on to recognize albumin when present in but small quantities.

#### TECHNIQUE OF ALBUMIN TESTING.

1. *Filter the freshly voided urine.* It is important that the urine be freshly voided, because in all stale urine what seems to be a trace of albumin can be found by the test I shall now describe. It is important to filter the urine since, by filtration, sedimentary matters, interfering with the test, are removed. Moreover, it is said that in certain urines the reaction due to mucin may mislead in unfiltered urine.

In order to filter the urine, fold three small, white, cut filter papers twice, the second time at right angles to the first. Insert the papers into a small glass funnel, set the tube of the funnel into a tall, *narrow* test-tube, and pour the urine into the funnel-shaped pouch made by the filters. [I advise use of three papers rather than one, because in my experience nearly all freshly voided urine filters clear through three thicknesses of paper. More are not advisable, because, of danger of traces of vegetable albumin.]

The urine filters slowly through into the test-tube and is *clear.* Let it fill the tube *three-fourths full.* Wipe off the outside of the tube with a rag until it is entirely clean and bright. Hold the tube up to the light, and see that both tube and urine are entirely clear and transparent.

2. *Boil the upper stratum of the urine in an alcohol lamp flame.* This is done by holding the tube *by the closed end* with the thumb and forefinger of the right hand, inclining it over the flame in such a way that the latter heats the urine about half an inch from the surface of the liquid. Use an alcohol flame so as not to crack the tube by too great heat. Do not let the flame at any time touch the tube above the surface of the liquid. Nearly all beginners fail to observe this precaution, with result that the tube is decapitated, so to speak, loses the upper quarter as neatly as if chopped off.

Boil *thoroughly* thirty seconds, removing from flame whenever the urine threatens to boil over, but do not boil the lower half of the urine at all.

3. *Add three to six drops of twenty per cent acetic acid to the boiling urine.* Shake to and fro gently until acid and upper stratum of urine have thoroughly mixed, then boil again for, say, thirty seconds.

4. *Hold the tube against a dark background*, as the coat-sleeve, or better still, hold it *below* a window sill of a north window or any window where there is no direct sunlight.

RESULTS.

A. If albumin is present, the upper, heated, acidulated quarter, or possibly third, is now distinctly turbid as compared with the lower, cool, remaining portion of the urine. If *much* albumin is present, the whole upper third or half of the urine is milky and flocks soon begin to fall. If only a *moderate amount* of albumin is present, the upper quarter or third is cloudy. If there is a distinct turbidity which cannot be seen when the tube is held *up* to the light we call it a *plain trace.* If there is an indistinct turbidity of the same character, requiring careful adjustment of eye and background, in order to see it, we call it *a trace.* If the turbidity is faint and only seen with great difficulty we call it a *faint* or *doubtful trace.* Such faint traces may possibly be due to mucin and not to albumin at all. They may be observed in the urine of nearly all

women. [Women who have leucorrhœa are nearly always found to have anywhere from a faint to a plain trace of albumin by this test in their urine. In such cases a vaginal tampon should be used, before the urine is voided for examination, or a cleansing vaginal injection taken.]

B. If no albumin be present in the urine, nothing will be seen, the upper, heated, acidulated portion of the urine resembling the lower in appearance.

C. If the urine be of deficient acidity, it will become cloudy when heated, owing to precipitation of *earthy phosphates*. The addition of six drops of the acetic acid and gentle to and fro shaking will usually dissolve the phosphatic cloudiness, and the urine beçomes *nearly* clear, in cases when albumin is absent, but *more cloudy still* if albumin is present.

Now, in nearly all cases when the acetic acid apparently dissolves the phosphatic cloud, careful observation will show a faint haze to remain. If this haze is really faint, and is not appreciably increased by further heating, I usually assume serum-albumin to be absent. Why not, it is asked, add the acetic acid *first* to the urine before boiling? When albumin is present in small quantities in acid urine, acidifying still further makes the albumin soluble when the urine is boiled, so that there would always be need to take the reaction beforehand, and to use judgment as to the amount of acid to be added, and so on.

If now, after boiling, a cloudiness appears, which, however, apparently disappears when acetic acid is added, but if after further boiling, a cloudiness in the upper portion is now again plainly seen, a plain trace of albumin is present, which was not seen at first, owing to the phosphatic cloudiness, and may not in the end be as noticeable as was the phosphatic cloudiness. Do not mistake a ring-shaped coagulum of phosphates remaining half way down the tube for albumin. This merely means that the acetic acid has not yet reached the lowest stratum of phosphatic cloudiness. The coagulum of albumin is to be seen in the *upper* part of the tube, always, when it is present.

Lastly, in strongly alkaline urine which foams when the acetic acid is added, be not sparing of acid, for the albumin in it is alkali-albumin, and will not be fully coagulated by heat until the alkalinity is overcome by the acid. In such cases, which are not very common, if *freshly voided urine* is tested, add acetic acid, drop by drop, and take reaction of the upper quarter with blue litmus paper, continuing to add acid until the blue slip is turned bright red, then boil again.

REMARKS.

For adding the acetic acid a medicine dropper (Fig. 38) is useful. Three drops may be added to urines

FIG. 38. Medicine-dropper.

which do not become turbid on boiling, but five or six will be necessary in cases where a cloud appears with heat alone.

The object of adding acetic acid is two-fold, first, to dissolve any phosphatic cloudiness; second, to convert alkali-albumin into albumin coagulable by heat.

The advantages of acetic acid over nitric acid are two-fold, first, the acid is neither dangerous nor corrosive; second, it does not act on the coloring matter of the urine as does nitric acid. *Plain traces of albumin shown by the heat and acetic acid test appear as faint or doubtful traces when the heat and nitric acid test is used.*

DISCUSSION.

The possible sources for error in my test are mucin and resins. Kirk claims that mucin alone will answer to the test but Saundby has failed to confirm his statement. So far as my own observation goes, I find that the urine of women will sometimes show a trace by my test, which other tests, as for example, Purdy's salt and acetic acid, do not confirm, yet microscopical examination of the sediment in such cases reveals presence of leucorrhœa. It is said, moreover, that when the patient is taking tolu, balsam of Peru, etc , that heat and acetic acid will precipitate the resin. Alcohol, however, will dissolve this precipitate. For clinical purposes, therefore, I regard the test as useful, and open to less criticism than any of equal readiness, simplicity, and expense.

## CHAPTER XXVI.

### LIFE-INSURANCE TESTING FOR ALBUMIN. COLD NITRIC ACID TESTS.

In this chapter and in the one following the physician will find the tests for albumin commonly recommended to examiners by life insurance companies. Under each test will be considered the following:

1. *Technique* of the test;
2. Chances for *error*;
3. *Different methods* of applying the test;
4. Practical *objections* or *advantages*.

Since most companies still prefer the older tests—those with nitric acid, heat, or both—special prominence will be given them in these pages.

**Preparing the Urine for Examination:**—Before the urine is tested for albumin it must first be *clear*.

To make the urine clear proceed as follows:—

A. The urine is already clear or but slightly turbid and of either acid reaction or but slightly alkaline:—

*Filter through three filter papers folded together.*

In a large majority of cases this is all that is necessary, especially in the case of freshly voided urines.

B. The urine does not filter clear through three filters:—

*Shake the filtered urine with magnesia usta and filter again.* This will usually suffice to clear it.

C. The filtered urine is still turbid.

If after the operations described in "A" and "B" the urine is still turbid *add to it*, after filtering as in B, *half its volume of a ten per cent solution of potassium hydroxide* (caustic potash) *and boil.* It becomes cloudy from precipitation of phosphates. Filter and in most cases the bacterial débris which has made it turbid will be precipitated with the phosphates and will remain on the filter, the urine coming through clear.

D. The filtered urine is still turbid.

*Add to it a few drops of magnesian fluid, boil, and filter again.*

NOTE:—Magnesian fluid may be made by dissolving 100 grammes (1554 grains) each of pure magnesium sulphate and ammonium chloride in 800 c.c. (27 fluidounces) of distilled water with addition of 100 c.c. (3 fl. oz) of ammonia water.

**Different albuminous substances in urine:**—In order to avoid confusion it must be understood that the urine may contain different albuminous substances. These are:

1. **Serum-albumin** and **serum-globulin.** These occur together and are coagulated both by heat (boiling), and by mineral acids, as nitric acid.

2. **Albumoses** (propeptones), may occur with or without serum-albumin. Are coagulated by mineral acids but *not* by boiling. *Peptones* are now not thought to be present in urine.

3. **Nucleo-albumin** (mucin) may occur with or without serum-albumin; not coagulated by boiling. Precipitated by strong acetic acid, especially in diluted urine.

The term *albuminuria* is applied to the voiding of urine containing serum-albumin. *Albumosuria* to that containing the albumoses. In addition to the substances named above the urine may contain *hæmoglobin*, *fibrin*, and *histon*, which will receive special attention later on.

### A. THE COLD NITRIC ACID TEST. HELLER'S TEST.

1. **Usual method of application:**—Pour half an inch of pure, colorless nitric acid into a test-tube, hold the latter inclined as in Fig. 39 (see page 170), and let an equal quantity of *clear* urine trickle down the inside of the tube. The urine *floats* on the surface of the acid.

**Results:**—If serum-albumin is present a *sharply-defined* zone of *whitish* color will be observed at the point of contact between the acid and the urine, becoming more or less pronounced according to the amount of albumin present. If but little albumin is

present, it may be necessary to hold the tube against a dark back-ground, as the coat-sleeve, in order to see the zone.

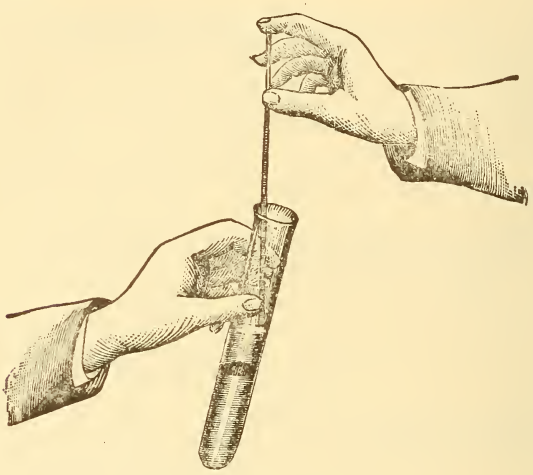


FIG. 39. Nitric acid test.

If no zone be seen, set the tube aside for half an hour or more. *A trace* of albumin may then be seen which is not visible at first.

**Chances for error:**

1. *A generally diffused haziness does not* indicate albumin. If the latter is present a distinctly and clearly-formed white *ring* is seen, provided the test be carefully performed without too hasty pouring of urine into acid.

2. A cloudiness *not at point of contact* but *higher up*, more diffused and spreading downward is *not* albumin, but due to precipitation of *urates* especially in urines of high specific gravity. In case of doubt perform the test again as follows: Dilute the urine with two or three times its volume of water, warm the nitric acid before adding the urine and now no cloud will be seen, if the previous cloud was due to urates.

3. A light cloudiness *near the surface* of the urine is *not* albumin but due to *nucleo-albumin* (mucin).

4. In all urines a *transparent zone of color*, more or

less intense, appears. This is *not* albumin but due to oxidation of the normal chromogens of the urine by the acid. The color is violet, reddish, or brownish, and its transparency can be observed by holding the tube up to the light.

5. A zone of slowly forming *crystals* may be observed in urines of high specific gravity containing 3 per cent or more of urea. The crystals are *nitrate of urea* and will not form if the test be tried again with dilute urine and warm acid as in 2.

6. A *yellowish-white zone*, less plainly defined than the albumin ring may be due to precipitation of certain resinous bodies, such as those contained in turpentine, balsam of *copaiva*, tolu, storax, cubebs, salicylic acid, etc., taken by the patient. Shake the urine-acid mixture with alcohol, which will dissolve the resins but not affect coagulated albumin.

7. If *blood* is present, the albumin ring will be colored *brown-red;* if bile, *greenish* or blue.

FIG. 40. Albumin tester.

8. If the nitric acid contains *nitrous acid* as an impurity, bubbles will rise, even in acid urine, and may obscure the rings. These bubbles are probably due in acid urine to decomposition of urea by nitrous acid. In alkaline urine the bubbles are due to carbon dioxide liberated from carbonates present by action of the acid, and will hence always be seen even if the nitric acid be free from nitrous acid, and no decomposition of urea take place.

**Different methods of applying the test:**

1. The Truax-Greene albumin tester:—By use of this instrument (Fig. 40) the various rings are seen better than when a test-tube is used.

2. The use of *conical glasses.* C. E. Simon recommends the use of conical glasses as follows:

About 20 c.c. (5 fluidrachms) of the clear urine are poured into one of the glasses and from 6 to 10 c.c. (1½ to 2½ fluidrachms) of nitric acid added by means of a pipette which is carried *to the bottom* of the vessel, when the acid is slowly allowed to escape by diminishing the pressure of the finger on the tube.

**Results:**—If *albumin* is present a whitish ring is seen from below upward at the zone of contact. If albumin is small in amount, the upper border, in time, though at first as well-defined

as the lower, becomes less so, the cloudiness extending upward in the form of small, irregular columns.

If **excess of uric acid** is present, after 5 or 10 minutes a distinct ring appears *from above downward* in the clear urine, about 1 to 2 centimeters (¾-inch to an inch) *above* the zone of contact. The degree of excess is indicated by the size of the ring.

If **uric acid is deficient** the ring above the zone of contact does not appear within 5 or 10 minutes.

If **excess of urea** is present an appearance like hoar-frost is seen on the sides of the glass. In such a case urea is 25 gm. per liter (12 grains per ounce) or more. When not less that 45 gm. per liter (22 grains per ounce) are present, spangles are seen. When urea is 50 gm. per liter (25 grains per ounce) or more, a dense mass of the urea nitrate may be seen to separate.

If the **urinary pigment** is normal, a transparent colored ring is obtained, of peach-blossom red, varying in tint from a faint rose to a pronounced brick color.

If *urobilin* is present a color ring like the above will be seen but the tint is *mahogany*.

If **indican** is present, a more or less violet-colored ring is seen *above* the peach blossom ring of normal color. The color of the indican ring varies from light blue to deep indigo according to the amount of indican present.

If **bile** be suspected, add a little nitrous acid to the nitric and a series of colors will be noticed *from above downward*, yellow, green, blue, violet, and red, of which the *green* is characteristic. Bile absent, no green.

NOTE:—Nitrous acid may be readily made by boiling a piece of wood with the nitric acid.

If **albumin and bile** together are present the bile color-play is beneath the albumin ring.

If **albumin, globulin**, and the *albumoses* are all present there is a cloud at the zone of contact as in case of albumin. If no cloud, probable absence of all three.

If **albumoses** alone are present, remove the cloudy urine (precipitated by the acid as above) with a pipette and heat. Urates are dissolved by gentle heat, albumoses by a higher temperature, reappearing on cooling while the urine turns *yellow*.

If **albumin and albumoses** together are present, the yellow color is noted as above, but the urine is only partially cleared by heat.

If **resins** are present, the turbidity produced by nitric acid is cleared by alcohol.

3. **Alexander's Method.** To distinguish albumin, nucleo-albumin (mucin), and resins Alexander proceeds as follows: Three glasses are used and into each is poured 8 or 10 c.c. of urine:—To the first glass is added 2 or 3 drops of hydrochloric acid; if *resins* are present a red-violet coloration is seen when the mixture is heated. To the second glass is added strong acetic acid:—a precipitate insoluble in excess, indicates *mucin*. To the third glass after heating is added half its volume of nitric acid: a turbidity indicates *albumin*.

## Practical advantages and disadvantages:—

1. Heller's test is a very convenient and simple one for clinical purposes.

2. It is said to precipitate $\frac{1}{500}$th of one per cent of albumin.

3. It precipitates various albuminous substances, resins, urates, urea (excess), and oxidized chromogens, but not phosphates, true peptones, or vegetable alkaloids.

4. The chief practical objection to it is the corrosive character of the nitric acid.

### B THE NITRO-MAGNESIAN TEST

1. **Preparation:** — Saturate distilled water with chemically pure magnesium sulphate, filter, and to the clear filtered liquid add nitric acid.

NOTE:—The amount of nitric acid used varies according to those who use this test. Dr. Roberts uses 1 volume of nitric acid to 5 of magnesium sulphate solution. Others use 1 of nitric acid to 2 of the magnesium sulphate. Some examiners prefer *equal parts* of acid and magnesium solution.

2. **Method of application:**—The contact method as in case of Heller's test.

3. **Advantages and disadvantages:** — The test is said to be as delicate as Heller's while the liquid is less corrosive. It is however, a more delicate test for nucleo-albumin and the ring of the latter is nearer the chemical fluid than in Heller's test.

# CHAPTER XXVII.

## LIFE INSURANCE TESTING FOR ALBUMIN—CONTINUED. HEAT TESTS.

Among the most important tests for albumin we find:—

### C. THE HEAT AND NITRIC ACID TEST.

This test was the first ever used for albumin in the urine by Cotugno in 1770. The urine is boiled and nitric acid is added to it. It is performed in several ways:—

Method I:—Fill a test-tube half full of clear urine, hold it with a test-tube clamp, boil, and add one-tenth its volume of nitric acid.

**Results:**—If any cloudiness, coagulum, or precipitate is seen after boiling and addition of nitric acid, albumin is present.

Method II:—Boil about an inch of the clear urine in a test-tube and add 2 or 3 drops of ten-per-cent nitric acid solution. If, after a few moments, there is no cloudiness, coagulum, or precipitate, boil again, add ten drops more of the dilute nitric acid and set aside. A trace of albumin may become visible after an hour or so, not seen at first.

Method III:—Clarify the urine by addition of a few drops of potassium hydroxide solution, boiling, and filtration. Fill a test-tube half full of it and add 15 to 18 drops of strong nitric acid. If the urine contain albumin it will become somewhat cloudy. Boil and let stand half an hour. There will be seen a sediment of whitish flakes or granules. Boil again, when if albumin be present, the flakes will *not* be dissolved by the second boiling.

#### DISCUSSION.

Authorities are not agreed as to the best method of performing the heat-and-nitric-acid test. Those who employ method I. do so

because (1) *too small* an amount of nitric acid may dissolve coagulated albumin, hence add to the urine one-tenth its volume of acid and not less; (2) *too large* an amount of the acid may also dissolve the albuminous coagulum to a certain extent, hence use not more than one-tenth its volume of acid.

**Chances for error:**—1. While the urine is hot, albumoses, urates, and vegetable alkaloids are not precipitated by this test. Urine rich in urates may on cooling, precipitate a pinkish-red sandy precipitate of uric acid.

2. The resins, thymol, etc., are precipitated by this test, but the precipitate is soluble in alcohol. The latter should not be added until the urine cools for fear of *explosion*.

3. When only a trace of albumin is present the characteristic appearance is either the formation of a few flakes of coagulated albumin or of a general turbidity which finally results in a fine flocculent separation, persisting when the solution is hot, and rendered more pronounced by the addition of alcohol.

4. If albumoses are present, the urine turns distinctly yellow after addition of nitric acid, and, on cooling, a whitish precipitate appears.

5. Faint hazes may be due to nucleo-albumin (mucin). See *differential testing* further on.

### D. HEAT AND ACETIC ACID TEST.

The writer advises that this test be used as described under the "Clinical Test," in Chapter XXV, namely, boiling the upper third and adding acetic acid.

If the acetic acid be added *drop by drop* after boiling, there is little or no danger that the albumin will be dissolved by excess. Resins may be excluded by use of alcohol. So far as the writer has been able to observe the chief chance for error is due to precipitation of what is probably nucleo-albumin (mucin). In case a slight cloudiness is obtained, not by heating, but only after addition of *several* drops of acid and further boiling, it may be well to try the following:

### E. ACETIC ACID AND HEAT TESTS.

I. Purdy raises the specific gravity of the urine 10 or 15 degrees by addition of a little saturated solution of common salt, filters clear, and to a test-tube two-thirds full of urine add 1 or 2 drops of 50 per cent acetic acid, and boils the upper third. He claims—and with reason I think—that by this test mucin is not coagulated, since this body is soluble in a strong solution of common salt.

II. Heynsius acidulates the clear urine strongly with acetic acid, then adds a few c.c. (about one fluidrachm) of saturated solution of common salt. The urine is then boiled, when a flocculent precipitate indicates presence of albumin.

III. The clear urine may be treated with *a few drops* of acetic acid until a *distinctly acid* reaction is obtained, and then *one-sixth* its own volume of a saturated solution of sodium chloride, magnesium sulphate, or sodium sulphate added. On boiling the urine a precipitation of even minimal amounts of albumin will take place.

### CHEMICAL EXERCISE XII.

1. To one volume of albuminous urine add six volumes of water. Mix well, fill a test-tube half full of the mixture, add a drop or two of nitric acid and shake: *albumin will be precipitated but will redissolve on shaking.* Keep on adding nitric acid, drop by drop, until finally the precipitated albumin is not dissolved.

This experiment shows that in dilute albuminous solutions a small quantity of nitric acid does not completely precipitate the albumin. In urine the neutral salts help small quantities of the acid to precipitate the albumin, but it is not safe to rely on the use of two or three drops.

2. Boil a sample of albuminous urine of *acid* reaction: a cloudiness appears which is undissolved by either acetic or nitric acid.

3. Boil a sample of albuminous urine to which liquor potassæ has been added: the urine becomes turbid: filter; boil again. The urine remains clear. Now add acetic or nitric acid in quantity sufficient to overcome the alkalinity and an abundant whitish coagulum of albumin appears. The first turbidity was due to precipitation of the phosphates. After filtering, although the urine was boiled, no coagulum of albumin appeared because the liquor potassæ had converted the albumin into what is called *alkali-albumin*, not coag-

ulated by heat. Addition of acid, however, broke up the alkali-albumin and then the albumin was coagulated by heat.

4. Let a sample of abundantly albuminous urine grow stale and ammoniacal. It will then be seen on boiling that only a slight turbidity due to phosphates appears, but on addition of acid, albumin will be coagulated and an abundant precipitate appear.

5. Filter a sample of acid urine containing but little albumin, fill each of the two test-tubes $\frac{3}{4}$ full of it and boil the upper third of each. To one add 15 to 30 drops of nitric acid after boiling, and to the other 2 or 3 drops of acetic acid. Which shows the precipitated albumin the plainer?

6. Compare either or both of these tests with the cold nitric acid test, using (*a*) the Truax-Greene apparatus, (*b*) a test-tube and pipette and (*c*) conical glasses and pipette.

7. To 10 c.c. of a sample of albuminous urine of *acid* reaction add 5 c.c. of 20 per cent acetic acid, boil, and compare with other samples to which acetic acid is added *after* boiling in various amounts.

# CHAPTER XXVIII.

## LIFE INSURANCE TESTING FOR ALBUMIN.—*Continued*

### THE FERROCYANIC AND TRICHLORACETIC TESTS.

**F. The ferrocyanic test:**—There are several methods of applying the ferrocyanide test, as follows:

METHOD I:—Make a solution of chemically pure potassium ferrocyanide, 10 grammes in 200 c.c. of distilled water (155 grains in 7 fl. oz.) Into the bottom of a *clean* test-tube pour 15 to 30 drops of acetic acid (30 per cent), then add two or three times that amount of the ferrocyanide solution and shake. The mixture should remain clear. Now add clear filtered urine, and if albumin be present it will be precipitated throughout the whole volume of the urine in the form of a more or less milk-like flocculent cloud, according to the quantity of albumin present.

METHOD II:—Fill an ordinary test-tube half full of clear filtered urine and add 3 or 4 c.c. (a fluidrachm or so) of the ferrocyanide solution. Mix thoroughly and add 10 or 15 drops of acetic acid, and, if albumin is present, a cloudiness or coagulum will be plainly seen.

METHOD III:—A few c.c. of urine are *strongly* acidulated with acetic acid (sp. gr. 1064). If (*a*) there is no turbidity, further add a few drops of a 10 per cent solution of potassium ferrocyanide, when if albumin be present, either a faint turbidity or a precipitate, according to quantity of albumin present, will be seen. Compare with tube containing clear filtered urine, both tubes being held against a dark background.

If (*b*) there is a turbidity seen on addition of the acetic acid alone (urates or mucin), the urine to which the acetic acid has been added should be filtered and diluted before the ferrocyanide is added.

METHOD IV:—The test by *contact* is as follows: To five cubic centimeters (one and a third fluidrachm) of 30 per cent acetic acid add five drops of the ferrocyanide solution, and cause the mixture to trickle down the side of a test-tube in which are 5 c.c. of clear filtered urine. A white ring at the surface of contact between the two fluids indicates the presence of albumin.

CHANCES FOR ERROR.

1. The ferrocyanide solution should be freshly made in pure distilled water, filtered clear, kept in a clean bottle, with a clean stopper, away from the light.

2. It is well to see that the acetic acid and the ferrocyanide solution when mixed together *without urine* remain clear.

3. The writer has noticed that, if the acetic acid be added from a pipette with a *rubber nipple*, a cloudiness or precipitate sometimes takes place. If pipettes are used they should be all glass.

4. Heating will cause a precipitate in the mixture without addition of urine.

5. When the amount of albumin is very small, cloudiness is not seen immediately after adding the urine *but only after a few minutes* have elapsed.

6. The ferrocyanide test precipitates albumin, globulin, acid and alkali-albumins, albumoses; nucleo-albumin from bile is said to be precipitated by it.

7. Urines of high specific gravity should be diluted with water lest albumin and albumoses be not precipitated.

8. Removing the coagulated substance with a pipette, and boiling it, will tell whether it is albumin or albumoses, since the latter clears when boiled and reprecipitates on cooling.

Partial clearing on boiling indicates a mixture of albumin with albumoses, but some care during the process is necessary, since boiling decomposes the ferrocyanide solution and makes it cloudy. The best way to manage it is to let the precipitate settle thoroughly, decant supernatant liquid, add water, let settle again, and remove with the pipette. This can be done rapidly by the use of the centrifugal machine.

**G. The Trichloracetic Acid Test:**—Trichloracetic acid, $CCl_3.COOH$, is a substance derived from acetic acid by treatment with chlorine in sunlight or by oxidizing chloral with nitric acid.

It is a monobasic acid, $HC_2Cl_3O_2$ and occurs in commerce in the form of *crystals*.

**Method of application:**—Make a saturated solution of the crystals, (half an ounce in an ounce of distilled water) and by means of a pipette carry 1 or 2 c. c. ( 16–32 minims) to the bottom of a test-tube containing the clear filtered urine so as to form a layer beneath the urine. If albumin be present, a *white ring* will be seen to form at the zone of contact between the two fluids, varying in intensity with the amount of albumin present.

**Chances for error:**—

1. Albumoses are precipitated but disappear upon boiling, to reappear on cooling.
2. Dilution of the urine prevents mistake which may be due to precipitation of urates; heat also serves to distinguish these substances.
3. Alkaloids, if precipitated, are soluble either by heat or by large excess of the reagent.

**Advantages:**—

1. This test will demonstrate albumin in urines in which the more common tests yields negative results but in which tube-casts may nevertheless be found.
2. Although showing 1 part of albumin in 100,000 of urine, the test is not so delicate as to demonstrate traces of nucleo-albumin in all urines.
3. Trichloracetic acid will detect albumin which has escaped observation on account of being dissolved by acetic acid, and not precipitated by picric acid or by heat.
4. No color rings are formed in the urine when this test is used.

# CHAPTER XXIX.

## MISCELLANEOUS TESTS FOR ALBUMIN

Inasmuch as different teachers prefer to teach medical students different tests I subjoin a list of a number of albumin tests with the hope that it will include all in common use.

**Acidulated brine test:**—This test as performed by Roberts is as follows: Make a saturated solution of sodium chloride and mix one pint of it with one fluidounce of strong hydrochloric acid (500 c.c. with 30 c.c.). Filter and apply by contact method, floating the urine on the reagent.

**Chromic acid test:**—Mix one part of a five per cent solution of chromic acid with three parts of urine in a test-tube. If albumin is present a cloudiness appears. If the mixture remain clear, boil the upper portion and a slight trace of albumin will be thus detected by cloudiness appearing in the heated portion. The chromic acid must be chemically pure, and the distilled water used for dissolving it also free from impurities.

**Metaphosphoric acid,** Hindenlang's test:—Into the clear filtered urine drop a fragment of metaphosphoric acid and, if albumin be present, a white precipitate is formed.

**Picric acid test:**—Make a saturated solution of picric acid, 6 or 7 grains to the ounce, of boiling distilled water. Float two inches of the reagent on a column of urine four inches deep. As far as the yellow color extends the coagulated albumin renders the mixture turbid. Albumin, peptone, mucin, urates, albumose, kreatinin, vegetable alkaloids, and piperazine are all precipitated. Hence add solution of citric acid (20 gm. per liter) first filter to eliminate mucin, then add picric acid, and carefully heat the precipitate formed. If albumin is present heat does not dissolve the coagulum as in the case of other bodies. The heat must not be too great or other precipitates will be formed.

Piperazine picrate is crystalline and disappears on heating.

**Potassio-mercuric iodide test:**—This test is performed with what is known as Tanret's solution, potassium iodide, 3.32 grammes; mercuric chloride, 1.35 grammes; acetic acid, 20 cubic centimeters; distilled water to make 100 cubic centimeters. Dissolve the two salts separately and then mix the solutions, add the acetic acid, and make up the whole to 100 c.c. with distilled water. Apply by contact method, floating the urine on the reagent. Gentle heat distinguishes albumin, pine-acids, and mucin from possible precipitates of albumoses and vegetable alkaloids.

**Phenic-acetic-acid test:**—This test as used by the late Dr. Millard of New York is performed with the following solution:

Glacial carbolic (phenic) acid, 95 per cent, 2 fluidrachms; acetic acid, C. P., 7 fluidrachms; liquor potassæ, 6 fluidrachms. Float the urine on the reagent. Heat distinguishes albumin, mucin, and pine-acids from albumoses and alkaloids.

**Platinocyanide of potassium:**—Same as the ferrocyanide test, and has the advantage of being a colorless solution.

**Sulphocyanide of potassium:**—Take 100 c.c. of a ten per cent solution of sulphocyanide of potassium and 20 c.c. of acetic acid, and add a few drops to the urine to be examined. If it contains the smallest quantity of albumin, a distinct cloudiness is at once obtained; if the urine contain much albumin a thick white precipitate is obtained. Any excess of the reagent has no effect. All normal urines, that is to say, such as are not affected by ferrocyanide of potassium and acetic acid, give negative results with this reagent. By successive dilutions of urine containing albumin it is found that this reaction is more delicate than ferrocyanide of potassium and acetic acid. It possesses the advantage of being colorless, so that the least cloudiness is more manifest than when ferrocyanide is used. Succinic acid may be substituted for the acetic acid. If to albuminous urine sulphocyanide of potassium and a little succinic acid be added, a distinct cloudiness is obtained, while normal urine remains clear.

This reaction possesses the advantage of being easily carried about, the sulphocyanide of potassium and the succinic acid being solid. If these reagents be mixed in equal proportions, and a small portion of the mixture be added to albuminous urine, an immediate cloudiness results with the smallest quantity of albumin.

**Reaction of albumin with perchloride of mercury and acetic acid:**—If a few drops of a ten per cent solution of perchloride of mercury be added to albuminous urine a distinct cloudiness is obtained, while in normal urine the cloudiness is hardly visible, except in very exceptional cases. If to the urine so rendered cloudy by perchloride of mercury, a few drops of acetic acid be added the precipitate disappears if it is not composed of albumin. On the contrary, if the urine contains albumin, the precipitate persists. A mixture of one part of acetic acid and a ten per cent solution of perchloride causes only a cloudiness when there is albumin in the urine; this appears immediately on the addition of the reagents and does not form a deposit, while the addition of the sublimate alone causes one. Peptones give no reaction with these agents in the proportions above indicated. The same applies to uric acid, urea, phosphates, and sugar. Further, very concentrated urine does not become cloudy on the addition of the sublimate and acetic acid.

**Spiegler's test for albumin:**—Spiegler's very delicate test for albumin in urine consists of a test solution composed as follows: Perchloride of mercury, 8 grams; tartaric acid, 4 grams; sugar, 20 grams; distilled water, 200 grams. The sugar serves to raise the specific gravity of the liquid to 1060, which is higher than that of nearly all urines. It is used by placing some of it in a test-tube, and gently adding some of the urine to be tested. If albumin is present a ring will form at the junction of the two liquids. The reaction will not take place in solutions of egg or serum-albumin save in the presence of chlorides.

**The sulpho-salicylic acid test:**—This test was first described by Reoch, and used independently by MacWilliam. It is said to

show traces of albumin in a dilution of 1 to 50000. Sulpho-salicylic acid, $C_7H_6SO_6 = C_6H_3.SO_3.H(OH)\ COOH$, is a white, crystalline substance, made by heating salicylic acid with concentrated sulphuric acid. It precipitates all proteids. It may be used either in form of a saturated solution, or by adding some of the crystals to a small quantity of filtered urine in a test-tube. In the latter case the tube should be shaken. If albumin is present in acid urine, a cloudiness or white homogeneous precipitate, according to the amount of proteid present, appears. *Uniform opalescence* is characteristic of this test. The test must be supplemented by heat to the boiling point, in order to distinguish the the serines from the albumoses, the latter being dissolved by heat as in the urine of the third stage of pneumonia, and the first passed after ejaculation of semen. The urine must be acid, or the test fails. Sulpho-salicylic acid gives no mucin reaction in normal urine, but only when larger quantities of mucin are present.

**Sodium tungstate** (Oliver's Test):—Mix equal parts of a 1 to 4 solution of sodium tungstate and saturated solution of citric acid. Apply by contact. Albumoses, mucin, and occasionally urates are also precipitated, but heat clears all but mucin and albumin.

**Jolles's test:**—This is said to detect 1 part albumin in 120.000 of water. The constituents are mercuric chloride, 10 grams; succinic acid, 20 grams; sodium chloride, 10 grams; water 500 c.c.

**Sharp's test:**—Dr. Sharp substitutes glycerol for the sugar in Spiegler's test.

**Tanret's reagent:**—Potassium iodide, 3.32 gm.; mercuric chloride, 1.35 gm.; acetic acid, 20 c.c.; distilled water, q. s. 100 c.c.

**Millard's reagent:**

| | |
|---|---|
| 95 per cent carbolic acid | f ʒ ij |
| Glacial acetic acid | ʒ vij |
| Liquor potassæ | ʒ xxij |

Mix.

## CHEMICAL EXERCISE XIII.

For five or six consecutive exercises the student should test urines for albumin, using *some one test*, until thoroughly familiar with it. The author advises either the heat and acetic acid, or heat and nitric acid tests to be used first. After familiarity with one or the other of these is gained, try either the trichloracetic acid test, the ferrocyanic test, or the sulpho-salicylic acid test.

## CHAPTER XXX.

### THE QUANTITATIVE DETERMINATION OF ALBUMIN IN THE URINE.

Clinical methods only will be considered in this chapter. A favorite one involves use of the *Esbach tube* (Fig. 41), which is a specially constructed tube which has an upper mark R, a second mark below it, U, and the figures 7, 6, 5, 4, 3, 2, 1, one above the other, indicating graduations of the tube, in parallel lines, beginning just below U, and going down to nearly the bottom of the tube. Between the mark 1 and the curved bottom of the tube is a short mark, not numbered, which is ½ of 1.

Fig. 41. Esbach tube.

In order to use the tube, first add eight or ten drops of the 20 per cent acetic acid to, say, half a fluid ounce (15 c.c.) of the urine to be tested, mix well, and pour the mixture into the tube until the latter is filled to the line indicated by the letter U. Then fill to the mark R with Esbach's reagent, a liquid made by dissolving 155 grains (10 grams) of picric acid and 310 grains (20 grams) of citric acid in 30 fluid ounces (900 c.c.) of distilled water and, after solution is accomplished, adding enough distilled water to make the total one litre (1.05 quart, or a little over 33 fluid ounces). The solution should be made in cold water and the chemicals powdered in a mortar before solution is attempted.

After the yellow reagent fluid has been added, close the mouth of the tube with the thumb, and invert a dozen times without shaking. Then close with a rubber cork and let settle for 24 hours. The precipitated proteids, if present, settle down to the bottom

of the tube, and the height of the deposited mass may be measured by the lines, 1, 2, 3, 4, etc., on the outside of the tube. The inventor, Dr. Esbach, claims that these lines indicate percentages of albumin *by weight*, *viz.: 1-10*, *2-10*, *3-10*, *etc.*, *of one per cent by weight.* These figures must be carefully distinguished from the old-fashioned method of reckoning albumin roughly *by bulk*, namely, 10 per cent, 20 per cent, etc., after boiling with heat and nitric acid. One per cent of albumin *by weight* is a very large quantity, but one per cent *by bulk* is an exceedingly small quantity, not much more than a plain trace. The Esbach tube is graduated so as to express percentages by weight, not bulk, and this must not be forgotten. I have, however, for clinical purposes, discarded reckoning by the Esbach tube save in the following way:

1. The precipitated proteids settle down below mark 1, *albumin is small in quantity.*

2. The precipitated proteids settle down below 3 but above 1, *albumin is moderate in quantity.*

3. The precipitated proteids settle down to any figure or letter above 3, *albumin is abundant*, very large in quantity if 5 to 7, enormous if much above 7. In such cases dilute the urine with an equal volume of water and multiply. In general it is better to dilute the urine, so that its specific gravity does not exceed 1008. It is said that albumoses and kreatinin are precipitated by the Esbach liquid, and a crop of uric acid crystals is often seen.

**Separation of albumin and globulin:**—First determine the total proteids by use of Esbach's albuminimeter, then saturate another portion of the urine with magnesium sulphate, filter, and determine the albumin in the filtrate with the Esbach tube again. The difference in the two results represents the amount of globulin precipitated by the magnesium sulphate, but allowance must be made for increase in the volume of the urine caused by saturation with the sulphate.

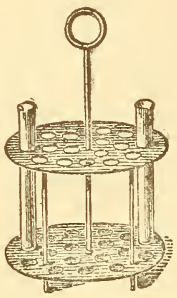


FIG. 42. Rack.

For a rack in which to set Esbach tubes the writer finds the metallic one (Fig. 42), convenient, since the Esbach tubes are too large to fit the apertures in many of the test-tube racks used.

For the determination of small quantities of albumin the original Esbach tube is not well suited. Dr. Hayward, of Liverpool, has modified the tube so that the base is conical, instead of round, by which means a small bulk of albumin may be measured.

**Determination of albumin by use of percentage tubes:**—Dr. C. W. Purdy, of Chicago, has our thanks for devising percentage tubes for the determination of albumin. They are the same as those already spoken of under chlorides (Fig. 35), and may be used either with or without the centrifugal machine. When the electric centrifuge is used, the determinations may be made at a definite speed for a definite time, for example, at 1000 revolutions per minute for five minutes. Purdy directs that a percentage tube be filled to the 10 c.c. mark with filtered urine, 3.5 c.c. of a 1 in 10 solution of potassium ferrocyanide added, and the mixture shaken, then 1.5 c.c. of 30 per cent acetic acid solution poured in, and the whole mixed thoroughly. Let stand 20 minutes and settle in the centrifuge. Settle for five minutes at a speed of 1000 revolutions, or till no further decrease in bulk of the precipitate occurs. Results are expressed in terms of *bulk*, not weight. If the sediment, for example, settles down to the mark 2 c.c , we have 20 per cent by bulk. If to the second small line, 2 per cent bulk.

These percentages do *not* correspond to percentages from boiling.

## CHEMICAL EXERCISE XIV.

### THE WRITER'S EXPERIMENTS IN DETERMINING BULK PERCENTAGES OF ALBUMIN.

Collect the twenty-four hours' urine of an albuminuric patient, filter a few hundred cubic centimeters of it, and for all experiments use 10 c.c. of this filtered urine, and a speed of 1,000 revolutions per minute in the centrifuge for five minutes. To different samples of the filtered urine add the following reagents respectively:

1. Purdy's ferrocyanic mixture as previously described.
2. Five c.c. of the Esbach fluid, previously acidulating the urine with 3 to 10 drops of 20 per cent acetic acid, according to reaction.
3. Boil the urine and then add 3 to 10 drops of 20 per cent acetic acid.
4. Boil the urine and add 20 drops of nitric acid.
5. Add 0.2 gm. of trichloracetic acid.
6. Add 2 gm. of trichloracetic acid—(solubility in excess).
7. Add 0.2 gm. of sulpho salicylic acid.
8. Add 2 gm. of sulpho-salicylic acid.
9. Add 0.2 gm. of metaphosphoric acid.
10. Add 2 gm. of metaphosphoric acid.
11. Add 5 c.c. of Oliver's sodium tungstate solution.

12. Add 5 c.c. of Jolles's test solution.
13. Add 5 c.c. of Tanret's reagent solution.
14 Add 5 c.c. of Millard's test solution.
15. Add 5 c.c. of Spiegler's test solution, or of the Spiegler-Sharp test liquid, etc.

All sorts of variations may be tried, especially in the way of adding small quantities of each reagent, and comparing results with those obtained by using an excess of the reagent. The difference in bulk between coagulated and precipitated albumin may be shown. The effect on the sediment of higher speed should next be shown, each sediment being subjected to a speed of 1,700 revolutions a minute for five minutes. It will be found that no two of the bulks will exactly agree, and that between the abundant precipitated bulk where the Esbach fluid is used, and the small coagulum obtained by heat and acetic acid, there is a marked difference in percentage.

The student will notice peculiarities of specific gravity and density, for example, the precipitate obtained by the ferrocyanic test is lighter apparently than that of some of the others. A small percentage, say 3, obtained by the ferrocyanic test at 1,000 revolutions can be reduced one-half by a speed of 1,700. If the quantity of proteids is very large, heat and acetic acid, or 0.2 gm. of sulpho-salicylic acid produce a denser sediment of smaller bulk than do the ferrocyanic, trichloracetic, or Esbach tests, at a speed of 1,000. When the amount of albumen is large, a speed of 1,700 for 15 or 20 minutes may be required to settle the precipitate properly.

Subject all the precipitates, settled at a speed of 1,000 per minute, to one of 1,700 per minute for 5 minutes and note which ones shrink in volume, and how much. Now pour off the supernatant urine in every tube (which can readily be done without losing any of the sediment), fill up to the 15 c.c. mark with cold, distilled water, shake well until all the sediment is dislodged, using a knitting needle or a small glass rod for stirring purposes, and settle again at a speed of 1,700 for five minutes. It will be found that this procedure reduces the percentage bulk of some of the sediments. Pour off the supernatant cold water and add hot water (above 150° F.), shake and stir as before, and settle while still warm at a speed of 1,700 revolutions. It will be seen that hot water reduces the bulk percentages materially in some cases. Let cool and after stirring and shaking, settle again at 1,700 and it will be found that, in some cases the proteid is *not* reprecipitated, on cooling, to its full previous bulk.

### CLINICAL NOTES ON AUTHOR'S CASES.

1. In a case of persistent albuminuria without other symptoms, and with but few casts in the urine, determination of the quantity of albumin, by the different reagents mentioned above, showed the following: Two examinations of the 24 hours' urine, made two weeks apart, showed about 4 per cent bulk of albumin by the heat and acetic acid, and by the heat and nitric acid tests, respectively, each time. On the other hand the ferrocyanic test showed 8 per cent the first time, and 14 per cent two weeks later; the trichloracetic test, precisely the reverse, namely, about 15 per cent the first time, and 8 per cent the second. In other words, the results were identical when the methods involving heat and acid

were used, but contradictory between the ferrocyanic and trichloracetic acid tests.

2. In a case of albuminuria, due to presence of pus and blood in the urine, the small bulk percentages obtained by use of the various reagents agreed quite closely.

3. In a case of chronic Bright's disease, ten days before death, when albumin was very large in amount in the urine, heat and 20 drops of nitric acid gave bulk percentages, which agreed more closely with those obtained by the precipitating reagents, than was the case in other urines containing small bulks of albumin.

4. The writer suggests to all teachers, who have the electric centrifuge, to encourage original work in the determination of bulk percentages of albumin, in order to answer the following questions: (*a*) Is the centrifugal method capable of yielding sufficiently constant results to be at all available for clinical purposes? What reagent or method gives the most satisfaction, *i. e.*, is most reliable? (*b*) Can the separation of albumin, globulin, and albumoses be made and the ratio of these substances to one another approximately determined?

N. B —The influence of the specific gravity of the urine on the bulk of the precipitates should be studied, and the size of the flakes observed, when boiling is used. Serum-albumin can be separated from globulin by rendering the urine amphoteric or faintly alkaline with sodium hydrate, and then saturating with magnesium sulphate in substance. Globulin is precipitated and serum-albumin remains in the filtrate. Determine the bulk percentage of the serum-albumin, by means, say, of boiling and addition of acetic acid, and by other reagents which do not react with magnesium sulphate.

For the Gravimetric Determination of Albumin see APPENDIX.

# CHAPTER XXXI.

## CLINICAL SIGNIFICANCE OF ALBUMINURIA.

Albumin occurs in the urine without serious significance much oftener than was formerly supposed, but at the same time the *permanent presence* of albumin in the urine must on the whole always be regarded as pathological. We may classify the various albuminurias not due to pus or blood as follows:—

1. **Functional Albuminuria:**—This much-abused term describes a number of albuminurias which in the past have been regarded as physiological, to wit: *transitory*, *intermittent*, or *cyclical* albuminurias. Albuminuria may follow severe muscular or mental exercise, cold baths, hearty meals, etc., and disappear; or it may continue several days or even weeks, disappear and reappear again. In the latter case the albuminuria is called *intermittent*. If it disappear and reappear with regularity, it is called *cyclical*. Cyclical albuminuria is called *postural* when it disappears after rest in bed, to appear again when the person stands on his feet.

These albuminurias may be observed in apparently healthy persons, but the writer is skeptical about any physiological basis for them. Among certain young men, whom the author has had under observation for years, no death has as yet occurred, and no disease of the kidneys can be demonstrated, but, as a rule, the subjects are pallid or neurasthenic and, in some cases, sexually weak.

Transitory albuminuria is noticed in anæmic children and masturbating boys. It is also found in pregnancy and in parturition.

Urines containing abundant sediments of uric acid or oxalate of lime are quite frequently found to contain albumin also. The latter most always disappears, when the urine becomes normal in other respects.

2. **Albuminuria due to febrile disorders:**—This in the experience of the general practitioner deserves second place. The albumin is seldom abundant, and disappears as the temperature becomes normal.

3. **Albuminuria due to renal disease itself:**—Far more common than has hitherto been recognized. Should be placed second in the list of any specialist who does not see many acute febrile diseases. The essential diagnostic features are, (*a*) increase in the quantity of night urine compared with the day, (*b*) decrease in the excretion of phosphoric acid, (*c*) presence of albumin in both day and night urine, (*d*) presence of casts, especially when in abundance, and of various kinds, (*e*) and presence of renal epithelium which, C. Heitzmann holds, is alone diagnostic of nephritis.

4. **Albuminuria of various chronic diseases:**—In these cases the kidneys are perhaps free from anatomical lesions, but the patient is himself suffering from some malady or other. The patients are weak, nervous, or anæmic. They often have diarrhœa. To this class belong pallid, ill-nourished young persons subject to various complaints as headache, nervousness, dyspepsia and diarrhœa. The albuminuria may be chronic, but is curable. In the writers experience it is fairly common among medical students, and especially among those who are either pallid in appearance, or nervous.

Many maladies are attended by presence of albumin in the urine, such as epilepsy, tetanus, mental diseases, painful paroxysmal affections of the abdominal organs (various colics), incarcerated hernia, etc,, etc.

The writer has found albumin quite constantly in the urine of epileptics, even when seminal fluid is absent, not only after paroxysms but persistently.

5. **Albuminuria from circulatory disturbances** as in cardiac insufficiency from valvular lesions, degenerations of the heart, coronary disease, impeded pulmonary circulation affecting the right heart, compression of renal veins by tumors, the pregnant uterus, etc. It is probable that febrile albuminuria is circulatory to a certain extent, due to renal hyperæmia produced by increased or diminished blood pressure.

The albuminuria of various choleras and in the simpler forms of intestinal catarrhs are, according to Simon, doubtless dependent upon such causes.

6. **Hæmic albuminuria:**—Albuminuria due to various diseases of the blood as in purpura, scurvy, leukæmia, pernicious anæmia, syphilis, jaundice, diabetes, oxaluria, uricæmia; in poisoning by mercury and lead; after inhalations of ether and chloroform.

7. **Albuminuria from mechanical pressure or interference:**—An impeded outflow of urine from the kidneys due to ureteral stenosis, impaction of calculus, pressure of tumor on ureter, etc., may be followed by albuminuria.

8. **Toxic albuminuria:**—Albuminuria may follow direct irritant action of poisons on the renal parenchyma. Substances like iodine, phosphorus, arsenic, lead, antimony, mineral acids, nitre, carbolic acid, oil of turpentine, cantharides, mustard, salicylic acid, tar, petroleum, alcohol, balsam of copaiba, cubebs, etc., etc.

In acute febrile diseases the albuminuria may be partly due to the direct irritant action of bacterial poisons.

## CLINICAL NOTES.

1. **Albuminuria due to presence of pus, blood, or leucorrhœal fluid in the urine:**—By far the most common of all seen in routine practice. In the urine of nearly all married women a trace of albumin may be found, or at any rate traces of a substance which responds both to the author's heat and acetic acid test and to the ferrocyanic test. Albumin is

found in greater or less quantity in the urine of most all elderly men, due to pus from bladder or prostatic troubles, also in the urine of young men who have had gonorrhœa, and its complications.

NOTE:—This form of albuminuria is known as *false*, or *adventitious.*

2. The writer has found by observation of the mortality among 500 patients with albuminuria, which have been carefully traced up to 1896, that, when the night urine *unaccountably* equals the day in quantity, the chances are very great that the patient has Bright's disease; and when the night urine habitually exceeds the day in quantity, the chances are three to one that Bright's disease is present.

Again it has been found that when the quantity of phosphoric acid falls below 20 grains (1.3 gm.) per diem, the chances are great that the albuminuria is of renal origin. When the phosphoric acid falls below 15 grains (1 gm.) the probabilities of rapidly fatal renal disease are greater than those of recovery.

Furthermore, by the author's heat and acetic acid test albumin unaccountably found in *both* day and night urine is likely to be renal in origin.

3. In typical cases of contracting kidney, as those with retinitis, soon terminating fatally, albumin may, however, either not be found at all in the morning urine, voided on rising, or may be present in traces only. In a case of this kind which the writer saw with Dr. C. Gurnee Fellows, a few months before death of the patient, albumin and casts were absent from the urine voided on rising, but present in the urine voided during the day.

4. Albuminuria not of renal origin occurs according to Dr. J. Hubley Schall of New York, as follows: In 34 cases (out of 510 recorded analyses) in neurasthenia, epilepsy, dilatation of the stomach, morphine habit, obesity, malassimilation in children, and after laparotomy. Bouchard finds it in obesity, gout, and diabetes. Schall finds intermittent albuminuria in physicians due to mental and physical excesses. Phosphaturia was marked in four cases and there was slight

excess of sulphates. Hawkins of London, reports a case of a physician who had albuminuria 43 years, without other symptoms of Bright's disease. Intermittent albuminuria, not of renal origin, may be due to elaboration of certain albuminoids by the liver, to excitation of the cutaneous nerves, to venous stasis from paralysis of the veins, as in morphine habit, to malaria, neurotic family history, prolapsus uteri, and, temporarily, as a result of over-study or powerful emotions in neurasthenic individuals.

5. According to Schall, diet seems to have no appreciable effect on the albumin in the cases just mentioned. Milk increases it, but kumyss has a tendency to improve the general condition and, in two cases, decreased the albumin. [This would seem to suggest an intestinal cause for the disturbance in view of the action of kumyss on aromatic sulphates See Ethereal Sulphates].

6 Dr A. W Stirling, of Atlanta Georgia, examined 369 boys between the ages of 12 and 16 on one of the large training ships near London. Nearly 21 per cent had albumin in their urine three hours after getting out of bed in the morning. Of the boys who played in a band 60 per cent had albuminuria Albumin increases with age. In 92 cases between 5 and 94 years of age, from 20 to 30 years the percentage was only 10; from 50 to 60, 66.6 per cent; 60 to 70, 75 per cent; 70 to 80, 75 per cent; 80 to 90, 83 per cent.

# CHAPTER XXXII.

## PROTEIDS CONTINUED. GLOBULIN, ALBUMOSES, [PEPTONE], HÆMOGLOBIN, FIBRIN, HISTON, NUCLEO-ALBUMIN.

THE proteids other than serum-albumin found in urine do not possess the clinical interest which attaches itself to albumin. A summary of our knowledge in regard to them may be given as follows:

### SERUM-GLOBULIN. PARAGLOBULIN.

**Detection in urine:**

METHOD 1.—Render the urine alkaline with ammonium hydrate, so as to precipitate phosphates. Let settle for an hour, filter, and to the filtrate add its own volume of a saturated solution of ammonium sulphate. If globulin be present, a flocculent, white precipitate occurs A yellowish or pinkish precipitate of ammonium urate may also form, but is distinguishable by its color.

METHOD 2.—Render the urine alkaline with sodium hydrate, filter, and carefully pour the filtrate down the side of a test-tube containing a saturated solution of sodium sulphate, so as to form a layer above this. If serum-globulin is present a white ring will appear at the zone of contact. *Paton's test.*

METHOD 3.—Dilute 30 to 50 c.c. of clear filtered urine with 10 times its volume of water. Add dilute acetic acid and pass into the solution a stream of carbonic acid gas. A turbidity, eventually becoming a precipitate, indicates the presence of globulin.

METHOD 4.—Drop albuminous urine, drop by drop, into a large volume of water. Each drop as it falls is followed by a milky streak if globulin is present.

METHOD 5.—Daiber separates globulin from albumin as follows: The urine is poured into a vessel and mixed with an excess of absolute alcohol, which precipitates all the albuminous substances. This mixture is left to settle for some hours, then filtered and washed with lukewarm, distilled water, then the deposit, together with the filter paper on which it is collected, is deposited in another vessel and distilled water at 30° C. (86° F.) is added and, drop by drop, diluted acetic acid up to complete dissolution of the albuminoid substances. After filtration a solution of 1 part sodium carbonate in 4 parts distilled water is added, until the solution becomes perfectly neutral or slightly alkaline, and then a 50 per cent solution of ammonium sulphate, which precipitates the globulin in the form of a flaky, white deposit. This latter may be dissolved in a 1 per cent solution of sodium chloride from which it is again precipitated when the liquid is treated. The globulin

remaining in the ammonium sulphate solution may be extracted as a precipitate by boiling the liquid.

**Quantitative determination:—**

1. In a rough way, Paton's test (method 2 above) will show by the size of the ring, whether much or little serum-globulin is present.

2. Collect on a dried and weighed filter the precipitate, obtained by method 1 above, with ammonium sulphate after it has settled for about an hour. Wash thoroughly with a solution of ammonium sulphate, one half saturated, until a sample of the washings treated with acetic acid and potassium ferrocyanide no longer gives a precipitate. Wash with alcohol and with ether to remove any fats present, and dry at 120° to 130° C. (248° to 266° F.) until it ceases to lose weight. The difference in weight, between the dry filter without precipitate and with it, represents the quantity of serum-globulin in the volume of urine used.

3. The Esbach tube may be used, as already described in the Chapter on Quantitative Determination of Albumin.

**Clinical Significance:—**

1. Globulin is not found in normal urine.

2. Its occurrence without serum-albumin is very rare, if it occurs at all without it.

3. The amount of globulin compared with that of albumin is increased in albuminuria due to digestive disorders, in chronic catarrhal cystitis, in acute nephritis and especially in *lardaceous disease* (amyloid degeneration of the kidney), and in the *albuminuria of pregnancy* in which the globulin may exceed the albumin.

4 The amount of globulin, compared with that of albumin, is *decreased* in chronic nephritis

**Clinical Notes:—**

1. The lower the state of nutrition of the renal epithelium, the more likely it is that globulin in increased amount will pass through it. (Boyd).

2. The proportion in which globulin is usually associated with albumin varies, so that it is not possible to determine the variety of renal disease by it. Even in lardaceous disease it may not be in excess. (Boyd).

3. In the albuminuria of heart disease the globulin is usually more abundant than in chronic interstitial nephritis. (Boyd.)

4. Senator holds that an increase of the globulin-albumin ratio is a fairly constant symptom of lardaceous disease, and is of some diagnostic importance

### ALBUMOSES.

The first products of the hydration of the native proteids are known as proto and hetero-albumose. The product most resembling peptone is called deutero-albumose. It is probable that there are a large number of albumoses, varying slightly according to the particular native albumin from which they are derived and the antecedents leading to their formation.

The albumoses, or proteoses as they are also called, are products of the digestive action of proteolytic ferments on all forms of proteid matter; they are the most important of the primary bodies resulting from gastric and pancreatic digestion. They are also produced by the growth of bacterial organisms and many of the toxic substances resulting from the growth of pathogenic bacteria, are peculiar albumoses. It is probable that the albumoses found in urine owe their origin to pyogenic micro-organisms, as the staphylococcus pyogenes aureus, although it is equally probable that the pneumococcus and streptococcus pyogenes are, likewise, active agents in the same direction. There is no question about pus containing albumose.

Albumoses thus formed under such different conditions, while resembling each other in their chemical properties, are not possessed of identically the same physiological properties.

Serum-albumin and globulin by hydration, as possibly from pepsin, frequently present in the kidneys and urine, may frequently be accompanied in the urine by traces of albumose.

**Reactions:**—The reactions characteristic of albumose according to Munk are as follows:

1. Not precipitated by heat.
2. Careful addition of cold nitric acid produces a precipitate which dissolves with a yellow color on boiling, to reappear again on cooling.
3. Addition of acetic acid and double the volume of a concentrated sodium chloride solution, gives in the cold a cloudiness or precipitate which clears on boiling to reappear on cooling.
4. The ferrocyanic test produces a cloudiness or complete precipitation.
5. Saturation with neutral ammonium sulphate precipitates them.

6. Addition of tannic and acetic acids, or phospho-tungstic acid solution, produces a cloudiness or precipitate.

7. The biuret reaction is obtained when albumoses are present, after removal of coagulable proteids by boiling with a little acetic acid.

**Detection in urine:**—The above reactions do not permit us to recognize *small* amounts of albumoses in urine either because they are not sufficiently delicate or else because they are characteristic of other albumins. Since in nearly all cases albumin or mucin or both are present, together with albumoses, the following methods must be tried.

1. When the albumoses are present in considerable quantity, they may be readily detected by filtering the hot solution described in reaction 2 above. Albumoses separate out in the filtrate on cooling. Or the hot filtrate will respond to the biuret test. Or, boiled with Millon's reagent, a red color is obtained.

2. If the biuret test is obtained after removal of coagulable proteids; test the filtrate for albumoses by first, nitric acid *and* heat (note order), second, acetic acid and potassium ferrocyanide; third, saturation with common salt and addition of a drop or two of nitric acid. In the latter test, the precipitate resulting is especially sensitive to heat, disappearing quickly on warming, reappearing on cooling.

3. For the detection of one part albumose or peptone in 50,000 parts of urine, M. L. Harris of Chicago, recommends the following:

The urine must first be freed from the last trace of all coagulable albuminoids before testing for albumose or peptone.

This is accomplished as follows:

To 20 c.c. of acid urine* in a test-tube are added six or eight drops of a saturated solution of salicyl-sulphonic acid (sulpho-salicylic acid) in distilled water, and 1 gm. of lead chloride. Shake well and boil about thirty seconds. Cool by shaking in running water from the cold water tap.

Filter through ordinary clean, white, filter paper until the urine is clear. Now add a few drops of a clear saturated solution of sodium sulphate in distilled water, in order to precipitate what lead is held in solution; raise to the boiling point, and cool under the cold water tap as before.

Filter again until clear. We should now have a perfectly clear urine, absolutely free of every trace of coagulable albuminoids, including nucleo-albumin, in which we may search for albumose or peptone. This clear filtrate is divided into three equal portions and placed in test tubes, one of which is kept for comparison, the other two for further analysis

To one of these are now added three or four drops of a saturated solution of salicyl-sulphotungstate of sodium in distilled water.†

*The urine must be fresh. If it must stand several hours before it can be examined, it should be preserved from the growth of bacteria in it by the addition of some antiseptic, preferably a few drops of formalin, which will keep it several days, and does not interfere with subsequent tests.

†Salicyl-sulphotungstate of sodium is prepared as follows: To a boiling saturated solution of tungstate of sodium in distilled water salicyl-sulphonic (sulpho-salicylic) acid is gradually added, under constant stirring, until the solution no longer turns red litmus blue; or in other words until the alkaline tungstate of sodium is completely neutralized. Upon cooling the salicyl-sulphotungstate of sodium crystallizes. A solution is now made of this in cold distilled water and filtered. A perfectly clear colorless fluid results.

If albumose or peptone be present a cloudiness will appear, varying in degree according to the amount of these proteids present.

As the amount of albumose present is often very minute, it may be necessary to compare the tube with the control tube in order to detect the cloudiness.

The cloudiness disappears entirely on gently heating the test-tube, to reappear on cooling.

In the third tube the test is varied by allowing about 5 c.c. of a dilute solution of the salicyl-sulphotungstate of sodium, made by adding about ten drops of the strong solution to 5 c.c. of distilled water, to flow very gently down the side of the tube so as to rest on the urine as a separate layer.

This should be very carefully done that the line of contact will be sharp and clear-cut, not diffuse. A cloudy line appears at the point of contact of the two liquids, if albumose or peptone be present.

When the amount present is very small, it may take two or three minutes for the line to develop and show best, the two liquids being clear, when held in front of a dark background.

As before stated, this test is extremely delicate, one part in 50,000 being readily detected; it is simple and can be easily applied in fifteen to twenty minutes.

Owing to the delicacy of the reactions it is necessary that all test-tubes be absolutely clean and the test solutions perfectly clear, otherwise a slight reaction may be easily overlooked.

The sodium sulphate solution must be added in slight excess in order to insure precipitation of all the lead, as any lead left in solution would be precipitated by the salicyl-sulphotungstate of sodium, and thus interfere with the test. This would be easily recognized, as the cloudiness in that case would not disappear on heating, but become more marked. The boiling during the application of the test, while not absolutely necessary, facilitates the reactions, and should always be done, the cooling, after boiling and before filtering, must never be omitted.

3. Salkowski's modification of Hofmeister's test for what was formerly called peptone is as follows: Albumin is first removed by boiling and filtering (and testing of filtrate with acetic acid and potassium ferrocyanide to see that the urine is sufficiently acid; if albumin is found in the filtrate, acidulate the urine, drop by drop with 30 per cent acetic acid, boiling after each drop, filtering and testing with ferrocyanide). Fifty c.c. of the albumin-free urine are acidified in a beaker with 5 c.c. of hydrochloric acid and precipitated with phospho-tungstic acid, the mixture being heated over the free flame when, in a few minutes, the precipitate will form a resinous mass, which closely adheres to the bottom of the vessel. The supernatant fluid is decanted off, and the mass at the bottom, which now becomes granular, washed twice with distilled water, which is likewise removed by decantation. The precipitate is then covered with about 8 c.c. of distilled water and treated with 0.5 c.c. of a sodium hydrate solution (specific gravity 1.16). Upon shaking the beaker the mass will dissolve, the solution assuming a dark blue color. This is heated on the free flame until the blue color turns to a dirty greenish-yellow. The solution at the same time becomes turbid but, at times, may turn yellow and remain clear. This decoloration may be hastened by the further addition of a few drops of sodium hydrate solution. As soon as this point

has been reached, some of the liquid is placed in a test-tube, allowed to cool and then treated with a very dilute solution of copper sulphate (1 to 2 per cent), drop by drop, when, in the presence of what were formerly called peptones, the solution assumes a bright red color, which may be brought out still more strongly if the specimen is now filtered. With this method which occupies only about five minutes, 0.015 gram of peptone pro 100 c.c. of urine may be demonstrated without difficulty. The quantity of urine used is so small that mucin may be disregarded.

**Clinical significance of albumosuria:**—Modern observers have agreed that true peptone has never as yet been found in urine. The products heretofore considered peptones by Hofmeister and others were not peptones at all, but albumoses. Hence the term albumosuria must be substituted for the term peptonuria, and the entire subject re-investigated. Harris's conclusions from many hundred examinations of urine are as follows:

As the albumose is due to the digestive action of invading microbes on the albumins of the fluids and tissues of the body, its presence in the urine simply indicates that we have to do with an infective condition in a state of more or less activity A word or two, however, in regard to the question of so-called peptonuria and the presence of suppuration within the body.

The digesting or peptonizing power of the ordinary pus microbes is usually quite active, and, whenever *suppuration is taking place anywhere within the body, albumose is always present in the urine.*

This albumosuria, however, can only be held indicative of suppuration when all other infective conditions can be excluded. The question may be stated thus: Given a patient with a probable circumscribed inflammatory condition in which the infective diseases can be excluded, the presence of albumose in the urine is quite positive evidence *that the condition is inflammatory, and that suppuration has taken place.*

1. True peptone being very rarely, if ever found in the urine, the term peptonuria should be substituted by the term albumosuria.

2. The albumoses are produced by the digestive or

peptonizing action of microbes on the albumins of the body.

3. This digestive action is one common to all forms of living organisms.

4. The albumoses are produced in quantities much in excess of what are appropriated by the microbes for their growth and development.

5. The albumoses being readily diffusible the excess in production is quickly absorbed by the blood, where being toxic and thus acting as foreign bodies they are eliminated by the kidneys and appear in the urine.

6. Albumosuria may be present in any condition or disease due to the action of micro-organisms within the body, and is thus simply indicative of an *infective* condition.

According to Harris, products corresponding to the class, albumose or proteose, are found in the following conditions:

All kinds of suppurative conditions, acute and chronic, such as pelvic abscesses, appendicular abscesses, peritonitis, suppurative lymphadenitis, subcutaneous suppuration, osteomyelitis, etc., and in the following infective diseases which he has had an opportunity to examine:

Acute croupous pneumonia, la grippe, phthisis pulmonalis, diphtheria, typhoid fever, syphilis, one case secondary stage, and one case of septicæmia of unknown origin.

Albumosuria very frequently accompanies albuminuria, in which case the condition is called *mixed albuminuria.* Albumosuria may alternate with albuminuria and precede as well as follow the latter, so that in any case in which albumoses are demonstrable in the urine, the appearance of albumin should be expected.

Dr. Sidney Martin found in a case of empyema that the amount of albumose in the urine varied inversely with the purulent discharge.

Drs. Dickinson and Fyffe noticed a complete disappearance of albumose from the urine when pus was evacuated.

Albumose is not found in the urine in many cases where there is a large collection of pus in the abdomen or in an hepatic abscess; doubtless due to thickness of the membrane surrounding the pus and interfering with its absorption.

In a case of acute bronchitis with pleural pain a peculiar albumose has been found in the urine most closely related to protomyosinose (a primary product of the digestion of myosin, the latter a native proteid of the globulin class, whose coagulation in muscle after death causes rigor mortis).

In most virulent and fatal cases of pneumonia, with extensive hepatization of the lung, albumoses are absent, and their appearance is possibly a favorable indication in this disease.

In many cases, however, of suppuration in the chest cavity with albumoses in the urine the noticeable features are severe character during primary fever, high mortality, and occasional serious sequelæ apart from development of empyema.

Finally it is said by Dr. Saundby (the International Annual for 1897) that albumose is found by delicate tests in the urine of the perfectly healthy.

### NOTES ON PEPTONURIA, FORMERLY SO-CALLED.

(*a*) According to Maixner *peptone is always present in urine when pus is forming*, the peptone constituent of leucocytes being absorbed into the circulation, whence it is eliminated by the kidneys.

(*b*) Again, extensive *destruction of the corpuscular elements of the blood* is a cause of peptonuria. Hence we find peptonuria in (*a*) the declining stages of pneumonia, in purulent pleuritis, suppurating tuberculosis, chronic bronchial catarrh, psoas abscess, purulent meningitis, acute articular rheumatism, and (*b*) acute infectious diseases and toxic conditions of the blood:—phosphorus poisoning, croupous pneumonia, typhoid-fever, small-pox, scarlet-fever, mumps, erysipelas, empyema, visceral cancer, especially of liver and intestines, catarrhal jaundice and apoplexy.

(*c*) Peptonuria (used in the former sense of the word) is almost invariably associated with cancer of the liver.

(*d*) Peptone is said to be a normal constituent of urine in the puerperal state.

(*e*) Ulcerative changes in the lungs being excluded, peptonuria is significant of epidemic cerebro-spinal meningitis as distinguished from tubercular. (Jaksch.)

(*f*) Peptonuria, it is said, distinguishes septicæmia from latent disseminated sarcoma.

(*g*) Peptonuria occurs in ulceration of the intestines, and when peptone is injected into the blood.

It seems quite probable that many of these conditions of so-called peptonuria may be found to be accompanied by presence of albumose

HÆMOGLOBIN.

Hæmoglobin, the red pigment of the blood, contains iron, and gives the proteid reaction. Hæmoglobinuria occurs whenever the liver is for any reason, unable to transform into bilirubin all the blood-coloring matter set free by destruction of red blood corpuscles. In such a case the urine contains few red corpuscles or none at all, but the coloring matter of the blood may be recognized by the following:

1. Tests:—*Guaiacum test:* —Mix equal parts of old oil of turpentine, which has become ozonized by exposure to the air and light, and tincture of guaiacum which has been kept in a dark-glass bottle, and then float carefully on the surface of the mixture an equal volume of the urine to be tested If hæmoglobin be present, a bluish-green ring, becoming a beautiful blue, appears when the two liquids meet, and, on shaking, the mixture becomes blue. If the urine contain pus, the latter will color the guaiacum alone without the turpentine and the blue color will disappear, when heated to the boiling point, which is not the case when the blue color is due to hæmoglobin. The urine tested should be fresh or made faintly acid.

2. Examine the urine *spectroscopically* as follows: Render feebly acid by means of acetic acid, and place before the open slit of the spectroscope in a test-tube, breaker, or similar vessel, when the two bands of oxyhæmoglobin (arterial blood), will be seen either at once, or upon carefully diluting with distilled water. If ammonium sulphide be now added, the spectrum of reduced hæmoglobin (venous blood) will be obtained. More commonly, however, the spectrum of methæmoglobin (a mixture of albumin, hæmoglobin, and hematin), is seen in cases of hæmoglobinuria.

3. *Heller's test:*—Boil urine to which solution of potassium hydroxide has been previously added to precipitate phosphates. The latter will present a bright-red color, if hæmoglobin is present. If it is difficult to appreciate the color, filter, and dissolve in acetic acid, when, if blood pigment be present, the solution becomes red, and the color vanishes gradually on exposure to the air. This test is quite as delicate as the guaiacum one.

**Clinical Significance:—**

1. Hæmoglobinuria is most frequently observed after poisoning by potassium chlorate, arseniuretted hydrogen, sulphuretted hydrogen, creasote, pyrogallic acid, naphthol, hydrochloric acid, tincture of iodine, carbolic acid, carbon monoxide, phosphorus, and also by morels (Helvella esculenta).

2. Hæmoglobinuria follows injection into the blood of solvents of the corpuscles as glycerin, solutions of bile-salts, or distilled water; also after transfusion of the blood of animals into man.

3. Hæmoglobinuria may occur in the course of any one of the specific infectious diseases, as scarlatina, icterus gravis, variola hemorrhagica, yellow fever, typhoid, typhus, and probably syphilis.

4. It occurs in pyæmia, scurvy, fat-embolism, some cases of jaundice, after extensive burns, occasionally in Raynaud's disease, and in leukæmia complicated by icterus.

5. From unknown causes as an epidemic among new born.

6. In the so-called paroxysmal hæmoglobinuria the attacks are frequently preceded by chills and fever closely simulating malarial fever. It must be, however, distinguished from malarial *hæmaturia*. Simon and others doubt the existence of malarial hæmoglobinuria while malarial hæmaturia is well-known.

NOTE:—Hæmoglobinuria is the voiding of urine containing the coloring matter of blood, but few or no corpuscles; hæmaturia is the voiding of urine containing both the coloring matter and corpuscles.

### FIBRIN.

**Fibrin** in the urine may be either in solution or coagulated. In the former case coagula separate or standing, covering the bottom of the glass or changing the entire bulk of urine into a gelatinous looking mass. In the coagulated state, fibrin is observed at times in the form of blood-coagula in hæmaturia.

**Test:**—Wash the clots thoroughly with water and dissolve by boiling in a 1 per cent solution of sodium hydrate or a five per cent solution of hydrochloric acid. On cooling, the solution is tested as for serum-albumin.

**Significance:**—Colorless coagula of fibrin are seen only in cases of chyluria or in diphtheritic inflammation of the urinary passages. In most cases of hæmaturia with clots, the fibrin comes from the kidneys, although it is often associated with hæmorrhages into the urinary tract, and is seen frequently in cases of villous tumors of the bladder.

### NUCLEO-ALBUMIN.

The term *nucleo-albumin* is given to the body occasionally present in urine, which is precipitated by acetic acid, and is insoluble in excess of this reagent, though soluble in nitric acid. It has been also called mucin, a mucinous body, and a globulin, and the term *mucinuria* has been applied to the condition in which urine contains it. Much contradiction exists in regard to the nature of it.

**Tests:**—The carefully filtered urine is treated in a test-tube, drop by drop, with an excess of *concentrated* acetic acid, when the occurrence of a turbidity will indicate presence of nucleo-albumin. Remove albumin first by simple boiling, and dilute the urine if necessary before testing.

**Albumin and nucleo-albumin:**—E. E. Smith's method of distinguishing albumin from nucleo-albumin is as follows: About an inch of clear filtered urine in a test-tube is heated to boiling, after which two or three drops of ten per cent nitric acid are added. If, after a few moments, there is no reaction for albumin, the contents of the tube are again boiled, and about ten drops of the nitric acid further added, and the tube set aside.

A quarter of an inch of a clear five per cent solution of potassium ferrocyanide is placed in a test-tube, an equal volume of dilute acetic acid is added, and the

whole poured into an inch of clear urine in another test-tube, the liquids being well mixed by pouring from one tube to the other several times. The test-tube is then set aside. A comparison tube is prepared as follows: An inch of the urine, clarified at the same time as that previously used, is placed in a test-tube, and two drops of dilute acetic acid are added. This tube is likewise set aside.

If both tests react positively, either a trace of true albumin or of mucus is present, to decide which, it is necessary to observe the comparison tube, in which, if mucus is present, there will be *some* turbidity from the partial separation of nucleo-albumin. If the urine in the comparison tube remains *perfectly clear*, and the reactions with heat and with ferrocyanide present the appearance characteristic of the albumin tests, then it is safe to conclude that *a mere trace of true albumin* is present, but the appearance of even a slight cloudiness in the comparison tube is to be taken as evidence of the presence of mucus, to which then the delicate heat and the ferrocyanide tests are to be attributed. Since the separation of nucleo-albumin in the comparison tube is only partial, it is evident that no comparison can be made between the *intensity* of this reaction and the heat and the ferrocyanide reactions.

The appearance characteristic of the heat and nitric-acid reaction with a trace of albumin is either the formation of *a few flakes of coagulated* albumin or the formation of a general turbidity which finally results in a fine flocculent separation, persisting when the solution is hot. The addition of one-third to one-half the volume of alcohol causes the flocculent appearance to become more pronounced, while any separated resinous substances, thymol, etc., pass into solution.

When *traces of true albumin* are present, the ferrocyanide test gives a *finely flocculent appearance*, while with *nucleo-albumin a mere opacity is more common.*

Finally, it is to be remembered that albumin is to be considered absent from a urine till its presence is demonstrated by methods which admit of its distinction from mucus. Undoubtedly the safest basis for

interpretation, except perhaps in the hand of the skilled analyst, is the requirement of three reactions. (The two above, and Heller's test) ignoring such traces as fail to respond to Heller's test.

Bladder mucus does not contain mucin but a proteid probably identical with nucleo-albumin, and only incompletely precipitated by acetic acid. To remove it from urine, C. E. Simon recommends treating the urine with neutral acetate of lead, carefully avoiding excess.

**Significance:**—Sarzin and Senator were unable to find nucleo-albumin in 200 urines from almost the entire list of hospital diseases.

C. E. Simon insists that an elimination of it from the blood through the kidneys does not exist, and that, when found, it is due to improper methods and referable to disintegrating epithelia.

Reissner, Obermeyer, and others claim to find it in various diseases. Reissner says it may precede albumin and continue longer than the latter. Obermeyer finds it in icteric urine and in that of other diseases.

Purdy says that in catarrhal inflammations of the urinary passages, mucin is much increased and may form ropy, tenacious strings, or settle in jelly-like mass.

Some author's allude to nucleo-albumin from bile. and it is said that the mucin of bile differs from that of mucous membrane in not being completely separated by acetic acid. The reader is referred to Fraser's Notes for January, 1895, and to Dr. Landon Carter Gray's well-known paper in the *American Journal of Medical Sciences*, for October, 1894, in which differential testing is described. It should be noted, however, that clarification of the urine by powdered French chalk, filtering through talc, etc., has recently been said to remove albumin as well as mucin from the urine.

Almost unsurmountable difficulties seem to beset us in the study of the albuminoid of mucus, and great difference of opinion exists as to its origin, nature, and properties.

### HISTON.

This albuminous body was first found by Kossel in the red-blood corpuscles of the goose. It has been shown to exist in the leucocytes of human blood, in combination with the acid leuko-nuclein, the so-called nucleo-histon of Lilienfeld. It has been found in the urine in a case of leukæmia by Kolisch and Burion as follows: Albumin being removed, the urine was precipitated with 94 per

cent alcohol, the precipitate washed with hot alcohol and dissolved in boiling water. On cooling, the solution was acidified with hydrochloric acid and let stand several hours, filtered, and precipitated with ammonia. Histon, if present, is now thrown down in addition to certain mineral constituents. The precipitate is collected on a small filter, and washed with ammoniacal water until the washings no longer give the biuret reaction. It is then dissolved in dilute acetic acid, and the solution tested with the biuret test; if this yields a positive result, and, if coagulation occurs, on application of heat, the coagulum being soluble in mineral acids, the presence of histon may be inferred.

# CHAPTER XXXIII.

## SUGAR IN THE URINE.

**Introductory.** The sugar found in the urine in the conditions known as glycosuria and diabetes mellitus is not cane sugar, as many medical students think, but a substance very like *grape-sugar*, which probably occurs in minute quantities in normal urine, and in greatly increased quantity in diabetes mellitus.

**Synonyms:**—*Sugar*:—GERMAN, *Zucker*; FRENCH, *Sucre*. Grape-sugar, dextrose, glucose:—GERMAN, *Traubenzucker; Glycose*, *Dextrose*, *Harnzucker*; FRENCH, *Glycose*, *Dextrose*.

**Chemical constitution:**—$C_6H_{12}O_6$, a *carbohydrate* containing 6 atoms of carbon; is one of the class of *monosaccharides*, group *hexoses*, sub-group *aldoses*.

**Reactions:**

1. Absorbs oxygen when heated with strong alkali solution, giving rise to characteristic color and odor.
2. Heated with alkaline solution of cupric salts, reduces them with (red) precipitate of cuprous oxide.
3. Reduces bismuth subnitrate to the metallic condition, when heated with it in presence of an alkaline solution.
4. Warmed with a solution of phenylhydrazin hydrochloride in water, to which a little sodium acetate is added, forms a yellow crystalline precipitate of phenylglucosazon.
5. Fermented by yeast splits into alcohol, carbon dioxide, and a number of other substances.
6. Boiled in faintly alkaline solution colored blue by indigo exhibits a beautiful color reaction.
7. Gives color reactions with various substances, as with alpha-naphthol and thymol in presence of sulphuric acid.

The method of application of these tests will be shown further on.

### A. CLINICAL TEST FOR SUGAR IN URINE.

One of the most satisfactory and reliable tests for sugar, if performed with care, is that made by use of Professor Walter Haines' test-liquid.

**Haines' test-liquid made by the metric system:**—2 grams of copper sulphate, 15 c.c. of water and

glycerine each, and 150 c.c. of liquor potassæ. Use 3.75 c.c. of the liquid in making the test.

**Haines' sugar-test liquid** (American measures):—A permanent, transparent, dark-blue solution containing cupric sulphate, and potassic hydroxide, dissolved in glycerine and water. It is made as follows:* Make a perfect solution of cupric sulphate ("free from iron,") 30 grains, in one-half fluidounce of distilled water; to this add one-half fluidounce of pure glycerine; mix thoroughly, and add liquor potassæ five fluidounces. Owing to the fact that even the best grade of cupric sulphate contains traces of the ferric salt, Haines' test-liquid will usually deposit, on standing, a slight reddish sediment. To avoid mistakes it is wise to let the solution settle before it is used and then decant from the sediment.

**Testing the quality of Haines' liquid**:—In order to be sure that the solution has been properly made, proceed as follows: Take one fluidrachm of the liquid (which quantity will fill a five-inch test-tube to the depth of about one inch), and boil it in a *clean* test-tube for thirty seconds or more. Now let it cool. Neither before cooling nor after should it show any change of color. Compare it after boiling with a fluidrachm which has not been boiled. The two should look exactly alike. Now take the second fluidrachm which has not yet been boiled and bring it to the boiling point, also in a clean test-tube. Add a drop of *normal* urine to it and bring to the boiling point again; repeat the process adding drop by drop till eight drops of urine have been added Then boil thirty seconds. Now let cool and see that no change in the *color* takes place, though perhaps *whitish flocks of phosphates* can be seen, suspended in the liquid, which in a short time settle, forming a *dirty-white sediment* in the tube. Compare with a third fluidrachm of the liquid which has not been boiled and the only difference seen will be due to the deposit of phosphates. *There should be*

* See Writer's "Diseases of the Kidneys" 2 Ed. p. 369.

*no reddish, greenish, nor yellowish tinge to the liquid after it is boiled with normal urine.*

**Detection of sugar with Haines' test-liquid:**— Having ascertained that the test-liquid is of good quality take a fluidrachm of it, boil it, and add one drop of the suspected urine to it. If much sugar is present in the urine, a change at once takes place; the whole liquid becomes turbid and changes color to yellow, reddish-yellow, or brown-yellow. If no such change takes place after adding a drop of urine, add another drop and bring to a boil again, and so on until the turbidity and discoloration are seen; urine which contains but a moderate quantity of sugar may require four drops to be added, boiling after each drop. Or it may be necessary in case but a small quantity of sugar be present to add eight drops of urine, boiling after each drop, and after the eight drops are added to boil for thirty seconds, before any change be seen. If, however, no change is seen even then, let the tube cool, when, provided but a small quantity of sugar be present, the liquid becomes greenish and turbid. But if no sugar is present, the brilliant blue transparency is unaffected on cooling.

**Precautions:**

1. The test depends on the reduction of the cupric sulphate to cuprous oxide. Normal urine has a slight reducing power on the solution in case of prolonged boiling, therefore *do not boil too long*, thirty seconds being enough.
2. Do not forget to set the tube aside after the test has been made and let it cool. A small quantity of sugar causes a turbidity only on cooling. A dirty test-tube is more often responsible for the change on cooling.
3. Do not use a sample of the liquid which contains a reddish sediment, lest the latter appear in the test-tube, and be mistaken for a reduction. Decant or filter the liquid before using.
4. Do not mistake the whitish flocks of phosphates precipitated in *all* urine, by this test, for sugar.
5. Do not use a dirty test-tube, since Haines' liquid is exceedingly sensitive to the presence of numerous organic substances. The test-tube must be *thoroughly* cleaned beforehand.
6. Do not use more than 8 or 10 drops of urine; a larger quantity of even normal urine may cause reduction.
7. Do not add any chemicals whatever before or after the test.
8. Use a clamp for holding the test-tube and not too great heat. An alcohol lamp is better than a Bunsen burner, unless the latter be turned low.

9. Point the mouth of the test-tube away from everybody when boiling, as the liquid sometimes "bumps."

NOTES.

1. Haines' test-liquid is affected by numerous organic substances even in small quantities: For example, 1 or 2 drops of 20 per cent acetic acid make it turbid and green on cooling; 2 drops of carbolic acid cause a precipitate, but the blue color is not entirely lost. The writer has found that a number of substances, left as samples by enterprising agents of various chemical manufacturers, either give copious characteristic precipitates, as in case of Panopeptone, Forbes' diastase, Sabalol balsam, or else a precipitate of some sort not typical, as in the case of a "non-saccharine solution of the hypophosphites," which gave a grayish-white precipitate, without changing the blue of the liquid. Chloral hydrate, chloroform, and sulfonal have a reducing power on the cupric tests, a fact which must be borne in mind, when these substances are added to urine for antiseptic purposes, or when taken internally.

2. The question then comes up as to the possibility of a reaction with Haines' test, when such substances are taken internally. So far as grape-sugar itself goes, the writer has proved in his own case that copious ingestion of solutions rich in glucose fails to render the urine saccharine, that is, no reaction with Haines' test has been obtained.

3. On the other hand there are those persons who, though free from diabetes, void, when taking strongly saccharine solutions, glucose in the urine. The writer published in the *Hahnemannian* of 1892 his observations on the reaction with Haines' test of the urine of a certain person, who was drinking freely of champagne, rich in glucose. It is thought by v. Noorden that such a condition is significant of a tendency to diabetes, and he tests the urine of his patients after administering 100 grams of grape-sugar to them.

4. In consequence of the above the writer is in the habit, when testing urine for sugar, to specify that the patient shall eat freely of saccharine articles and to test the urine of each micturition separately. It has been found that the urine voided *in the afternoon, about 3 or 4 o'clock*, is most likely to affect Haines' solution. When a marked reaction occurs at this time, the writer subjects the urine of this particular hour to *fermentation* so as to avoid error from possible presence of various organic substances including those of the urine, as glycuronic acid.

It goes without saying that all glasses used shall be rigorously cleaned, before any conclusions as to presence of a trace of sugar can be arrived at.

5. Some curious facts as to this afternoon reaction with Haines' liquid have come under the writer's observation: One patient would manifest it in the urine voided after eating bananas; another whenever he drank ordinary tap beer, but not when he drank bottled imported beer.

6. In several cases where this doubtful reaction has been found, prohibition of saccharine articles of food together with reduction in starchy foods has been followed by an improvement in the general health of the patient and disappearance of the reaction.

ADVANTAGES OF THE HAINES' TEST-LIQUID.

1. The solution is stable being known to keep fifteen years when properly made from pure materials. The writer keeps it in a dark place.

2. By adding the urine, drop by drop, the chances of reduction by the other substances than sugar are lessened.

3. An idea as to the amount of sugar present may be had approximately as follows:—If one or two drops of urine give an immediate yellow or red precipitate, sugar is abundant, 4 per cent or more; if several drops are necessary to produce the yellow precipitate, sugar is moderately abundant; if eight drops of urine are required before any change occurs, sugar is in small amount; if no change occurs until after cooling mere traces are present. It is understood, however, that the tube is not allowed to cool while the urine is being added.

# CHAPTER XXXIV.

## USUAL LIFE INSURANCE TESTS FOR SUGAR.

One of the most commonly used test solutions is *Fehling's*, which is made as follows:—(1) Dissolve 69.28 grams of pure *recrystallized* copper sulphate in enough distilled water to make one liter; (2) Dissolve 100 grams of sodium hydroxide, "by alcohol," in sticks, in 500 c.c. of distilled water. Heat to boiling, and add gradually 350 grams of pure *recrystallized* Rochelle salt. Stir until all is dissolved. Allow the solution to stand 24 hours in a covered vessel, then filter through asbestos into a liter flask, and add water to make 1 liter. Keep each of these solutions in a separate bottle. There are several methods of applying the test:

Method I:—Mix equal parts of the two solutions described above using about a fluidrachm (4 c.c.) of each. Pour 4 c.c. (one fluidrachm) of the blue solution thus made into a test-tube and test its stability by boiling. If no change occurs on boiling, add 3 or 4 drops of the urine to be tested and boil again. If much sugar be present, after a short time there results a dense, opaque, yellow color, and a yellow-red precipitate soon settles to the bottom of the tube. In case of no change of color with 3 or 4 drops, continue adding urine until an amount equal to the amount of the solution has been added; that is, if the amount of solution used is 4 c.c., add in all 4 c.c. of urine but no more. If no precipitate or change occurs, sugar is absent.

Method II.—Pour 4 c.c. of the solution into a test-tube, and add an equal amount of water. Boil and the solution must remain clear. Then add ½ c.c. of urine and boil, when, if sugar is present in amount greater than one-tenth of one per cent, the yellow

color appears. If not, add more urine and boil again, and so on until an equal amount of urine has been added.

METHOD III:—Mix equal parts of the two solutions, dilute with four times as much water, boil, add a small amount of urine and *warm*, not boil.

PRECAUTIONS.

1. It is important *not to mix* the two solutions *until just before the test* is made, as the blue liquid formed does not keep well.
2. Even when the solutions are kept separately, it is said that the tartrate used is likely to decompose, racemic acid being formed, which reduces cupric salts.
3. A greenish flocculent precipitate always occuring in greater or less quantity when the urine is added, is due to *precipitated phosphates.*
4. A *clear* dark green solution sometimes formed, when the urine is heated with Fehling's solution, is not significant of sugar, but is due to partial reduction by normal constituents of the urine as uric acid, kreatinin, etc. A colorless mixture is indicative of the same partial reduction. Drugs taken internally may cause the same reaction.
5. If, however, with this change of color a red precipitate takes place, the urine must be tested with the bismuth test or by fermentation. Occasionally uric acid is so abundant as not only to discharge the color of the mixture, but also to cause precipitation of the red oxide of copper, and hence cause doubt.
6. The same precautions in regard to cleansing the tubes are necessary as in case of Haines' liquid.
7. It is also advised to remove albumin before applying the test. This is done by boiling and filtering.
8. Some companies recommend their examiners to neutralize the urine before applying Fehling's test.
9. Morphine, tannin, salicylic acid, salol, cubebs, copaiba, rhubarb, senna, sulfonal and antipyrin reduce Fehling's solution. Internal administration of chloral, camphor, etc , produce glycuronic acid in the urine, which affects Fehling's test. Glycosuric acid gives a positive reaction, but is rare in urine.
10. When the quantity of sugar is small and there is a fear that the reduction of Fehling's solution has resulted from uric acid or from kreatinin, some advise to filter the urine first three times through animal charcoal. If Pavy's ammoniated cupric test is used instead of Fehling's, a larger quantity must be employed and the urine added to the depth of two inches in the tube. Boil the upper portion of the mixture, which loses its blue color, if sugar be present. Fermentation over mercury is probably safest in such cases.

NOTES.

1. Fehling's solution made as above is used for quantitative determinations.
2. Fehling's solution is said to detect even traces of sugar, and to be more delicate than Trommer's test.

3. A very convenient arrangement for keeping the two solutions separately, is described by J. H. Long as follows:—Two bottles, each holding about 200 c.c., are fitted with perforated rubber stoppers. Through the opening in each stopper the stem of a 2 c.c. pipette with very short tip is passed, and left in such a position that, when the bottles are half filled, the bulbs and stems to the mark will be covered with the liquid. One bottle contains the standard copper sulphate solution, the other the mixture of alkali and tartrate solution. The rubber stoppers should be covered with vaseline so that they will permit the pipette stems to slide easily in the perforations, and also close the bottles perfectly. When the stoppers are inserted, the pipettes should stand full to the mark, ready for use.

On withdrawing the stoppers with forefinger closing the pipettes, exactly 2 c.c. of each liquid can be taken out without delay, and on mixing in a test-tube yield the Fehling solution, fresh and ready for use, directly, or after dilution with distilled water, as thought necessary. As the solutions are used the pipette stems are pushed farther through the stoppers so as to leave the marks always at the surface of the liquids. The solutions may be kept in this manner for years, and their use is not attended with any inconvenience. The open ends of the pipette stems should be kept closed with small rubber caps, or a bit of soft paraffin wax.

### THE BISMUTH TEST.

The bismuth test is used for the reason that *bismuth salts are not reduced by uric acid.*

**Principle:**—Bismuth oxide in alkaline solution is reduced by glucose, a precipitate of lower oxides of bismuth taking place.

**Method of Preparation:**—Nylander's modification of Almén's test is prepared by dissolving 4 grams (62 grains) of potassium sodium tartrate in 100 grams of an 8 per cent solution of caustic soda, warming the fluid and adding as much subnitrate of bismuth as will remain in solution, namely, about 2 grams Filter, on cooling, and keep in a colored glass bottle.

**Method of Application:**—Add 1 c.c. of the bismuth solution to 11 of the urine and boil for a few minutes. If sugar is present, the solution becomes first yellow, then yellowish-brown, and lastly nearly black, due to formation of lower oxides of bismuth.

**Chances for Error:—**

1. When abundance of albumin, pus, or blood is present, sulphide of bismuth is precipitated, which is a black deposit similar to that caused by presence of sugar.

2. The reaction occurs in urines containing melanin or melanogen.

3. When the urine contains a large proportion of reducing substances without sugar, the reaction occurs; but uric acid and kreatinin do not reduce the bismuth test. The substances which reduce the bismuth oxide are glycuronic acid combinations, and substances formed after use of kairin, rhubarb, eucalyptus tincture, large doses of quinine, turpentine, and other drugs.

4. Glycosuric acid gives a blackish discoloration.

5. In the presence of but very little sugar the solution is not black or dark brown but only deeper colored, and after some little time we see merely a dark or black edge on the upper layer of the phosphatic precipitate.

6. After standing for a time it is natural that a black deposit should be found in the tube, the supernatant liquid becoming clearer but still colored.

7. It is said that urines containing less than 0.3 per cent of sugar do not react with Nylander's test.

Since a small amount of albumin does not interfere with this test, it is easier to boil the urine and filter it before applying the bismuth test than to use Brücke's test, which requires some little time and skill for performing it.

In the writer's opinion the cupric test and the bismuth tests are all that are necessary for life insurance purposes.

### THE FERMENTATION TEST.

This test may be used to confirm the bismuth test. It should be performed as follows:—Fill three test-tubes each half full of mercury. To the first add the urine to be tested, to the second add water, and to the third add a 1 per cent solution of grape-sugar. Into each of the tubes drop a piece of compressed yeast, of the same size in each. Cover the mouth of each tube in turn with the thumb, invert over a small vessel of mercury, and set the whole aside for several hours. If sugar is present, the urine in the first tube should be displaced by the carbonic acid gas formed to a greater extent than in the second. If the yeast is active, the displacement in the third tube should be more noticeable than that in the second.

**Chances for Error:**

1. The urine, if not acid, should be made faintly acid by addition of a little tartaric acid.

2. Less than one per cent of sugar may not be detected, since the carbonic acid gas formed, is somewhat soluble in the urine.

**Remarks:**

The fermentation method may be used in conjunction with the bismuth test as follows:—When the bismuth test gives only a faint reduction, treat the acid urine with yeast whose activity has been tested by the solution known to contain sugar, and allow it to stand 24 to 48 hours in a warm place. Again test with the bismuth test, and if the reaction now gives negative results, sugar was previously present. But if the reaction continues to give positive results, other reducing bodies than sugar or perhaps sugar with other reducing bodies is present.

## CHEMICAL EXERCISE XV.

**A.** 1. Make up a four per cent solution of glucose or grape-sugar and note the change which takes place when *a single drop* of this solution is added to 4 c.c. (one fluidrachm) of Haines' solution heated to boiling.

2. Dilute the glucose solution with equal parts water, and add several drops successively to the Haines' solution heated to boiling.

3. Dilute the glucose solution with two and four parts of water respectively, and add 8 drops of each

to the boiling Haines' solution. If no change occurs in either case, let the tube cool and note change if any

4. Dilute the glucose solution until no change occurs until after the tube cools. Note carefully the character of the change.

**B.** 1. For several successive exercises test urines containing different quantities of sugar with Haines' test.

2. Repeat the operation with Fehling's test.

3. Repeat the operation with the bismuth test.

# CHAPTER XXXV.

## DELICATE TESTS FOR SUGAR.

For clinical purposes the tests already given viz. preferably by Haines' test-liquid, or Fehling's, Almen's (Nylander's), and the fermentation method are all sufficient. The remaining tests are, however, exceedingly delicate and hence will be included:—

### TROMMER'S TEST.

To about one fluidrachm (4 c.c.) of urine in a test-tube add enough cupric sulphate solution to make the urine light-green in color; then add an equal volume of liquor potassæ. A blue precipitate of hydrated cupric protoxide occurs at first, which, on shaking the tube, dissolves, forming a beautiful, clear, blue solution. If allowed to stand half an hour or so, reduction gradually takes place, especially if much sugar be present, a yellow or yellowish-red precipitate of suboxide of copper being formed. If instead of letting stand half an hour gentle heat be applied, the test becomes more delicate and reduction occurs at once. The objections to the test are that, if it be not boiled it is not very sensitive, and when it is boiled, especially if long, other substances than sugar may reduce the copper salt. (See notes in next Chapter).

### MODIFICATIONS OF FEHLING'S TEST.

Boil 8 c.c. of urine with 5 c.c. of cupric sulphate solution of the strength used in Fehling's test. Let cool and add 1 to 2 c.c. of a saturated sodium acetate solution. Filter, add 5 c.c. of alkaline tartrate of the usual strength, and boil 15 to 20 seconds. The test, when hot, shows as little as one-quarter of one per cent of sugar and less still on cooling. (Allen's test).

Another modification is to remove alkaloids by filtering through animal charcoal, make alkaline with mercuramin, and then any reduction of an alkaline copper tartrate solution is due to dextrose.

### THE PHENYLHYDRAZIN TEST.

Phenylhydrazin, $C_6H_5.NH - NH_2$ is a derivative of hydrazin, $NH_3 - NH_2$, formed by the replacement of a hydrogen atom by the aromatic radical phenyl, $C_6H_5$. Hydrazin or diamin, $N_2H_4$, is a substance in many ways resembling ammonia gas. Phenylhydrazin itself is a colorless oil of powerful reducing properties which forms crystallizable salts with acids, of which the *hydrochloride* is used as a test for small quantities of sugar.

**Principle:**—Phenylhydrazin has the property of forming with grape-sugar a highly characteristic crystalline compound known as *phenylglucosazon*.

**Methods of application:**—There is difference of opinion as to how the phenylhydrazin test should be applied; one method is as follows: Treat 6 or 8 c.c. of urine with two points of-a-knifeful of phenyl hydrazin hydrochlorate and 3 parts of acetate of sodium and warm until the salts have been dissolved, a little water being added if necessary. Plunge the tube in boiling water for twenty to thirty minutes, and then suddenly plunge into cold water. If sugar be present in moderate amounts, a bright yellow crystalline deposit will at once be thrown down, partly adhering to the sides of the tube. Traces of sugar will be revealed by the presence of crystals of phenyl glucosazon, very delicate, bright yellow needles, singly or in bundles and sheaves, insoluble in water. **Fig. 43.**

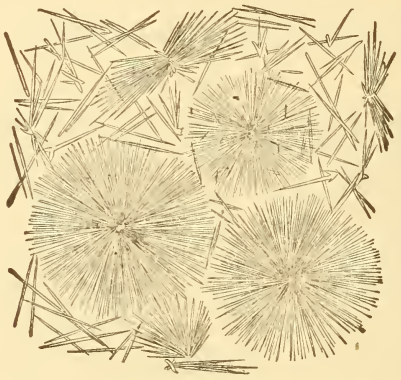


FIG. 43. Crystals of phenylglucosazon.

Jolles uses the test by boiling the test-tube in a water bath for one hour, and then letting stand for 12 to 14 hours. The method by use of the water bath is generally given as follows:

To 25 c.c. (6½ fluidrachms) of the urine to be tested add 1 gram (15 grains) of phenylhydrazin hydrochloride, 0.75 gram (11 grains) of sodium acetate and 10 c.c. (2⅔ fluidrachms) of distilled water. Place the whole, contained for convenience in a porcelain capsule, on the water bath, and warm for at least an hour. Remove, let cool, and if sugar be present, even in minute quantity, a yellow precipitate settles out, which under the microscope is seen to consist of *minute needles*, generally arranged in *rosettes*, which melt at 204° C. (399° F.). (See notes below).

**Precautions:**

1. The mixture must not be warmed for less than an hour, or a glycuronic-acid crystalline compound is formed, melting at 150° C. (302° F.). (See notes below).

2. Phenylhydrazin is poisonous and, moreover, the hydrochloride causes a troublesome *eczema*, so that caution must be observed not to get it on the hands.

3. To *determine the melting point* of the crystals pour off the supernatant liquid, add water, let settle, pour off again and repeat

this process several times. Transfer the crystals to a watch-glass, dry them over sulphuric acid in a desiccator, place a small amount in a thin, narrow tube, fasten the latter to a thermometer in such a way that the substance in the bottom of the tube is near the bulb of the thermometer, then immerse both in a vessel containing oil and gradually heat until the crystals begin to fuse, noting the temperature indicated by the thermometer.

**Remarks:**—This test is applicable in the presence of albumin and gives no reaction with urates, uric acid, kreatin, or kreatinin; nor with oxybutyric acid, urochloralic acid, uroxanthic acid, tannin, morphine, salicylic acid, or carbolic acid. Glycuronic acid and pentose are the only things likely to cause confusion. The microscopic appearance of the osazon from maltose is different from that of the glucose and the melting point of the latter is higher.

### THE INDIGO-CARMINE TEST.

This test, known as Mulder's may be employed for the detection of small quantities of sugar but apparently possesses no advantages over the preceding.

**Preparation:**—Make a solution of 0.2 per cent of sodium-indigo sulphate in acidulated distilled water, and a 25 per cent solution of crystallized sodium carbonate in distilled water. Add 5 drops of the indigo solution to 3.75 c.c. (one fluidrachm) of the sodium carbonate solution and heat to boiling. A green color results.

**Method of application:**—Add 10 drops of the urine to the above prepared green solution, heat again to boiling, and keep the fluid as near boiling as possible without ebullition, by holding the tube in the flame, withdrawing and replacing at short intervals. If sugar is present, the color will pass from green to violet, purple, red and finally *straw-color* without further change, the latter indicating presence of sugar. Urine containing 0.01 per cent of sugar will change the test to a red, while 0.02 per cent changes it slowly to the straw-color. On shaking the tube to admit oxygen of the air and cooling, the colors will return in the inverse order to that by which they appeared. The greater the proportion of sugar the more rapid the change to yellow.

### DELICACY OF THE TESTS.

| | |
|---|---|
| Trommer's test | 0.0025 per cent. |
| Fehling's test | 0.0008 " " |
| Nylander's test | 0.025 " " |
| Fermentation test | 0.1–0.05 per cent. |
| Phenylhydrazin test | 0.05 0.001 " " |
| Polarimetric test | 0.025-0.05 " " |

It must be remembered, however, that testimony as to the delicacy of these tests in urine is conflicting, some saying, for example, that Nylander's test does not reveal less than 0.3 per cent of sugar. Williamson says that the phenylhydrazin test gives a reaction in dilute urine with 0.015 per cent of sugar, and that it is too delicate for prolonged boiling in the water bath.

# CHAPTER XXXVI.

## QUANTITATIVE DETERMINATION OF SUGAR.

The easiest method of determining the quantity of sugar is that by fermentation with yeast, but it requires 24 hours' time for its performance. Results are approximate, but, if certain precautions be taken, sufficiently accurate for clinical purposes.

**Quantitative fermentation method*** :—Collect the whole urine for 24 hours, warm some of it to 77° F. (25° C.) and take the specific gravity with an urinometer, standardized at 77° F. Make a note of the specific gravity obtained. Measure off 120 c.c. (4 fluidounces) of the urine into a bottle, add half a cake of compressed yeast, crumbled into small bits, cork loosely, or with a nicked cork, and set aside in a warm place for 24 hours. Filter, warm or cool to 77° F. (25° C.) again, take specific gravity again. The specific gravity is now less than before and each degree lost indicates one grain of sugar per fluidounce of urine, or about 2.1 grams to the liter of urine. Hence if the specific gravity before fermentation was 1040 and after fermentation was 1020, this urine contains 20 grains to the ounce of urine or 42 grams to the liter.

**Calculation of results** :—The *percentage* of sugar in the urine may be calculated by multiplying degrees of specific gravity lost, by 0.23. Thus in the above example 20 times 0.23 equals 4.6 per cent, approximately.

**Example for practice** :—Urine of 24 hours measures 900 c.c. Specific gravity before fermentation 1030, after fermentation 1025. Required percentage of sugar and total sugar voided in 24 hours. *Solution:*—1030 minus 1025 equals 5, hence the urine contains 5 grains of sugar per ounce, or 10.5 grams per liter.

*The writer greatly prefers this method to all those given on pp. 221–225.

Degrees lost, 5, multiplied by 0.23 equals 1.15 *per cent* of sugar present. Total urine 900 c.c., or 30 fluidounces, therefore total sugar equals 900 times 10.5 divided by 1,000, or 9.45 *grams* in 24 hours; or 30 times 5 equals 150 *grains* in 24 hours.

**Precautions necessary**:—Do not set the urine to be fermented in a *hot* place or it will evaporate measurably in 24 hours, and an error, due to condensation of volume, will affect the specific gravity. A Jaksch fermentation flask is best for this purpose.

NOTES.

The process may be hastened, if to every 100 c.c. of urine 2 grammes of sodium potassium tartrate and 2 grammes of sodium dihydrophosphate be added with 10 grammes of compressed yeast, and the mixture allowed to stand at a temperature of from 30° to 34° C. Add 0.022 to the specific gravity taken before fermentation to allow for addition of salts to the fermented sample.

**Quantitative determination by cupric solutions**:—Fehling's test-liquid may be used as follows:—Measure off 10 c.c. of Fehling's solution in a glass flask and dilute with 40 c.c. water. Dilute the urine with ten parts of water, unless the quantity of sugar is very small when five are to be used. Into the boiling Fehling's solution add the diluted urine from a burette, ½ c.c. at a time, until the solution is almost colorless, then add, drop by drop, until decolorization is complete. The degree of dilution of the urine multiplied by 5, and the result divided by the number of c.c. of diluted urine employed, will then indicate the per cent of sugar.

Cause's modification of this process is to dilute 10 c.c. of Fehling's solution with 20 c.c. of distilled water, and treat with 4 c.c of a 1 to 20 solution of potassium ferrocyanide. While boiling, the diluted urine is now added, drop by drop, until the blue color has entirely disappeared, a precipitate not appearing at all with this method.

The objections to this method are first, the great care necessary in preparing Fehling's solution, and second the difficulty of determining the end reaction. It should be used only by experts.

Purdy uses a solution and method as follows:—Cupric sulphate (C. P.) 4.742 grams, potassium hydroxide, (C. P.) 23.50 grams, strong ammonia water (Sp. Gr. 0.9) 450 c.c., glycerin (C. P.) 38 c.c., distilled water to make 1,000 c.c. The cupric sulphate and glycerin are dissolved in 200 c.c. of water with aid of gentle heat. The potassium hydroxide is dissolved in another 200 c.c., and the two solutions are mixed. When cold the ammonia water is added, and the whole diluted to one liter; 35 c.c. of the solution are measured into a flask of 200 c.c. capacity, diluted with about 2 volumes of distilled water, and the whole thoroughly boiled. A graduated burette of 20 c.c. capacity is filled to the zero-mark

with the urine to be tested, and the urine *slowly* discharged into the *boiling* solution, drop by drop, until the blue color begins to fade; then still more slowly, three to five seconds elapsing after each drop, until the blue color completely disappears, and leaves the test solution perfectly transparent and colorless. If 2 c.c. of urine reduce 35 c.c. of the solution, 1 per cent of sugar is present; if 1 c.c. of urine, 2 per cent; ¾ c.c., 3 per cent; ½ c.c. 4 per cent; ¼ c.c. 8 per cent.

**Carwardine's Saccharimeter:**—By means of this apparatus

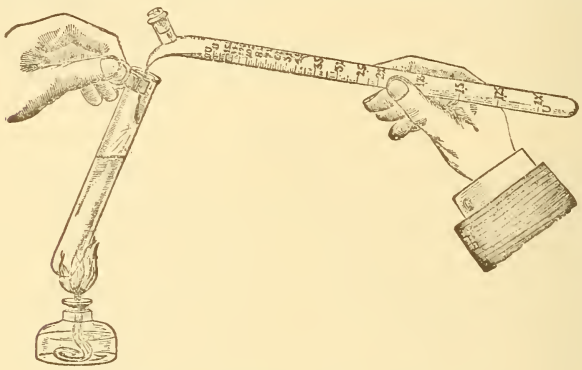


FIG. 44. Carwardine's Saccharimeter.

(Fig. 44) the percentage of sugar can be determined, it is said, at the bedside without calculations as follows:

A. 1.—Fill measure to "F" with Fehling's solution.
   2.—Dilute by adding water to 'D F.
   3.—Pour this into test-tube.
B. 1.—Fill burette to "U" with urine.
   2.—Dilute by adding water to 'D U.'
   3.—Mix.

**To estimate:**—Boil A, and whilst boiling gently, add B as in figure. When blue color has gone quite from A, hold B upright, and read off percentage of sugar.

**Picric acid determination:**—Dr. Johnson of England uses a method by which the sugar in the urine reduces picric acid and the color produced when compared with that of a standard solution of ferric acetate indicates the percentage of sugar present. The apparatus, reagents, and directions for use can be obtained of Muller & Co., 405 W. 59th St., New York, who are also agents for Carwardine's Saccharimeter.

**Polarimetric method:**—The saccharimeter of Soleil-Ventzke (Fig. 45) is convenient for determining sugar in urine. It is constructed in such a way that, if a solution of glucose be employed, every entire line of division on the scale will indicate 1 per cent of sugar. In every case the filtered urine should be free from albumin, and if markedly colored, previously treated with neutral acetate of lead in substance and filtered. If it be desired to demonstrate the presence of sugar only, the compensators are first brought to the zero position. If now, upon the interposition of

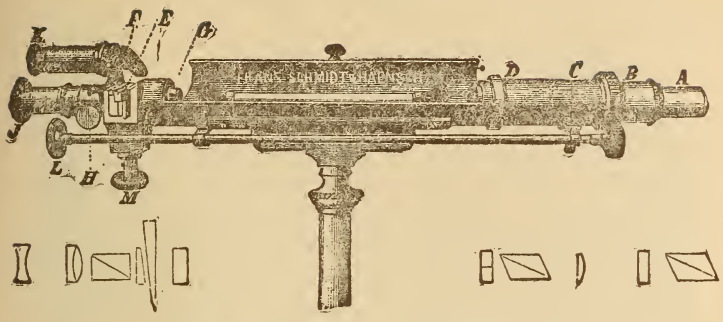


FIG. 45. Soleil-Ventzke Saccharimeter.

the tube filled with urine, a difference in the color of the two halves of the field of vision be noted, the presence of an optically active substance in the urine may be assumed and. if at the same time the deviation be to the right, the presence of glucose is highly probable.

**Ultzmann's polarizing saccharimeter** has advantages in that it may be adjusted to a microscope stand. The arc or fixed scale is so divided that one division of it represents 1 per cent of grape-sugar at 20° C. Results are uncertain, according to Purdy, when the quantity of sugar is less than 1 per cent.

Maltose is a source of error in the polarimetric test, so that this substance must be tested for by the phenylhydrazin test beforehand. Large quantities of B-oxybutyric acid may neutralize or overcome any rotation to the right due to glucose. In such cases the fermented urine will turn the plane of polarization still more strongly to the left, indicating the presence of a dextro-rotatory substance, in all probability glucose.

**Williamson's Method:**—A test-tube of ordinary size is filled for about half an inch with powdered phenylhydrazin hydrochloride; powdered sodium acetate is added for another half inch. The test-tube is next half filled with urine and boiled over a spirit lamp. By shaking, the salts soon dissolve, and after the liquid has reached the boiling point the boiling is continued for two minutes. The tube is then allowed to stand and is finally examined for sugar, which is indicated by a yellowish deposit of needle-shaped crystals at the bottom of the tube. A urine which gives no reaction may be declared quite free from sugar for all practical purposes.

**Whitney's volumetric method:**—F. Waldo Whitney of New York uses a solution and method as follows:

The formula of the standard solution (parts by weight) is:

| | GRAMMES. |
|---|---|
| Ammonii Sulphatis (C. P.) | 1.2738 |
| Cupri Sulphatis (C. P.) | 2.5587 |
| Potassii Hydroxid. (C. P.) | 19.1620 |
| Aquæ Ammon. (Sp. gr. 0.80) | 312.2222 |
| Glycerini (C. P.) | 60. |
| Aquæ (dest.) | qs. |

One cubic centimeter of the reagent is the equivalent of:

| | GRAMMES. |
|---|---|
| Cupro-diammonium Sulphate $(N_2H_6Cu)SO_4$ | 0.03832 |
| Cupric Hydroxide, $CuOH_2O$ | 0.41062 |
| Grape Sugar, anhydrous, $C_6H_{12}O_6$ | 0.00526 |

The sulphates of ammonium and copper are chemically combined as a double salt. It is best prepared for this reagent by adding chemically pure ammonium hydrate to a solution of cupric sulphate; a bluish precipitate falls, which redissolves in excess of the alkali, to form a deep blue solution. Strong alcohol floated on the surface of the solution separates long right rhombic prisms, which are very soluble in water; this solution constitutes aqua sapphirina. (Witthaus). The crystals should be dried on bibulous paper *in vacuo* and used immediately, for if they are exposed to the air they part with their ammonia and are converted into a mixture of basic sulphates. In Fehling's, Pavy's and Purdy's solutions the solution of cupric sulphate is added to the solution of caustic potash, which forms cupric hydroxide. If added to the ammonia, it throws down the cupric hydroxide unless added to excess, yielding a deep purplish-blue solution that will only keep a longer or shorter period, according to the purity of chemicals used and care employed. A permanent reagent can only be prepared by chemical combination of these salts before adding to the caustic potash solution.

The official potassium hydroxide contains (other than fifteen to twenty-eight per cent of water), from five to ten per cent of impurities—viz., oxide of iron, chloride, sulphate, and carbonate of potassium, silica, lime, and alumina—and should be purified by the alcohol process. Digest the caustic potash in alcohol, which only takes up the alkaline hydrate, decant the solution from the precipitate, evaporate to dryness, and fuse the dry mass obtained.

Prepare the reagent with the chemicals as described, and add sufficient distilled water, so that 3.696 cubic centimeters (one drachm) are decolorized by 0.00526 gramme (one thirtieth of a grain) of anhydrous grape sugar.*

The following tables will give the amounts of sugar in analytical testing:

| If reduced by | It contains to the ounce, | Percentage. |
|---|---|---|
| 1 minim. | 16. grains or more. | 3.33 |
| 2 minims. | 8. grains. | 1.67 |
| 3 " | 5.33 " | 1.11 |
| 4 " | 4. " | 0.83 |
| 5 " | 3.20 " | 0.67 |
| 6 " | 2.67 " | 0.56 |
| 7 " | 2.29 " | 0.48 |
| 8 " | 2. " | 0.42 |
| 9 " | 1.78 grain. | 0.37 |
| 10 " | 1.60 " | 0.33 |

*Physicians can procure the reagent, accurately compounded as described, from the Lewis Chemical Company, No. 1300 Broadway, New York.

The Method of Procedure:—Heat one drachm of the reagent in a test-tube to boiling; add the urine slowly, drop by drop, until the blue color begins to fade; then more slowly, boiling three to five seconds after each drop, until the reagent be perfectly colorless, like water, or until ten drops only are added.

It will be noted after reduction that the reagent, on cooling, resumes the blue color again. This change is due to the absorption of oxygen from the atmosphere, changing the reduced suboxide held in solution to the blue protoxide again. This should not be mistaken for imperfect reduction or defect in the reagent. The change takes place quickly by shaking the tube, and the reduction can be repeated, if done immediately, before the evaporation of the ammonia by the addition of the saccharine urine as before, though not with the same degree of accuracy.

If albumin is present or a large amount of coloring matter, more or less of a yellow tint will be noticed.

In samples of urine loaded with sugar, dilution with water is necessary, for example, if one minim of *undiluted* urine reduces the reagent there is no telling how great a percentage of sugar above 3.33 is present. Therefore, dilute the urine with, say, four parts of water and multiply the amount found by the table by the amount of dilution. That is if three minims of urine *diluted* with four parts of water reduce the reagent then 5.33 (see table), multiplied by 5 (number of volumes of urine plus water, or 1 + 4) equals 26.65 grains per ounce. To find percentage multiply 1.11 (table) by 5, equals 5.55 per cent.

Dilution also serves to yield more accurate results, for example, if 7 minims of *undiluted* urine reduce the reagent the urine may contain anywhere from 2.29 to 2.67 grains per ounce. More precise figures may be obtained by diluting the urine, say, with one part water, when, if 14 minims of this diluted urine are necessary then the undiluted urine contains 2.29 grains to the ounce; 13 minims, 2.46 grains; dilution with 2 parts water would show 2.29, 2.42, and 2.54 grains.

To determine small amounts of sugar add lead acetate to the urine in proportions of one-third of a grain for each degree of specific gravity above 1,000 up to 1,024. if pale, or 1,030 if high-colored; the lead salt precipitates all albumin, phosphates, sulphates, chlorides, and coloring matter, but does not affect the dextrose; filter until perfectly transparent and colorless, and examine. This treatment should be given all dense urine loaded with uric acid, urates, and abnormal coloring matters, even when less than ten minims are required, if any doubt exists in the mind of the examiner about the reduction of the reagent.

Any shade of blue or green remaining in the reagent does not indicate sugar. The reduction with urine, thus treated, leaves the reagent colorless or a light amber tint, according to the amount required. If no sugar be present, the blue or green tint is not wholly dissipated, even if the dilution be carried much higher than in the tables given.

For experimental use with prepared urine, or with distilled water with a known trace of glucose added, a continuation of the table is appended:

| If reduced by | It contains to the ounce, | Percentage. |
|---|---|---|
| 11 minims. | 1.455 grains. | 0.308 |
| 12 " | 1.333 " | 0.278 |
| 13 " | 1.231 " | 0.256 |
| 14 " | 1.144 " | 0.238 |
| 15 " | 1.067 " | 0.222 |
| 16 " | 1.000 " | 0.208 |
| 17 " | 0.941 " | 0.196 |
| 18 " | 0.889 " | 0.185 |
| 19 " | 0.842 " | 0.175 |
| 20 " | 0.800 " | 0.167 |

Experiments with the small traces, as shown in the above table, are of no particular clinical importance, for small traces of sugar, not continuous, would not indicate pathological changes, but show the delicate and sensitive nature of the reagent, and require the utmost care and precision in performing the analysis.

In some urines a white or grayish cloud due to cuprous urate may be noticed or the blue color may fade to greenish but this has no significance. There is no reduction as long as any blue or green tint remains.

### MISCELLANEOUS NOTES ON SUGAR TESTING.

**Trommer's test.**—According to Charles Platt, of Philadelphia, the best way to apply this test is as follows: To urine in a test-tube add one-fourth its volume of 30 per cent sodium hydroxide, and then 10 per cent cupric sulphate solution, drop by drop, until a slight permanent precipitate is formed. Heat to boiling and, in presence of glucose, a reddish-yellow precipitate of cuprous oxide separates. If glucose be present it will be noticed that the cupric sulphate will form a greenish-blue precipitate on coming in contact with the urine, but that on agitation this precipitate will dissolve, forming a dark-blue solution, itself a satisfactory test for glucose in absence of sucrose and of glycogen. As most of the reducing substances other than sugar, which are apt to be present in the urine, react only at the boiling temperature, a second test may be prepared as described, and, without heating, allowed to stand twelve to twenty-four hours. If sufficient sugar be present a red precipitate of cuprous oxide will be obtained. The test so performed is practically free from the objection of other reducing substances, but requires a somewhat larger amount of sugar to be present; in other words, it is less delicate. A decolorization of the solution without separation of cuprous oxide is not necessarily indicative of sugar, nor is a precipitate forming only on cooling of the test. In the former case the smallest amount of cuprous oxide may be detected by Hoppe-Seyler's reaction with hydrochloric acid.

As an introduction to Trommer's, or, for that matter, to any sugar test, filtration through charcoal may be resorted to. By continued filtration a highly-colored urine may be reduced to a colorless solution practically free from reducing substances, sugar

included, unless the latter be in large amount. Seegen proposed to filter repeatedly through charcoal, to reject the filtered urine, to wash the charcoal carefully with distilled water, and to apply the tests to the washings. Charcoal filtration is, however, by no means so perfect a process as is Brücke's method with lead acetate. In this the phosphates, carbonates, sulphates, coloring-matter, etc., are removed by precipitation with neutral lead acetate, or boiling saturated solution of lead chloride. To the filtrate ammonium hydroxide is added in excess, the precipitated plumbic glucosate is filtered off, washed carefully, suspended in water, decomposed by passing hydrogen sulphide, and the hydrogen sulphide removed by boiling. The clear solution is then evaporated to the original volume of urine, allowed to stand several hours, again filtered, if necessary, and, finally, the filtrate is tested by any reliable sugar test.

A less tedious manner of securing at least a partial separation of other constituents of the urine from the sugar is by Allen's method. (See above).

**Purdy's test.**—Dr. Charles Platt finds that in the case of Purdy's solution many normal urines will show a reducing power equivalent to from 0.2 to 0.3 per cent of glucose, this substance, however, being entirely absent. Deduct, therefore, 0.2 per cent for each 5 c.c. of undiluted urine.

**Haines' solution.**—Dr. Platt says that small amounts of sugar 0.30 per cent, or less, are not detected by this reagent. Allen's modification of Fehling's test, the phenylhydrazin test, and the fermentation tests are more delicate.

**Brücke's modification of the bismuth test.**—Dr. Platt recommends this as one of our most reliable methods. Make up Frohn's reagent by dissolving 7 grammes of potassium iodide in 20 c.c. of water. Heat and add 1.5 grammes of freshly precipitated bismuth subnitrate and about 1 c.c. of strong hydrochloric acid. Add a few drops of this to 10 c.c. of water in a test-tube, then add hydrochloric acid, drop by drop, until the precipitate which has formed just disappears. To 10 c.c. of urine add the same amount of reagent and of acid as in the preliminary trial test. Filter, make the filtrate strongly alkaline with sodium hydroxide, and boil. A black precipitate will indicate glucose.

**The Phenylhydrazin test.**—Dr. Platt performs this test as described above in the second method, but uses 2 grammes of sodium acetate. In case the crystals are not clearly revealed, the yellow precipitate may be separated and dissolved in hot alcohol, the alcoholic solution added to water in a beaker, the alcohol removed by evaporation and the deposit again examined. This test is exceedingly delicate, responding to 0.001 per cent of glucose in aqueous solution and to 0.05 per cent in the urine.

**The fermentation method.**—Dr. Platt says that rather better results may be obtained by Antweiler's and Breitenbend's method of fermentation in presence of Rochelle salts and determination of the loss in weight due to evolution of carbon dioxide. This loss in weight multiplied by 2.045 gives the amount of glucose in the sample taken (2.0454 parts of glucose producing one part of carbon dioxide on fermentation).

# CHAPTER XXXVII.

## CLINICAL SIGNIFICANCE OF GLYCOSURIA.

Glucose is found in the urine under the following circumstances:

1. **In traces** in normal urine, but not recognized by the tests usually employed. Patients who view glycosuria calmly are in the habit of asking the writer whether "sugar" is not found in *all* urine. To such the answer "No," should be given, especially since Jolles denies that even traces are present.

2. **Transitory and due to alimentary causes:**—If a person have glycosuria from ingestion of so small an amount as 100 grams (about 3 ounces) of chemically pure glucose the condition is to be regarded as pathologic, showing a diminished power of utilizing carbohydrates in the system. Diffuse cerebral lesions referable to alcohol and syphilis are likely to give rise to this digestive glycosuria, which may follow the ingestion of 100 grams of glucose. In lead colic this glycosuria has been observed and as a constant symptom of functional neuroses (grand hysteria and traumatism); also in phosphorus poisoning.

3. **Transitory** in many nervous diseases:—Lesions affecting the central as well as the peripheral nervous system, such as tumors and hemorrhages at the base of the brain, lesions of the floor of the fourth ventricle, tetanus, sciatica, cerebral and spinal meningitis, concussion of the brain, in about 10 per cent of cases of head injury, fracture of the cervical vertebræ; following epileptic, hystero-epileptic, and apoplectic seizures, mental shock produced by railroad accidents, etc., (traumatic neuroses), mental strain and worry, fatigue, and anxiety. (Probably due to distinct or reflex influence affecting the floor of the fourth ventricle).

Transitory also in certain acute febrile diseases, par-

ticularly during convalescence, namely, typhoid fever, scarlatina, measles, cholera, diphtheria, influenza, and especially malaria. (Due possibly to action of ptomains or leukomains on the floor of the fourth ventricle).

Transitory also in cases of poisoning by a number of substances: — Curare, chloral hydrate, sulphuric acid, alcohol, carbon monoxide, morphine, etc., and even after simple transfusion of normal salt-solution into the blood.

Phloridzin (a glucoside from the bark of the root of the apple tree), will likewise cause sugar to appear temporarily in the urine, ceasing with the withdrawal of the drug.

4. **Persistent** in connection with certain brain lesions, particularly those affecting the floor of the fourth ventricle.

5. **Persistent** in the disease known as *diabetes mellitus*, together with more or less polyuria, and increased elimination of solids, except uric acid, and associated in advanced cases with *acetonuria*, *lipuria*, and *lipaciduria*. (See further on).

FLUCTUATIONS IN THE QUANTITY OF SUGAR IN DIABETES MELLITUS.

According to Simon the following is true:

1. Cases have been known in which 360 grams (5,580 grains, or about one pound) of sugar in 24 hours have been passed.
2. The severity of the pathologic process cannot be measured by the amount of sugar eliminated. The total amount of sugar may not exceed a few grams daily, and yet the disease rapidly tend toward fatal termination.
3. Absence of sugar from the urine in one or even more urinary examinations does not exclude diabetes. In such a case give the patient 100 grams of glucose, and test the urine three or four hours afterward.
4. A light case of diabetes in which the sugar has disappeared under dietetic treatment may suddenly become severe, and apparently severe cases may suddenly assume a more benign type.
5. In a type described by Hirschfeld a specific gravity of 1012 and greatly diminished elimination of solids is noticed.

THE BEGINNING OF DIABETES MELLITUS.

According to Loeb the following is true:

1. Little is known with respect to the earliest stage of diabetes.
2. The temporary occurrence of a small quantity of sugar in the urine ought not to be regarded lightly; severe diabetes sometimes follows.

3. Some cases of diabetes are acute from the first.
4. Some cases of slight and temporary diabetes recover completely.
5. In a great number of cases of diabetes before a large quantity of sugar is excreted, small quantities are excreted temporarily, often for years.

### NOTES ON THE WRITER'S CASES.

In the writer's experience the urine of all persons should be tested in the afternoon, about two hours following the noonday meal. Traces of sugar discoverable by Haines' test may be present at that time but absent at other hours of the day.

In the writer's experience polyuria is not a constant symptom among well-cared for Americans with diabetes. Not over 50 per cent of 70 cases seen by the writer had noteworthy polyuria, and in his private practice the largest amount ever collected and *accurately* measured was 18 pints. The mortality among all the polyuric cases seen in 7 years was 42 per cent, but no typical case of glycosuria *without* polyuria and other marked symptoms proved fatal in that time. Half the writer's patients voided 20 to 40 grams of urea per 24 hours. The mortality was directly proportioned to the quantity of urea, the safest excretion being 20 to 30 grams. The mortality in those voiding over 60 grams of urea was very great.

The author has had several cases in which the patient although intelligent, was not aware of having any disease, even when there was considerable polyuria and over 1,000 grains of sugar daily.

The thirst is greatest in cases where the percentage of sugar rises above 4 per cent. In a case in which there was 6 per cent of sugar, thirst was intense, but when, under the writer's mineral water treatment, the sugar fell to 4 per cent, the patient declared that he drank no more water than was prescribed for him, namely 8 glasses per 24 hours, and was no more thirsty than usual.

### REDUCING SUBSTANCES OCCASIONALLY FOUND IN URINE.

Besides glucose there are found in the urine the following carbohydrates: Lactose, levulose, maltose, dextrin, laiose, pentose, inosite, and animal gum; cane sugar, and glycogen may also occur. In addition to these, certain acids are found which have reducing properties, viz., glycuronic acid and glycosuric acid.

**Levulose:**—The usual tests show presence of a reducing substance, and polarimetric examination shows a deviation to the left or none at all. Occasionally present in diabetic urine.

**Lactose.** See Chapter XIX.

**Maltose:**—The phenylhydrazin test gives crystals differing in appearance from those of glucose, and they melt at a temperature about 16° C. lower than that of the glucososazon crystals. Found in the urine of a person supposedly with pancreatic disease, associated with acholic stools.

**Dextrin:**—On application of Fehling's test the blue liquid becomes first green, then yellow, and sometimes dark brown. Has been found in diabetic urine.

**Laiose:**—Titration with Fehling's solution shows from 1.2 to 1.8 per cent more sugar than the polarimetric method.

**Pentose:**—This sugar occurs in milk, tea, coffee, and wines, in normal urine and in diabetic urine. Salkowski says that in order to test for pentose take 200 to 500 c.c. (6¾ to 16 fluidounces) of urine, and for each 100 c.c. (3¼ fluidounces) add 2½ grams (39 grains) of phenylhydrazin dissolved in a quantity of acetic acid, sufficient to render the solution acid. Heat the mixture in a Bohemian-glass vessel until it begins to boil, then place in a water bath for an hour and a quarter. When cooled, the crystals of phenylpentosazon will be obtained. The crystals melt at 158° C. (316.4° F.), and are dissolved by water of 60° C. (140° F.) temperature. Fermentation by ordinary yeast destroys pentose. Tollen's test (heating the urine with a saturated solution of phloroglucin in hydrochloric acid), shows pentose to be present in most diabetic urines, and in the urine of dogs rendered diabetic by ablation of the pancreas or by ingestion of phloridzin.

**Inosite** and **animal gum** have already been considered. See Chapter XIX.

**Cane sugar** may occur in traces in the urine. If containing other sugars as impurities it may reduce copper tests, otherwise not. *Glycogen* has been found in some diabetic urines.

### ACIDS WITH REDUCING POWER.

**Glycuronic acid:**—This substance, $C_6H_{10}O_7$, occurs in the urine abundantly after administration of such drugs as chloral, butyl-chloral, morphine, chloroform, camphor, curare, nitrobenzol, etc. It is occasionally found in the urine of apparently healthy people. *Detection:*—Urine containing glycuronic acid reduces Haines' and Fehling's solutions, giving a yellow or even red precipitate, and rotates the plane of polarized light to the right, but fermentation with yeast shows no glucose present. Phenylhydrazin forms crystals, with glycuronic acid, but they differ from those of phenylglucosazon, being in the form of rosettes, while the needles are thick and plump, the whole resembling crystals of ammonium urate. They melt at 150° C. (302° F.)

**Glycosuric acid:**—This substance, called also uroleucinic acid, urrhodinic acid, and *alkapton*, occurs very rarely in urine. Urines which contain it are normal in color, when voided, but turn dark on standing. Glycosuric acid is more frequently found in the urine of children than in adults, the condition at times occurring in families, and persisting for years. Its significance is not known, though Dr. Marshall, of Philadelphia, noticed a gradually increasing weakness in a case coming under his observation. Glycosuric acid reduces Fehling's solution, but merely causes a blackish discoloration when the bismuth test is used. Fermentation is negative. When Ehrlich's test is applied, a dark-brown color develops on standing for fifteen minutes, while at the end of an hour the urine has turned almost black. The first person to isolate glycosuric acid was Marshall of Philadelphia.

# CHAPTER XXXVIII.

## ACETONE AND ALLIED SUBSTANCES.

Acetone has already been alluded to in describing diabetes mellitus, as it frequently occurs in the urine of that disease. This substance, a thin, colorless liquid of peculiar fruit-like odor, dimethyl-ketone, $CH_3 — CO — CH_3$, occurs in small amount in normal urine, blood, and secretions; the amount is notably increased in diseases. A purely albuminous diet increases it after 48 hours and, in general, acetonuria is always due to increased albuminous decomposition. Continuous administration of white of eggs causes its appearance. It has been found in febrile diseases of long duration, in certain nervous diseases, as in general paresis, melancholia, tabes, and after epileptic seizures; also in Addison's disease, general carcinomatosis, eclampsia, and other conditions where there is increased albuminous decomposition.

*Detection:*—Distill 500 to 1,000 c.c. of urine adding 1 gram phosphoric acid pro liter and employ the first 10 to 30 c.c. for the following tests:

1. Luben's test:—Treat a few c.c. of the distillate with several drops of a dilute solution of iodo-potassic iodide and sodium hydrate; iodoform is formed, recognized by its odor. Lactic acid and alcohol, if present, also form iodoform.

2. Baeyer's indigo test:—This test may be applied to the urine directly. Dissolve, by aid of heat, a few crystals of nitro-benzaldehyde in the urine; on cooling the aldehyde separates in the form of a white cloud. Make the solution alkaline with dilute solution of sodium hydroxide and, if acetone be present, first yellow, then green, and lastly an indigo-blue color will appear within ten minutes.

3. Reynold's test:—A few c.c. of the distillate are treated with a small amount of freshly precipitated yellow oxide of mercury. (The latter is made by precipitating solution of mercuric chloride with an alcoholic solution of sodium hydrate). Shake the mixture, filter, and add a few drops of ammonium sulphide to the clear filtrate. If acetone be present, a black color due to formation of mercuric sulphide is seen.

Inasmuch as few physicians have the facilities for distilling urine, it is easier in diabetes mellitus to test for the next constituent to be considered, namely,

### DIACETIC ACID.

This substance, a colorless, strongly acid liquid, also known as ethyl-diacetic acid, $CH_3.CO.CH_2.CO_2H$, when found in urine, is always of pathologic significance. It is found especially in diabetes, in various forms of digestive disturbance, and in the high and continued fevers of children and others. It strikes a Bordeaux-red with solution of ferric chloride and is tested for as follows: To a few c.c. of urine add a strong solution of ferric chloride (perchloride of iron), drop by drop, until the precipitation of phosphates ceases. This may be readily observed by letting the precipitate settle, after a few drops of the iron solution have been added, which it will do in about ten minutes. Filter, and to the filtered urine add more of the iron solution. If now a Bordeaux-red color is seen, another portion of the urine is boiled and similarly treated, and if this second sample give no reaction, suspect presence of diacetic acid. Confirm by treating a third portion of the urine with sulphuric acid, shake the mixture with ether, and draw off the ether. Test the ethereal extract with the iron solution as above, and if the Bordeaux-red color be obtained, which disappears on standing for 24 to 48 hours, diacetic acid is present, especially if acetone can be detected in the distillate.

It is necessary to boil the urine, as in the second case above, since this procedure prevents the reaction

with diacetic acid but not the reaction with the urine of those who have taken various drugs, (thallin, antipyrin, salicylic acid, and phenol), also fatty acids and other compounds. If then, *after* boiling, the Bordeaux-red appear, it is due to something else besides diacetic acid.

CLINICAL NOTES ON ACETONE AND DIACETIC ACID.

1. The writer deems the test for diacetic acid an important one, as he has found it in the urine of several diabetics who speedily died, and has not found it in cases which have been apparently cured by his mineral-water treatment. (See *Hahnemannian*, January and April, 1897).

2. Jaksch proposes to substitute the term diacetic coma for diabetic coma, deeming the coma due to diacetic acid in the blood.

3. Diaceturia is least significant and not uncommon in febrile conditions in children.

4. Diaceturia is especially common in the diabetes of children and the writer finds it an ominous sign. Its appearance is often preceded by diminution in the quantity of sugar.

5. Diaceturia in the height of acute fevers in *adults* is of grave significance.

6. Diaceturia is sometimes a sign of anto-intoxication, so-called *diacetæmia*, accompanied by vomiting, dyspnœa, and jactitation, soon ending, in case of adults, in coma and death without other discoverable disease or lesion. Children may recover from it. When acetone without diacetic acid is present, such cases may recover whether adults or children.

7. The breath gives the odor of acetone (chloroform and acetic acid) in diabetic coma, and also, in case of children suffering from various febrile affections.

8. The urine, also, in long continued fevers may have the odor of acetone.

9. In the gastric crises of diabetes, now well recognized, especially in cases serious from the beginning, acetone may be present in the urine, and the odor of it may be noticed in the breath.

10. Although acetone, diacetic acid, and oxybutyric acid appear to be connected with the phenomena of diabetic coma yet it is possible that they are a result rather than a cause of it. The presence of toxins circulating in the blood, causing an increased tissue-destruction, with simultaneous formation of abnormal acids, may possibly be the cause of the coma. (C. E. Simon).

OXYBUTYRIC ACID.

There is no easy method of detecting this substance in urine though its occurrence is of great clinical interest. It is an odorless syrup, B-oxybutyric, or hydroxybutyric acid, $C_3H_6OH.COOH$, optically active, lævo-rotatory, and its presence may be inferred if, after fermentation, the urine rotate the plane of polarized light to the left

# CHAPTER XXXIX.

## ABNORMAL COLORING MATTERS IN URINE.

The following abnormal coloring matters will now be considered: Blood-pigments, biliary pigments, pathologic urobilin, melanin, the chromogen giving Ehrlich's reaction, and some others of less importance.

**Blood-pigments:**—The tests for these have already been given. (See Hæmoglobinuria). *Hæmatin* is a rare pigment which is identified by the spectroscope. *Urorubrohæmatin* and *urofuscohæmatin* are two rare pigments observed by Baumstark in the urine of a case of pemphigus leprosus complicated with visceral lepra.

**Hæmatoporphyrin** is attracting some attention now, as it is found in the urine during long continued administration of sulfonal. Urines rich in this pigment present an abnormal color, varying from a sherry or port-wine tint to Bordeaux-red. Clinically it does not appear to be of any special significance. Its formula is $C_{16}H_{18}N_2O_3$, and it is probably closely related to the hæmatoporphyrin resulting from action of sulphuric acid on hæmatin.

## BILE IN THE URINE.

Choluria shows itself by presence of the bile pigments in urine. Of these bilirubin alone occurs in freshly voided urine, the others forming on standing. Whenever the outflow of bile into the intestines becomes impeded, bilirubin is absorbed by the lymphatics and eliminated in the urine, icterus at the same time resulting.

**Color of urine containing bile:**—This varies from a bright yellow to a greenish-brown, sometimes almost black. After bile has been abundant in the urine and has diminished to small quantities, the urine has an intense yellow color, resembling somewhat dilute potassium chromate solutions.

**Odor of urine containing bile:**—The odor strongly suggests ox-gall, and those who are familiar with this substance can detect bile in the urine without chemical tests.

**Foam of urine containing bile:**—The foam of biliary urines is increased and may show, if held in the right light, a peculiar color, usually greenish-yellow.

**The sediment of biliary urines:**—One of the easiest ways to detect bile is to examine the sediment with the microscope. Epithelia are stained an intense golden-yellow, tube-casts also. Granular casts show a peculiarity in this respect, certain parts of them being darker and more opaque than others. Filter-paper is also stained by biliary urine.

**Chemical tests:**—Of the legion of tests for bile only two will be considered.

1. *Rosenbach's:*—This, according to Jolles, is the most delicate and is a modification of Gmelin's. The urine is filtered through thick Swedish paper, the latter removed, and, on the inner surface of it, is placed a drop of concentrated nitric acid, which has been allowed to stand exposed to the air for a short time. In the presence of bilirubin rings presenting the colors of the rainbow will form around the nitric acid.

2. *Huppert's test:*—This is a favorite among chemists; 10 to 20 c.c. of urine are precipitated with milk of lime, or a solution of barium chloride, and the precipitate, after filtering, brought into a beaker by perforating the filter and washing its contents into the latter with a small amount of alcohol acidulated with sulphuric acid. The mixture is boiled, when, in presence of bilirubin, the solution assumes an emerald-green color. Urine tested for bile should be freshly voided.

CLINICAL NOTES.

1. The bile pigments in urine may appear several days before icterus is perceptible.

2. They are found in urine in numerous diseases of the liver, in which icterus may or may not be present.

3. The diseases in which bile is most often seen in

the urine are, besides catarrhal jaundice, biliary calculus, parasites, compression of the duct by tumors of the liver, of the gall-bladder, the duct itself, and of neighboring structures, namely, the pancreas, stomach, and omentum. In diseases in which the blood pressure in the liver is lowered. In cases in which degenerative processes are affecting the glandular epithelium, as in acute yellow atrophy or where the destruction of red corpuscles is going on rapidly so that the liver cannot transform into bilirubin all the blood pigment carried to it, as in pernicious anæmia, malarial intoxication, typhoid fever, poisoning with arseniuretted hydrogen, etc.

### BILIARY ACIDS.

These occur together with bile pigment and their significance is essentially the same. Dr. Oliver's method of detection is simple, and as follows:

To 20 minims of clear filtered urine reduced to 1,008 in specific gravity add 60 minims of test-fluid prepared as follows:

| | |
|---|---|
| Pulverized peptone | gr. xxx; |
| Salicylic acid | gr. iv; |
| Acetic acid (B. P.) | m. xxx; |
| Distilled water to | fl. oz. viii. |

To be filtered repeatedly until transparent.

If bile salts are present in quantity greater than normal, a distinct milkiness promptly appears, becoming more intense in a moment or so. If the bile salts are in normal or less than normal quantity, there is no immediate turbidity, but in a short time a slight tinge of milkiness is seen.

For **Cholesterin** see SEDIMENTS.

### PATHOLOGIC UROBILIN.

This substance must not be confounded with normal urobilin (urochrome). It may be obtained, according to Gautier, from urochrome by submitting the latter to the action of reducing agents. It represents a lower form of oxidation than normal urobilin, and, like it, is derived from the coloring-matter of the blood and bilirubin.

**Color of urine containing pathologic urobilin:**—This is usually dark yellow, resembling that due to bile, and even the foam may be colored.

**Tests:**—

1. Huppert's test for bile (see above) gives a brownish-red precipitate where urobilin is abundant, disappearing upon boiling with acidulated alcohol, the liquid at the same time becoming colored a brownish or pomegranate red. If but a small amount of the pigment is present, the liquid is colored only a light reddish tinge. (Jaksch's test).

2. Gerhardt's test:—Shake 10 to 20 c.c. of the urine with chloroform and treat the extract with a few drops of a dilute solution of iodo-potassic iodide. On the further addition of a dilute solution of sodium hydrate the chloroform extract is colored a yellow or yellowish-brown, and exhibits a beautiful green fluorescence which is even more intense than in the case of normal urobilin.

3. If these tests fail, recourse must be had to the *spectroscope*. In acid urines or solutions urobilin presents a distinct band of absorption between "b" and "F," extending beyond "F" to the right, while in alkaline solutions a band is likewise seen between "b" and "F" which does not extend beyond "F," and is less intense.

CLINICAL NOTES ON PATHOLOGIC UROBILIN.

1. In 12 cases of atrophic and hypertrophic cirrhosis Jaksch was able to find urobilin in the urine in every instance.

2. Simon has found it in a few cases of hepatic cirrhosis, chronic malaria, and pernicious anæmia, in all of which the skin showed a light icteric hue, but bile pigment was absent from the urine.

3. Urobilinuria occurs most commonly in the course of extensive cutaneous hemorrhages due to scars, carcinoma, the hemorrhagic diathesis, etc. Individuals in whom this process is going on exhibit a yellowness of skin, but there is no bile in the urine and no obstruction of the bile ducts. (Jaksch).

4. Binet has found urobilin *increased* in digestive disturbances, infectious diseases, measles, scarlatina, typhoid fever, and pneumonia, but *scanty* in uncomplicated diphtheria.

5. Riva believes that the greater part of urobilin and its chromogen is of intestinal origin, but under the influence of modifications in the biochemical function of the liver not yet understood.

6. According to Hayem urobilinuria is an early sign of hepatic incompetence, as in the beginning of cirrhosis of the liver, in cardiac cases where hepatic lesions are imminent, and in numerous acute affections in alcoholics. He thinks it a bad sign in typhoid fever. He finds it in newly-delivered and in nursing women; also in most forms of cachexia. Relatively pale urines may contain it.

7. Mya thinks urobilinuria a sign of destruction of the red blood corpuscles; he finds it in pneumonia,

febrile polyarthritis, typhoid fever, and anæmias, in poisoning by pyridin, antipyrin, acetanilid, and other similar substances; also in grave hepatic lesions.

### MELANIN.

In cases of melanotic disease the urine, normal in color when voided, gradually darkens on exposure and finally becomes black. Such urines generally contain melanin and its chromogen in solution. Deposits of melanin are not by themselves at all characteristic of melanotic tumors, being found in malarial conditions. Moreover melanin itself may be absent in cases of melanotic tumors and present in wasting and inflammatory conditions. Its occurrence is merely confirmatory of other symptoms of melanotic tumor.

**Tests:—**

1. A few c.c. of urine are treated with bromine-water, when, in presence of melanin or melanogen, a precipitate will be obtained, which is yellow at first, and then gradually turns black.
2. The addition to melanotic urine of a few drops of a strong solution of perchloride of iron will cause the appearance of a gray color, which is imparted to the precipitate of phosphates occurring at the time if more of the reagent be added, and which dissolves again in an excess.

### VARIOUS COLORS IN URINE.

**Phenol urines:**—Certain urines darken on standing when melanin is absent. The color may be due to presence of various oxidation products of hydrochinon, as in cases of poisoning by *carbolic acid* or following the ingestion of pyrocatechin, salol, hydrochinon, salicylic acid and its compounds in large doses.

**Tests:—**

1. Ferric chloride solution develops a marked violet color which does not disappear on standing, when salol and salicylic acid have been taken.
2. In suspected carbolic acid poisoning, if the ratio of mineral to conjugate sulphates, normally 10 to 1, becomes greatly diminished, without other cause, the diagnosis of poisoning by carbolic acid may be inferred.
3. Tests for melanin are negative.

**Alkapton:**—This substance has already been described under the name glycosuric acid. Urines containing it, though normal in color when voided, darken on standing.

**Blue urines, etc.:**—These are usually referable to internal use of methyl blue, which is administered in the treatment of malaria, chyluria, cystitis, and other diseases. Sometimes, however, indican is formed within the urinary passages and colors the urine blue, but the occurrence is of unknown significance. Indigo taken internally will also color urine blue.

*Green* urines occur, but the cause of the color is not definitely known. See Chapter IV.

Urines containing *copaiba* turn red on addition of hydrochloric acid, and the red color is changed to violet on application of heat.

During administration of *iodine* or the *iodides*, nitric acid turns urine dark mahogany and the Stokvis-Jaffé indican test develops a beautiful rose-red color in the chloroform.

INFLUENCE OF DRUGS, ETC., ON THE COLOR OF URINE.

The drug substances, named below, when taken internally, influence the color of the urine as follows:

Aloes, reddish.
Alizarin, reddish.
Analgen, blood-red after large doses or continued use.
Anilin chlorhydrate, external use, may cause dark red color in urine.
Antipyrin, urine darker than normal.
Arseniuretted hydrogen, poisoning by this agent, black urine.
Bilberries, reddish.
Blackberries, darker than normal.
Carbolic acid, in time the urine assumes a dark to olive-green color, changing to blackish.
Carrots, reddish-yellow.
Chelidonium, brownish yellow or red; blood-red in alkaline urine.
Cascara, yellow or reddish-yellow.
Chrysophanic acid, yellow or orange-color.
Coffee, strong coffee darkens the urine.
Creosote, darkens the urine.
Frangula (Buckthorn), yellow or reddish-yellow.
Fuchsin, reddish.
Gallic acid, may darken the urine.
Gamboge, yellow more intense than normal.
Hydrochinon, darkens the urine.
Indigo, blue color.
Kairin, urine darker than normal or greenish-brown.
Logwood, darkens the urine.
Madder, reddish.
Methyl-blue, imparts blue color to urine.
Mulberries, red.
Naphtol, dark to blackish-brown color.
Phenocoll, brown-red to blackish brown.
Picrotoxin, yellow.
Potassium chlorate, poisoning by this agent, black.
Pyrocatechin, darkens the urine.
Pyrogallic acid, external use may give urine a brown tint.
Quinine, urine darker than normal.
Resin, grayish-yellow.
Resorcin, darkens the urine.
Rhamnus, see Cascara.
Rheum, bright-yellow, deep-yellow or greenish; alkaline urine, intense red.
Salicylic acid, in large doses, smoky hue.
Salol, dark-brown color.
Santonin, yellow, more intense than normal; alkaline urine, intense red or orange-red.
Senna, like Rheum.
Sulphuric acid, poisoning by this agent, black urine.
Sulphonal, at times clear dark-red, due to hæmatoporphyrin.
Tannic acid, may darken the urine.
Tar, darkens the urine, when applied by inunction to the body.
Thallin, yellow to brownish with a greenish tint.
Trional, see sulphonal.
Turpentine, often darkens the urine.
Uva Ursi, color darker than normal.

### EHRLICH'S DIAZO REACTION.

This reaction has been called the *typhoid fever reaction*, due to presence of a chromogen in urine, which, when treated with a solution of diazo-benzene-sulphuric acid and ammonia imparts a color to urine varying from eosin to deep garnet-red.

**Method of application:**—Simon advises the test to be made in the following way: A few c.c. of urine are poured into a small test-tube, an equal quantity of the sulphanilic-acid mixture (see (*c*) below), is added and the whole thoroughly shaken: 1 c.c. of ammonia water is then allowed to run carefully down the side of the tube, forming a colorless zone above the yellow urine containing the acid. At the junction of the two, a more or less deeply colored ring will be seen, the color of which is readily distinguished, the slightest *carmine* tinge being shown readily by contrast with the colorless zone above and the yellow below. If, now, the mixture be poured into a porcelain basin containing water, a *salmon-red color* will be obtained if the chromogen in question is present, but a yellow or orange-red when it is absent.

NOTE:—The solutions required are made as follows: (*a*) 50 c.c. of hydrochloric acid are diluted to 1,000 c.c. with distilled water, then saturated with sulphanilic acid; (*b*) 5 grams of sodium nitrite are dissolved in 95 c.c. of distilled water; (*c*) a mixture is then made of 40 c.c. of the sulphanilic acid mixture made as in (*a*) with 1 c.c. of the sodium nitrite mixture made as in (*b*) and this mixture (*c*) is used in performance of the tests.

Ehrlich's original method was to add the mixture (*c*) to the urine in equal parts with ammonia in excess. His modified method was to add about 50 c.c. of absolute alcohol to 10 c.c. of urine, filter, and add to the alcoholic urine the mixture (*c*) from a burette, 20 c.c. of the mixture to 30 c.c. of the alcoholic urine, adding the mixture in small quantities at a time and shaking thoroughly. Then on addition to the whole of a few drops of ammonia the characteristic color appears, which disappears on shaking and becomes permanent only after adding excess of ammonia.

**Colors obtained:**—The characteristic color is *carmine-red*; it may vary from eosin to deep garnet-red. An orange color may be obtained in normal urine. Urines containing bile may exhibit a dark cloudy discoloration changed to reddish-violet on boiling. Urine containing alkapton may exhibit a dark-brown color on

standing. In rare instances of diseases associated with well marked chills, Ehrlich's original method (see above) develops an intensely yolk-yellow color, even imparted to the foam.

### CLINICAL NOTES ON THE DIAZO REACTION.

1. The reaction when found between the 5th and 13th day of a disease, the diagnosis of which is in doubt, disappearing later, points to typhoid fever.
2. The reaction may occur in other acute febrile diseases, as scarlatina, measles, small-pox, malaria, pneumonia, etc.
3. The reaction is found in phthisis pulmonalis, and its presence for any length of time is of bad omen.
4. Differentiation between acute miliary tuberculosis and typhoid fever may be made as follows: In typhoid fever the reaction is usually present as early as the 5th or 6th day, and disappears not later than the 22d day; in acute tuberculosis it does not appear earlier than the beginning of the 3d week and then persists almost to the end.
5. Absence of the reaction from the 5th to 9th day in typhoid usually indicates a mild case, except in children. Exceptions are, however, occasionally noted as when in severe cases the reaction is not obtained before the third week, and lasts only a few days.
6. Rötheln is distinguished from measles by absence of it.
7. Tubercular phthisis is differentiated from chronic pulmonary disease by presence of it.
8. The reaction is occasionally obtained in the healthy; invariably in typhoid fever and pneumonia; generally in pleurisy; frequently in measles, peritonitis, suppurative inflammations, erysipelas, and phthisis; occasionally in rhachitis and diabetes mellitus.
9. It is absent in malignant and chronic non-tubercular lesions.
10. Its absence is very valuable testimony in showing that an affection is not typhoid fever.

11. Morphine, even in dilute solution, yields the diazo reaction according to Hewlett.

### CHEMICAL EXERCISE XVI.

1. Obtain some urine containing bile; note the color, odor, and color of the foam.

2. Examine the sediment with the microscope, and note that epithelia and various elements are stained by the pigments.

3. Try Rosenbach's test and Huppert's test on freshly voided biliary urine.

4. Note that the filtered urine will in most cases show a trace of albumin.

5. Obtain the urine of a patient with typhoid fever after the fifth day and demonstrate Ehrlich's reaction in it.

# CHAPTER XL.

## ANIMAL BASES IN URINE. TOXICITY OF URINE.

Animal substances of a basic nature occur in urine, in small quantities in normal urine, but in larger quantities during certain pathological conditions. They are called *ptomains* or putrefactive bases, transition products of decomposition, that is, temporary forms through which matter is being transformed from the organic to the inorganic state by agency of bacteria and *leucomains*, products either of fermentative changes other than those of bacteria, or of retrograde metamorphoses. These compounds are of the greatest interest and importance in modern medical study since they may be regarded as the chemical causes which lie at the bottom of all infectious diseases, but as yet it must be admitted that the whole subject is wrapped in the deepest obscurity

**Chemical properties of the animal bases:—**

1. They resemble alkaloids, containing nitrogen, are all alkaline in reaction, insoluble in water, but soluble in acids forming compounds with the latter, from which compounds they are precipitated by ammonia.

2. They are energetic reducing agents decomposing chromic acid, iodic acid, and silver nitrate; they give Prussian-blue with potassium ferrocyanide and ferric chloride.

3. They are all oxidizable and unstable, especially under the influence of an excess of mineral acid, which colors them red and then converts them to a resinous mass.

4. They are precipitated by numerous reagents, as picric acid, iodine and potassium iodide, potassio-mercuric iodide, phosphomolybdic acid, metatungstic and phosphotungstic acid, tannin, auric chloride, and iodide of potassium and bismuth in dilute solutions acidulated with sulphuric acid.

**Detection:**—Methods for detection are tedious. The Gautier, Stas-Otto, or Brieger methods are usually employed. That of Brieger is perhaps best suited for urinary work as follows:— Sufficient hydrochloric acid is first added to render the urine acid, and the mixture is then boiled for a few minutes and filtered. The filterate is concentrated at first over a flame, and subsequently over a water bath, to a syrupy consistence. If the urine is foul, it is especially advisable to evaporate in vacuo and at the lowest

possible temperature, and as a general thing this procedure is useful on account of the instability of the bodies sought.

The thick fluid is next mixed with 96-per cent alcohol, filtered, and the filtrate treated with a warm alcoholic solution of lead acetate. The resulting lead precipitate is removed by filtration and the filtrate concentrated—preferably *in vacuo*—to a syrup, and again taken up in 96-per cent alcohol. The alcohol is next evaporated, and the residue, disolved in water, is freed from lead by the addition of sulphuretted hydrogen and filtration. The filtrate is acidified with hydrochloric acid and evaporated to a syrupy consistence. It is then diluted with alcohol, and alcoholic solution of mercuric chloride is added. The resulting precipitate is boiled in water, and certain ptomains may separate at this stage in consequence of different solubilities of the double salts of mercury. The better to secure this, the precipitate may be treated successively with water at various temperatures. Should it be thought that the lead precipitate may have retained some of the ptomains, it may be suspended in water, the lead converted into sulphide, and the fluid treated in the manner just described.

The solution obtained as above is filtered, freed from mercury, and evaporated; the excess of hydrochloric acid is carefully neutralized with sodium carbonate (the reaction is kept feebly acid), then it is again extracted with alcohol to free it from inorganic salts. The alcohol is evaporated, the residue dissolved in water, the remaining traces of hydrochloric acid neutralized with alkali, the whole acidified with nitric acid and treated with phosphomolybdic acid. The phosphomolybdate double compound is separated by filtration and decomposed by neutral lead acetate or, more readily, by heating over a water bath. The lead is next removed by means of sulphuretted hydrogen (hydrogen sulphide); the filtrate is evaporated to a syrupy consistence and taken up with alcohol. Several ptomains are thus separated as hydrochlorates, and may be obtained in the form of double salts of gold, or platinic chloride, and of picric acid. The chloride of the base is obtained by removing the metallic base by precipitation with sulphuretted hydrogen, while the picrate is taken up with water, acidified with hydrochloric acid, and repeatedly extracted with ether to remove the picric acid. The last step is to ascertain if any ptomains remain in the phosphomolybdic acid filtrate after precipitation of the phosphomolybdic acid.

Brieger has obtained some of his ptomains by a simpler modification of his above complete method. Thus he has obtained *neurodin* by treating the aqueous extract of the organic matter, after boiling and filtration, with mercuric chloride, collecting the precipitate, decomposing it with sulphuretted hydrogen, evaporating the filtrate over a water bath, and extracting the base with alcohol.

**Character of the bases:**—Most of the members of the *uric acid leucomains* have been found in urine, namely, xanthin, paraxanthin, heteroxanthin, the alloxuric bodies and bases, hypoxanthin, methyl-xanthin, carnin, episarkin, epiguanin, etc. These bases are commonly spoken of as xanthin bases or nuclein bases since they are derived from the nucleins. [Kossel suggested that the nuclein bases be divided into two groups: *Xanthin* bases including guanin, xanthin, and its methyl derivatives, and *sarkin* bases including adenin, hypoxanthin, and their methyl derivatives. Uric acid constitutes a third group. Kossel and Krüger have

lately used the term *alloxuric bodies* to include uric acid and the xanthin bases, since these contain alloxan and urea-residues. On the other hand, *alloxuric bases* include xanthin, guanin, adenin, hypoxanthin, heteroxanthin, paraxanthin, also theobromin, theophyllin, caffein, and carnin. Episarkin would not be included in this group, as it probably has only an alloxan residue].

Other bases which have been found are reducin, parareducin, and a base containing an aromatic nucleus and giving a compound with platinum chloride. Thudichum thinks urochrome and kreatinin basic. Pouchet has found carnin and another base of the composition $C_7H_{12}N_4O_2$ or $C_7H_{14}N_4O_2$; also a base which he called extractive matter of urine, $C_3H_5NO_2$. He regards urine as containing small quantities of certain pyridin bases like those from decomposing fish. Baumstark isolated a compound having the composition $C_3H_8N_2O$, which could just be detected in forty liters of urine. Selmi succeeded in obtaining from pathological urines various bases which he calls pathoamins. The term urotoxin is likewise sometimes used to designate the urine poison. Bouchard, Villiérs, Lépine, Gautier, and others have apparently found basic substances in pathological urine.

In general, however, it may be said that it is comparatively easy to find alkaloids by the so-called alkaloidal tests in urine but much more difficult to isolate them in a chemically pure condition, such that their exact constitution can be determined.

The diamins, cadaverin, and putrescin have been isolated in a perfectly pure condition.

### SPECIAL METHODS OF DETECTION AND ESTIMATION.

**Luff's method:**—The urine of infectious diseases is examined as follows: Render a large quantity of the urine alkaline with sodium carbonate, and agitate with half its volume of ether. Let stand, remove ether, filter, shake with solution of tartaric acid. The alkaloids are removed as tartrates. Render the aqueous acid solution alkaline with sodium carbonate, shake with half its volume of ether, remove ether, evaporate spontaneously, dry residue over sulphuric acid, and test for alkaloids by dissolving in hydrochloric acid and precipitating with phosphomolybdic acid, potassio-mercuric iodide, etc.

**The alloxuric bodies and bases:**—Krüger and Wulff use a copper method as follows: 100 c.c. of the urine freed from albumin are placed in a beaker and boiled; then 10 c.c. of a 1 in 2 sodium bisulphite solution and 10 c.c. of a 13 per cent solution of copper sulphate are added and the whole raised to boiling. Finally 5 c.c. of a 10 per cent solution of barium chloride are added. This causes the precipitate to settle rapidly and permits washing. The precipitate is allowed to stand two hours, then filtered through a 10-12 cm. Swedish plaited filter and washed about five times with warm water (60° C.). The filter and

its moist contents are placed in a Kjeldahl round digestion flask (150 c.c.), and 15 c.c. of concentrated sulphuric acid added, together with 10 gm. of potassium sulphate and 0.5 gm. copper sulphate. On boiling for about one hour the solution becomes clear. The solution is then transferred to a flask, rendered alkaline with sodium hydrate, and distilled. Talc can be advantageously used to prevent bumping. The distillate is titrated with $\frac{N}{10}$ oxalic acid, using rosolic acid as an indicator.

By subtracting now from the nitrogen thus obtained, the nitrogen calculated from the uric acid estimated by the Salkowski-Ludwig method (see APPENDIX), the difference gives the nitrogen in the alloxuric bases in 100 c.c. of the urine. According to Baginsky, 2.8-3.8 mg. of xanthin bases are present in 100 c.c. of urine. This corresponds to 0.042-0.057 gm. per day. Krüger and Wulff found by the method just given that on an average 0.1325 gm. of alloxuric bases was excreted in the urine per day. The proportion of uric acid nitrogen to the nitrogen of the alloxuric bases was, on an average, 3.82 :1.

In a case of leukæmia, Bondzynski and Gottlieb found this proportion to vary from 1.06 :1 to 3.22 :1. The daily excretion of alloxuric bases was 0.5-0.6 gm.

### CLINICAL SIGNIFICANCE OF THE BASES.

1. In acute febrile diseases, as typhoid fever, pneumonia, pleurisy, and acute yellow atrophy, large amounts of the bases are found. Bouchard points out that these substances are probably formed in the lower portion of the intestinal tract.

2. The diamins, putrescin and cadaverin, have been found in cases of cholera, pernicious anæmia, and in connection with cystinuria.

3. Ptomains in notable amounts have been found in the urine of maniacs.

4. In cases of extensive skin-burns, a basic substance, presumably peptotoxin, has been found.

5. Toxins which in animals produce (*a*), convulsions;

(*b*), anæmia; (*c*), effects similar to those of Basedow's disease, have been extracted from urine.

6. A base behaving like cholin has been found in the urine of Addison's disease, and a base has been found by Hunter in pernicious anæmia.

7. Interest in the alloxuric bodies has been stimulated of late by investigations which go to show that aseptic surgical fever is due to increase of these substances.

8 Xanthin is said to be increased ten fold in acute nephritis. Vaughan finds xanthin in the sediment of urine in cases of enlarged spleen.

9. Xanthin and hypoxanthin are increased in leucocythæmia owing to the increase in nucleated white blood corpuscles.

Hypoxanthin is thought to be the substance once observed as a deposit by Bence Jones in the sediment, and called xanthin by him (see Sediments).

10. Paraxanthin is thought by Rachford to be the cause of migraine and other troubles. Its physiological action is to produce an almost *rigor mortis*-like condition when injected into the muscles.

11. Modern investigators are seeking to show that Bright's disease is due to irritation of the kidneys by passage through them of toxins, in all probability formed in the intestinal tract.

The work in this field of urinary toxins already done is enormous. To describe it in full would be a volume in itself. But as yet it has neither become sufficiently exact to be reliable nor is it capable of being used for clinical purposes. It is safe to say, however, that medicine of the future will achieve brilliant results from research work in these substances. The reader is referred to Vaughan and Novy (third edition), for much that is interesting in connection with the subject.

### THE TOXICITY OF URINE.

Bouchard's book on auto-intoxication has recently aroused much interest in this subject although Feltz and Ritter, as long ago as 1881, demonstrated the toxicity of normal urine by injecting it into the blood

of animals. Bocchi and Schiffer, Dupard, Lépine, Guérin, next investigated the subject, followed by Bouchard, Lenoir, and Charrin. Bouchard finds seven toxic agents in urine, namely, one diuretic, one narcotic, one sialogenous, three convulsive (two organic, one inorganic), and one reducing bodily heat.

Bouchard's intravenous injections on rabbits of normal urine show the following toxic symptoms:

A. Myosis (contraction of pupils), accelerated respirations, somnolence and coma; also lowered body temperature, diminished reflexes, death from convulsions or coma.

B. The toxicity *varies* under certain *circumstances:*

1. The urine is twofold as toxic during the day as during the night.
2. The night urine is strongly convulsive.
3. The day urine is strongly narcotic.
4. Active muscular exercise diminishes the toxicity.
5. The toxicity increases the longer the urine stands.
6. If urine is decolorized, by filtering through charcoal, its toxicity is diminished about one-third.
7. An aqueous extract (chiefly of the mineral elements) causes contraction of the pupil, convulsions, lowered temperature, but no coma, diuresis, or salivation.
8. An alcoholic extract causes deep coma and diuresis, but no convulsions nor myosis.

C. In diseases the following is found:

1. In acute uræmia the urine is non-toxic.
2. In acute infectious diseases and fevers, if the kidneys remain unaffected, the urine is more toxic than in health.
3. In kidney diseases, the urine is *much less toxic* than in health.
4. In tetanus the urine is powerfully toxic.
5. In pneumonia it is strongly toxic, producing convulsions similar to tetanic urine.
6. In typhoid fever it is then no more toxic than normal urine.
7. In cholera it produces cyanosis, convulsions, lowered temperature, albuminuria, and diarrhœa.

8. In leucocythæmia the urine is highly toxic, causing convulsions and death.

In kidney diseases, if it require 80 c.c. of urine to kill a rabbit of one kilogram weight, it may be assumed that the capacity of the kidneys is crippled about one-half; if a week later only 60 c.c. are required the condition of the kidneys is improved.

Apropos of this subject it may be of interest to quote the following from Vaughan and Novy:

"The chemical theory of so-called uræmia has received support in recent researches, notwithstanding the fact that the old idea that urea is the active poison and the theory of Frerichs that ammonium carbonate is the active agent, has been abandoned.

"Landois laid bare the surface of the brain in dogs and rabbits, and sprinkled the motor area with kreatin, kreatinin, and other constituents of the urine. Urea, ammonium carbonate, sodium chloride, and potassium chloride had but slight effect; but kreatin, kreatinin, and acid sodium phosphate caused clonic convulsions on the opposite side of the body, which later became bilateral. The convulsions continued at intervals for from two to three days, when, growing gradually weaker, they disappeared. Landois concludes that chorea gravidarum is a forerunner of eclampsia. These experiments have been confirmed by Leubuscher and Zeichen.

"Falck injected into both sound and nephrotomized animals fresh urine, urine and the ferment of Musculus and Lea, and urine which had undergone spontaneous decomposition, without producing any symptoms which were comparable with those observed in uræmia. However, he did find that if a few drops of an infusion of putrid flesh were added to the urine before injection, all the typical symptoms of uræmia were induced. That the infusion of putrid flesh alone had no effect was also demonstrated. This would lead us to believe that some ferment in the infusion converts some constituent of the urine into a highly poisonous body. In this connection attention may be called to the fact that kreatin may be converted by the action of certain

germs into methyl-guanidin, which produces convulsions. Whether such conversion occurs in uræmia or not, and if it does what the cause of it is, are questions which must be left for future investigations to decide. It would be well for some one to test the brain and blood of a person, who had died in uræmic convulsions, for methyl-guanidin."

# CHAPTER XLI.

## URINARY SEDIMENTS.

URINE on standing deposits a sediment which may be recognized as follows:

**Chemical tests for sediments:**—Let the glass containing the urine settle for several hours. When the sediment forms, remove it with a pipette. An ordinary glass tube will serve as a pipette. Close the upper orifice of the tube tightly with the finger, dip the lower end into the sediment and remove the finger; urine rich in sediment runs up into the tube; again close the upper orifice of the tube with the forefinger and remove the tube from the glass. The urine and sediment in the tube do not flow out as long as the finger is tightly pressed over the upper orifice. Insert the lower orifice into a test-tube, remove the finger, and the sediment will now flow out into the test-tube where it may be tested in various ways as provided further on. In this book under the heading Chemical Tests for Sediments it is always assumed that the sediment to be tested has been removed to a test-tube in this way, unless the centrifugal machine is used. When several chemical tests are to be tried, it is best to use several samples of the sediment in different test-tubes.

The centrifugal machine accelerates and simplifies chemical tests for sediments. Instead of waiting several hours for the urine to deposit its sediment, pour well-shaken urine into the two or more tubes of the centrifuge, revolve at moderate speed (say 1,700 revolutions) for five minutes and the sediment has collected in the bottom of the tubes. By a clever device of Dr. Purdy the urine can be poured off from the sediment in his tubes without loss of sediment. Chemical tests

may then be tried without necessity of transferring the sediment to a test-tube.

The following figure shows a centrifuge of modern make. The force exerted is enormously greater than that of gravity.

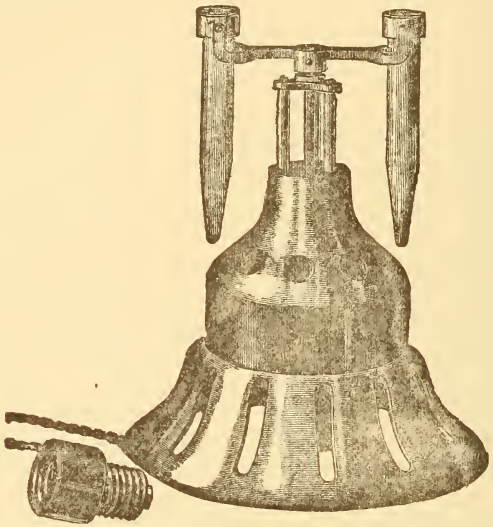


FIG. 46. Purdy's electric centrifuge, used by the author.

The sediments easily recognized, either by chemical means or by inspection are:

| | |
|---|---|
| Urates, | Blood, |
| Uric acid, | Pus, |
| Phosphates, | Calcium oxalate (less easily). |

We shall consider the sediments according to the reaction of the urine, whether acid or alkaline.

**Acid urine:—**

1. Hold the tube containing sediment in water heated to 60° C. (140° to 150° F.). If it clears wholly or partly, *urates* compose the sediment.

2. If it does not clear with heat, is of a brownish or yellowish color, and consists of small grains looking like "red-pepper grains," add a few drops of liquor potassæ to the sediment and shake; if it dissolves, *uric acid* is present.

3. If the sediment is small in amount and colorless divide into three portions, add acetic acid to one and hydrochloric acid to the other, shake thoroughly. If the second is dissolved and the first is not, *calcium oxalate* is probably present. Confirm by adding a few drops of liquor potassæ to third portion and notice insolubility.

4. If the sediment is whitish and especially if it is dense and creamy white, add a few drops of liquor potassæ to it. If it becomes greenish and gluey, perhaps forming viscid strings when poured from the tube, *pus* is present. The urine itself, if pus is present, will always respond to the albumin test, showing from traces to ½ on Esbach tube.

5. If the sediment is reddish in tint and does not respond to tests for urates nor appear as uric acid crystals, test for *blood* as follows: Mix equal parts of freshly made tincture of guaiac and old spirit of turpentine,* shake well, and cause a like amount of urine containing the sediment to trickle down the side of the tube into the guaiac-turpentine mixture. A dense yellowish precipitate (guaiac) is seen in all urines but, if blood be present, at the juncture of the yellow precipitate and fluid above it, is seen *a blue color*, slowly appearing.

Use freshly voided urine in making this test. The urine itself will always respond to the albumin test, showing from traces up to the 2d mark on Esbach tube according to amount of blood.

**Feebly acid, neutral, or alkaline urine:—**

1. Test a *whitish* sediment for phosphates by adding acetic acid and shaking well. If phosphates alone are present, the sediment is wholly dissolved. If the sediment is only partly dissolved, seen by comparison with some of the original sediment in another tube to which nothing has been added, phosphates are present together with other constituents, probably micro-organisms, mucus, epithelia, and perhaps pus.

*The turpentine should be well ozonized by exposure to air *and light.*

2. In alkaline urine a slimy, viscid sediment, which sticks to the glass or is clotted and gelatinous, is pus mixed with mucus and needs no chemical test. Acid urine containing a whitish sediment, if set in a warm place until alkaline, will then have this stringy sediment if pus is present.

**Urine of any reaction:—**

1. Sediments not readily recognized by any of the above tests are probably composed of mucus, micro-organisms, epithelia, and fungi. The urine of nearly all women contains an abundant mucous sediment which does not respond to the tests above. Excess of mucus in the urine is recognized by the slowness with which the urine filters.

2. Micro-organisms in urine are readily recognized by the hazy appearance they give to the urine. No matter how long the urine stands, the haze due to micro-organisms will not settle. It requires a high speed of the centrifugal machine to settle them, 2,000 revolutions or more. Stale urine of women with leucorrhœa exhibits this haze due to countless micro-organisms.

3. In urine containing sugar an abundant whitish sediment forms as the urine grows stale, composed of *penicillium glaucum*, a fungous growth not answering to the tests above given.

*In general, chemical tests for urinary sediments are not as satisfactory as microscopical examination, and are often wholly negative unless more or less tedious processes of separation are resorted to.*

4. Urine, if containing albumin, in no matter how small quantity, and depositing, if only a scanty sediment, should be carefully examined for tube-casts with the microscope. A sediment so slight as hardly to be seen with the naked eye may contain a considerable number of casts. In such cases the centrifugal machine is of great service in concentrating the scanty sediment.

# CHAPTER XLII.

## MICROSCOPICAL EXAMINATION OF URINE.

Let the urine settle six hours in a conical glass in case the physician does not possess a centrifugal machine, but if the latter be at hand proceed as in chemical testing, settling for five minutes at a speed of 1,700 revolutions, or higher if bacteria are to be examined. Remove a little of the sediment by means of a pipette and place a small drop on a glass slide. *Do not use cover glass* at first. Procure a Bausch & Lomb microscope (Continental BB stand) with half-inch and one-fifth inch objectives. Always use half-inch first, focus by raising, not lowering the tube, and study the field.

In a general way consider whether the objects seen are (*a*), crystalline, *i. e.*, of definite geometrical form and strongly refractive of light, or (*b*), whether they are shapeless and granular, or (*c*), whether they are pale and more or less regular in form.

We shall first suppose the objects seen are either crystals, or amorphous granules, and take up those occurring in acid urine first.

The sediments commonly found in acid urine are uric acid, urates, calcium oxalate; less commonly, cystin, hippuric acid, kreatinin, leucin and tyrosin, calcium sulphate.

### SEDIMENTS OF URIC ACID.

**Occurrence:**—In acid, usually sharply acid, urine, especially when below 1020 in specific gravity.

**Color and appearance:**—Crystals visible to the naked eye, looking like red-pepper grains, prone to cling to the sides and bottom of the glass, very heavy, falling quickly to the bottom of the glass when the urine stands. Best seen by holding the glass *above*

the head and looking upwards. Of deep yellow or orange-red color, in some urines pale-yellow.

**Crystalline structure:**—Primary form is a rhombic prism, and the crystals occur in various combinations or modifications of this form.

**Solubility:**—

1. Insoluble in acids, as hydrochloric or acetic.
2. Soluble in fixed caustic alkalies (potassium hydroxide).
3. Converted into ammonium urate by ammonia.

**Microscopical appearances:**—Uric acid crystals (Fig. 47) have a rich yellow or orange color, or at least

FIG. 47. Various forms of uric acid crystals. (*Finlayson.*)

a pale yellow color. They occur as lozenge-shaped, rounded, barrel-shaped, compound, twin, cross, or rosette forms. In over-acid urines there are also seen spear-shaped or comb-and-brush-shaped crystals. They are easily seen with a low power (150 diameters) and look large with a high power (500 diameters). They may occur in enormous quantities, filling the entire field with beautiful forms of rich coloring.

In some urines the crystals are a pale lemon-yellow color and must, if hexagonal, be differentiated from cystin. (See Cystin).

**Physiology:**—The uric acid sediment is normally found in some urines after standing ten hours or more. The tendency to sediments of this kind is increased by rich food, animal or vegetable, and by bodily exercise. In the urine high acidity, poverty in mineral salts, low pigmentation, and high percentage of uric acid tend to accelerate the precipitation of uric acid in form of concretions or sediment.

**Pathology:**—The sediment is probably pathological, if occuring in urines less than six hours old. The sooner it is deposited the greater the danger of formation of gravel and calculi. The deposit is found:—

1. In acute febrile disorders, and convalescence from scarlatina.
2. When function of the heart, lungs, kidneys, and diaphragm is impeded.
3. In the so-called "uric acid diathesis" (defective action of the liver with errors in diet, and sedentary life).
4. In mental and physical strains (over-work, sleeplessness).
5. In early stages of contracting kidney (interstitial nephritis).

## Diagnostic hints:

1. In chronic nephritis if uric acid sediments occur, one kidney only is involved (Heitzmann). In later stages of nephritis the sediments are not often seen.

2. Spear-shaped crystals indicate hyper-acid urine, as in gout or rheumatism.

FIG. 48 Sharp-pointed crystals of uric acid.

3. Clusters of uric acid crystals found in fresh urine, especially if spear-shaped, together with epithelia from pelvis of the kidney and blood corpuscles, mean

hemorrhage in pelvis of the kidney due to deposition there of sharp crystals.

4. Constant deposit of uric acid crystals in fresh urine is to be regarded as a a sign of functional derangement of the liver, and possibly of undue production of uric acid in the body.

**Clinical notes:—**

1. Patients, in whose fresh urine uric acid crystals are found, quite commonly complain of pain along the course of the ureter and in the median line above the symphysis pubis. Copious ingestion of fluids has several times in my experience relieved such pains.

2. Patients who have inflammatory diseases of the urinary organs are worse when they pass uric acid crystals, the latter irritating sensitive mucous surfaces. This should not be forgotten in the treatment.

3. Uric acid sediments in diabetic urine seem to be related to the "rheumatic" pains from which some diabetics suffer; at any rate in one or two instances treatment based solely on the uric acid condition has resulted in marked alleviation of the pains.

### SEDIMENTS OF MIXED URATES.

**Composition:**—Acid urates of sodium, potassium, ammonium, and (rarely) calcium.

**Occurrence:**—In acid urine. (Ammonium urate in alkaline urine). Especially in urines of high specific gravity, above 1025.

**Color and appearance:** — Amorphous, reddish, granular sediment, in color faint pinkish, fawn-color, reddish, or brick-red, forming what is known as the "brick-dust" sediment which adheres so closely to the sides of containing vessels, especially at the surface line of the urine. Scanty urines of high specific gravity are frequently turbid from presence of suspended urates. In the urine of children the mixed urate sediment frequently gives the urine a "milky" appearance with but faint tint of color.

A pellicle of urates is frequently noticed on the surface of urines containing this sediment.

The sediment of urates is of different color from the urine containing it, being deeper in hue.

**Crystalline structure:**—The acid urate of sodium is usually amorphous, sometimes crystalline (various forms). The acid potassium urate is amorphous, as is the calcium urate. The ammonium urate is crystalline, and consists of dark spheres with fine sharp spicula.

**Chemical tests of the mixed urate sediment:—**

1. Characteristic test: Dissolved by heat* (120° F. or upwards), reappearing as the liquid cools.
2. Insoluble in 20 per cent acetic acid.
3. Soluble in caustic alkalies, as liquor potassæ.
4. Responds to the murexide test (see uric acid).
5. Decomposed into uric acid on addition of hydrochloric acid, the former separating as brownish grains (crystals).
6. Not readily soluble in water; the sodium urate soluble with difficulty (1150 parts cold, 124 parts boiling); calcium urate very sparingly soluble.

**Microscopical appearances:—**

1. The mixed urates, when amorphous, appear under the microscope with a low power (150 diame-

FIG. 49. Amorphous urates.

*The books say "gentle heat dissolves urates." If a bottle of urine, turbid from urates, be set in water of temperature 140° F. (60° C.), in about three minutes the sediment will dissolve, when the urine is heated to 120° F. (50° C.).

ters) as flocculent masses filling the entire field. With a high power (500 diameters) they appear (Fig. 49) as brown granules in a moss-like arrangement.

2. Sodium urate, when crystalline (Fig. 50*a*), occurs in a great variety of forms. In one of Dr. Heitzmann's slides showing urate of sodium from a dermoid cyst of the kidney some of the crystals are much smaller than those in the figure. The crystals are more or less colored, brown or pink, and appear as needle-like clusters, in double fan-shape arrangement, or leaf-shaped.

3. Ammonium urate appears with a low power (150 diameters) as dark-brown spheres which, with a high power (500 diameters), are seen (Fig. 50) to be studded

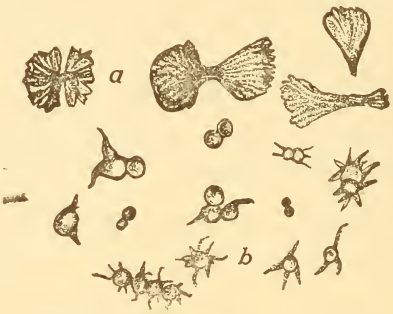



FIG. 50. Sodium urate (*a*), and ammonium urate (*b*).

with fine, sharp-pointed spicula, so-called thorn-apple crystals.

**Physiology:**—Normal urine precipitates urates (*a*) in cold weather; (*b*) when stale. Urine two or three days old may first, when more acid, throw down a sediment of amorphous mixed urates and uric acid; later, when four or five days old and ammoniacal, the amorphous urate sediment becomes transformed into ammonium urate.

The freshly voided urine of a healthy person shows no sediment of urates at ordinary temperatures, except possibly after profuse perspiration with diminution of amount of urine.

**Pathology:**—The sediment of mixed urates may occur temporarily in:—

1. Slight disturbances of health from over-eating or drinking or prolonged abstinence from either, after great exertion, revelry or excitement, hard study, or fright.

2 Temporarily in slight colds, digestive disturbances in children, and during attacks of gout.

3. During fevers and inflammatory diseases; in febrile exacerbations of chronic diseases.
4. More constantly in visceral disorders attended by wasting; in chronic affections of the heart, liver, and spleen; in functional disorders of the stomach; in congestions of the kidneys.
5. In the scanty high-colored urine of dropsical patients.

**Diagnosis:—**

1. The presence of uric acid and of urates in the urine in form of deposits is one of the most constant signs of functional derangements of the liver.

2. If without errors of diet a patient under 40 habitually passes urine which soon deposits a pinkish sediment, or which though clear when voided soon becomes thick and opaque, there is undoubtedly an undue tendency to produce uric acid.

3. In such cases as the above, possibility of the presence or formation of gravel or calculus is to be borne in mind.

4. The richer the color of the urate sediment, the more the evidence of functional derangement of the organ in question.

5. In acute lung diseases the larger the amount of the urate sediment, the more insufficient the respiration.

6. Rose-red urates are common in articular rheumatism, acute and chronic; in acute articular rheumatism the urates are more highly colored (by uroerythrin) on the advent of pericarditis.

7. The paler the color of the urate sediment the worse, usually, the condition of cutaneous functions.

8. The sediment of urates is now thought to be indicative of total absence or relative insufficiency of disodic phosphate in the urine.

**Clinical notes:—**

1. An occasional sediment of urates is not serious since it occurs even in slight disturbances of health. Regulation of the digestion, avoidance of late hours and irregular living, together with copious ingestion of fluids will quickly cause it to disappear.

2. In eight or ten rapidly fatal cases from cardiac or renal diseases I have noticed the urine to be constantly cloudy from urates. But as in all these cases the urine was scanty, 15 to 20 ounces (450-600 c.c.)

daily, I can assign no special prognostic significance to the sediment.

3. In looking for tube-casts in urine containing urate sediments, be sure first to dissolve the sediment with heat just short of boiling. (See Tube-Casts). This is done by immersing the bottle or tube in water heated to 140° F. (60° C.). The urate sediment will dissolve when the urine containing it is of a temperature of 120° F. (50° C.).

### SEDIMENTS OF CALCIUM OXALATE (OXALATE OF LIME).

**Chemical constitution and derivation:**—$CaC_2O_4$.

**Occurrence:**—Usually in acid urine, sometimes in alkaline.* When occurring in profusion and in several forms, urine usually hyper-acid.

**Color and appearance:**—Light, easily-moving sediment, usually of small bulk, and colorless.

**Crystalline structure:**—Octahedra, made up of four-sided pyramids, situated base to base, as seen in their long diameters; or less commonly, ovoid or circular discs.

**Chemical tests:**

1. Soluble in hydrochloric acid, insoluble in acetic acid.

2. Insoluble in alkalies, as liquor potassæ.

**Microscopical appearances:**—

Common forms:—Small, colorless crystals (Fig. 51), seen with difficulty with a low power (150 diameters), best studied with a power of 400 or 500 diameters octahedral in form, highly refracting; have appearance of rear of a letter envelope, *i. e.*, squares crossed obliquely by two sharp lines. When small, the two lines form a bright spot at their crossing in the centre.

*I cannot understand the statement of certain authors that oxalate of lime is a sediment characteristic of alkaline urine. Between January 1, 1895, and June 1, 1896, I found sediments of calcium oxalate in 116 samples of the 24 hours' urine. Of these 98 were urines acid in reaction, 1 neutral, and 17 alkaline. In every case but two where there was great profusion and different forms of crystals, the urine was hyper-acid in reaction.

FIG. 51. Various forms of calcium oxalate crystals. *(Peyer)*

Edge view of the octahedra shows them as four-sided pyramids, base to base. Concretions of these crystals may occur as shown in the figure.

Calcium oxalate also occurs in small circular crystals, sometimes smaller than blood corpuscles.

Rare forms:—Large octahedra, double octahedra ("twins"), discs, and tablets with rounded corners. The dumb-bell, according to Heitzmann and others, is the disc seen in edge view. Uric acid sometimes crystallizes as dumb-bells, but they are brownish in color.

Calcium oxalate crystals are more easily found after any phosphates present have been dissolved by addition of acetic acid, or urates cleared up by heat.

**Physiology:**—Oxalate of lime, $CaC_2O_4$, formed by the combination of oxalic acid with calcium (lime) occurs in the urine as sediment after eating heartily of apples especially those of the Spitzbergen variety, bananas, and rhubarb. In the spring when "pie-plant pie" is a favorite dish, oxalate sediments are common. A case is on record where a boy ate so much "pie-plant" and drank so much hard water that the oxalate crystals formed in his body caused hæmaturia! Cabbage, carrots, spinach, asparagus,

sorrel, onions, tomatoes, turnips, gooseberries, cresses, parsnips and saccharine articles of diet may also be responsible for the sediment, as also an excess of fat meat. Certain beverages may cause a sediment of oxalate of lime; these are alkaline waters, carbonated drinks, fermented liquors, and sparkling wines.

In cases when the sediment is due to food or drink it is temporary. Persistent presence of the sediment regardless of diet is probably pathological, when the sediment occurs before the urine is 24 hours old.

**Pathology:**—Insufficient activity of that stage of oxidation in the body which changes oxalic acid into carbonic. Hence oxalate of calcium sediments are found in a great variety of disorders.

1. Due to the action of certain drugs as gentian, rhubarb, squill, valerian, and others.
2. In febrile disorders.
3. Pulmonary and cardiac affections in which respiration is impeded.
4. Disorders of the hepatic system.
5. Depressed conditions of the nervous system.

The tendency to oxaluria is now regarded as indicating even more defective oxidation than the condition known as lithiasis (uric acid sediments).

According to Debout d' Estrées oxaluria is more common in America, lithiasis more common in Europe.

## Clinical hints:—

1. Oxalate sediments in urines of high specific gravity, 1026 to 1040, are found in many cases of nervous dyspepsia, hypochondria, or melancholia. Symptoms suggesting locomotor-ataxia may occur which, however, disappear when the digestive trouble is remedied.

2. Patients with urine, as above, quite frequently complain of pain in the region of one kidney or the other, urinate frequently, and cannot retain their urine at times.

3. Open air life especially in dry climates or in the mountains is a sovereign remedy for this class of patients.

4. The tendency to "oxaluria" lasts a long time. I have one patient still suffering from recurrences of the symptoms after 14 years.

5. Severe attacks of prostato-urethritis may occur in protracted cases of oxaluria.

6. Stone formation is fairly common in chronic cases of oxaluria. Stone may be present in the kidney and yet oxalate crystals not always abundant, sometimes even absent from the urine. This I have

observed in two cases in which calculus was subsequently passed, after renal colic.

### CYSTIN IN THE SEDIMENT.

**Chemical Composition and Synonyms:**—Formula, $C_3H_6NSO_2$, amido-sulpho-pyruvic acid, an amide of the lactic acid series; contains more than 25 per cent of sulphur. *Cystine.* GERMAN, *Cystin.* FRENCH, *Cystine.* An organic substance.

**Occurrence:**—A sediment seldom occurring, especially in strongly acid urine; when occurring is commonly in faintly acid, pale urine which on standing gives off odor of sulphuretted hydrogen as well as that of ammonia.

**Color and appearance:**—Of pale-lemon, or dirty yellowish gray color often changing to green on standing.

**Solubility:—**

1. Insoluble in cold and hot water, ether, alcohol.
2. Insoluble in acetic acid.
3. Soluble in ammonia, and in solutions of sodium and potassium hydroxides, as liquor potassæ, but insoluble in solution of ammonium carbonate.
4. Soluble in hydrochloric acid.
5. Soluble in solutions of oxalic acid.
6. Soluble in large excess of hot water.

**Characteristic test:**—None.

**Chemical recognition:***—Let urine settle, decant, filter sediment, wash latter with water, and (1) test on platinum foil. Cystin does not fuse but burns with a bluish-green flame and without melting, while a sharp, acid odor like hydrocyanic acid, is evolved. (If in solution in the urine, it may be precipitated by acetic acid, and its solubility ascertained in reagents mentioned under *Solubility* above.) (2) Heated with nitric acid, it dissolves with decomposition and, on evaporation, leaves a reddish-brown mass which does not give a purplish color with ammonia.

**Microscopical appearances:**—Cystin may occur as hexagonal tablets superimposed upon or contiguous to one another and which with a power of 500 diameters are seen to have radii, which are fine lines of secondary crystallization. In many the angles become worn off, approximating a circular form. The crystals may have a faint greenish tinge, or possess an opalescent lustre suggesting mother of pearl. Less commonly cystine occurs as highly refractive four-sided square prisms, whose sides are dark, when out of the direct line of vision, but brilliant white when presented vertically to the light.

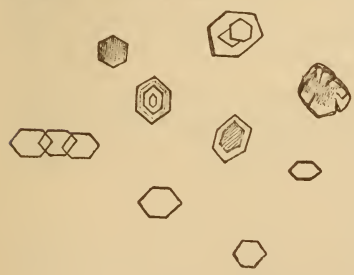


FIG. 52. Cystin. (*Daiber.*)

*The value of the ferrocyanide of sodium test has been disputed by Krukenberg.

**Micro-chemical reactions:**—Differentiate from uric acid by its solubility in oxalic and hydrochloric acids; from triple phosphate by its solubility in ammonia.

**Physiology:**—Cystin sediments may be noticed in the urine for years, especially in young men, without impairment of the health of the individual but they can hardly be called physiological.

**Pathology:**—Some families are prone to cystin sediments and calculi as others are to uric acid, hence it is probably associated with hepatic disorders. Cystin has been found in the urine of Bright's disease, chlorosis, and acute articular rheumatism. Little is known about it.

### HIPPURIC ACID IN THE SEDIMENT.

**Microscopical Appearances:**—Colorless four-sided prisms (Fig. 53) whose sides, when seen with a power of 500 diameters, sometimes show indentations. It also occurs in clusters of very fine needles.

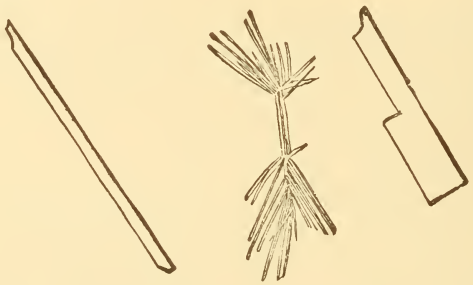


FIG. 53. Hippuric acid.

NOTE:—The writer having seen a slide of hippuric acid actually deposited in urine, prefers to give a cut as above of a drawing of it rather than to copy those more elegant but less typical ones usually given in the books.

**Micro-chemical tests:**—Differentiate from uric acid by solubility in alcohol; from triple phosphate by insolubility in acetic acid. The crystals are soluble in ammonia, but insoluble in hydrochloric acid.

**Significance:**—Usually due to ingestion of certain berries as cranberries or bilberries; also to administration of benzoic acid, benzoates, and other drugs. Heitzmann says it is sometimes found in the sediment of the urine of diabetes.

### CALCIUM SULPHATE IN THE SEDIMENT.

**Chemical constitution and synonyms:**—Calcium sulphate, $CaSO_4$. Formed by union of sulphuric acid or sulphates with calcium or its compounds. Sulphate of lime, gypsum. GERMAN, *schwefelsaurer Kalk, Gyps.* FRENCH, *sulphate de chaux.*

**Occurrence:**—A rare sediment in concentrated urines of highly acid reaction.

**Form:**—Crystalline and sometimes amorphous.

**Color and appearance of sediment:**—A whitish, heavy, dense, sediment.

**Solubility:—**

1. Sparing soluble (1–400) in cold water.
2. More soluble in large bulk of hot water.
3. Insoluble in ammonia and in strong hydrochloric acid.

**Characteristic test:**—None.

**Chemical recognition:**—Let urine settle, decant supernatant urine from sediment, filter the sediment, wash latter with cold water, dissolve in large bulk hot water, divide into two portions, test one with barium chloride, the other with ammonium oxalate.

### KREATININ IN THE SEDIMENT.

**Microscopical appearances:**—According to Heitzmann kreatinin sometimes appears in the sediment of acid urine. The crystals (Fig. 54) are colorless or at most light greenish in shape

FIG. 54. Kreatinin.

somewhat like those of uric acid, but seen with a power of 500 diameters, have striations both concave and radiating.

NOTE:—The cut given above is from a drawing made of a slide belonging to Dr. Charles Heitzmann. None of the books on urinary analysis in ordinary use give cuts resembling these forms.

**Significance:**—The crystals shown in the figure were found in the urine in a case of uræmia, and are regarded by Heitzmann as an unfavorable sign. Small crystals of it may be found after excessive muscular exertion.

### LEUCIN AND TYROSIN IN THE SEDIMENT.

**Chemical constitution and synonyms:**—*Leucin*, (leucine) $C_6H_{13}NO_2$, or $C_5H_{10}(NH_2)COOH$, amido-caproic acid, and *tyrosin*, (tyrosine) $C_9H_{11}NO_3$, or $C_6H_4OH.CH_2.CH(NH_2).COOH$, also an amido-fatty acid, a monobasic phenol acid. Both leucin and tyrosin are decomposition products of the albuminoids. GERMAN, *Leucin, Tyrosin.* FRENCH, *Leucine, Tyrosine.*

**Occurrence:**—In urine containing excess of biliary coloring matters. Possibly also in urine not containing bile. It is the opinion of Jaksch that in some instances when these bodies were supposed to have been in the urine that they were not sufficiently identified.

**Form:**—Crystalline.—Leucin, yellowish and of greasy feel. Tyrosin, snow-white crystalline masses, tasteless and odorless.

**Solubility of leucin:—**

1. Insoluble in ether.
2. Insoluble in cold hydrochloric acid.
3. Soluble in caustic alkalies, as liquor potassæ, and ammonia.

4. Partly soluble in water and in alcohol, more readily in hot alcohol.

**Solubility of tyrosin:—**

1. Insoluble in alcohol and ether.
2. Insoluble in acetic acid.
3. Soluble in hydrochloric acid.
4. Soluble in caustic alkalies.
5. Difficultly soluble in cold water.
6. Readily soluble in hot water.

**Chemical recognition of leucin:**—Concentrate the urine slightly over the water bath, let settle, decant, collect sediment on filter, wash with cold water, dissolve in ammonia with addition of ammonium carbonate, set aside, allow to evaporate, then separate from tyrosin by treating with absolute alcohol, which dissolves some of the leucin but not the tyrosin. Let the alcoholic solution evaporate and test as follows:

(*a*) Scherer's test:—Place some of the residue on platinum foil, add a few drops of nitric acid and heat until it is consumed. A colorless residue is left. Now heat again with a drop or two of caustic potash solution and, if leucin is present, drops of an oily fluid will form, which does not adhere to the platinum. (*b*) Hofmeister's test:—Dissolve another part of the original ammoniacal residue in hot water and further heat with some proto-nitrate of mercury; a deposit of metallic mercury occurs on the tube. (*c*) Heat cautiously some of the residue in a glass tube open at both ends to about 170° C. (338° F.), and if leucin is present it sublimes without fusing into woolly masses, and a smell of amyl-amin is given off.

**Chemical recognition of tyrosin:**—Go back to the residue from which leucin was separated by treatment with absolute alcohol and test as follows: (*a*) Place a very small particle of it on a watch-glass, moisten with a drop of sulphuric acid, cover over, let stand half an hour, dilute with water, saturate while hot with calcium carbonate, filter, and treat the colorless filtrate with a very dilute solution of acid-free perchloride of iron (made by subliming the perchloride and dissolving sublimate in water). A violet color appears readily destroyed by excess of the iron solution. (Piria, Städeler). (*b*) Dissolve another portion of the residue in hot water, add a few drops of Millon's reagent (made by dissolving 1 part by weight of mercury in 2 of nitric acid, heating gently, and adding 2 parts of water) and there arises a red precipitate, the supernatant fluid being colored red to purple-red. (Hoffmann's test).

Hoffmann's test may be applied directly to an urinary sediment supposed to contain tyrosin.

**Microscopical appearances:**—Leucin (Fig. 55) appears as yel-

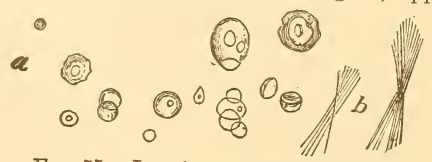



FIG. 55. Leucin (*a*) and tyrosin (*b*).

lowish, highly refracting spheres somewhat resembling fat granules, though not so highly refracting, and which, with a high

power (500 diameters), look large. Tyrosin appears as very fine needles in sheaf-like collections. Crystallized from an alkaline solution it may occur in form of rosettes composed of fine needles arranged radiately.

**Micro-chemical tests:**—Differentiate leucin from fat granules by its insolubility in ether; from ammonium urate by no decomposition nor separation of uric acid crystals when treated with hydrochloric acid.

**Physiology:**—The amido-fatty acids being products of decomposition of proteids are not found in normal urine. They are said to occur physiologically in the axilla and between the toes.

**Pathology:**—When retrograde changes are rapid in the body, as in extensive suppuration and gangrene, leucin and tyrosin are formed in the body in large amounts, may pass into the urine, and largely supplement or replace urea.

**Significance:**—Sediments of leucin and tyrosin are found in acute yellow atrophy of the liver and in acute phosphorus poisoning. Whether they occur in other diseases, as infectious diseases, is doubted. Prus has found abundance of leucin in a case of leukæmia.

### CALCIUM SULPHATE.

**Microscopical appearances:**—Long, colorless needles, (Fig. 56),

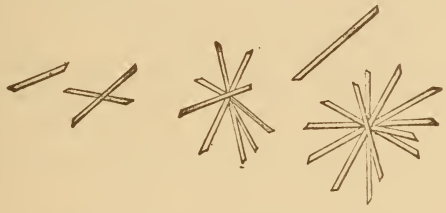


Fig. 56. Calcium Sulphate. (*Daiber*).

or elongated tables with abrupt extremities; sometimes also in dumb-bell shaped amorphous masses.

**Micro-chemical tests:**—The crystals and the amorphous masses are both insoluble in ammonia and in strong hydrochloric acid.

**Physiology:**—Not found normally in urine.

**Pathology:**—Concentrated urine of highly acid reaction is thought to be necessary for the presence of this sediment.

**Clinical significance:**—Unknown or none other than given under *Pathology.*

### XANTHIN (HYPOXANTHIN) IN THE SEDIMENT.

**Occurrence:**—A very rare sediment in acid urine.

**Form:**—Crystalline.

**Microscopical appearances:**—Lemon-shaped or whetstone-shaped crystals somewhat like uric-acid. (Fig. 57).

Fig. 57. Xanthin, (Hypoxanthin?) (*Neubauer*).

**Micro-chemical tests:—**

1. Differentiate from uric acid by solubility in ammonia without formation of ammonium urate crystals, and by solubility in hydrochloric acid.
2. Insoluble in acetic acid.

**Significance:**—Found by Bence Jones in the sediment of urine in case of a boy who passed a calculus composed of it.

NOTE:—It is now thought that the substance is really hypoxanthin, not xanthin.

# CHAPTER XLIII.

## SEDIMENTS FOUND USUALLY OR ALWAYS IN ALKALINE URINE.

These are ammonium-magnesium phosphate, simple phosphates, and ammonium urate; less commonly calcium carbonate, magnesium phosphate, soaps, indigo.

### SEDIMENTS OF AMMONIUM-MAGNESIUM PHOSPHATE OR TRIPLE PHOSPHATE.

**Occurrence:**—Always in urine either alkaline or verging on alkalinity.

**Chemical composition:**—$(NH_4)MgPO_4.6H_2O$. Called "triple" because of $6H_2O$ forming the third part of the formula. Result of decomposition of urea into ammonium carbonate and union of latter with magnesium phosphate.

**Color and appearance:**—Phosphatic sediments are whitish or dirty-white. If triple phosphate crystals are present in large numbers, they sparkle like minute diamonds when the sediment is held up to a strong light. The urine containing it is turbid when freshly voided.

**Crystalline form:**—Triangular prism.

**Chemical tests:**—

1. Readily soluble in acids even in 20 per cent acetic acid.
2. Insoluble in solutions of the caustic alkalies, as liquor potassæ.
3. Red-litmus paper turned blue by ammoniacal urine reddens again when dry, allowing us to infer that the phosphatic sediment contains triple phosphate.
4. Urine has an odor of ammonia.

5. A rod moistened with hydrochloric acid held near the urine shows fumes of ammonium chloride.

6. Urine effervesces *vigorously* when acids are added to it. (Carbonate of ammonium decomposed by acid, and carbonic acid gas given off.) The foam may rise so fast as to bubble over from the test-tube before the inexperienced urine tester knows what is happening.

**Microscopical appearances:—**

Triple phosphate (Fig. 58) occurs in the form of

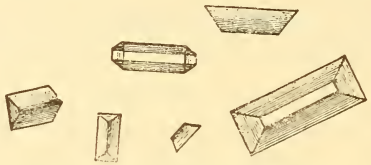


FIG. 58. Ammonio-magnesium phosphate. (*Daiber*).

triangular prisms, complete and incomplete. The colorless crystals are easily seen with a low power (150 diameters) and with a high power are very large. The incomplete forms are seen alone in slightly alkaline urine, or in urine which having been acid is verging on alkalinity. The complete forms appear in profusion in strongly alkaline ammoniacal urine. The ends of the prisms are beveled. The term "coffin-lid" is used in describing them. Seen in edge view they appear as squares. Formed artificially they appear as star-shaped, feathery crystals (Fig. 32). Both forms may be artificially prepared by adding a small lump of ammonium carbonate to two or three ounces of urine and setting aside. The crystals are beautiful objects when seen by polarized light.

**Physiology:**—Normal urine which has become stale and ammoniacal deposits triple phosphate. If occurring in freshly voided urine, the sediment is pathological.

**Pathology:—**

1. Sediment due to ammoniacal decomposition of the urine within the body; urea is converted into ammonium carbonate, which in turn gives up its ammonium to magnesium phosphate which is present.

2. Sediment found in obstructive diseases of the lower urinary tract: retention of urine in bladder or pelvis of the kidney. Hence

in diseases of the spinal cord, paralysis of the bladder, enlarged prostate, etc.

3. Sediment sometimes occurs in vegetarians who are under mental strain; in time phosphatic stone may form in such cases, as well as in others.

**Clinical notes:—**

1. Triple phosphate crystals in freshly voided urine are common in conditions preceding "surgical kidney" viz., septic inflammations of the urinary tract.

2. The first introduction of the catheter, especially in cases of elderly men, is dangerous when triple phosphate crystals are found in freshly voided purulent urine.

3. An immense number of triple phosphate crystals in urine should always suggest presence of calculus, especially in cases where other causes for the patient's condition are not evident. In several cases, operations, or renal colic and passage of stone, have verified diagnoses of calculus made by the writer.

4. The fact that the patient is voiding phosphatic urine does not necessarily mean presence of *phosphatic* calculus. The stone may be of any variety and set up inflammation with decomposition of urine and formation of triple phosphate.

6. In one of the writer's cases in which immense numbers of triple phosphate crystals were deposited, without pus, in the urine of a man under great mental strain for years, renal colic finally took place and the patient voided a phosphatic calculus weighing 0.4 gramme (about six grains). The patient was after this free from the phosphatic sediment except occasionally when greatly fatigued or under nervous strain. He has gained 50 pounds in weight and in 8 years there has thus far been no recurrence of renal colic.

7. In the case in which Dr. Chas. Adams removed a renal calculus weighing nearly half a pound (Fig. 59), the writer found immense numbers of triple phosphate crystals, together with pus, in the fresh urine.

FIG. 59. Renal calculus (actual size) removed by Dr. Chas. Adams.

SIMPLE PHOSPHATES (EARTHY PHOSPHATES).

**Chemical constitution:**—Basic phosphates of calcium and magnesium. $Ca_3(PO_4)_2$ and $Mg_3(PO_4)_2$. Neutral calcium phosphate, $CaHPO_4$.

**Occurrence:**—In alkaline urine. Neutral calcium phosphate in feebly acid, neutral, or alkaline urine.

**Color and appearance:**—The phosphatic sediment is light colored, usually dirty white; may occur as a flocculent turbidity in freshly voided urine, which settles rather slowly and is easily disturbed by shaking. Occasionally the sediment is so abundant as to have a creamy white color and may be mistaken by the patient for seminal fluid.

**Chemical tests:**—

1. Urine more or less cloudy when freshly voided, but the sediment is not dissolved by heat. (Differentiated from urates).
2. Readily dissolved by acids, even by 20 per cent acetic acid.
3. Red litmus paper colored blue; does not become red again when dried, if triple phosphate is not present in large quantity. (Urine alkaline from fixed alkali).
4. The urine does not smell ammoniacal, if triple phosphate is not present in great quantity.
5. A rod moistened with hydrochloric acid does not fume (if triple phosphate is not abundantly present).

NOTE:—Both simple phosphates and triple phosphate may occur in the same sediment, hence tests 3, 4 and 5 are of value only when triple phosphate is absent or present in relatively small amount, ammoniacal decomposition not having as yet taken place.

6. Urine effervesces on addition of acids but not so vigorously as when triple phosphate has been deposited by ammoniacal decomposition.
7. Urine when heated becomes turbid from further deposit of phosphates, but the turbidity disappears with effervescence when an acid is added. (Differentiated from albumin).

**Microscopical appearances:**—The simple phosphates are either amorphous in form or, less commonly, crystalline. If amorphous, (Fig. 60, A), the

sediment appears in the form of minute pale granules arranged in irregular patches and sometimes mistaken for granular masses of organic matter. A drop of 20 per cent acetic acid quickly dissolves this sediment on the slide.

When crystalline the sediment usually consists of neutral calcium phosphate, stellar or stellate phosphate, (Fig. 61) a rarer sediment than any other phosphatic deposit, save crystalline magnesium phosphate.

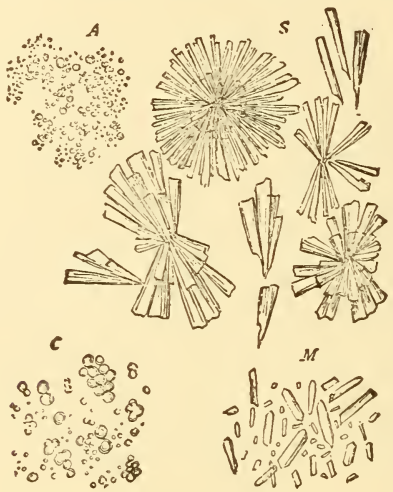



FIG. 60. Simple Phosphates and Carbonate of Lime.

*A.* Amorphous simple phosphates. *S.* Star-shaped simple phosphates (crystalline calcium phosphate). *C.* Amorphous carbonate of lime. *M.* Combination of carbonate of lime with magnesium salts. Magnified 300 diameters. (After Heitzmann).

**Physiology:—**

1. A slight sediment of amorphous simple phosphates recurring after a full meal, when the urine is naturally less acid than at other times can hardly be regarded as abnormal.

2. It is said that deposits of crystalline calcium phosphate may take place in the urine of healthy people during the summer.

**Pathology:**—*Circumstances favoring increase of alkalescence of the blood.* The sediment of earthy phosphates is in the main due to alkalinity of the urine and not merely to excess of phosphates in the urine. The latter occurrence is rare at least in Chicago and vicinity and not necessarily accompanied by any sediment at all unless the urine at the same time happens to be neutral or alkaline. Urine alkaline from fixed alkali deposits

earthy phosphates with usually a few crystals of triple phosphate, since ammoniacal decomposition usually quickly takes place in such urines.

The sediment is found in cases of accumulation of carbonic acid in the system, as:

1. Debility with feeble respiration, convalescences from acute diseases.

2. Flatulent dyspepsia; fatty acids, formed by fermentative changes, being oxidized in the blood into carbonic acid, and carbonates formed which increase alkalescence of the blood and diminish acidity of the urine.

**Diagnosis:—**

1. The persistent sediment of earthy phosphates most frequently means flatulence of the small intestine. The urine when heated becomes turbid; but when acetic or nitric acid is added there is effervescence and the urine clears up.

2. Phosphatic sediments are thought to be a sign of "nerve waste" but the writer has shown that they are not often, in fact very rarely, accompanied by any increase in the total phosphorus in urine, estimated as phosphoric acid.

3. Ralfe speaks of cases in which there is, in addition to the phosphatic sediment, a real increase in the total phosphorus in the urine; such cases are more serious, may be attended by emaciation, and associated with phthisis, may result in diabetes insipidus, or alternate with diabetes mellitus.

4. Crystalline calcium phosphate may occasionally be found in the urine of persons during the summer. Roberts regards it as often an accompaniment of serious disorder as cancer of pylorus, phthisis, and exhaustion from obstinate chronic rheumatism. It is also said to be found in diseases of the brain.

**Clinical notes:—**

1. The term phosphaturia is used to designate the conditions in which phosphatic sediments occur in the urine.

2. The patient with phosphatic sediment of simple phosphates is usually low-spirited, thinks he is losing seminal fluid, has to urinate often, is sallow, constipated or of irregular bowels, and perhaps loses flesh. These symptoms are quite regularly associated with

flatulent dyspepsia in debilitated persons and do not result from the condition of the urine.

3. Phosphaturia has been noticed to follow gonorrhœa and it then has a particularly depressing effect on the patient. It is also common during the period of sexual activity in men.

4. It is true that spermatozoa are quite frequently found in urine depositing a phosphatic sediment; but this is not invariable nor is spermatorrhœa a necessary concomitant of phosphaturia.

5. The phosphatic sediment in urine may be easily cleared up by administration of acids as benzoic, boracic, or phosphoric in sufficient doses to make the urine acid. This often has a beneficial effect on the patient's spirits. But radical treatment is that of flatulent dyspepsia in most cases.

### CRYSTALLINE CALCIUM PHOSPHATE.

**Chemical constitution:**—Hydrogen calcium orthophosphate, $CaHPO_4$, $2H_2O$; (neutral calcium phosphate, neutral phosphate of lime), a combination of phosphoric acid with calcium in which one atom of the hydrogen of the acid still remains; in urinary sediments called *stellate* or *stellar* phosphate.

**Synonyms:**—GERMAN, *neutrales phosphorsaures Calcium phosphat.* FRENCH, *phosphate de chaux neutre.*

**Occurrence:**—In pale, abundant, feebly-acid, neutral, or alkaline urine. When found, is usually in feebly-acid urine verging on alkalinity.

**Color and appearance:**—Occurs either in the whitish sediment of amorphous phosphates, or together with oxalate of lime in a light colored, flocculent sediment of small bulk.

**Solubility:**—

1. Not dissolved when the sediment is heated.
2. Soluble in acids, even in twenty per cent acetic acid, especially when shaken with it.
3. Decomposed by ammonia.

**Chemical recognition:**—If necessary the sediment may be separated by filtration, washed, dissolved in acetic acid, tested for phosphoric acid with uranium nitrate, and for calcium with ammonium oxalate.

**Microscopical appearances:**—Stellar phosphate occurs essentially as crystalline rods, usually grouped in stellar or rosette form, or in form of lances or wedges, but sometimes lying entirely unarranged. The crystals are colorless, but under the microscope look dark towards the centre of the clusters. (Fig. 61). They can be easily seen with a low power, 150 diameters, but are best studied with higher. From triple phosphate they are distinguished by their form.

FIG. 61. Stellar phosphate. (*Beale*).

**Micro-chemical tests:—**

1. Easily distinguished from uric acid by solubility without effervescence, when a drop of twenty per cent acetic acid is placed on the margin of the cover glass.

2. Not dissolved when the sediment is warmed on the slide. (Differentiation from crystalline urates).

**Physiology:**—The appearance of crystalline calcium phosphate depends on an excess of calcium phosphate in a feebly-acid urine. According to Bence Jones this sediment may be produced at pleasure by taking lime-water.

It is said that this sediment may occur in the urine of healthy persons during the summer.

**Pathology:**—Any condition in which an excess of calcium phosphate is found in feebly acid urine.

**Clinical notes:—**

1. According to some writers the sediment of stellar phosphate is found in cases of serious disorder of the brain.

2. Roberts takes a gloomy view of the sediment; he regards it as an accompaniment of some grave disorder, as cancer of the pylorus, phthisis, and exhaustion from obstinate chronic rheumatism. The crystals are then plenty.

3. My own experience is as follows: Out of 640 urinary sediments recently examined, stellar phosphate occurred 9 times, or 1

in 70. The patients were 6 men and 3 women. The cases were (1) chronic prostato-urethritis with impotence and profound mental depression; (2) paresis of the bladder from injury; (3) hyperæmia of the liver; (4) urine following recovery from uræmia; (5) nervous prostration from over-work; (6) renal calculus, removed by Dr. Chas. Adams; (7) debility; no other diagnosis; (8) pregnancy; (9) post-gonorrhœal cystitis.

But two of these were examined during the summer. The crystals were plenty in all cases.

### CALCIUM CARBONATE.

**Chemical composition:**—Normal or basic calcium carbonate, $CaCO_3$. carbonate of lime, a combination of carbonic acid with calcium, in which the hydrogen of the acid is completely replaced by calcium.

**Synonyms:**—GERMAN, *kohlensaurer Kalk.* FRENCH, *carbonate de chaux.*

**Occurrence:**—A rare sediment found in alkaline urine.

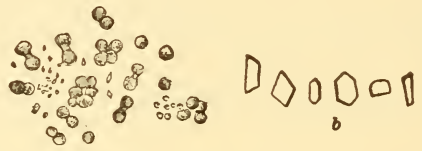
**Color and appearance:**—Whitish sediment like that of phosphates.

**Form:**—Amorphous and crystalline.

**Solubility:**—

1. Soluble in acids, even 20 per cent acetic acid, with *effervescence* (evolution of carbonic acid gas).

**Microscopical appearances:**—Should be studied with a high power, 300 to 500 diameters, when it appears as dumb-bell shaped masses, and coarsely granular concretions. According to some observers it appears also as minute spherules like the spherules of calcium oxalate. Heitzmann's slide of carbonate of lime shows them somewhat prismatic in form. Fig. — gives the different appearances. See also Fig. 60.



*a* *b*

FIG. 62. Calcium carbonate.

(*a*) *Daiber.* (*b*) *A few crystals from one of Heitzmann's slides.*

**Micro-chemical tests:**—Readily distinguished from uric acid and calcium oxalate by solubility with evolution of bubbles, when a drop of 20 per cent acetic acid is placed on the margin of the cover glass (calcium phosphate dissolves, but without bubbles).

**Pathology:**—According to Heitzmann the sediment occurs in cases of bone caries and tuberculosis; also in rickets.

### CRYSTALLINE MAGNESIUM PHOSPHATE.

**Chemical constitution:**—Tribasic, or normal magnesium phosphate, $Mg_3(PO_4)_2.22H_2O$, phosphate of magnesia, a combination of phosphoric acid with magnesium, in which the hydrogen of the acid is completely replaced by magnesium.

**Synonyms:**—GERMAN, *Magnesium phosphat; phosphorsaure Magnesia.* FRENCH, *phosphate de magnésie.*

**Occurrence:**—A very rare sediment, which occurs in concentrated urine of feebly acid, neutral, or alkaline reaction.

**Color and appearance:**—Whitish sediment.

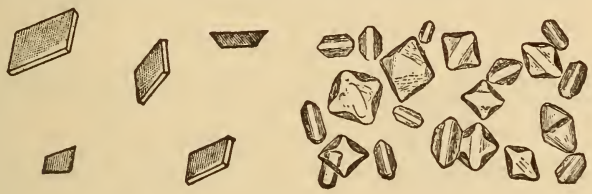
**Form:**—Crystalline.

**Solubility:**—

1. Readily soluble in acetic acid and re-precipitated on addition of sodium carbonate solution.

2. In a solution of one part by weight ammonium carbonate in five of water it is in time partly dissolved. (See Micro-chemical Tests).

**Microscopical appearances:**—Crystallizes in large, highly refracting, rather long rhombic tablets or plates. (Fig. 63). They



*a* *b*

FIG. 63. Crystalline magnesium phosphate.
*a* (*Daiber*). *b* (*Jaksch*).

can be seen with a low power, 150 diameters; best studied with 500 diameters.

**Micro-chemical tests:**—

1. Differentiate from calcium oxalate by ready solubility in acetic acid.

2. From triple phosphate by the action of ammonium carbonate solution which makes them faint and after some minutes eats away the edges. (Triple phosphate not changed by ammonium carbonate).

### SOAPS OF LIME AND MAGNESIA.

**Chemical constitution:**—Calcium and magnesium salts of the higher fatty acids.

**Occurrence:**—In feebly acid urine.

**Microscopical appearances:**—Crystals (Fig. 64) closely resembling tyrosin, but not yielding the characteristic reactions of that body.

**Pathology:**—Seen once by Jaksch in the case of a woman with severe puerperal septicæmia.

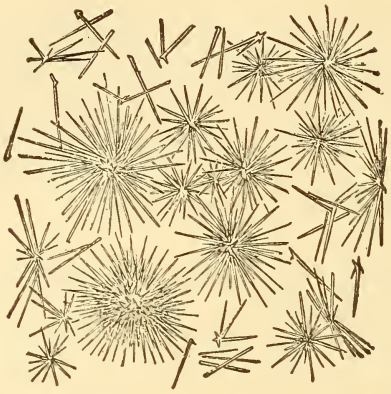


FIG. 64. Soaps of lime and magnesia. (*Jaksch*).

INDIGO IN THE SEDIMENT.

**Chemical constitution:**—Derived from the decomposition of indoxyl sulphate (indican), the indoxyl being oxidized into indigo blue, thus: $2\,(C_8H_6NOH) + O_2 = C_{16}H_{10}N_2O_2 + 2H_2O$.
(Indoxyl.) (Indigo-blue.)

**Occurrence:**—Not rare in decomposing (alkaline) urine which sometimes shows a bluish-red pellicle of microscopic crystals of indigo-blue owing to the decomposition of the indican. Found also at the bottom of the glass.

**Microscopical appearances:**—Blue rhombic crystals and fine blue needles (Fig. 65), mostly cohering in clusters; also amorphous in flakes.

FIG. 65. Indigo. (*Daiber*).

**Chemical test:**—The substance when heated sublimes in violet vapors.

**Pathology:**—Jaksch has found it in remarkable abundance in the ammoniacal fermentation of the urine of jaundice, and also in the *acid* urine of a case of abscess of the liver.

# CHAPTER XLIV.

## SEDIMENTS OF INFREQUENT OCCURRENCE.

CERTAIN sediments of infrequent occurrence not confined to urine of any particular reaction are the following:

Fat, Cholesterin, Hæmatoidin, Melanin.

### SEDIMENTS OF FAT. (LIPURIA).

**Synonyms:**—GERMAN, *Fett.* FRENCH, *Graisse.*

**Occurrence:**—In urine of any reaction.

**Appearance:**—If abundant the urine becomes milky, but the milkiness is cleared by addition of ether.

**Chemical tests:**—Soluble in ether; also in hot alcohol, carbon disulphide, and chloroform. Less soluble in benzol, insoluble in water.

**Microscopical appearances:**—Fat appears in the sediment under the microscope as bright, highly refracting granules, usually requiring a high power, 300 to 500 diameters for recognition, except when very abundant or of extraneous origin, from lubricants, etc. The margins of the granules are dark and somewhat irregular. Micro-chemically the granules may be seen to be dissolved by ether, by placing a drop of the latter on the margin of the cover-glass.

It may occur in the form of needles (Fig. 66), or be grouped about margaric acid needles. See also Fig. 67.

FIG. 66. Margaric acid needles with fat granules grouped about them. (*Daiber*).

**Physiology:**—Fat occurs in the urine physiologically in or during:

1. Pregnancy.
2. Administration of fatty substances, as olive oil, cod-liver oil, etc.
3. After inunctions of fatty substances.

**Pathology:**—Fat is found in the urine pathologically in or during the following conditions:

1. Chyluria.
2. Fatty degeneration at some point in the urinary apparatus as in fatty degeneration of the kidneys, and chronic parenchyma-

tous nephritis; also where pus from an old abscess finds its way into the urinary passages; in pyonephrosis.

3. Constitutional affections associated with marked cachexia or dependent on systemic intoxication, as phthisis, long-continued suppuration, pyæmia, yellow fever, poisoning by phosphorus or carbonic oxide, poisoning from external use of carbolic acid, chronic poisoning by turpentine, severe injuries to the bones, diabetes.

**Diagnostic Hints:—**

1. If large fat granules are abundantly seen in the sediment with the microscope, use of the catheter may be inferred.

2. When small fat granules are found, not due to extraneous matters, fatty degeneration of the kidneys is the condition, more certainly if fatty casts are also found.

3. Connective tissue studded with fat granules is probably derived from the kidneys.

4. In the urine of women, fat granules of sebaceous origin (smegma) may be seen with the microscope in vaginal epithelia, and in epidermal scales from the nymphæ. These are particularly noticeable in cases of vaginitis and vulvitis, as from masturbation in female children, but are not significant of the latter unless connective tissue be also found. (Heitzmann).

**Clinical Notes:—**

1. Recovery from parenchymatous nephritis is possible, at least in children, even when the sediment for months is a mass of fatty casts and free fat granules. In one such case, which I saw, the patient, a boy of eight, had for six months such a sediment in his urine together with a very large percentage of albumin—constantly above all figures on the Esbach tube.

2. Purdy speaks of seeing a large amount of fat in the urine occurring intermittently and alternating with sugar.

3. Cushing, of Boston, saw a case in which a large amount of fat in the urine indicated not only an abscess opening into the urinary tract, but also sufficient sloughing going on to set free the oil of the fatty tissue.

4. Ebstein speaks of fat in a case of hydronephrosis; Henderson in heart-disease; various authors in diseases of the pancreas; in acute yellow atrophy of the liver.

5. Jaksch says it may occur in the form of needles (Fig. 67), especially in connection with chronic nephritis and septicæmia.

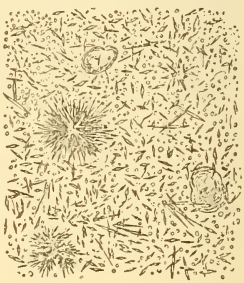


FIG. 67. Fat in crystalline form. (*Jaksch*).

## CHOLESTERIN IN THE SEDIMENT.

**Chemical constitution:**—$C_{24}H_{44}O.H_2O$, a fatty substance of alcoholoid constitution.

**Synonyms:**—GERMAN, *Cholesterin; Gallenfett.* FRENCH, *Cholestérine.*

**Occurrence:**—A very rare sediment.

**Form:**—Crystalline.

**Microscopical appearances:**—Large, very thin, rhombic plates overlapping (Fig. 68) each other. Occasionally found in urine voided late at night, when patient is exhausted.

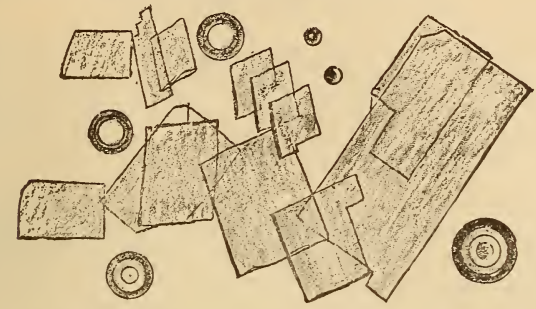


FIG. 68. Cholesterin and fat granules. (*Long*).

BILIRUBIN AND HÆMATOIDIN IN THE SEDIMENT.

Bilirubin, $C_{16}H_{18}N_2O_3$, is an extremely rare occurrence in the sediment of urine. It may appear as amorphous *yellow* granules, *red-brown* rhombic tablets, or needle-form bodies (Fig. 69) imbedded in other substances (mucus, or connective tissue), as in nephritis or in cancer of the liver.

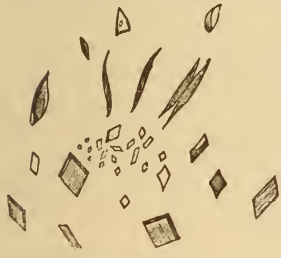


FIG. 69. Hæmatoidin. (*Daiber*).

Hæmatoidin occurs in forms similar to bilirubin. Chemically it is said to differ, being insoluble in potassium hydroxide solutions, as liquor potassæ, and colored transient blue by nitric acid. (Bilirubin soluble in caustic potash, colored green by nitric acid).

MELANIN IN THE SEDIMENT.

**Constitution:**—A black pigment of organic composition containing sulphur and iron, in addition to carbon, hydrogen, and nitrogen.

**Synonyms:**—GERMAN, *Melanin.* FRENCH, *Mélanine.*

**Occurrence:**—Usually in solution in the urine, rarely as a sediment.

**Solubility:**—

1. Soluble in boiling strong mineral acids, and in boiling acetic and lactic acids.
2. Soluble in strong solutions of the caustic alkalies and ammonia.
3. Insoluble in cold alcohol and ether.
4. Insoluble in acetic acid and in dilute mineral acids.

**Recognition:**—Occurs in the sediment in form of small, lumpy granules much resembling carbon particles.

**Tests:**—Best applied to the urine itself. (See Melanuria).
**Pathology:**—See Melanuria.

## MICROSCOPICAL EXERCISE III.

1. Examine crystals of uric acid, noting color, and observe whether the crystals are sharp-pointed or not. Observe action of solution of sodium or potassium hydroxide on the crystals, and of acetic acid (20 per cent).

2. Examine crystals of triple phosphate, noting size and shape; also appearance of fragments. Observe action of acetic acid (20 per cent) on the crystals, and of sodium hydroxide.

3. Examine crystals of calcium phosphate as above.

4. Examine crystals of calcium oxalate, noting small size, different forms, and action of reagents as above, also of nitric acid.

# CHAPTER XLV.

## ANATOMICAL SEDIMENTS IN THE URINE.

If the objects seen with the microscope are not affected by the chemical or micro-chemical tests already described, they are probably anatomical in character and will, as a rule, appear pale in color, and not refract light sharply, though they may be regular or irregular in form. We distinguish corpuscles, epithelia and scales, tube-casts and similar formations, fungi and micro-organisms, spermatozoa, and shreds of connective tissue.

Among corpuscles we find blood corpuscles, pus corpuscles, and mucous corpuscles. Corpuscles of all kinds are small, roundish bodies, visible, but not clearly distinguishable, with a power of 150 diameters, and requiring 400-500 for identification. They are nearer in size to small octahedra of calcium oxalate than to any of the other common crystals.

**Blood corpuscles:**—Blood corpuscles in the urine present different appearances. They may be (*a*) normal, like those freshly obtained, as from the finger by puncture with a needle; (*b*) crenated; (*c*) spherical or shrunken, with irregular outline; (*d*) in form of faint transparent rings, devoid of coloring-matter (hæmoglobin) from long stay in the urine. These last are known as blood-shadows, or ghosts, and are smaller than normal.

Figure 70 shows the different ways in which blood corpuscles may appear in the urine, *a* being normal with biconcave appearance; *b*, blood shadows or "ghosts"; *c*, crenated as in acid urine; *d*, spherical and swollen from imbibition of water.

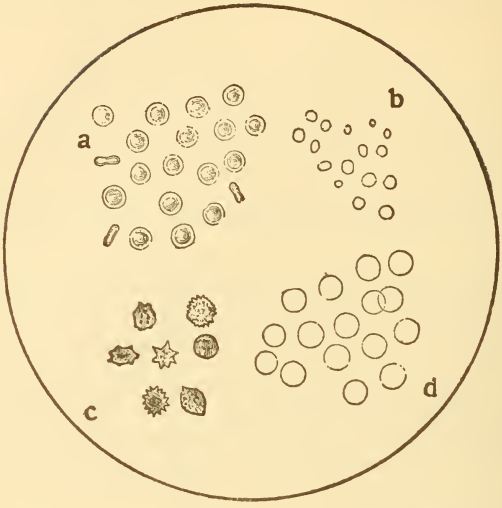



FIG. 70. Different appearances of blood corpuscles in the urine.
*a*. Normal blood corpuscles. *c*. Crenated, as in acid urine.
*b*. Blood shadows. *d*. Swollen from imbibition of water.

### RECOGNITION OF BLOOD CORPUSCLES.

1. When blood corpuscles are abundant, urine deposits a sediment varying in color from bright red to dark-brown or almost black. If pus is also present, the blood settles on top of the pus.

2. When blood corpuscles are abundant, albumin is *always* found in the urine.

3. The corpuscles must be examined with a high power, 400-500 diameters.

4. If at all abundant in the urine, the microscopical field is seen to contain an immense number of small roundish objects, whose mass exhibits a rusty color, sometimes with tinge of green-yellow.

5. The individual corpuscles show no nuclei and are not granular, owing to absence of cell contents.

### SIGNIFICANCE OF BLOOD CORPUSCLES.

Presence of blood corpuscles in abundance constitutes the condition known as *hæmaturia*. Blood in the urine occurs under the following conditions:

**Renal hæmaturia:**—In nephritis, acute or chronic; also in renal hyperæmias, in lardaceous disease, in renal abscess, in cystic diseases of the kidney, in hydatids, in stone, in rare instances in aneurism and embolism of the renal artery and thrombosis of the renal vein, in cancer of the kidney, in tuberculosis of the kidney, in malignant forms of acute infectious diseases as small-pox, yellow fever, malaria, etc.; and in leukæmia, purpura, scurvy, hæmophilia, and filariasis; also in poisoning by turpentine, creosote, carbolic acid, cantharides, and the new synthetic compounds; in cases of uterine and crural phlebitis; as a consequence of injuries, blows or wounds, or indirectly from concussion.

Lastly, it is possible to find renal hæmaturia in healthy kidneys, from paralysis of the vaso-constrictor nerves of the blood-vessels and consequent escape of the red blood corpuscles.

### DIFFERENTIAL DIAGNOSIS IN RENAL HÆMORRHAGES.

In *renal hæmorrhages* the urine is usually acid in reaction (sometimes alkaline in pyelitis), of homogeneous reddish-brown color, of lowered specific gravity, containing *blood-casts* and renal epithelium. (See Casts and Epithelium). The sediment is usually more or less brown or coffee-colored in hue. The blood in most cases is intimately mixed with the urine (except in angio-neurotic cases, where the kidneys are healthy) and blood shadows or "ghosts" are numerous. Clots are usually absent, except those long, slender, pencil-shaped molds, due to passage through the ureter. (The writer has, however, seen one case of hæmorrhage from the membranous and prostatic urethra in which such pencil-shaped clots were to be found).

**Differential diagnosis in renal hæmaturias:—**

1. *Nephritis:*—Presence of albumin, out of proportion to amount of blood, together with tube-casts, decrease in ratio of day urine to night; deficiency of urea or of phosphoric acid or increase in urea-phosphoric acid ratio (above 12 to 1). Symptoms and history of nephritis.

NOTE:—If the proteid deposit in the Esbach tube rises above the figure 4 the albumin is in all probability in excess of what the blood would account for except possibly in excessive, persistent, and *prostrating* hæmorrhages. Doubtful cases are those where, *without casts*, the proteid deposit in the Esbach tube is between 1 and 3. The writer has seen cases where blood alone in the urine, without casts or evidences of nephritis, gave rise to albumin in quantity such that the proteid deposit in the Esbach tube was between the figures 3 and 4. Albumin in such cases leaves the urine, when the blood disappears.

2. *Renal hyperœmia:*—Not much blood, not much albumin, few casts, scanty urine, urates or uric acid in sediment.

3. *Renal carcinoma:*—Troublesome, profuse, and repeated attacks of bleeding. Persistent, burning pain in the back, partially relieved by rubbing and by change of position. Renal tumor and cachexia. Pus not abundantly present in the urine. Albumin not in excess of blood. Bleeding much more profuse at times than at others, with weeks or months interval.

4. *Renal tuberculosis:*—Urine contains, besides blood, more or less pus, broken-down débris settling with difficulty; intermittent hæmaturia, usually no pain, but tumor may be present. Emacia-

tion, elevation of temperature; detection and propagation of *bacillus tuberculosis.*

5. *Renal stone:*—Blood usually diminishes. when the patient is at rest. Albumin small in quantity, pus corpuscles always found, crystals usually. Fixed pain in region of the kidney, wincing on part of patient on deep pressure over kidney at a certain point, pain down course of ureter, sometimes with retraction of testicle, and often extending down the thigh.

6. *Malarial hæmaturia:*—Absence of nephritis and other signs with history of malaria and presence of *plasmodium malariæ* in blood.

7. *Bleeding from healthy kidneys*, often symptomless:—Due to over-exercise, hæmophilia, or angio-neurosis. In the latter cases there may be renal tenderness on deep pressure. In one purely angio-neurotic case (diagnosis verified by operation), which the author saw, the blood on some occasions separated completely from the urine, leaving clear normal urine above the sediment. In such cases settle the blood in the centrifuge at low speed, pour off supernatant urine, and settle this at high. The urine settled at high speed shows nothing but blood-corpuscles, as does that at low. [In cases of symptomless hæmaturia put the patient on milk-diet, give baths, and keep quiet for several weeks, using also suggestive treatment. (The writer has found 30-drop doses of tincture of Thlaspi Bursa Pastoris useful in the purely angio-neurotic cases, but it was of no value in a case of hæmophilia in which it was tried). If the hæmorrhage is overcome by the above treatment, it is probably angio-neurotic. The writer thinks these cases not so rare as might be imagined].

**Hæmaturia from bladder:**—The urine is usually alkaline, often ammoniacal and thick from muco-pus, clots are commonly found, blood is brighter red and not intimately mixed with urine. Blood clots of irregular form and large size are from bladder; epithelia from middle layers of the bladder are quite commonly found. The ratio of day urine to night is not usually permanently or seriously changed in purely vesical hæmorrhages.

### DIFFERENTIAL DIAGNOSIS IN VESICAL HÆMORRHAGES.

1. Blood in the urine in small quantities, together with pus, in the case of old men, is quite common, as in the cystitis from enlarged prostate.

2. Blood in cases of stone in the bladder is almost normal in appearance, and is passed mostly at the end of micturition.

3. In inflammations of the neck of the bladder, blood, in small quantity, may be passed at the end of micturition. History of recent gonorrhœa, and presence of considerable albumin (½ to 1½ in the Esbach tube) will serve to distinguish from stone.

4. Profuse vesical hæmorrhages occur in connection with growths in the bladder. Dilute the urine abundantly with water; the blood-corpuscles are dissolved, and flesh-colored fibers or shreds easily found. (See Connective Tissue for figure). Epithelia from middle layers of the bladder are usually abundantly present in such cases.

**Hæmaturia from urethra:**—Recognized by flow of blood between micturitions or when blood can be squeezed out of the meatus by pressure. Usually due to gonorrhœa (acute stage), chancre, growths, injuries, or surgical operations.

MISCELLANEOUS CLINICAL NOTES.

1. An alternation of clear and bloody urine in the same day is never seen in hæmaturia due to bladder tumors.
2. The urine voided three hours after eating is sometimes more than ordinarily bloody in cases of calculous pyelitis, or in cancer of the kidney.
3. Blood from the seminal vesicles will be clotted and mixed with yellow bodies and spermatozoa. If the spermatic fluid is bloody, the blood probably comes from the prostatic sinus.
4. Symptoms of malarial hæmaturia sometimes resemble those of stone in the bladder, namely, frequent painful micturition, vesical tenesmus, sacral pain, and sleeplessness; but in addition there are in malarial hæmaturia, rigors, usually daily, fever, and sweat for several hours, and beginning usually at the same hour.
5. Laceration of the kidney may occur from accident without external appearance of injury; the symptoms are hæmaturia, pain in the loins, possibly pus in the urine, typhoid condition, and death in a few weeks.
6. Keyes reports that much albumin and tube-casts may be found in some cases of hæmaturia from enlarged prostate.
7. Vicarious menstruation by the kidneys is possible and spontaneous, and even regular monthly hæmaturia has been noticed in males.
8. Renal hæmaturia may follow the high temperature of typhoid fever, disappearing on the fall of the fever.
9. Renal hæmaturias may be due to over-doses of turpentine, and also to certain well-known and much-puffed synthetic compounds now on the market. Vesical hæmorrhages may be due to overdoses of cantharides.
10. Hæmorrhage from the bladder is sometimes due to rupture of varicose veins, especially in elderly patients.

# CHAPTER XLVI.

## PUS CORPUSCLES IN THE URINE. MUCOUS CORPUSCLES.

Recognition of pus by chemical means has already been described. Microscopically we find *pus corpuscles;* these are about one-third larger than blood corpuscles, granular, and sometimes showing nuclei. The latter may be brought out by addition of acetic acid.

Figure 71 shows pus corpuscles.

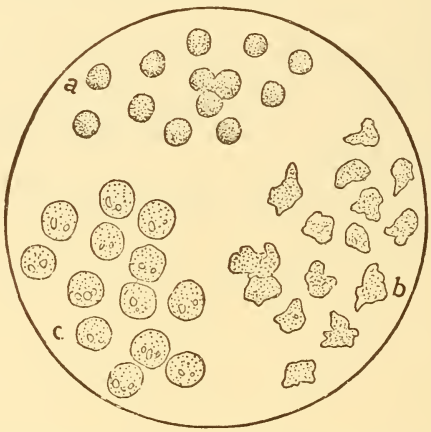



Fig. 71. *a.* The usual globular pus corpuscles of acid urine. *b.* Irregular pus corpuscles of acid urine, provided with processes. *c.* Swollen pus corpuscles of a strongly dilute or alkaline urine, with visible nuclei. (*Ultzmann*).

### RECOGNITION OF PUS CORPUSCLES.

1. Urine containing abundance of pus corpuscles deposits a dense white or greenish-white sediment. In less abundance the deposit is flocculent.

2. At least a trace of albumin is to be found in the urine, but seldom a large quantity. The precipitated

proteids in the Esbach tube will settle below the figure 1.

3. The corpuscles must be examined with a high power, 400-500 diameters.

4. If at all abundant, the field is seen to contain an immense number of small, colorless, roundish objects, granular and sometimes exhibiting nuclei.

5. In ammoniacal urine it is hard to see the individual corpuscles, which have broken up and coalesced to form a granular mass.

6. In strongly dilute or alkaline urine they are much swollen, and have visible nuclei in the central portion, while the peripheral portions show only a small number of granules.

7. In acid urine they are small and either globular, or else irregular, sending out processes. The latter occur in the more obstinate cases of pyuria.

8. Solution of iodine in potassium iodide colors pus corpuscles a fine yellow, while the nuclei appear darker and of a brown-yellow color.

### SIGNIFICANCE OF PUS CORPUSCLES.

In the urine of women pus corpuscles may merely indicate leucorrhœa. Whenever found, the urine should be examined after a cleansing vaginal injection or use of vaginal tampon. Pus in the urine is found in a large number of pathological conditions. It may be due to chronic diffuse nephritis, renal abscess, tuberculosis, cancer, or calculus; and is found in pyelitis, pyelo-nephritis, pyonephrosis, cystitis due to various causes, urethritis, prostatitis, etc., etc.

### DIFFERENTIAL DIAGNOSIS IN PYURIA

1. Pus from the kidneys is usually found in acid urine together with casts and renal epithelium. It settles quickly on standing, and is flocculent. The patient is usually sensitive to pressure over one kidney or the other, and may show presence of a tumor. When pus is retained in the calices, *chills* are often present. If the pus is only in the pelvis of the kidney, casts will be absent or scanty, and albumin not large in amount, below 1 on the Esbach tube. Frequent urging to urinate will not be a *persistent* symptom, though it may be complained of for a time.

2. When pus is from the bladder, the deposit is glairy and sticky, if the urine is ammoniacal, and there are found triple phosphate crystals with large, flat, and often round epithelia. Frequent and painful micturition is the rule in such cases.

In acute inflammation of the neck of the bladder the urine is acid, and it may appear that the pus is from the kidney, but albumin will be fairly abundant, perhaps settling to 1, or higher,

in the Esbach tube with frequency, straining after urination, and doubtless a history of recent gonorrhœa.

Pus from the prostate may show itself in the form of "threads" in the urine. The microscopic appearance of these threads is shown in Fig. 72.

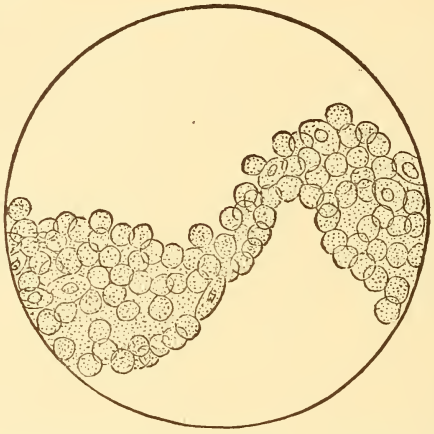


FIG. 72. A so-called gonorrhœal thread, consisting of pus corpuscles and urethral epithelium. (*Ultzmann*).

3. Pus from the urethra may be squeezed out between the acts of micturition, and the bulk of the pus is in the first glass, if the urine be voided into two glasses.

### CLINICAL NOTES ON PYURIA.

1. Pigmented pus corpuscles justify a diagnosis of chronic catarrhal cystitis. (Heitzmann).

2. Pus corpuscles with delicate red-brown hæmatoidin crystals in them signify previous hæmorrhage, as in the tubules or pelvis of the kidneys. (Heitzmann).

3. In chronic abscess of the kidney large quantities of hæmatoidin may be mixed with the pus. (Heitzmann).

4. In diseases affecting the renal parenchyma the amount of pus, as a rule, is small, except when a large abscess, located in the kidney structure proper, has suddenly burst into the renal pelvis.

5. Pus corpuscles are more abundant in the urine of acute nephritis than in that of chronic.

6. In the course of well-recognized chronic nephritis

an increase in the number of pus corpuscles indicates either an acute intercurrent nephritis or a complicating pyelitis, ureteritis, or cystitis.

7. In cases of simple renal hyperæmia pus corpuscles are never abundant.

8. As a rule the sudden appearance of a large

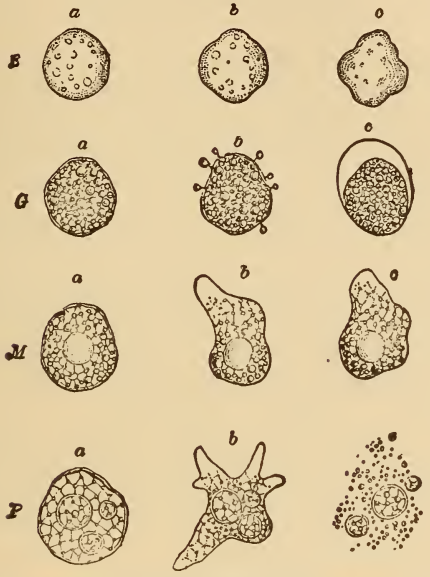



FIG. 73. Diagram of pus corpuscles of persons of different constitutions.

*E*, Pus corpuscle of an excellent constitution; the bioplasm nearly compact, containing a few small vacuoles, alive in *a*, alive and contracted in *b*, dead and contracted in *c*. *G*, Pus corpuscle of a good constitution, the bioplasm coarsely granular, alive in *a*, alive and contracted in *b*, dead and contracted in *c*. *M*, Pus corpuscle of a middling good constitution; the bioplasm less coarse, with a compact nucleus, alive in *a*, amœboid in *b*, dead in *c*. *P*, Pus corpuscle of a poor constitution; the bioplasm comparatively scarce, finely granular, vesicular nuclei very distinct; alive in *a*, amœboid in *b*, dead and burst in *c*.

Series *P*, indicates a broken-down constitution and rapidly approaching death.

NOTE:—Jagged forms of pus corpuscles found on drying, or evaporation of the highly ammoniacal urine of chronic cystitis, should not be mistaken for a result of amœboid motion.

quantity of pus in urine, previously normal or nearly, may most always be referred to the rupture of a neighboring abscess into the urinary passages.

9. Heitzmann holds that the constitution of an individual may be told by study of the pus corpuscles in his urine. Fig. 73 illustrates his idea.

10. When pus is from the kidneys, free oil may sometimes be found, when casts are absent. In a recent case, confirmed by operation on the kidney, the writer found abundance of free oil by sedimenting the pus in the centrifuge, at a speed of 1,000 revolutions, decanting the supernatant urine, and sedimenting this at a speed of 1,700 revolutions.

11. Catheterization of the ureters is a most useful process for determining the locality whence pus is derived.

12. In posterior urethritis if the urine is voided into two glasses the urine in the first glass will always be cloudy, but that in the second will sometimes be clear, sometimes cloudy, while the urine is acid in reaction.

### MUCOUS CORPUSCLES.

These resemble pus corpuscles but are irregular in size and in shape, have no nucleus but are granular; they are less compact than the pus, and are more like collections of fine granules.

### MICROSCOPICAL EXERCISE IV.

1. Examine blood corpuscles (*a*) in acid urine, (*b*) in urine which has stood for some time, and (*c*) in urine diluted with water.

2. Examine pus corpuscles (*a*) in acid urine, (*b*) in alkaline urine or urine diluted with water, (*c*) in strongly ammoniacal stale urine.

3. To a field of pus corpuscles of the usual globular form add a drop of acetic acid, and note effect on nuclei.

4. Obtain, if possible, pus from an old case of pyelitis and note microscopical appearance of corpuscles.

5. Sediment pus in centrifuge at 1,000 revolutions for 5 minutes; decant, sediment decanted portion at 1,700, and look for oil.

# CHAPTER XLVII.

## EPITHELIUM IN URINE.

Epithelium, the normal product of mucous surfaces, in greater or less amount occurs in nearly all urine, and is exceedingly abundant in the urine of women, when it forms a whitish flocculent sediment.

Whether diagnosis can be made with certainty by identification of epithelium is a disputed point. The late Charles Heitzmann, one of the ablest pathologists in this country, was emphatic in his opinion as to the possibility of recognition of the locality whence epithelium was derived. He proved his own ability to do so in several instances, when urine was referred to him by the writer, from cases the symptoms and history of which were known to me but unknown to him. There is not a shadow of doubt in my own mind about Heitzmann's ability to make diagnoses from observation of what other writers are loth to recognize as significant.

The epithelia found in urine are shown in the following, Figure 74, taken from Heitzmann:

### SIGNIFICANCE OF EPITHELIA.

In urine of *males:*—

1. The largest *columnar* epithelia from the urethra occur in deeply seated blenorrhœic inflammation, and in ulcerations which often lead to formation of a stricture.

2. *Cuboidal* epithelia, somewhat smaller than the average cuboidal epithelia of the bladder, come from the prostate in catarrhal prostatitis (young men), and hypertrophy of the prostate (men over 40).

3 *Ciliated columnar* epithelia, distinctly surpassing in size those from the mucosa of the uterus, indicate slight catarrhal inflammation of the ejaculatory ducts. They are rarely seen ciliated, as the cilia break off very easily; delicate parallel rods in the interior indicate original ciliation.

In urine of *females:*—

1. Large, flat, vaginal epithelia indicate catarrhal vaginitis. The largest cuboidal and columnar epithelia are observed in cases of intense, deeply-seated, or ulcerative vaginitis.

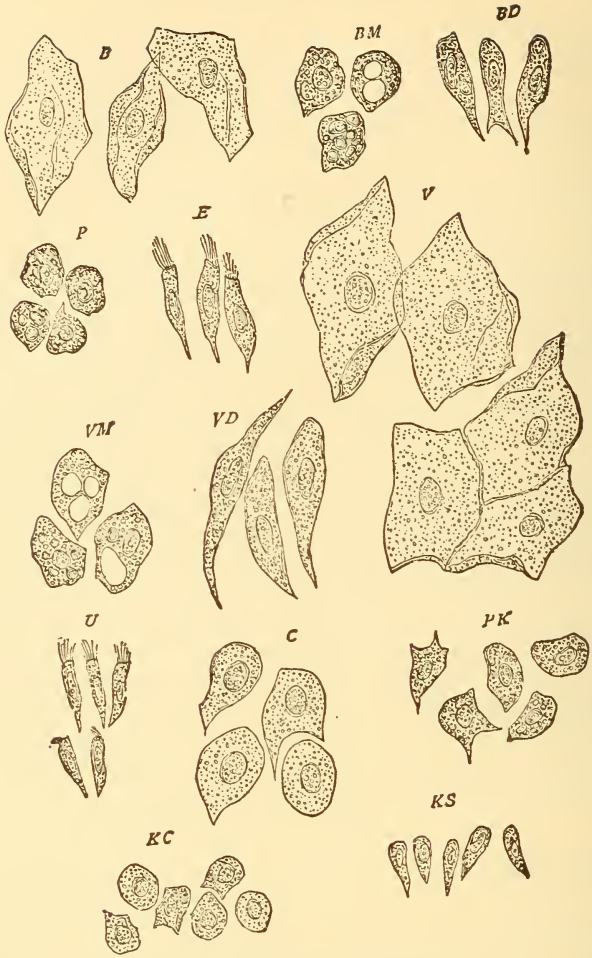



FIG. 74. Epithelia found in urine.

*B*, Bladder epithelia from upper layers; *BM*, bladder epithelia from middle layers; *BD*, bladder epithelia from the deepest layer; *P*, prostatic epithelia; *E*, epithelia from the ejaculatory ducts; *V*, vaginal epithelia from upper layers; *VM*, vaginal epithelia from middle layers; *VD*, vaginal epithelia from the deepest layer; *C*, epithelia of the cervix uteri; *U*, epithelia of the mucosa of the uterus; *PK*, epithelia from pelvis of the kidney; *KC*, kidney epithelia from the convoluted tubules; *KS*, kidney epithelia from the straight collecting tubules. Magnified 500 diameters. (*Heitzmann*). Bartholinian epithelium corresponds to prostatic.

2. Flat cuboidal epithelia (smaller in size than vaginal and as a rule finely granular, often with offshoots) are found, together with pus and blood corpuscles and shreds of connective tissue, in ulceration of the cervix uteri.

NOTE:—Cuboidal epithelia are originally angular, polyhedral formations, but, by swelling in the urine, they assume a more or less regular or even perfectly spherical form.

3. Delicate, columnar, ciliated epithelia from the mucosa of the uterus, accompanied by ciliated pus corpuscles, indicate catarrhal endometritis.

In urine of *both sexes:*—

1. Flat epithelia of the bladder, in small numbers and without pus corpuscles, are normal.
2. Flat epithelia in larger amount (with pus corpuscles and epithelia from middle layers of the bladder, exhibiting endogenous new formation of pus corpuscles) indicate acute catarrhal cystitis.
3. If the cuboidal epithelia largely outnumber the flat, or are scanty in comparison with the large amount of pus corpuscles, and especially if some pus corpuscles contain dark-brown pigment granules, the case is one of chronic cystitis.
4. Clusters of uric acid crystals in freshly voided urine, together with caudate epithelia somewhat smaller than those of the middle layers of the bladder, indicate deposit of uric acid in the pelvis of the kidney.
5. Pelvic epithelia, together with epithelia from the uriniferous tubules, indicate pyelo-nephritis.
6. Pelvic epithelia with red blood corpuscles, and shreds of connective tissue, indicate hemorrhage and ulceration in the kidney pelvis.
7. Renal epithelia, together with pus corpuscles, signify catarrhal (interstitial) nephritis.
8. Renal epithelia, together with pus corpuscles and tube-casts, signify croupous (parenchymatous nephritis).
9. The same with large quantities of pus corpuscles signify suppurative nephritis.

### EPIDERMAL SCALES.

These are irregular in size and in shape and somewhat resemble epithelia, but are without nucleus. They are of no significance.

## MICROSCOPICAL EXERCISE V.

1. Obtain the urine of a woman who has borne children, and study the white sediment of vaginal epithelia. Note epithelia from upper and middle layers in cases where leucorrhœa exists. Note also pus corpuscles. (Fig. 75).

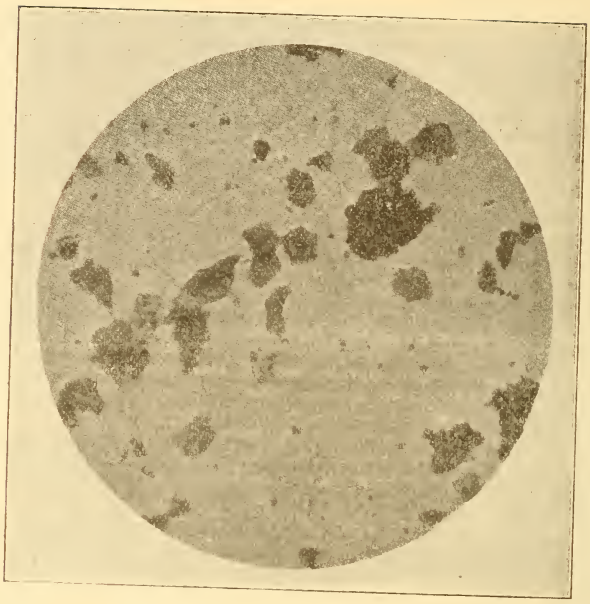


FIG. 75. Sediment common in urine of women; vaginal epithelia and debris. (Photo-micrograph).

2. Obtain urine from the same woman voided after a cleansing vaginal injection, or drawn off by the catheter, and note smaller quantity of epithelia and absence of pus corpuscles.

3. Let the urine, obtained as in 1, stand in a cold place until urates have deposited, and notice how they hide the epithelia.

4. Obtain the urine from a case of cystitis and demonstrate pus corpuscles and epithelia from the middle layers of the bladder. Demonstrate prostatic epithelia in the urine of old men with enlarged prostate.

5. If possible, obtain urine from a case of suppurative nephritis and pyelitis, and demonstrate renal and pelvic epithelia.

6. Obtain urine from a man who has the so-called "clap-threads" in the urine and study their appearance. Of what are they composed?

# CHAPTER XLVIII.

## TUBE-CASTS IN THE URINE.

Casts are in all probability composed of the coagulable elements of the blood which, after gaining access to the renal tubules, entangle in them any free or partly-detached products of the tubules, and form molds of the latter. The substance of which they are composed is a proteid not identical with any that we recognize.

Tube-casts proper consist of a uniform, transparent, gelatinous matrix to which other elements (epithelia, corpuscles, and even various salts, both crystalline and amorphous) may be accidentally attached.

They must be distinguished from (*a*) *cast-like formations*, *i. e.*, groupings of salts, corpuscles, etc., which lack uniform matrix, and (*b*) the band-like formations known as *cylindroids* and *mucous cylinders*.

### IDENTIFICATION OF CASTS.

Study Figures 76, 77 and 78.

1. Casts should be sought for with a low power and without cover-glass. The urine should be *acid*. Alkaline urine rapidly dissolves casts.

2. They may be recognized by use of a power of 150 diameters, when they will look small, yet much larger than corpuscles, spermatozoa bacteria, or small crystals, as oxalate.

3. They are of *uniform breadth*, and usually longer than they are broad.

4. They have usually at least one well-rounded extremity, and well-defined borders.

5. They are not longitudinally striated, not jagged, nor provided with processes, not jointed, segmented, nor serrated. They may possibly be spirally twisted at one or both ends.

6. They are distinguished from large epithelia by absence of the nucleus, and by the well-rounded extremity. They refract, also, differently.

7. They are distinguished from bacteria, corpuscles, spermatozoa, and oxalate crystals by their larger size, uniform breadth, greater length than breadth, and rounded extremity.

8. They are distinguished from large crystals by absence of geometrical form and less refraction.

9. In some cases one end of the cast tapers off considerably, and presents a spirally twisted appearance, which may go on to such an extent that the entire cast becomes transversely striated. Broad hyaline casts may sometimes be branched dichotomously at one end.

10. Their kind must be determined by use of a high power, 500 diameters.

11. To find hyaline casts tilt the mirror of the microscope, so as to darken the field gradually, when the outlines or shadows of delicate hyaline casts may be seen, which otherwise might escape detection.

KINDS OF CASTS.

**Hyaline casts:**—These are colorless, usually very pale, transparent, and readily soluble in acetic acid, a fact which must be borne in mind, when this reagent is added to a sediment in order

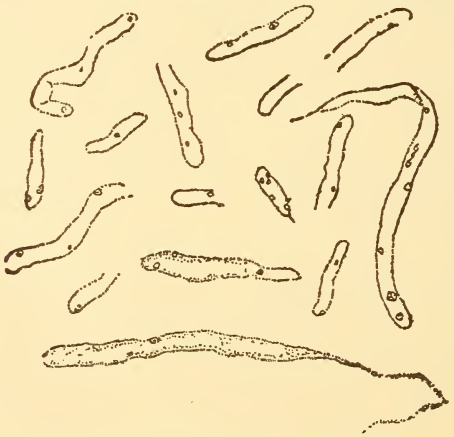


FIG. 76. Hyaline casts. (*Simon*).

to dissolve phosphates. Small granules may almost always be seen imbedded in or adhering to their matrix. In breadth these casts are usually between 0.01 and 0.05 m.m.; in length they vary greatly, in some cases being not much longer than they are wide, but in others extending across the entire microscopic field.

It has often been said that it is impossible to reproduce hyaline casts in cuts so that they appear at all natural. The writer thinks, however, that figure 76, taken from C. E. Simon, is an excellent representation of them, barring the borders, which instead of being dotted should be continuous, as in Figure 77.

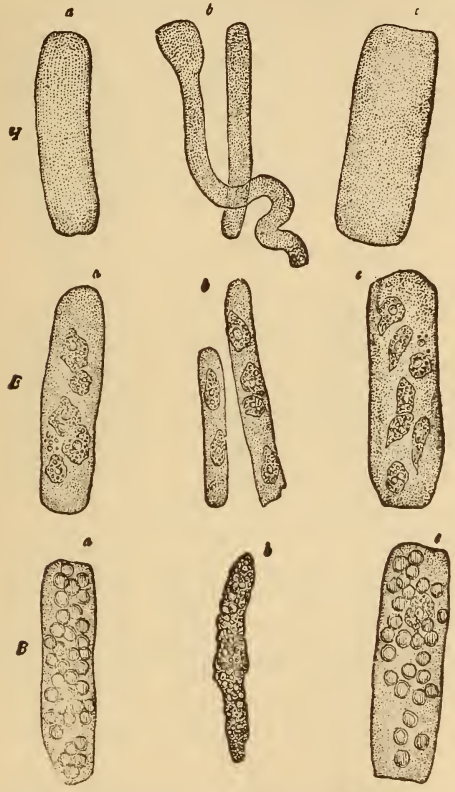



FIG. 77. Hyaline, epithelial, and blood casts, seen with a high power.

The series *a* shows casts from convoluted tubules of the second order; the series *b*, casts from the narrow portion of the loop-tubules; the series *c*, casts from the straight collecting tubes. *H*, hyaline casts; *E*, epithelial casts; *B*, blood casts. Magnified 500 diameters. (After *Heitzmann*).

**Epithelial casts:**—These have the hyaline matrix more or less concealed by epithelia. Close observation will usually show a fine boundary line at some portion of the structure, even when epithelia are very numerous, and a drop of acetic acid serves to dissolve the matrix and set the epithelia free.

**Blood casts and pus casts:**—These consist of the hyaline matrix with blood corpuscles or pus corpuscles imbedded in or adhering to the matrix. Pus casts are exceedingly rare and no cuts of them appear in the majority of our text-books. In a recent case observed by the author, in which operation disclosed pus in one kidney, several pus casts were found in the urine.

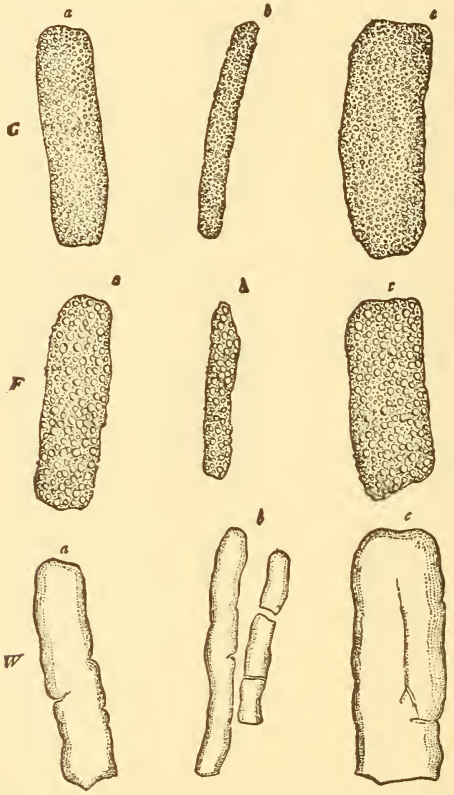



FIG. 78. Granular, fatty, and waxy tube-casts, seen with a high power.

The series *a* shows casts from convoluted tubules of the second order; the series *b*, casts from the narrow portion of the loop-tubules; the series *c*, casts from the straight collecting tubules. *G*, granular casts; *F*, fatty casts; *W*, waxy casts. Magnified 500 diameters. (After *Heitzmann*).

**Granular casts:**—These have the hyaline matrix, and well-defined boundary with granular matter imbedded in or adhering to the matrix. Granular casts are of several kinds, as finely granular, or coarsely granular. The latter are usually of more serious significance. Coarsely granular casts may at times be very long, large, and dark in color, especially in rapidly fatal cases.

**Fatty casts:**—These have the hyaline matrix dotted with fat granules. Free fat is usually also discoverable in the field.

**Waxy casts:**—These are strongly refractive of light, have a yellow or yellow-gray color, and are but slowly attacked by acetic acid, if at all. As a rule only small fragments of them occur, but these are broad and stout. They may be coated with urates, or may contain crystals of calcium oxalate, etc., but do not commonly present these features. Some of these waxy casts give the amyloid reaction, that is, assume a mahogany color when treated with a dilute solution of iodo-potassic iodide, turning to dirty violet on addition of dilute sulphuric acid, but this is not pathognomic, as formerly supposed, of amyloid kidney, but due probably to degeneration, due to long stay in the uriniferous tubules.

### CAST-LIKE FORMATIONS.

These are composed of various elements having the cast form, but lacking the matrix soluble in acetic acid.

*Amorphous urates* may occur simulating granular casts in form (Fig. 79).

*Bacteria* may be grouped in a cast-like manner, but close inspection shows irregular outline, and abundance of groupings not in cast form.

*Hæmatoidin* and *granular detritus* may also assume the cast form.

*Epithelia* may be found in cast form. Such formations are hollow, being thrown off *en masse* from the uriniferous tubules. Seen only in parenchymatous nephritis.

FIG. 79. Cast-like formations of amorphous urates.

*Blood corpuscles enmeshed in fibrin* are common in renal hæmorrhages, and may assume the cast form.

The differential diagnosis between a true cast and a cast-like formation can be made by addition of a drop of acetic acid, which dissolves the hyaline matrix of a true cast, but has no effect on a cast-like formation.

### CYLINDROIDS AND MUCOUS CYLINDERS.

*Cylindroids* have the appearance of hyaline tube-casts, but are very large and band-like. They have uniform breadth and often contain crystals, epithelia, and corpuscles. They are soluble in acetic acid. They are of renal origin. True casts are sometimes seen, which terminate at one or both ends in cylindroids.

*Mucous cylinders* are never of uniform breadth, seldom or never contain morphologic or mineral constituents, and are insoluble in acetic acid. They are found in any urine containing abundance of mucus, and are of no other significance.

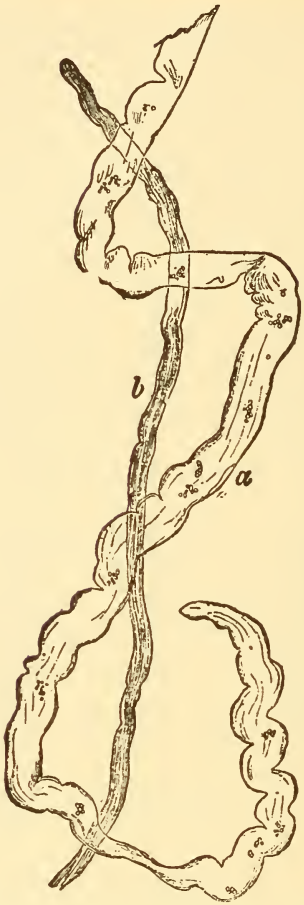



FIG. 80. *a* and *b*, cylindroids. (*Jaksch*).

EXTRANEOUS OBJECTS SOMEWHAT RESEMBLING CASTS.

These are very numerous and may be divided into fibers, wool, feathers, and fungi, as mycelium, leptothrix, and bacteria. Figure 81, from Heitzmann, shows the most common ones found in urine.

*Cotton fibers* are wavy and twisted with edges more compact than the centre is.

*Linen fibers* are straight, composed of smaller fibrilla, with breaks and breaches from hackeling.

*Sheep's wool* has fine serrations along the edges; cuticle on surface is imbricated.

The *mycelium*, especially of penicillium glaucum, is very common in urine; with a high power it appears segmented as in the figure —.

*Leptothrix* is small and very slender.

*Bacteria* are very small, and cannot be easily recognized with 150 diameters.


FIG. 81. Accidental occurrences in the sediment of urine.

*S*, Silk fibers; *C*, cotton fibers; *L*, linen fibers; *W*, sheep's wool; *F*, feather; *St*, starch-granules of rice; *Cr*, cork particles; *O*, oïdium, the seed of mildew; *M*, mycelium of mildew; *Mc*, micrococci; *B*, bacteria; *Lt*, leptothrix. Magnified 500 diameters. (After *Heitzmann*).

*Zoöglœa masses* of bacteria, exceedingly common in the urine of women, are often mistaken for granular casts by beginners. They have no matrix, are irregular in outline, and occur in great abundance without definite shape.

### SIGNIFICANCE OF CASTS.

1. The writer finds that with the centrifugal machine a few casts may be found in 1 out of every 3 specimens of the 24 hours' urine examined. Such casts are usually 2 or 3 small hyaline, or 1 or 2 small granular, per sediment of 15 c.c. urine.

2. In cases in which stimuli, as severe exercise, cold baths, etc., occasion albuminuria, casts may also be found.

3. When casts and albuminuria occur together, it may be assumed that the albuminuria is renal.

4. Albuminuria and a few hyaline casts, especially if latter are only temporarily present, signify a mild circulatory disturbance of the kidneys.

5. Continuous presence of hyaline casts in abundance, together with albuminuria, especially if marked, indicates the existence of a nephritis.

6. Numerous hyaline, epithelial, and blood casts signify acute croupous (parenchymatous) nephritis. (*Heitzmann*).

7. Numerous granular, fatty, and waxy casts signify chronic croupous (parenchymatous) nephritis. (*Heitzmann*).

8. Casts of both acute and chronic forms indicate a subacute form, chronic inflammation with acute recurrences. (*Heitzmann*).

9. The greater the number of casts, the more serious the nephritis. (*Heitzmann*).

10. A large number of blood casts in the urine of adults indicates a fatal termination in a short period of time. (*Heitzmann*).

11. The size of the casts is of great prognostic value (Fig. 77). Narrow casts together with a small number of casts of medium width, signify a mild degree of nephritis. Casts of medium width denote inflammation of the cortical substance. Casts of all three sizes,

the largest arising from the straight collecting tubules, signify inflammation in the whole organ, in which case there is a very unfavorable prognosis. (*Heitzmann*).

12. Hyaline casts studded with fine granules may be called "verging on granular," and indicate an incipient chronic nephritis as in third or fourth week of scarlet fever. When casts have distinct outlines they are "verging on waxy," as granular-waxy, fatty-waxy. Epithelial casts may be "verging on fatty and waxy," either or both. Hyaline, epithelial, fatty, and granular casts have indistinct outlines, but when verging on waxy the outlines are distinct. Fatty casts may be told from casts of cocci by their glossy, distinct granules; cocci are smaller, sharply defined, as in zöoglœa, and darker. Fat granules are larger, less sharply defined, and not so dark. (*Heitzmann*).

13. Fatty casts are most commonly associated with subacute or chronic inflammations of the kidney of protracted course, with tendency to fatty degeneration of the renal tissues. (*Jaksch*).

14. Epithelia found in tube-casts, if shrunken and atrophic, indicate an inflammatory renal process complicated with degenerative changes. Epithelial casts without presence of distinct changes affecting the renal parenchyma are probably never seen.

15. Pus corpuscles in small numbers on hyaline casts are common in various nephrites, especially in acute cases.

16. Pus-casts indicate suppurative inflammation of the kidneys.

17. Cylindroids accompany hyaline casts, and are of the same significance.

### THE WRITER'S OBSERVATIONS ON MORTALITY IN ALBUMINURIA WITH AND WITHOUT CYLINDRURIA.

In an article in the *New York Medical Times*, July, 1895, the writer gave the statistics of mortality in 500 cases of albuminuria as follows:

SUMMARY NO. 1. 1888-1895.

| | | |
|---|---|---|
| I. | Non-albuminuric cases whose present condition is known with certainty | 253 |
| | Deaths | 28 |
| | Percentage of mortality thus far | 11 |
| II. | Albuminurics without casts | 255 |
| | Deaths | 37 |
| | Mortality per cent thus far | 14 |
| III. | Albuminurics with casts | 304 |
| | Deaths | 89 |
| | Percentage of mortality thus far, about | 30 |

SUMMARY NO. 2.

| | | |
|---|---|---|
| I. | Albuminurics with casts | 304 |
| | Without granular, fatty, or waxy casts | 177 |
| | Deaths | 36 |
| | Percentage of mortality thus far | 20 |
| II. | With granular, fatty, or waxy casts | 127 |
| | Deaths | 53 |
| | Percentage of mortality thus far | 41 |
| III. | Mortality in those of II, according to sex: | |
| | (*a*) Total number of men | 93 |
| | Deaths | 37 |
| | Percentage of mortality thus far | 40 |
| | (*b*) Total number of women | 34 |
| | Deaths | 16 |
| | Percentage of mortality thus far | 47 |

From these figures it will be seen (1) that the death-rate was greater among those who had albuminuria without casts than among those who had no albuminuria at all, and (2) that the death-rate among those who had albuminuria with casts was greater than in those without casts, while (3) the death-rate of those albuminurics with granular, fatty, or waxy casts was double that of those with only hyaline, epithelial, or blood casts.

## MICROSCOPICAL EXERCISE VI.

**1.** Obtain the urine of a patient with post-scarlatinal nephritis and study the different kinds of tube-casts. Notice in a severe case the large number of objects in the field and the variety of them, not less than four different constituents being present in abundance. (Fig. 82).

FIG. 82. The field in nephritis. (Photo-micrograph). Note tube-casts, corpuscles, epithelia, etc.

2. Obtain the urine from a case of chronic nephritis, preferably with dropsy and high-colored, scanty, albuminous urine, and study the casts. What are the prevailing ones?

3. Obtain the urine of a man over 40 with chronic interstitial nephritis and look for casts? Are they numerous? What kind?

4. Add dust from the dustpan to a sample of normal urine and study the sediment for extraneous objects.

# CHAPTER XLIX.

## SPERMATOZOA, CONNECTIVE TISSUE, MICRO-ORGANISMS, PARASITES.

**Spermatozoa:**—(Fig. 83), are found in the urine of healthy adults after pollutions or coitus and are then of no significance.

FIG. 83. Spermatozoa.

*Constant* presence of spermatozoa in the urine is noted in spermatorrhœa due to sexual excesses or masturbation.

In cases in which semen is passed during defecation or from irritation of ammoniacal urine, as in cystitis, no deleterious effects seem to appear.

Spermatozoa are found in the urine after epileptic seizures and sometimes after hystero-epileptic attacks; also in certain spinal diseases, and in severe illness as typhoid.

In the urine spermatozoa are almost always quiescent; they are in form thread-like bodies provided with a head and a long, tapering, tail-like extremity. The entire length is about 1-600 of an inch and they must be searched for with a high power.

**Connective tissue:**—Little is to be found in medical literature regarding this substance in the urine, except what has been written by Heitzmann. The appearance of connective tissue fibers in the urine is a frequent phenomenon. They are, as a rule, small and are distinguished from mucous threads by their greater refraction, their almost invariable occurrence in bundles of varying size, their fibrillary or finely granular appearance, and of the presence in them at times of formations similar to nuclei. Linen fibers possess strong refraction but split in a way essentially different from connective tissue.

Shreds of connective tissue are found in the urine in:

1. Ulcerations.
2. Abscesses.
3. Tumors.
4. Hæmorrhages.
5. Trauma.
6. Cirrhosis and atrophy of the kidneys.
7. Hypertrophy of the prostate.

Connective tissue studded with fat is probably from the kidneys.

Figure 84, a photo-micrograph, by Dr. Charles Gordon Fuller, of Chicago, from one of the writer's slides obtained from Dr.

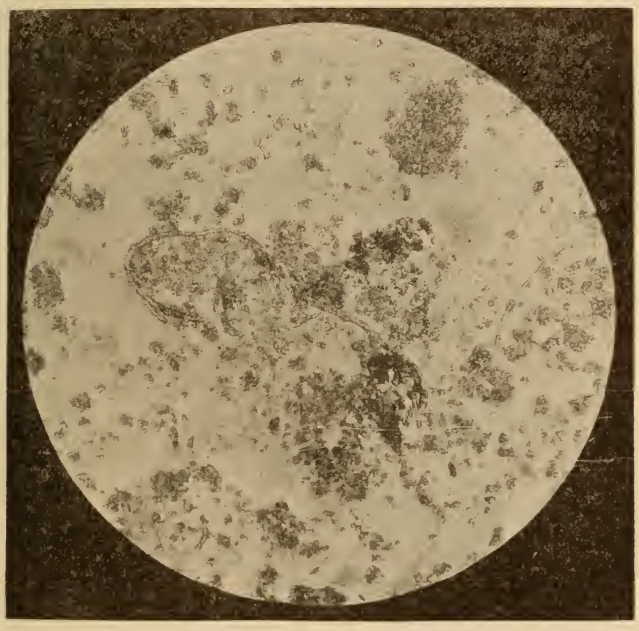


FIG. 84. Shred of connective tissue in urine of a case of tumor of the bladder. Photo-micrograph by Dr. Charles Gordon Fuller, of Chicago.

Heitzmann, shows a shred of connective tissue found in the case of a tumor of the bladder.

When tumors are present in the urinary tract, connective tissue is most abundant. If papilloma of the mucous membrane of the bladder exist, there will be found, especially on diluting the urine with water and sedimenting with the centrifuge, much elongated shreds of connective tissue, which, under the microscope, appear spread out like branches, knotted or convoluted, shriveled, and containing blood vessels in which are but few inflammatory corpuscles and no epithelium-nests.

**Micro-organisms:**—Healthy urine is an aseptic fluid which, on standing exposed to the air, soon contains great numbers of micro-

organisms. Abnormal urine nearly always contains micro-organisms: These are fungi, pathogenic and non-pathogenic. Non-pathogenic fungi are molds, yeasts, and fission-fungi. Molds are found on the surface of old saccharine urine which has undergone alcoholic fermentation, or less frequently on the surface of putrid urines containing no sugar. (See Fig. —).

The yeast plants (saccharomyces urinæ) are found in acid urine and abundantly in saccharine urine. The sporules occur as small roundish bodies (Fig. —), suggesting blood corpuscles in size and shape, but are irregular, sometimes of large size with nuclei, and are more elongated or oval. They are often arranged in bead-like forms, some of which may have several small bud-like bodies attached to them. In great numbers they are indicative of presence of sugar.

*Fission fungi* are found as the urine begins to putrefy; it is then cloudy, not easily filtered clear, never sharply acid, and usually neutral or feebly alkaline. Such urine is common in the case of delicate women and in men with stricture or who use catheters or bougies. The fungi in these conditions are the micrococcus ureæ (Fig. 85), and various rod-like bacteria; occasionally long spiral bacilli with large spores and cocci occur. Nearly all these microbes possess the power to transform urea into ammonium carbonate.

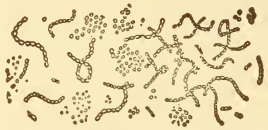


FIG. 85. Micrococcus ureæ.

The micrococcus ureæ occurs in almost pure culture on the surface of fermenting urine in the form mostly of characteristic chains as in the figure. The individual coccus is large and is sometimes mistaken for a blood-shadow or "ghost." The diagnosis of ammoniacal fermentation within should not be made unless the presence of ammonia can be demonstrated in freshly voided urine, as some urines undergo fermentation, particularly in warm weather, shortly after being voided, and especially if the vessel employed is not absolutely clean.

Sarcinæ (Fig. 86) occur in urine and are smaller than those found in the stomach, being in point of size comparable to those of the lung. The writer has noticed them particularly abundant in a case of chronic cystitis occurring in a patient with paralysis agitaus.

FIG. 86. Sarcinæ in urine.

*Pathogenic fungi* are numerous and belong to two orders, micrococci and bacilli. In suppurative diseases we find the characteristic micrococci as the staphylococcus pyogenes albus, aureus, citreus, and the streptococcus pyogenes. The bacilli found include the bacillus coli communis the urobacillus liquefaciens septicus, the bacillus tuberculosis, and many others. As a general rule the organisms causing the morbid processes are elimi-

nated. Pathogenic organisms have been found in the urine in erysipleas, measles, scarlatina, relapsing fever, sepsis, typhoid fever, tuberculosis, etc., but unfortunately it is only exceptionally that the diagnosis of specified fevers can be made by bacteriologic examination of the urine.

Even the search for the tubercle bacillus in the urine is frequently fruitless. By use of Dr. Purdy's small tubes, designed for sedimentation of bacteria, and a high speed, 5000 or more revolutions per minute, of the centrifuge one is more likely to find the tubercle bacillus, which should always thus be sought for in the case of pyuria accompanied by anæmia, wasting, and evening temperature. The urine must be obtained with the catheter to avoid admixture with the urine of smegma bacilli which can be with difficulty distinguished from the tubercle bacilli. Injection of a few drops of the sediment of such urine into the anterior chamber of the eye of a rabbit; the urine being obtained under bacteriologic precautions, is advisable, the development of miliary tubercles of the iris being watched for. The search for the bacillus is made as in sputum and should only be undertaken by an expert. Those not familiar with bacteriology do not realize the care and experience necessary in this operation.

The relation of micro-organisms to nephritis is now occupying the minds of a number of observers and some interesting studies have been made, as for example, of the rôle of the bacillus coli communis. In general, however, nephritis is referable to ptomain intoxication rather than to the action of bacteria, although their presence in the kidneys may be regarded as indicating the existence of some definite alteration of the renal parenchyma.

Non-pathogenic bacteriuria has occasionally been noticed but the occurrence is very rare and possibly not associated with any pathologic condition, although the bacillus coli communis has been obtained in pure culture from cases of pyelitis.

*Gonococci* may be found in the cellular elements in urinary sediments, but in making the examination for them a drop of the discharge should be taken from the meatus on a cover-glass, spread out in as thin a layer as possible, allowed to dry, passed three or four times through the flame of a Bunsen, and stained with a drop of carbol fuchsin without application of heat. Excess of coloring matter is removed by rinsing in water, the specimen is dried between layers of filter-paper mounted in a drop of water and examined, preferably with an oil immersion lens. The gonococci consist of minute roll-shaped cocci, chiefly met with as diplococci, the individual cocci being seemingly divided by a bright, transverse band often presenting the so-called roll form; also called the kidney or bean shape. The cocci usually appear in pairs lying close together, their flattened surfaces usually presented to each other. Presence of gonococci *within* the cellular elements is deemed characteristic. The reader is referred to works on Bacteriology for figures.

**Animal parasites:**—The ova of distoma hæmatobium and the filaria sanguinis hominis occur in the urine. The parasites cause various serious urinary diseases, as hydronephrosis, pyonephrosis, pyelitis, and pyelonephritis, and the ova serve as nuclei for stone. Echinococcus, ascarides, strongylus gigas, and infusoria are also found. Filaria are found in our Southern States, and cause chyluria. The eggs of distoma are oval, flask-shaped bodies.

# CHAPTER L.

## THE URINE AND CHARACTERISTIC SYMPTOMS OF DISEASES OF THE KIDNEYS.

The following pages show the clinical features of the most common urinary diseases:

**Acute renal hyperæmia** (*active congestion*):—
Frequency, urgency, possibly vesical tenesmus. Urine contains less than 10 per cent bulk of albumin, a few hyaline casts, and perhaps a little blood. Suppression possible.

**Chronic renal hyperæmia** (*passive congestion*):—
Cardiac symptoms, dropsy, dyspnœa, cyanosis (not in milder cases); weak, thready pulse; hacking cough. Urine decreased in quantity, specific gravity increased, albumin small, casts few, hyaline; urates and mucus.

**Acute diffuse nephritis** (*including post-scarlatinal nephritis*):—
Dropsy, pallor, high pulse and temperature, nausea, vomiting, headache, stupor, coma, convulsions. Blood the urinary feature. Albumin abundant, numerous hyaline, epithelial, and blood casts; later, granular and perhaps fatty casts.

**Chronic diffuse nephritis** (*including parenchymatous or croupous, formerly so-called*):—
Obstinate dropsy, anæmia, pallor and puffiness of face, debility and loss of flesh. Night urine exceeds day. Albumin abundant. Dark granular, fatty, and waxy casts. Later, urine more abundant, lighter in color, less albumin.

**Chronic interstitial nephritis** (*contracting kidney, terminating in cirrhosis*):—
Rising at night to urinate; full, hard pulse; displacement of apex beat of heart, accentuation of second sound (at second right intercostal space, one-half inch from the sternum), retinitis, post-cervical neuralgia, dizziness, drowsiness, coma, convulsions. Slow course, sudden death. Polyuria. Deficiency of phosphoric acid marked. Trace of albumin, increased at times. Casts, few hyaline. Night urine equals or exceeds day.

NOTE:—The kidneys finally become contracted, small, and hard. The actual size possible is shown in figure 87.

FIG. 87. Cirrhotic kidney, actual size. (*McNutt*).

**Lardaceous disease** (*amyloid disease*):—
Gastro-intestinal symptoms the feature: diarrhœa. Sallow complexion. History of syphilis or suppurations. Tuberculous family history. Dropsy. Enlarged spleen and liver. Albumin abundant; casts not abundant, large hyaline or waxy.

**Cystic disease of kidneys:—**
Cardiac symptoms of chronic interstitial nephritis. Soft, non-fluctuant, kidney-shaped, bilateral renal tumor of slow growth. Urine of chronic interstitial nephritis, plus blood; more albumin and large granular casts. Cystitis may complicate, with pyuria.

**Puerperal nephritis:—**
Headache, visual troubles, dizziness, nausea, vomiting, convulsions. Urine suddenly becomes scanty, urea suddenly increases *in grains per ounce* (12 to 14), albumin jumps from a trace to a large quantity, in twenty-four hours or less; casts present, not always abundant unless patient previously have chronic nephritis.

## DIAGNOSTIC DIFFERENTIATION.

Chronic renal hyperæmia is to be differentiated from chronic interstitial nephritis as follows:—

| THE URINE IN CHRONIC RENAL HYPERÆMIA, | THE URINE IN CHRONIC INTERSTITIAL NEPHRITIS, |
|---|---|
| Oliguria; | Polyuria; |
| Solids increased in grains per ounce; | Solids decreased in grains per ounce; |
| Color increased; | Color decreased; |
| Albumin small; | Albumin small; |
| Casts few, hyaline; | Casts few, hyaline; |
| Urates and uric acid in sediment; | No crystalline sediment; |
| Usually blood corpuscles in sediment. | Usually no blood unless cystic disease. |

| THE SYMPTOMS OF CHRONIC RENAL HYPERÆMIA, | THE SYMPTOMS OF CHRONIC INTERSTITIAL NEPHRITIS, |
|---|---|
| Valvular diseases; | No valvular diseases; |
| No hypertrophy of heart; | Hypertrophy of heart; |
| Weak thready pulse; | Full hard pulse; |
| Dropsy, chiefly of lower extremities; | No dropsy till late; |
| No uræmia; | Chronic uræmia; |
| No rising at night to urinate; | Nocturnal micturition common; |
| No visual disorders. | Visual disorders. |

Chronic diffuse nephritis must be differentiated from lardaceous (amyloid) disease.

| THE URINE OF CHRONIC DIFFUSE NEPHRITIS, | THE URINE OF LARDACEOUS DISEASE, |
|---|---|
| Urinary sediment abundant; | Urinary sediment scanty; |
| Albumin large; | Albumin large; |
| Casts abundant, including dark granular and fatty; | Casts few but large size, broad hyaline and waxy. |
| Pus corpuscles, epithelia, granular debris abundant in sediment. | Few cellular elements. |

| CHRONIC DIFFUSE NEPHRITIS, | LARDACEOUS DISEASE, |
|---|---|
| Dropsy; | Dropsy; |
| Anæmia striking, pallid puffy face; | Cachexia:—face sallow or bronzed; |
| Uræmia not till late; | Uræmia rare; |
| Dyspepsia and diarrhœa not permanent; | Dyspepsia and diarrhœa are notable features; |
| Liver and spleen not enlarged. | Liver and spleen enlarged. |

Cystic disease of the kidneys must be differentiated from chronic interstitial nephritis and from renal cancer:—

| CYSTIC DISEASE. | CHRONIC INTERSTITIAL NEPHRITIS. | CANCER. |
|---|---|---|
| Non-fluctuant swelling in the sides; | No swelling; | Nodular growth of unequal resistance; |
| Recurrent severe hæmaturia; | No hæmaturia; | Irregular intermittent hæmaturia; |
| Slow growth of tumor; | No growth; | Rapid growth: |
| No pain; | ---------- | Pain; |
| Sallow, cachectic appearance; | Patient well-preserved; | Emaciation and cachexia; |
| Age, 40 to 55. | Age over 40. | Age under 5 or over 60. |

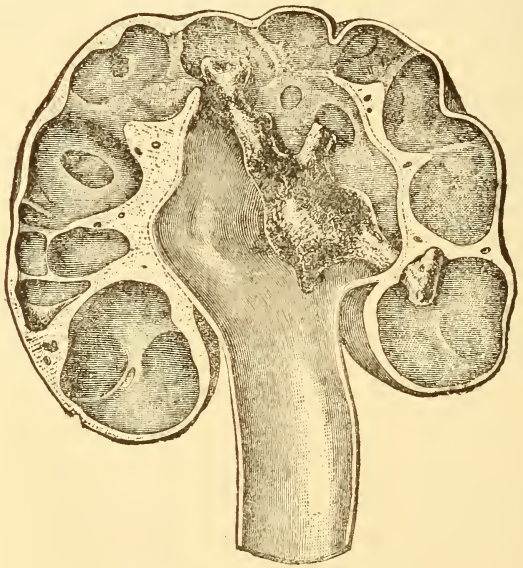


FIG. 88. Stone in the kidney.

**Renal embolism:—**

History of endocarditis; sudden renal pain, perhaps with repeated chills and cardiac symptoms; if renal pain severe, vomiting and collapse. Sudden albuminuria gradually diminishing in two to four weeks; hyaline, epithelial, and leucocyte casts for a few days, then disappearing.

**Renal calculus:—**

Dull ache deep in loin; patient flinches on deep pressure with thumb over one kidney; renal colic, violent unilateral pain down the course of the ureter to the testicle; gastric disturbances; general nutrition good. Urine contains blood which is increased by exercise; crystals, especially sharp-pointed uric acid, and oxalate concretions. Figures 88 and 89 show stone in kidney.

**Renal cancer:—**

Symptoms are increasing tumor between the costal arch and the crest of the ilium; lobulated; nearly always fixed; pain early, usually persistent, sometimes intermittent; dull ache in beginning, later lancinating not affected by movements. Emaciation; anæmia; cachexia (brownness or sallowness of the skin); debility.

*Urine* contains blood, appearing and disappearing at intervals without cause. Pus very small in amount, albumin corresponds to blood. Acetone present. Urination frequent.

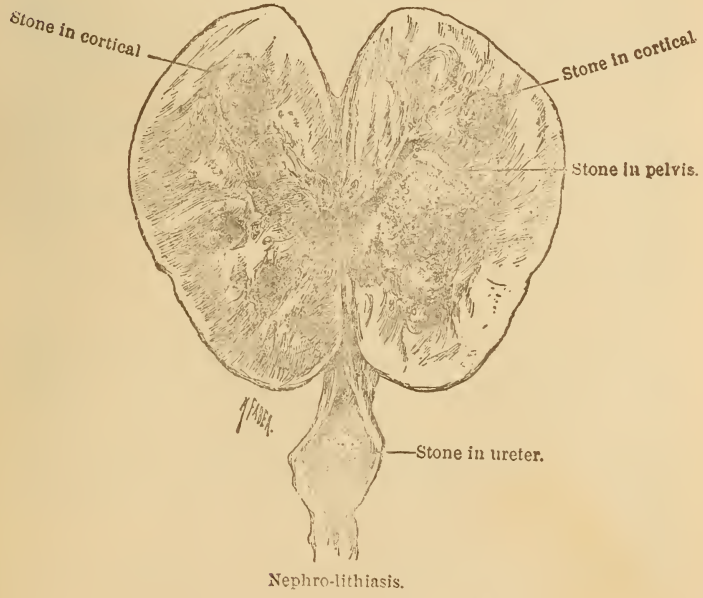



FIG. 89. Stone in the kidney. (*McNutt*).

**Sarcoma of kidney:—**

Microscopical diagnosis of small round-cell sarcoma: The urine contains: 1, Pus corpuscles; 2, red blood corpuscles; 3, shreds of connective tissue; 4, sarcoma corpuscles, in size midway between red blood corpuscles and pus corpuscles, either coarsely granular or homogeneous, *i. e.*, composed of compact living matter, non-nucleated They are larger than red blood corpuscles, and more granular; differ from pus in having no nucleus. The diagnosis of sarcoma is not possible unless ulceration of the tumor is present, which involves the presence both of red blood corpuscles and shreds of connective tissue.

**Renal tuberculosis:—**

Polyuria; dysuria prominent and increasing progressively until the bladder is comfortable only when empty, usually no pain at end of urination. More or less pain in renal region, with tenderness on deep pressure. Rise of 2 to 4 degrees in the temperature at night; or periods of fever for several days, with periods of remission. Profuse night-sweats, loss of appetite, debility, loss of flesh, cough, and diarrhœa.

*Urine* increased, traces of albumin, a few blood corpuscles, and pale cloudy urine, acid and of low specific gravity; followed, when ulceration sets in, by alkaline milky urine containing pus, the latter remaining in suspension even on long standing. Blood in 1 case out of 4, may be small, but sometimes is abundant. Finally, offensive ammoniacal urine, with ropy muco-pus, triple phosphate, cheesy masses, and with more albumin than pus and blood accounts for. The bacillus tuberculosis, if present, is best recognized by cultures in gelatin and inoculation of animals.

**Hydronephrosis:—**

Tumor in loin, sudden diminution of which corresponds with sudden increase in non-purulent urine which sometimes contains blood or blood-clots causing renal colic.

**Pyonephrosis:—**

Tumor in loin with scanty purulent urine, chills, evening temperature, debility; all symptoms relieved by copious flow of urine containing blood and pus.

**Acute pyelitis:—**

Accompanies pyonephrosis and suppurative nephritis.

**Chronic pyelitis:—**

ching and dragging lumbar pain, worse on pressure and exercise. Polyuria; greenish urine; odor slightly of rotten eggs; pus not sticky, if the urine is acid; albumin more or less abundant; pus corpuscles, with tooth-like projections; triple phosphate crystals in acid urine. Frequent painless micturition.

**Acute pyelo-nephritis** (*Suppurative nephritis; surgical kidney*):—

Copious pyuria with constitutional symptoms: chills, high temperature, brown tongue, etc. Sediment of urine contains pus, blood, casts, bacteria, bacteria casts. Albumin abundant. Disease rapidly fatal, if both kidneys affected.

**Movable Kidney:—**

Patient commonly a thin woman who has rapidly borne children. Dull, aching, dragging pain in the side with severe paroxysms., Gastro-intestinal symptoms, more or less mobile tumor manipulation of which causes peculiar, sinking, or fainting sensations, or nausea. Scanty high-colored urine or short suppression

followed by short polyuria. Hæmaturia not infrequent. Slight albuminuria. Differentiation from tumors, etc. difficult.

**Cystitis** (*Inflammation of the Bladder*):—

*Causes:*—Local bladder infection by bacterial germs: hence many causes, as gonorrhœa, stricture, enlarged prostate, stone, sexual excess, etc.

*Symptoms:*—Pus in the urine, frequent urination and pain especially after urinating. No persistent constitutional symptoms.

*The Urine:*—In "acid cystitis" or more recent disease of the bladder, the urine is acid when voided. More turbid in the first glass than in the second, plainly albuminous, with flocculent pus; microscopically, large round epithelia from middle layers of the bladder, pus corpuscles, blood corpuscles, and possibly bacteria, with a few imperfect crystals of triple phosphate. In "alkaline cystitis" or older cases the color of the urine is lighter, reaction alkaline, odor ammoniacal or pungent or both; albumin in traces only, sticky pus; microscope always shows bacteria, chiefly the pathogenic, as *bacillus coli communis* and *staphylococcus pyogenes aureus*, pus corpuscles, blood corpuscles, bladder epithelia, and plenty of triple phosphate.

**Stone in the Bladder:**—

*Symptoms:*—The features are pain and interruption of micturition. The pain may be felt along urethra, at end of penis, in testicles, or down the thighs, is severe with spasm at close of micturition, worse on motion, frequency of urination is present, worse on motion.

*Urine:*—At first urine normal in appearance with deposit of crystals. Later the urine of cystitis plus crystals, and blood at the close of micturition aggravated by motion.

**Tuberculosis of the Bladder:**—

*Symptoms:*—Patient 15 to 30 years old of tuberculous family; increased frequency of urination during the day, followed by hematuria and rising at night; severe tenesmus at close of micturition with constitutional symptoms of tuberculosis; evening temperature, night-sweats, etc. Features are relief from pain when bladder is empty, persistent perineal pain, pain in the middle of the penis, hæmaturia without cause and not dependent on exercise.

*The Urine:*—Pyuria; hæmaturia, sometimes slight, sometimes pronounced; finally urine of cystitis.

**Cancer of the Bladder:**—

*Symptoms:*—Features are pain just before the beginning of urination with frequency of micturition. In some cases sharp pain radiating to the thighs above symphysis or in perineal region. Hæmaturia.

*The Urine:*—Irregular and very large shreds of connective tissue. Epithelia with very large prominent nuclei; blood; features of cystitis. Epithelial nests in granular connective tissue are suspicious and very irregular shreds with nests characteristic.

**Benign Growths of the Bladder:**—

Typical shreds, in the urine, of connective tissue of yellow brown color like yellow casts. Great size is characteristic, and more regular form than in cancer.

## MISCELLANEOUS.

**Diabetes Mellitus:—**
Polyuria; glycosuria, diaceturia; lipuria; lipaciduria, with emaciation, thirst, hunger, debility, nervous disorders, and sub-normal temperature. Pale urine of high specific gravity.

**Diabetic Coma:—**
Gastric pain, dyspnœa, and drowsiness in course of diabetes mellitus.

**Diabetes Insipidus:—**
Great polyuria; thirst; emaciation and debility; sub-normal temperature; pale urine of low specific gravity.

**Chyluria:—**
Milky urine, which does not settle, with a pink tinge of blood, tending to coagulate spontaneously. Urine contains fat, fibrin and albumin.

### THE DIAGNOSIS OF PREGNANCY.

Dr. Wm. B. Gray, of Richmond, Virginia, places 1¼ inch of urine in a small-sized test-tube, adds one-third its volume of magnesian fluid and lets precipitate settle 15 to 20 minutes. In pregnancy the triple phosphate crystals formed by the above procedure differ in appearance from the normal. The normal triple phosphate formed by precipitation is stellate and markedly feathery. Soon after conception (20 days) the crystals lose their feathery appearance, the change beginning at the top and progressing toward the base. One side only may be affected, or both, leaving only the shaft and perhaps a few fragments, the shaft assuming a beaded or jointed appearance These changes are most marked in the early months and occur in a very large percentage of pregnant women. Examine freshly voided urine.

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NOTE:—For pathology and treatment of these disorders see the author's new book, "The Clinical Features and Treatment of Urinary Diseases."

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SPECIAL:—The APPENDIX of this book on Urinary Analysis is published separately and contains a complete course in the quantitative analysis of research work, including the Kjeldahl process for nitrogen, the Liebig-Pflüger process for urea, the Ludwig-Salkowski process for uric acid, the Salkowski-Volhard process for chlorides, determination of the urotoxic coefficient, etc., etc. Also a complete method for the analysis of urinary calculi, and Charles Heitzmann's method of preserving and mounting urinary sediments.

# APPENDIX.

This Appendix contains standard methods for quantitative determinations of the acidity of urine, urea, total nitrogen, uric acid, kreatinin, xanthin, paraxanthin, chlorine, sulphuric acid (preformed and conjugate sulphates), phosphoric acid, glycero-phosphoric acid, oxalic acid, albumin, sugar, and the urotoxic coefficient. Those engaged in research work will appreciate the convenience of an arrangement by which the quantitative determinations are consecutively described, instead of being scattered throughout the whole of the preceding pages. In addition I have included Mœschel's resumé of drugs which interfere with sugar and albumin tests, Long's methods of analysis of calculi, and Heitzmann's method of preserving and mounting urinary sediments.

At the end of the Appendix are certain tables which the author finds convenient for reference, and to which frequent allusion has been made in the clinical part of the book.

## DETERMINATION OF THE ACIDITY OF URINE.

Solutions required are (*a*) phenolphthalein, 1 gm. in a mixture of 200 c.c. water and 300 c.c. alcohol, best prepared fresh for each determination, and (*b*) decinormal potassium hydroxide solution made by diluting 100 c.c. of normal potassium hydroxide solution to 1,000 c.c. with pure water.

Normal potassium hydroxide solution is made as follows: Dissolve 75 gm. of potassium hydroxide in 1050 c.c. of water at 15° C. (60° F.), and fill a burette with this solution. Dissolve 0.63 gm. of pure oxalic acid in crystals in about 10 c.c. of water and add to it a few drops of phenolphthalein. Now add the potassium hydroxide solution from the burette, until the oxalic acid is just neutralized, a faint pink tint being seen in the solution. Note the number of c.c. of potassium hydroxide used, and dilute the remainder so that 10 c.c. of it will exactly neutralize 0.63 gm. of oxalic acid. The method of determining the total acidity of the urine is as follows: To 50 c.c. of urine add several drops of phenolphthalein and add decinormal potassium hydroxide solution until the pink color appears. Each c.c. of the potassium hydroxide solution used is equivalent to 0.006285 gm. of oxalic acid. The total acidity of the 24 hours' normal urine averages an equivalent of 2 gm. of oxalic acid.

Highly colored urine should first be shaken with animal charcoal and filtered.

The acidity of urine at different times of the day can be determined by this method. Since recognition of the true end reaction is impossible, owing to the action of the alkali employed on the acid sodium phosphate, a mixture of neutral and acid sodium phosphates resulting at first which produces an amphoteric reac-

tion, it is necessary to add slight excess of the hydroxide and the reading taken when the reaction has become faintly alkaline, the degree of acidity found being a trifle too high.

## DETERMINATION OF UREA (LIEBIG-PFLUEGER METHOD).

(*a*). **Mercuric Nitrate Solution.**—Weigh out a quantity of pure mercury and heat in a porcelain dish with two or three times its weight of strong nitric acid, sp. gr. 1.42. Evaporate the dissolved mercury to the consistence of a thick syrup, adding from time to time a few drops of nitric acid to complete oxidation which is shown by cessation of red fumes. Pour the syrupy residue into ten times its volume of water with constant stirring. Let settle, pour off supernatant liquor, dissolve sediment in a few drops of nitric acid and add to the liquid poured off. Dilute with distilled water so that 71.5 gm. of mercury is contained in one liter of solution.

(*b*). **Baryta Solution.**—To one volume of a cold saturated solution of barium nitrate add two volumes of a cold saturated solution of barium hydroxide. Keep in a well-stoppered bottle. The solution is used to precipitate phosphates and sulphates which interfere with the mercuric nitrate reaction.

(*c*). **Sodium Carbonate Solution.**—Heat pure sodium carbonate in a platinum dish to low redness, weigh out 53 gm. of the salt thus dried, dissolve in distilled water, and dilute to one liter.

(*d*). **Standard Urea Solution.**—Dissolve 2 gm. of pure urea in distilled water and dilute to make 100 c.c.

## PRELIMINARY TEST.

1. To exactly 10 c.c. of the urea solution add 19 c.c. of mercuric nitrate solution. Shake, let stand a minute, filter. Wash precipitate with a little distilled water, and to the mixed filtrate and washings add enough of a weak solution of methyl orange to give a pink color. Next from a burette run in enough sodium carbonate with constant shaking until the pink changes to yellow; not over 11.5 c.c. of the alkaline solution should be required. From this calculate the amount needed for each c.c. of mercuric nitrate.

2. To exactly 10 c.c. of the urea solution now add 19.5 c.c. of mercuric nitrate solution. Also add the correct number of c.c. of soda solution required to neutralize the acid of the nitrate.

3. Make a pasty mass of chloride—free sodium bicarbonate in water, washing off excess of the bicarbonate, if necessary, with a little cold water in a beaker and pouring off the water.

4. By means of a stirring rod transfer a drop of the liquid obtained in 2 to a dark glass plate and there mix it with a drop of the semi-fluid obtained in 3. The color should be white.

5. Continue adding the mercury solution to the urea-carbonate solution as in 2, drop by drop, and stirring well, and after addition of each drop of mercury solution, test as in four. A slight yellow color on the plate will finally be obtained, and if the mercury solution is correct just 20 c.c. should be necessary for this.

## TEST OF THE URINE.

1. To 50 c.c. of urine add 25 c.c. baryta solution. Shake thoroughly, filter through dry filter into a flask. Filtrate should be (*a*) alkaline, if not (*b*) precipitate over again with equal parts urine and baryta solution.

2. Take 15 c.c. of the alkaline filtrate obtained in 1 (*a*) or 20 c.c. if of (*b*), and neutralize by adding carefully one drop at a time dilute nitric acid. Test with litmus after each drop.

3. The filtrate thus prepared is titrated with the mercury solution. Begin by adding a c.c. at a time, and after each addition bring a drop of the mixture in contact with a drop of the semi-fluid sodium bicarbonate on a plate of dark glass. The drops should be placed side by side and mixed at the edges. At first the mixture remains white, even after stirring, but as the addition of mercury is continued a point is reached where the drop from the beaker brought in contact with the moist bicarbonate gives a light yellow shade. On stirring the drops together this yellow should disappear, but this shows that the end of the reaction is nearly reached. Add now the mercury solution in drops and test after each addition. When the point is reached where a faint yellow shade persists after stirring together the drop from the beaker and the sodium bicarbonate, it is time to neutralize with the normal sodium carbonate solution. Run in the right number of cubic centimeters corresponding to the mercury used and now make the test for the final reaction again and continue until the yellow color appears.

Regard this test as preliminary and make a new one with 15 c.c. of the filtrate neutralized as before. Run in directly within 1 c.c. of the amount of mercury required, as shown by the first test, neutralize and complete as before. For each cubic centimeter used, after deducting for chlorides, calculate 10 mg. of urea.

4. Deduct for chlorides by determination of the chlorides present in 10 c.c. of urine (see Chlorides), calculate to sodium chloride, and for each milligram of it found deduct .0238 c.c. from the volume of the mercuric nitrate, or approximately deduct 2 c.c. from the volume of the mercury solution.

5. If more than two per cent of urea is present more than 20 c.c. of mercuric solution will be needed in the titration. If the volume of the latter solution is greater than the sum of the volumes of the prepared urine and soda solution used in neutralization, this sum must be subtracted from the volume of the mercury solution and the result multiplied by 0.08. The product is added to the number of cubic centimeters of mercuric nitrate used, to give the corrected result. If, on the other hand, the volume of mercuric nitrate used in titration is less than the sum of the volumes of prepared urine and soda solution, the difference is multiplied by 0.08 and the product taken from the number of c.c. of mercuric solution used, to give the corrected result. In these calculations the volume of mercuric nitrate taken up by the chlorides must be considered as part of the diluting liquid. The same must be remembered in adding sodium carbonate for neutralization.

The correction may be expressed in this formula, according to Pflueger:

$$C = -(V_1 - V_2) \times 0.08,$$

in which

C = the correction to be added or subtracted.
$V_1$ = the sum of the volumes of the urine, soda solution and mercuric nitrate combined with the chlorides.
$V_2$ = the volume of mercuric nitrate taken by urea.

In illustration we may take an actual case:

15.0 c.c. = the prepared urine (neutralized).
15.8 c.c. = the sodium carbonate used.
1.8 c.c. = the mercuric solution used by chlorides.

$V_1$ = 32.6 c.c.
$V_2$ = 26.0 c.c.

6.6

$$-(V_1 - V_2) \times 0.08 = -0.528 = C.$$

Therefore, 26—0.5 = 25.5 is the corrected volume of mercuric nitrate, indicating, with the latter solution of standard strength, 25.5 gm. of urea in a liter.*

## KJELDAHL PROCESS FOR TOTAL NITROGEN.

**Solutions required:** (*a*). Normal sulphuric acid made by mixing 30 c.c. of pure concentrated acid, specific gravity 1.835, with enough water to make 1050 c.c. The mixture is cooled and its strength determined with normal potassium hydroxide (see Acidity). It is then diluted with water until 10 c.c. will exactly neutralize 10 c.c. of the normal potassium hydroxide solution.

(*b*). Fuming sulphuric acid.
(*c*). One-fifth normal potassium hydroxide solution.
(*d*). Solution of sodium hydroxide, specific gravity 1.3.
(*e*). Solution of litmus.

The one-fifth normal potassium hydrate is prepared by introducing 100 c.c. of normal potassium hydrate solution into a 500 c.c. graduated flask and filling with distilled water to the mark.

The sodium hydrate solution is made by dissolving 320 grams of the pure sticks in about 500 c.c. of distilled water, allowing to cool, and when cold, introducing into a 1,000 c.c flask and filling with water to the mark.

The litmus solution is made by pulverizing 50 grams of litmus, introducing the powder into a flask containing 300 c.c. of distilled water, warming an hour or two in a water bath with frequent shaking, and decanting through a filter. Divide the filtrate into two equal volumes and redden one by introduction of small quantities of dilute nitric acid, using a glass rod. Then mix the two volumes, add 50 c.c. of strong alcohol, and keep in a dark, cool place in small bottles filled to the neck, each closed with a cork, having a groove cut in one side to allow access of air.

## APPARATUS REQUIRED.

A 200 c.c. round-bottom Bohemian flask.
A 750 c.c. Erlenmeyer flask.
A condenser.
A 400 c.c. flask as a receiver.
A safety tube, 50 c.c. burette, etc.

*Long's *Chemical Physiology.*

## PROCESS OF DETERMINATION.

Introduce 5 c.c. urine from a burette into a 200 c.c. round-bottom flask, and add 10 c.c. fuming sulphuric acid. To prevent loss while the fluid is heated, introduce (according to Arnold) into the mouth of the flask a test tube which fits loosely into its neck, having been enlarged in its upper third by heating in the flame of a blast lamp and blowing out. If the enlargement of the test tube is near or in the middle third, remove the upper part of the tube with a file. Place the flask on wire gauze secured at an angle of 45°, and heat the fluid with a gas or spirit lamp. Continue the application of heat until the fluid becomes light yellow in color. This usually takes place in one to one and one-half hours. The fluid should be kept in constant ebullition. After cooling, place the flask in cold water, as heat is generated by diluting, and add water in small quantities, mixing well by shaking gently after each addition, and when the dilution has reached about 100 c.c. the fluid is introduced into the 750 c.c. Erlenmeyer flask. Rinse several times with water, and add the rinsings to the fluid. The quantity of fluid in the Erlenmeyer flask should not exceed 200 c.c. Into the 400 c.c. flask to receive the distillate, introduce 10 c.c. normal sulphuric acid from a burette. The condensing tube of the cooler should be somewhat long, and the end to enter the receiver bent, that its orifice may be brought as near the acid as possible without coming in contact. As the fluid is dense when the solution of sodium hydrate is introduced, it is liable to bump during the distillation, to prevent which small fragments of zinc are introduced into the flask. By the action of NaOH on zinc, hydrogen is evolved, which prevents the bumping; but it was found (Pfeiffer and Lehmann) that the hydrogen and aqueous vapor a small quantity of sodium hydrate is carried over, hence a safety tube is introduced between the Erlenmeyer flask and condenser. This is made by drawing out the end of a combustion tube, 20 c.m. long and 18 m.m. internal diameter, in the flame of a blast lamp to 8 or 10 m.m. which passes through a hole in the cork of the Erlenmeyer flask.* The upper end of the tube is connected with the cooler by means of a cork, through which passes a bent glass tube. To the fluid to be distilled add 60 c.c. of the solution of sodium hydrate (sp. gr. 1.30) and three fragments of zinc as nearly spherical as possible, the weight of which not to exceed 0.5 grm. The sodium hydrate and zinc having been introduced, connection with the condenser is made at once to prevent loss of ammonia Distill slowly until the ammonia separates from the fluid and is carried into the receiver and absorbed by the sulphuric acid. This is usually accomplished by distilling thirty minutes. To determine with greater accuracy if all the ammonia is distilled, place a small piece of red litmus paper at the orifice of the condensing tube, and if ammonia is still passing over, the red litmus paper turns blue.

The quantity of ammonia absorbed by the 10 c.c. normal sulphuric acid is determined by titrating with the one-fifth normal

*It was found by Dr. Van Nuys that by a safety tube of the dimensions here given, the purpose is accomplished as well as with others more complex in construction which have been recommended.

potassium hydrate. For this purpose, the solution of litmus is added to the fluid in quantity sufficient to impart a distinct red color, when the solution is titrated with the one-fifth normal potassium hydrate from a 50 c.c. burette, until by the addition of 0.1 c c., after shaking, the solution turns purple or blue.

## CALCULATION OF RESULTS.

In 1 c.c. normal ammonia there is 0.017 gram $NH_3$ or 0.014 gram nitrogen. 1 c.c. normal acid will neutralize 1 c.c. normal ammonia; therefore, by multiplying the number of c.c. normal acid neutralized by 0.017, the product is the quantity of $NH_3$ in grammes, or by multiplying by 0.014, the number of grams nitrogen is determined.

Example: 31 c.c. of one-fifth normal potassium hydrate was required to neutralize the acid instead of 50 c.c., as would be the case in the absence of ammonia 31 c.c. one-fifth normal solution is equal to 6.2 c.c. of the normal ($\frac{31}{5}=6.2$), and as 10 c.c. of the normal sulphuric acid was employed, 3.8 c.c. was neutralized by the ammonia formed from 5 c.c. urine (10—6.2=3.8), and as 3.8 c.c. normal ammonia would neutralize 3.8 c.c. normal sulphuric acid, there is in 3.8 c.c. normal ammonia the quantity of nitrogen found in 5 c.c. urine, which is 0.0532 gm. (3.8×0.014=0.0532), and in 100 c.c. urine there is 1.064 gm. nitrogen (0.0532×20=1.064).

## THE GUNNING METHOD.

In this method neither potassium permanganate nor sulphide is used, but 10 gm. of powdered potassium sulphate and ordinarily 20 c.c. of concentrated sulphuric acid. Digestion as in the Kjeldahl process, as also dilution, neutralization and distillation. In neutralizing it is convenient to add a few drops of phenolphthalein by which one can tell when the acid is completely neutralized, remembering that the pink color which indicates an alkaline reaction is destroyed by considerable excess of strong fixed alkali. Titration as in Kjeldahl method.

A very satisfactory apparatus is now used by the Connecticut Agricultural Experiment Station, which is described in full in their annual report for 1889. For use in determining nitrogen in the urine the flasks may be made smaller.

Dr. Long advises use as standard acid one-tenth normal sulphuric acid, which is colored with a *single drop* of methyl orange; the standard acid must still show a pink color after the distillation process.

## DETERMINATION OF URIC ACID.

The principal methods now in vogue are the Salkowski-Ludwig and the Haycraft.

### THE SALKOWSKI–LUDWIG.

**Solutions required:**

(*a*). *Ammoniacal silver nitrate* solution made by dissolving 25 gm. of silver nitrate in 100 c.c. of water, adding ammonia water until the precipitate first appearing is completely dissolved, making up to 1,000 c.c. with water and keeping in a dark bottle away from the light.

(*b*). *Magnesia mixture* made as follows: Dissolve 100 gm. of magnesium sulphate and 100 gm. of ammonium chloride in 800 c.c.

of water, add 100 c.c. of strong ammonia water, allow mixture to stand 24 hours and filter. It must be strongly alkaline and almost or quite clear.

(*c*). *Solution of sodium sulphide* made by dissolving 25 to 30 gm. of pure crystals ($Na_2S$, $9H_2O$) in 1,000 c.c. of distilled water. To make the test measure out 200 c.c. of the urine of 24 hours and put it in a beaker. Add 20 c.c. of the silver solution to an equal volume of the magnesia mixture and then ammonia enough to clear up any precipitate which forms. Pour the clear mixture into the urine in the beaker and stir well. A precipitate of silver urate and phosphates (silver and earthy) forms.

The beaker is allowed to stand at rest about an hour, after which the contents are filtered and the precipitate washed with weak ammonia on the filter. To do this the ammonia is sprayed into the beaker from a wash bottle and rinsed around thoroughly. This is done several times, the liquid being poured on the filter. Where available a Gooch crucible serves well for the collection of the precipitate, as the filtration is slow on paper without aspiration. It is not necessary to remove any of the precipitate which clings to the beaker, as will be seen. When the washing is complete transfer the precipitate and filter paper, or asbestos if the Gooch crucible is used, back to the beaker and pour over it a boiling mixture of 20 c.c. of the sulphide solution (*c*), and 20 c.c. of distilled water. Stir up thoroughly, allow to stand some time and then add 50 c.c. of boiling water. Place the beaker on a sand bath or gauze and bring the contents to boiling, stirring continually. Keep hot some minutes and then allow to stand until cold, the precipitate being stirred meanwhile occasionally.

The treatment with the sulphide solution decomposes the silver urate with precipitation of black insoluble silver sulphide, the uric acid remaining in solution as soluble urate. The cooled liquid is filtered into a porcelain dish, and the precipitate washed with warm water, the washings going also into the dish. Enough hydrochloric acid is now added to combine with all the bases present and liberate the uric acid, which is the case when the liquid becomes acid in reaction. It is now slowly evaporated to a volume of about 10 c.c., best on a water bath, and then allowed to stand an hour for the complete separation of the uric acid. This is then collected on a weighed Gooch crucible, the crystals being transferred gradually by aid of the filtered liquid. When the crystals are on the asbestos they are washed with a little acidulated water several times. The crucible is dried at 100° C. (212° F.), put back in the funnel and treated with a small amount of pure carbon disulphide to remove traces of sulphur. Finally wash with ether, dry at 110° C., and weigh with a chemical balance.

Results obtained show the amount of uric acid in grams in 200 c.c. of urine; multiply by 5 to find grams per liter and by the number of liters of urine in 24 hours (1,000 c.c. = 1 liter) to find total quantity of uric acid in 24 hours. Reduce this to grams by multiplying by 15.43.

### THE HAYCRAFT METHOD FOR URIC ACID.

**Solutions required:**

(*a*). *Ammoniacal solution of silver nitrate:* Dissolve 5 gm.

of silver nitrate crystals in 100 c.c. of water and then enough ammonia water to give solution strong alkaline reaction. Make up to 200 c.c. with the ammonia.

(*b*). *Ammonium sulphocyanate solution:* A fiftieth normal solution of ammonium sulphocyanate is used which is made by diluting 100 c.c. of decinormal ammonium sulphocyanate to 500 c.c. in a measuring flask.

[Decinormal ammonium sulphocyanate is made as follows: Dissolve about 7.7 gm. of the pure crystals of ammonium sulphocyanate in water and make up to a liter. Determine its strength by titration with decinormal silver nitrate solution made as follows: Weigh out *accurately* 10.766 gm. of *pure* silver and dissolve in a flask with pure nitric acid. Remove excess of nitric acid by evaporation and blow air through to drive out nitrous fumes. Cool and dilute to one liter. This solution may also be made by dissolving 16.954 gm. of the crystals of silver nitrate (fused at low temperature before weighing) in water to make a liter, but its strength must be tested, as described under chlorides.

Determination of the strength of the decinormal ammonium sulphocyanate solution is made as follows: Measure into a flask or beaker 25 c.c. of the decinormal silver solution, and add to it 2 or 3 c.c. of a nearly saturated solution of ferric alum free from chlorine. This gives some color and a slight opalescence. Now add about 2 c.c. of pure, strong nitric acid which decolorizes and clears the mixture. Into the mixture now let the sulphocyanate flow a little at a time, shaking after each addition. When the red color disappears more slowly on shaking, then add the sulphocyanate drop by drop till at last a single drop is enough to give a permanent reddish tinge. Less than 25 c.c. will do this. Repeat the test and if the same result is found dilute the sulphocyanate so that 25 c.c. will exactly do the work. That is, if 24.2 c.c. were required, then if you have 900 c.c. of sulphocyanate solution, $24.2 : 25 = 900 : x$, or $x = 929.75$. That is, add 29.8 c.c. of water to the 900 c.c. of sulphocyanate.]

(*c*). *Ammonium ferric sulphate* (ferric alum), saturated solution, as indicator.

One cubic centimeter of a fiftieth normal ($\frac{N}{50}$) solution of the sulphocyanate liberates and indicates .00336 gm. of uric acid.

If a solution of a sulphocyanate is added to a solution of a silver salt containing nitric acid and ferric sulphate, a complete reaction takes place between the sulphocyanate and silver before the characteristic reaction between the former salt and the ferric compound appears. In other words, the sulphocyanate and the silver combine first, and then any further amount of sulphocyanate added unites with the iron, producing a red color (of ferric sulphocyanate), *indicating* the completion of the first reaction.

The process for determining uric acid in the urine is as follows: Measure out 50 c.c. of the urine and warm it gently if it contains a sediment of urates. Add 3 to 4 gm. of pure sodium bicarbonate and then ammonia enough to give a strong alkaline reaction. This may give a precipitate of phosphates which need not be heeded. Next add 5 c.c. of the silver solution (*a*), and mix thoroughly. This produces a precipitate of silver urate along with the bulky phosphates thrown down by the ammonia. Allow to stand half an hour and then filter. A paper filter and funnel may

be used in the usual manner, but much better results are obtained by the use of the Gooch crucible and asbestos with the aid of an aspirator. Rinse the sides of the beaker thoroughly with weak ammonia and pour this on the precipitate in the funnel or crucible. Continue the washing of the precipitate with weak ammonia water until all traces of silver are washed out, as may be shown by allowing a few drops of the filtering washings to fall into some dilute hydrochloric acid in a test tube. The washing is complete when a cloudiness is no longer obtained in this test.

Now pour some pure dilute nitric acid into the beaker in which the precipitation was made, and which was washed free from silver by the ammonia, and shake it around until any traces of the silver urate precipitate are dissolved. Put the funnel or Gooch crucible over a clean receptacle and pour this acid liquid on the precipitate. Silver urate dissolves completely in dilute nitric acid, and enough of this is added, a little at a time, to bring about complete solution. It now remains to titrate the silver in the solution. To this end add 5 c.c. of the ferric alum solution, and if the mixture is not clear and colorless, about 2 c.c. of pure strong nitric acid. Then from a burette run in the sulphocyanate (*b*), a little at a time, shaking after each addition until a faint red shade of ferric sulphocyanate becomes permanent. Toward the end of the titration a red appears as each drop of liquid from the burette falls into the silver solution below, but this color fades out on shaking and does not persist until the last particle of silver has been taken up by the sulphocyanate. Supposing now that 15 c.c. of the latter solution are required to reach this point we have $15 \times .00336 = .0504$ gm. as the amount of uric acid in the 50 c.c. of urine taken. A volume as large as this would seldom be required, 5 to 10 c.c. corresponding to 16.8 to 33.6 mg., is usually sufficient.

**The Hopkins method** is one in which, after removal of phosphates, titration by potassium permanganate is used. While easier in some respects than the two previous methods, there are certain difficulties in it which make it not so preferable to the two methods just described as to warrant description in full.

## QUANTITATIVE DETERMINATION OF KREATININ IN THE URINE.

In 240 c. c. of urine the phosphates are first removed by rendering the urine alkaline with milk of lime and then adding calcium chloride as long as a precipitate forms. If the volume now be less than 300 c. c., water is added to that amount. The mixture is filtered after having been allowed to stand for one-quarter to one-half hour, and washed with a little water; 250 c. c. of the mixture are then measured off, slightly acidified with dilute hydrochloric acid so as to prevent any transformation of kreatinin into kreatin during the long process of evaporation. This amount is evaporated on a water-bath to a syrupy consistence, and then thoroughly mixed with 20 to 30 c. c. of absolute alcohol. The mixture is poured into a stoppered flask provided with a 100 c. c. mark, and after thoroughly rinsing out the evaporating dish with absolute alcohol, the washings are also placed in the bottle and absolute alcohol added to the 100 c. c. mark. The bottle is thor-

oughly shaken and set aside in a cool place for twenty-four hours, the mixture being agitated from time to time. It is now filtered and rendered slightly alkaline with a drop or two of sodium carbonate solution, as kreatinin hydrochloride is not precipitated by chloride of zinc. The reaction, however, should be only *faintly* alkaline, as otherwise zinc oxide will be precipitated. The mixture is now slightly acidified with acetic acid. Eighty c. c., corresponding to 160 c. c. of urine, are treated with 10 to 15 drops of an alcoholic solution of zinc chloride, prepared by dissolving the salt in 80 per cent. alcohol and diluting with 95 per cent. alcohol to a specific gravity of 1.2. The mixture is then well stirred and set aside in a cool place for two or three days. The crystals, which are usually deposited upon the sides of the vessel in the form of wart-like masses, are then collected upon a dried and weighed filter, always using portions of the filtrate to bring the crystals completely upon the filter. These are washed with a small amount of 90 per cent. alcohol until the washings are without color and give only a slight opalescence when treated with a drop of nitrate of silver solution. The crystals are finally dried at a temperature of 100° C. (212°F.), and weighed. By multiplying the weight thus found by 0.6243 the amount of kreatinin is obtained.

Precautions: 1. Albumin and sugar, if present, must first be removed. In diabetic urines it is best, after having removed the sugar by fermentation, to take one-fifth of the total quantity eliminated in 24 hours, and to evaporate this to about 300 c.c. before removing the phosphates. 2. The weighed material should be examined microscopically to see whether notable quantities of sodium chloride be present. Should such be the case it is necessary to determine the amount of zinc present and to estimate the kreatinin from this. To this end the alcoholic solution containing the kreatinin-zinc chloride is evaporated to dryness after the addition of a little nitric acid. The residue is incinerated, extracted with water, washed, dried, fused and finally weighed.

As 100 parts of kreatinin-zinc chloride correspond to 22.4 parts by weight of zinc oxide, the corresponding amount of the compound is found according to the following equation: $22.4 : 100 = y : x$ and $x = 4.4642$, in which $y$ represents the amount of zinc oxide found, and $x$ the corresponding amount of kreatinin-zinc chloride. By multiplying the number thus ascertained by 0.6243 the corresponding amount of kreatinin is found.

3. Instead of doing this the precipitate in the alcoholic solution may be examined microscopically before filtering, and if sodium chloride crystals be found, providing that the kreatinin-zinc chloride crystals adhere to the sides of the vessel, the sodium chloride may be dissolved in a little water and poured off.

4. If the crystals of kreatinin-zinc chloride adhere very firmly to the sides of the vessel, so that their removal would be incomplete, it is perhaps best to dissolve them in a little hot water, to evaporate to dryness, and to weigh the kreatinin compound directly.

5. If the urine shows an alkaline reaction it is best to acidify with sulphuric acid and to boil for half an hour, before removing the phosphates, so as to transform any kreatin that may be present into kreatinin, when the examination should be continued as described. (Simon.)

## DETECTION OF PARAXANTHIN AND XANTHIN.

In the examination of the urine Rachford assumes, for reasons given in his paper, the following propositions: 1. Four liters of normal urine is too small a quantity to determine the presence of paraxanthin. 2. Three liters of pathological urine are quite enough to determine whether paraxanthin occurs in sufficient excess in this urine to make it a probable factor in disease.

In every case at least two specimens of urine should be examined. One of three liters of urine passed during and just after the attack, supposed to be due to leucomain poisoning; and the other of four liters of urine passed, in an interval between the attacks, when the patient is at his best.

*Method* (from E. Salkowski and Salomon).—The phosphates are precipitated with ammonium hydrate; after twenty-four hours the urine is filtered or decanted from the precipitate, and a three per cent. solution of nitrate of silver is added to it; the silver solution should be added as long as precipitation occurs. The urine is removed from the precipitate of silver compounds, and this precipitate is washed five or six times with distilled water, the water being removed each time from the precipitate by decantation. This process may require a week. The silver compounds suspended in water are now decomposed with hydrogen sulphide, the current of $H_2S$ is made to pass through the water. in which the silver compounds are suspended, for hours; the liquid is now filtered, to separate it from the precipitate, and evaporated down to about 50 c.c. if 2,000 c.c. of urine have been used. the remaining uric acid is thereby separated; this liquid being filtered, ammonia is again added; after twenty-four hours it is again filtered and precipitated with silver nitrate, the silver being added as long as precipitation occurs; the silver compounds are again separated from the liquid by filtration; they are allowed to remain on the filter paper and kept in a dark place for twenty-four or thirty-six hours; the filter paper holding the dry precipitate of silver compound is put in hot nitric acid of 1.1 specific gravity; the acid dissolves the nitrates of xanthin and paraxanthin in the precipitate, and thus separates them from the nitrate of hypoxanthin, which is insoluble in nitric acid; if working with three liters of urine, from 6 to 7 c.c. of acid should be sufficient to dissolve the xanthin and paraxanthin. After two hours the nitric acid is again heated and filtered while hot, so as to insure the solution of the xanthin and paraxanthin; the nitric acid solution is now carefully neutralized with ammonium hydrate, and for the third time xanthin and paraxanthin are precipitated; the precipitate is washed, suspended in water, and again decomposed with hydrogen sulphide; this fluid is filtered while hot, and the nitrate is evaporated to 10 c.c.; a little ammonium hydrate is now added, and after twenty-four hours the last traces of phosphates and oxalate will be precipitated; the liquid is again evaporated on a sand-bath, and when the liquid begins to get turbid evaporation is suspended, and as the liquid cools the xanthin, if present, will separate out; filter and again evaporate to 2 c.c. Again the liquid is allowed to cool. so that the xanthin may crystallize out, and the 2 c.c of "final fluid" is added to 3 or 4 c.c. of distilled water, and this dilute "final fluid" is tested for paraxanthin. If this fluid contain paraxanthin—*a*, the needle-shaped crystals can be

obtained by evaporating a drop on a glass slide; *b*, the characteristic white precipitate should result when a drop of this fluid is added to a solution of potassium hydrate; *c*, a few drops of this fluid when injected hypodermically into a mouse or rat should produce the symptoms of paraxanthin poisoning.

That the crystalline mass that separated out in the final evaporations was xanthin may be proven as follows: Dissolve the supposed xanthin crystals and add picric acid, and if xanthin be present a precipitate of long white glistening crystals of picrate of xanthin will form; or a better test is to mix two or three drops of suspected xanthin solution with two or three drops of nitric acid, chemically pure, in a porcelain dish, and evaporate over flame to dryness, and a yellow precipitate results; to this yellow precipitate add ammonium hydrate and heat; if the precipitate takes on a purple color xanthin is present.

The quantity of xanthin present can be determined by carefully weighing the crystals that separate out in evaporating down to the "final fluid." But for clinical purposes this is scarcely necessary, as one can judge by the mass of crystals formed whether there be a great excess of xanthin or not If there only be a thin layer of xanthin crystals at bottom of the final fluid, then the xanthin is not very greatly increased, but if the xanthin crystals separate out in much larger quantities, adhering to the sides of the glass vessel and forming a mass that cannot be redissolved in 6 or 8 c.c. of distilled water at room temperature, then it may be safely asserted that the xanthin is very greatly increased in quantity.

The stomach contents should be diluted with distilled water and boiled, and then filtered through filter paper with the aid of a vacuum filter; the mass remaining on the filter should be again mixed with distilled water, boiled, and again filtered; this fluid is then treated in the same way as the urine.

## DETERMINATION OF CHLORIDES.

The method of Salkowsky-Volhard is as follows:

**Reagents necessary:**

1. A solution of silver nitrate of such strength that every c.c. corresponds to 0.01 gram of sodium chloride.
2. A solution of potassium sulphocyanide of such strength that 25 c.c. correspond to 10 c.c. of the silver nitrate solution.
3. A solution of a ferric salt saturated at an ordinary temperature, such as ammonio-ferric alum.
4. Nitric acid (specific gravity 1.2).

Preparations of these solutions:

1. The silver nitrate to be used for this purpose must be pure, the crystallized salt being used. In order to test the purity of the salt, about 1 gram is dissolved in distilled water, heated to the boiling point, the silver precipitated by dilute muriatic acid and filtered off. The filtrate when evaporated in a platinum crucible should leave either no residue at all or only a very faint one; otherwise it is necessary to recrystallize the salt and test again, until the desired degree of purity is obtained.

To bring the solution to its proper strength 0.15 gm. of sodium chloride which has been previously dried carefully by heating in a platinum crucible is accurately weighed off, dissolved in a little

distilled water and further diluted to 100 c.c. To this solution a few drops of a solution of chromate of potassium are added and the mixture titrated with that of silver nitrate containing 29.059 gm. in 100 c.c. of water. The nitrate of silver will first precipitate every trace of sodium chloride present and then combine with the potassium chromate forming red silver chromate. The slightest orange tinge remaining after stirring indicates the end of the reaction. Were the solution of silver nitrate of the proper strength exactly, 15 c.c. should have been used, as every c.c. is to represent 0.01 gm. of sodium chloride As a matter of fact, less will in all probability be needed, the solution having been purposely made too strong. Its correction then becomes a simple matter, it merely being necessary to determine the degree of dilution required. Supposing that 29.059 gms. of silver nitrate to have been dissolved in 900 c.c. of water, and that 14.5 c.c. instead of 15 c.c. had been required to precipitate the 0.15 gm. of sodium chloride, it is evident that every 14.5 c.c. of the remaining solution must be diluted with 0.5 c.c. of water. It is hence only neccessary to divide the number of c.c. of the silver nitrate solution remaining by 14.5; the result multiplied by 0.5 represents the amount of water which must be added in order to bring the solution to the required strength.

Hence the rule for the correction of a solution which has been found too strong:

$$C = \frac{N \cdot d}{n},$$

in which C represents the number of c.c. which must be added to the solution remaining; N the total number of c.c. remaining after titration; and the number of c.c. consumed in one titration; and the difference between the number of c.c. theoretically required and that actually used in one titration.

In the example given the equation would then read:

$$C = \frac{936.5 \times 0\ 5}{14.5} = 32.29$$

32.29 c.c. of distilled water are added to the remaining 936.5 c.c., and the strength of the solution tested by a second titration. If the solution be found too weak, it is best to make it too strong and then to correct, as described.

2. Preparation of the potassium sulphocyanide solution.

In order to bring this solution to its proper strength, 10 c.c. of the silver nitrate solution are diluted to 100 c.c., 4 c.c. of nitric acid (specific gravity 1.2) and 5 c.c. of the ammonia-ferric alum solution added, and the mixture titrated with the KSCN solution; the end reaction is recognized by the production of a slightly reddish color, which persists on stirring. The KSCN solution having been purposely made too strong, it will be found that less than 25 c.c. will be needed in order to precipitate all the silver present. The quantity of water necessary for dilution is ascertained as above according to the formula:

$$C = \frac{N \cdot d}{n},$$

3. The solution of ammonia-ferric alum is a solution saturated

at ordinary temperatures, care being taken to insure the absence of chlorides in the salt, which may be effected, if necessary, by recrystallization.

Method applied to the urine: 10 c.c. of urine are placed in a small stoppered flask bearing a 100 c.c. mark, diluted with 50 c.c. of distilled water and acidified with 4 c.c. of nitric acid. From a Mohr's burette 15 c.c. of a standard solution of silver nitrate are added, the mixture is thoroughly agitated and diluted with distilled water to the 100 c.c. mark, the silver chloride formed is filtered off through a *dry* folded filter into a *dry* graduate, 80 c.c. of the filtrate are placed in a beaker, and after the addition of 5 c.c. of the ammonio-ferric alum solution, titrated with the potassium sulphocyanide solution until the end reaction—i. e., a slightly reddish tinge—is seen. If necessary, two such titrations should be made, the sulphocyanide solution being added 1 c.c. at a time in the first, while in the second the total number of c.c. needed to bring about the end reaction, less one c.c., are added at once and then one-tenth of a c.c. at a time.

The amount of chlorides present in the urine is calculated as follows: Example:—Total quantity of urine 600 c.c.; 6.5 c.c. of potassium sulphocyanide solution were required to bring about the end reaction in 80 c.c. of the filtrate. This would correspond to 8.125 c.c. for the total 100 c.c. of filtrate representing 10 c.c. of urine, as is seen from the equation.

$$\begin{aligned} N : 80 &= x : 100 \\ 80x &= 100\,n \\ x &= \frac{100\,n}{80} = \frac{5n}{4} \end{aligned}$$

in which x represents the number of c.c. corresponding to 100 c.c. of the filtrate and N the number of c.c. actually used.

These 8.125 c.c. were used in precipitating the remaining c.c. of the silver nitrate solution not decomposed by the chlorides. As 25 c.c. of the potassium sulphocyanide solution correspond to 10 c.c. of the silver nitrate solution, the excess of silver solution in c.c. is found by the equation:

$$\begin{aligned} 25 : 10 &= N : x \\ \text{then } 25x &= 10N \\ x &= \frac{10N}{25} = \frac{2N}{5} \end{aligned}$$

in which x represents the excess of silver nitrate solution in c.c., N that sulphocyanide solution as found in the equation above, x in this case being 3.25 c.c.

The difference between the total amount of silver solution employed (*i. e.*, 15 c.c.) and the excess (*i. e.*, 3.25 c c.) indicates, of course, the number of c.c. necessary for the precipitation of the chlorides in 10 c.c. of urine. In the case under consideration 11.75 c.c. were employed. As 1 c.c. of the silver solution represents 0.01 gram of NaCl, there must have been present in the 10 c.c. of urine 0.1175 gram; in 100 c.c., hence, 1.175 grams, and in the total amount—*i. e.*, 600 c.c. of urine—7.05 grams.

From these considerations the following short rule results: Instead of first multiplying the number of c.c. of the potassium sulphocyanide solution corresponding to 80 c.c. of the filtrate by

$\frac{5}{4}$, as seen from the equation above, and the result by $\frac{2}{5}$, in order to find the number of c.c. of the potassium sulphocyanide solution representing the excess of silver nitrate in 100 c.c. of the filtrate and then deducting the result from 15, it is simpler to multiply by ½ directly and deduct the result from 15, the number of grams of sodium chloride contained in 1000 c.c. of urine being thus found. This figure is then corrected for the total amount of urine.

Hence the equations, I., $x = 15 - \frac{n}{2}$; II., 1000 : x : : A : Ch, or the combined formula $Ch = \frac{A(15 - \frac{n}{2})}{1000}$,

in which Ch represents the quantity of chlorides contained in the total amount of urine, A the amount of urine actually passed, n the number of c.c. of the potassium sulphocyanide solution used in the precipitation of the excess of chlorides in 80 c.c. of the filtrate.

So in the above case $Ch = \frac{600(15 - \frac{6.5}{2})}{1000} = 7.05$.

The method described may be employed in the presence of albumin, albumoses, peptones and sugar; the urine, however, must be fresh, so as to insure the absence of nitrous acid. (Simon.)

## DETERMINATION OF THE SULPHATES.

(a) total sulphates: 100 c.c. of clear, filtered urine are treated with 8 c.c. of hydrochloric acid (1.12), and heated to the boiling point; when 20 c.c. of a saturated solution of barium chloride are added. The mixture is kept in the water-bath until the barium sulphate has thoroughly settled, which it will do in about half an hour. Filter through a Gooch filter with a close-fitting plug of asbestos, the whole having been previously dried and weighed. Care should be taken never to allow the filter to become dry, and small amounts of hot water must be added to the last c.c. remaining, the final traces being placed upon the filter with the aid of a rubber-tipped glass rod. The precipitate is washed with boiling water until a specimen of the washings is no longer rendered cloudy, even on standing for a few minutes, on the addition of a drop of dilute sulphuric acid. Gum-like substances, as well as pigments, are removed by washing with hot alcohol (70 per cent.), and then filling the filter two or three times with ether. A suction apparatus is necessary, and in the absence of a special pump a simple glass tube bent upon itself may be employed.

If a paper filter has been used, it is placed in a weighed platinum or porcelain crucible and ignited. The ash is then heated, at first moderately, and almost completely covered with the lid. It is then heated, only half covered, from five to seven minutes, until the contents of the crucible are white. The crucible when

cooled is placed in a desiccator and weighed, the difference between the first and the second weight giving the weight of the barium sulphate obtained from 100 c.c. of urine.

A reduction of some of the barium sulphate usually takes place during the process of combustion, owing to the presence of organic material, so that the weight of the barium sulphate obtained is actually too low. This error may be corrected in the following manner: The barium sulphate is washed into a small beaker with a small amount of water, colored red by a few drops of an alcoholic solution of phenolphthalein, and titrated with a one-tenth normal solution of sulphuric acid until the red color has disappeared. Every c.c. of the one-tenth normal solution corresponds to 0.004 grams of barium sulphate, so that the actual amount of barium sulphate contained in 100 c.c. of urine is ascertained by adding the figure thus found to that obtained by weighing (see below).

Quantitative Estimation of the Conjugate Sulphates. One hundred c.c. of clear, filtered urine are mixed with 100 c.c. of an alkaline solution of barium chloride (see above), the mixture being thoroughly stirred. After a few minutes this is filtered through a dry filter into a dry graduate up to the 100 c.c. mark. This portion, corresponding to 50 c.c. of urine, is now strongly acidified with dilute hydrochloric acid and brought to the boiling point. It is kept upon the boiling water-bath until the barium sulphate formed has settled and the supernatant fluid is clear. The precipitate is filtered off, washed, dried and weighed, as described above. The barium sulphate thus obtained multiplied by 2 and deducted from the amount found according to the first method indicates the amount referable to the performed sulphates. The molecular weight of barium sulphate$_4$ being 232.82, that of $SO_3$ 79.86, of $H_2SO_4$ 97.82, and of S 32, the figure expressing the amount of $H_2SO_4$, $SO_3$, or S, corresponding to 1 gram of barium sulphate, is found according to the following equations:

232.82:79.86: :1:x, and x=0.34301. ∴ 1 gram of barium sulphate=0.34301 gram of $SO_3$.

232.82:97.82: :1:x, and x=0.42015. ∴ 1 gram of barium sulphate=0.42025 gram of $H_2SO_4$.

232.82:32. :1:x, and x=0.13744. ∴ 1 gram of barium sulphate =0.13744 gram of S.

To calculate results it is only necessary to multiply the weight of barium sulphate found by 0.34301, 0.42015, or 0.13744 in order to ascertain the amount of sulphuric acid contained in 50 c.c. of urine in terms of $SO_3$, $H_2SO_4$, or S, respectively.

## PREPARATION OF VOLUMETRIC SOLUTIONS FOR DETERMINATION OF PHOSPHORIC ACID.

(See page 147.)

1. Weigh out 44.78 gm. of uranium nitrate and dissolve in about 900 c.c. of distilled water.

2. Dissolve 10.085 gm. of pure dry and non-deliquescent disodic hydrophosphate to make 1000 c.c. of distilled water.

3. Dissolve 100 gm. of acetate of sodium in distilled water, add 100 c.c. of 30 per cent. acetic acid and dilute the whole to 1000 c.c.

4. Make a solution of ferrocyanide of potassium 10 gm. to 100 c.c. of distilled water. Keep in a dark place.

Transfer 50 c.c. of the phosphate solution to a beaker, add 5 c.c. of the acetate solution and heat on the water bath.

Fill a burette with the uranium solution and by means of a glass rod place a number of drops of the ferrocyanide solution on a white plate. Run in the uranium solution, stir well with a rod and from time to time bring a drop of the liquid in the beaker in contact with one of the drops on the plate. As soon as the reddish precipitate appears stop, read off number of c.c. of uranium used, and repeat the operation several times until the exact number of c.c. necessary to cause the red color to appear be determined. Dilute the uranium solution according to the formula:

$$C = \frac{N \cdot d}{n}$$

in which C will represent the number of c.c. of water to be used for dilution, N the total volume of uranium solution left after the testing is over, n the number of c.c. of uranium solution necessary to cause appearance of the red color on the plate, and d the difference between the n and 20 (the latter being the number of c.c. theoretically required to precipitate 50 c.c. of the phosphate).

Suppose, for example, after the tests are over there are 750 c.c. of uranium left and that 18 c.c. were required to cause appearance of red color on the plate, then $C = 750 \times 20 - 18 \div 18$. That is $750 \times 2 \div 18$, or 83.33. Dilute the 750 c.c. of uranium solution with 83.33 c.c. of distilled water. Test again and it will be found that 20 c.c. of the diluted solution will exactly precipitate 50 c.c. of the phosphate solution, as shown by the red color on the plate. The process with the urine has been described on page 147.

## OXALIC ACID.

**Neubauer's Method, modified by Fuerbringer.**—The quantity of urine passed in twenty-four hours is measured and treated with a few c.c. of alcoholic solution of thymol to prevent bacterial growth. Treat the urine with ammonium hydrate until, after stirring, the odor of ammonia is perceptible. Add a solution of calcium chloride until a precipitate ceases to form, and with acetic acid render distinctly acid, avoiding a great excess. The phosphates of calcium and magnesium dissolve in acetic acid, while calcium oxalate precipitates with more or less uric acid. Let stand twenty-four hours, filter through a small filter paper, collect and transfer the precipitate to the paper, with a glass rod provided with a small piece of rubber tubing on one end. Wash with water until the wash water is free of chlorides, known by testing with a solution of silver nitrate and a few drops of nitric acid. When washed, transfer the filter, with precipitate, to a small beaker and treat with dilute hydrochloric acid and water, avoiding a great excess of the former; warm on a water bath, and stir with a glass rod so the acid will come in contact with every part of the precipitate. The calcium oxalate will dissolve in the acid, while any uric acid present will remain undissolved. Filter, through a small filter paper, into a beaker of 250 or 300 c.c. capacity, wash with water and determine when washed, as before. Evaporate the filtrate with wash water to about 200 c.c., transfer from the dish to

a beaker, rinse the dish with water and add rinsings to the fluid in the beaker when the fluid is rendered alkaline with ammonium hydrate, known by turning turmeric paper dark red after the fluid is well mixed by stirring. Having stood well protected from dust twenty-four hours, filter through a small filter paper free of ash, wash with water until the wash water is free of chlorine, known by producing no turbidity when tested with a solution of silver nitrate with a few drops of nitric acid. Dry the filter with precipitate and ash in a platinum crucible, and by the heat of a blast flame reduce the oxalate to oxide. Cool in a desiccator and weigh. Repeat the process of heating and weighing until the weight becomes constant. Multiply the weight of the oxide by 1.6071 to find the weight of oxalic acid.

## QUANTITATIVE DETERMINATION OF ALBUMIN.

**Scherer's Method.**—Urine in which albumin is to be estimated, if not clear, is filtered. Into a beaker of about 200 c.c. capacity, 100 c.c. urine is introduced. If the reaction of the urine is not strongly acid, add acetic acid until the reaction is decidedly acid, but avoid an excess of the acid. Suspend the beaker in a water bath and keep the water in the bath at the boiling temperature. At the expiration of thirty minutes, if, by transmitted light, the urine is clear between the flakes of coagulated albumen, the precipitation is complete. If, however, the urine is cloudy, a small quantity of acetic acid is added, the urine stirred, and the heat continued, when the separation of albumin in flakes will take place. Filter through a filter, having been dried at 110° C. between watch glasses and cooled in a desiccator and weighed. The albumen, having been transferred to the filter, is washed with water. As the filtering and washings are likely to require several hours, a filter pump or aspirator bottle may be employed with advantage, the filter having the support of a platinum cone. The washing is continued until no cloudiness is produced when tested with a solution of silver nitrate and some nitric acid. Having been washed with water, wash with about 50 c.c. absolute alcohol, followed by about the same quantity of ether. Any fat present is removed by the alcohol and ether, and the water is so far removed as to facilitate the drying. The funnel is covered with paper or a glass plate and placed upright in an air bath and heated gradually until the paper and precipitate are somewhat dry, when the filter, with the precipitate, is placed between the watch glasses employed before. The heating in the air bath at 110° C. is continued until the weight becomes constant, which is ascertained by heating two hours, cooling in a desiccator and weighing, repeating the process until the weight becomes constant. The difference in weight caused by the precipitate is taken as the weight of albumin, except in case the urine contains much albumin; when the filter paper and precipitate are ashed and the ash weighed in a platinum crucible. By subtracting the weight of the ash from that of the precipitate, the remainder is the weight of albumin, or, instead of ashing, 50 c.c. urine may be taken and 50 c.c. water added before acidifying and heating. The albumin, when dry, should not exceed 0.3 gm. in weight; if less, the quantity of inorganic matter present is very small.

## QUANTITATIVE DETERMINATION OF SUGAR BY FEHLING'S SOLUTION.

As a rule urines of specific gravity of 1030 should be diluted five times, and if the density be still higher ten times. To be certain that the proper degree of dilution has been reached, 5 c.c. of Fehling's solution are treated with 1 c.c. of the diluted urine, a little caustic soda and distilled water being added to make in all about 25 c.c. This mixture is thoroughly boiled, and if the fluid still remains blue another 1 c.c. of diluted urine added, and so on until the last two tests differ by 1 c.c. of urine, the last c.c. added causing a separation of cuprous oxide. In this manner the percentage of sugar may be approximately determined. Albumin, if present, must first be removed by boiling.

Ten c.c. of Fehling's solution, diluted with 40 c.c. of water, are placed in a porcelain dish and boiled. While boiling, the diluted urine is added from a burette, ½ c.c. at a time, when, as a rule, the precipitated cuprous oxide will rapidly settle, so that gradually a white bottom may be seen through the blue fluid, the color of which becomes less and less intense upon the further addition of urine until, finally, the solution is almost colorless. When this point is reached the urine is added only drop by drop, until the decolorization is complete. The degree of dilution multiplied by 5 and the result divided by the number of c c. of diluted urine employed will then indicate the percentage amount of sugar.

Unfortunately, it is difficult as a general rule to determine exactly the point when all the copper has been reduced, *i. e.*, the point at which the blue color has entirely disappeared. When it is thought that this has been reached, about 1 c.c. should be filtered through thick Swedish filter paper, and the filtrate, which must be absolutely clear, acidified with acetic acid and treated with a drop or two of a solution of potassium ferrocyanide. If unreduced copper be still present in the solution, a brown color will result, indicating that insufficient urine has been added. But if, on the other hand, no brown discoloration be noted, it is possible that the desired point has already been passed, when the titration should be repeated. At times the precipitate will not settle at all, and even pass through the filter, so that it is almost impossible to determine the end of the reaction. In such cases the following procedure, suggested by Cause, will be found serviceable:

Ten c.c. of Fehling's solution are diluted with 20 c.c. of distilled water and treated with 4 c.c. of 1-20 per cent. solution of potassium ferrocyanide. While boiling, the diluted urine is now added drop by drop, until the blue color has entirely disappeared, a precipitate not appearing at all with this method.

In order to obtain reliable results, however, the Fehling's solution must be prepared with great care, and its strength determined. This may be done in the following manner: 0 2375 gram of crystallized cane sugar, pure and dried at 100° C., is dissolved in 40 c.c. of distilled water, to which 22 drops of a 1-10 per cent. solution of sulphuric acid have been added. This solution is kept upon a boiling water-bath for an hour, when it is allowed to cool and diluted to 100 c.c. with distilled water. Twenty c.c. of this solution will then contain exactly 0.05 gram of glucose, corresponding to 10 c.c. of Fehling's solution, if this be of the required

strength. If too strong, so that 21 c.c., for example, of the sugar solution are required to obtain a complete reduction of the copper, the strength of Fehling's solution may be determined according to the equation: 20:0.05: :21:x, and x=0.0525. If too weak, on the other hand, so that 19 c.c , for example, are required, its strength is similarly determined: 20:0.05: :19:x, and x=0.0475. If necessary, the solution may of course be brought to the exact strength in the manner indicated elsewhere, by first making it too strong and then ascertaining the required degree of dilution. (Simon.)

## DETERMINATION OF GLYCERO-PHOSPHORIC ACID.

Sotnischewsky's process is to render the 24 hours' urine alkaline with milk of lime and precipitate with calcium chloride. Filter, evaporate filtrate, and extract residue with alcohol. The residue not dissolved with alcohol is dissolved in water. To both solutions add a solution of ammonia and magnesia and allow the mixture to stand 24 hours in order to remove traces of the inorganic phosphoric acid that may still be present. Filter, render the filtrate strongly acid with sulphuric acid and boil for some time in order to separate the glycero-phosphoric acid. After cooling, solution of ammonia is to be added, when, on standing, crystals of ammonium-magnesium phosphate are deposited. These are to be collected and weighed, whence the amount of phosphoric acid derived from the organic compounds can be deduced.

**Another method.**—Acidify 250 c.c. of urine strongly with nitric acid and boil 30 minutes. (The fumes given off have an overpowering odor, so that the flask should be provided with a delivery tube dipping into water.)

When cold precipitate the phosphoric acid by rendering the solution alkaline with ammonium hydrate, and treating with 50 c.c. of magnesia mixture and ammonium hydrate (50 to 100 c c.). Mix well and let stand 6 to 12 hours. Filter, and transfer the precipitate to the filter by means of a stirring rod provided with a small piece of rubber tubing placed on its end. Wash the precipitate with water containing one-third its volume of ammonium hydrate. The washing is continued until some of the wash water, having been boiled in a test tube to drive off excess of ammonia, and rendered acid with nitric acid, ceases to yield a turbidity with a solution of silver nitrate. When the precipitate is washed it is immediately transferred to a graduated 250 c.c. flask. This is brought about by perforating the filter with a glass rod, and with a fine stream of water from a wash bottle every trace of the precipitate is removed from the paper. Dissolve the precipitate with acetic acid, and with water fill to the mark. (The writer finds that it is not easy to dissolve *all* the precipitate with acetic acid as directed; in which case dissolve in nitric acid and reprecipitate with magnesia mixture and ammonia as above.)

Mix well by shaking. With a pipette introduce 50 c.c. of the solution into a 200 c.c. flask, add 5 c.c. of the solution of sodium acetate, heat to the boiling point (preferably on a sand-bath), and from a burette containing the uranium solution titrate while hot and determine as under phosphoric acid.

Multiply the number of c.c. of uranium solution used by 0 005, the product of which is the weight of $P_2O_5$ in 50 c.c. of the solu-

tion. Multiply by 20 to get into grams per liter and by the number of liters of urine in 24 hours to get grams per 24 hours. Subtract from the total grams for 24 hours the result of a determination of the total phosphoric acid itself, exclusive of glycero-phosphoric acid, and the result is the quantity of glycero-phosphoric acid.

## DETERMINATION OF SUGAR BY THE POLARISCOPE.

Soleil-Ventzke's apparatus is constructed in such a manner that if a solution of glucose be employed, the length of the tube being 10 cm., every entire line of division on the scale will indicate 1 per cent. of sugar.

The tube of the saccharimeter should be carefully washed out with distilled water, and at least once or twice with the filtered urine, when it is placed on end upon a flat surface, and filled with the urine to such a degree that this forms a convex cup at the end. The little glass plate is now carefully adjusted, so as to guard against the admission of bubbles of air. The metallic cap is then placed in position, care being taken to avoid undue pressure. The examinations are made in a dark room, an ordinary lamp being used, and several readings taken, until the differences do not amount to more than one-tenth or two-tenths per cent. The tubes should be thoroughly cleansed *immediately* after the experiment.

In every case the filtered urine should be free from albumin, and, if markedly colored, previously treated with neutral acetate of lead in substance and filtered.

If it be desired to demonstrate only the presence of sugar, the compensators are first brought to the zero position. If now, upon the interposition of the tube filled with urine, a difference in the color of the two halves of the field of vision be noted, the presence of an optically active substance in the urine may be assumed, and if at the same time the deviation be to the right, the presence of glucose is rendered highly probable, while a deviation to the left will generally be referable to levulose or oxybutyric acid. Indican, peptones, cholesterin, and certain alkaloids, it is true, also turn the plane of polarization to the left, but as a rule these substances need not be considered, cholesterin occurring but rarely, while indican in diabetic urines is usually present in only small amounts, and a concurrence of sugar and peptones has not as yet been observed Lactose and maltose, which also turn the plane of polarization to the right, may be distinguished from each other and from glucose by the phenylhydrazin test. Levulose turns the plane of polarization to the left. Oxybutyric acid is practically always associated with the presence of glucose, and may be recognized by allowing the urine to undergo fermentation, when the filtered urine will become distinctly gyro-rotatory. (Simon.)

## DRUGS WHICH INTERFERE WITH ALBUMIN AND SUGAR TESTS.

A very suggestive resumé is given by Mœschel as follows:

I. **Albumin Tests** are interfered with by:

| | | |
|---|---|---|
| Alkaloids. | Benzoates. | Oil of Santal. |
| Analgen. | Benzoinum. | Piperazine. |

| | | |
|---|---|---|
| Antipyrine. | Chloroform. | Plums. |
| Balsam Peru. | Copaiba. | Styrax. |
| Balsam Tolu. | Cranberries. | |
| Benzosol. | Hypnone. | |

After the administration of acids, some tests for albumin in the urine do not respond. Neutralize such urine with a few drops of sodium hydrate and filter. Acidify slightly with acetic acid before applying *any* test. Cloudy urines, also such containing a precipitate (mucin, medicinal balsams and resins), should be faintly acidulated with acetic acid and carefully filtered before applying any tests.

II. **Sugar Tests** are interfered with by:

| | | |
|---|---|---|
| Acetanilide. | Kalmia. | Salicylates. |
| Antifebrin. | Morphine. | Salol. |
| Antipyrine. | Mercurialis perennis. | Senna. |
| Betol. | Ol. gaultheriæ. | Sulphonal. |
| Chloral hydrate. | Phenacetine. | Uva ursi. |
| Chloroform. | Rheum. | Urethan. |
| Copaiba. | Rumex. | Vaccin. myrtillus. |
| Epigæa. | | |

To which may be added:

| | |
|---|---|
| Ammonium salts. See *b* below. | Glycerin. |
| Benzoates. | Glycosuric acid. See *e*. |
| Bromides. | Iodides. |
| Camphor. | Pyrocatechin. |
| Carbohydrates. See *c*. | Serum globulin. |
| Cubebs. | Turpentine. |
| Creatinine. See *d*. | Uric acid, urates. See *d* and *f*. |

*a*. Temporary glycosuria may be occasioned by poisoning with alcohol, amyl nitrite, carbonic oxide, chloral, hydrocyanic acid, morphine, sulphuric acid.

*b*. Ammonium salts should be removed before testing. Such is accomplished by boiling with NaOH until no more ammonia is given off.

*c*. Under certain conditions some carbohydrates (animal gum) may be present in the normal urine, causing reduction.

*d*. Creatinine (also uric acid and urates) can be removed by precipitating with mercuric chloride, which operation does not affect any glucose present.

*e*. To remove glycosuric acid in urine of diabetics, acidify the urine with $H_2SO_4$ and shake with ether, from which it may be crystallized.

*f*. To test for glucose in urine in which salicylates are the disturbing compounds, the following course may be adopted: Add solution of lead subacetate to the urine, which precipitates almost all the salicylic acid, also the chlorides, phosphates and sulphates, uric acid, urates, albumin, glycuronic acid, and coloring matter. The lead remaining in solution is precipitated with dilute sulphuric acid, and the excess of acid carefully neutralized with soda or potash. Thus prepared, the urine may be tested for glucose with the usual reagents.

*g*. Nylander's test is interfered with by the use of arsenic, iodides, mercurials, large doses of quinine, salicylates, and sulphur.

III. **Spectroscopic Influences** are exerted by:

| | | |
|---|---|---|
| Acetanilide. | Chloral hydrate. | Salol. |
| Antifebrin. | Copaiba. | Santonin. |
| Antipyrine. | Epigæa. | Sulphonal. |
| Benzosol. | Frangula. | Uva ursi. |
| Betol. | Kalmia. | Vaccin myrt. |
| Cascara sagrada. | Salicylates. | |

IV. **Important Suggestions:**

1. The reactions obtained should always be compared with the perfectly clear, untested urine contained in the same sized test-tube holding an amount of fluid equal to that tested.

2. Filtration is assisted by slightly acidulating with acetic acid. Use a good filtering-paper, preferably doubled, and moisten thoroughly with distilled water before using. The filter fulfills its purpose only after all the cellulose fibers have swollen by absorption.

3. Filtration through talcum, to remove mucin and bacteria, also removes large quantities of albumin and glucose.

4. Animal charcoal is likewise objectionable.

## DETERMINATION OF THE UROTOXIC COEFFICIENT.

Acid urine being carefully and exactly neutralized with sodium bicarbonate and filtered is injected into the veins of a weighed rabbit. The posterior marginal vein on the dorsal part of the face is convenient for injection. The weight of the person voiding the urine is taken beforehand and the amount of urine voided by him is measured. Day urine should be collected separately from night and the toxicity determined separately. The urine is injected in small quantities at a time, and the result of each injection studied.

The quantity of normal urine necessary to kill a rabbit varies between 30 c.c. and 60 c.c. for each kilogram of weight of the animal, or 45 c.c. per kilo on an average.

Pathological urines are some more poisonous, others less poisonous than normal.

The amount of cubic centimeters of urine necessary to kill one kilogram of animal is found as follows: Multiply the amount of urine injected before the death of the animal by 1,000, and divide product by weight of the animal in *grams*.

Thus, suppose 46 c.c. of urine required to kill a rabbit weighing 1,600 grams, then,

$$\frac{46 \text{ times } 1{,}000}{1{,}600} = 28.95 \text{ c.c.}$$

of urine for each kilogram of animal.

To calculate the urotoxic coefficient of any man, divide the quantity of his urine passed in a given period, day or night, or better, each separately, by the number of c.c. of urine required to kill each kilogram of animal. Thus, suppose a man void 700 c c. of urine during the working hours, 46 c.c. of which are needed to kill a rabbit weighing 1,720 grams. Then,

$$\frac{46 \text{ times } 1{,}000}{1{,}720}$$

or 26.74 equals the number of c.c. of urine necessary for each kilogram of rabbit, and $\frac{700}{26.74} = 26.178$ *urotoxics.*

so-called. If the period during which the urine was collected was 16 hours, then $\frac{26.178}{16}$

or 1.6361, is the urotoxy or unit of toxicity per hour. If the man weigh 81 kilograms, then $\frac{1.6361}{81}$ or 0.2002

represents the urotoxic coefficient per kilogram of the man's weight in an hour.

In other words, this man voids for each kilogram of his weight in one hour what would kill 20.02 grams of living material.

In determining the toxicity of the 24 hours' urine collect the day and night separately, ascertain the toxicity of each in c.c. per kilogram of animal, and add together, otherwise if the urines be mixed before the toxicity is determined, there will be a loss of about one-third A person eliminates during sleep something which is partly antidotal to the day urine.

## COMPLETE ANALYSIS OF CALCULI.

The writer prefers Dr. Long's methods, as follows:

1. Heat test: Reduce some of the calculus to a powder and heat to bright redness on platinum foil. If the powder is completely consumed suspect uric acid, ammonium urate, cystin, xanthin, organized matter; if the powder is either not consumed at all, or only partly so, calcium oxalate, phosphates.

**Uric Acid** may be recognized by dissolving a little of the powder in weak alkali, precipitating by hydrochloric acid, and examining the precipitate with the microscope. [The writer finds, however, that in the West calculi of uric acid are frequently coated with phosphates; hence after dissolving what is possible in the alkali, filter and precipitate filtrate with hydrochloric acid, letting stand some hours.]

**Ammonium Urate** acts as above like uric acid and is further recognized by liberation of ammonia (odor) when heated with a little pure sodium hydroxide solution.

**Cystin:** Dissolve powder in ammonia, filter and allow drops of filtrate to evaporate spontaneously on slide. Identify by microscope. (See cut of Cystin in the book.)

**Organized Matter** is recognized by odor of burnt feathers when heated to redness.

**Calcium Oxalate.**—Stones of this substance are very hard and break with a crystalline fracture. They are often called "mulberry calculi." When the powder is heated it decomposes, leaving carbonate, which may be recognized by its effervescence with acids.

**Calcium and Magnesium Phosphates.**—These leave a residue in which the metals and phosphoric acid may be detected by simple tests of qualitative analysis. The ignited powder is soluble in hydrochloric acid without effervescence. When ammonia is added to this solution in quantity sufficient to give an alkaline

reaction, a precipitate of triple phosphate or calcium phosphate appears, which may be recognized by the microscope.

The above tests are generally sufficient to tell all that is practically necessary about the calculus. If more detailed information is desired a systematic analysis may be made according to the usual methods.

The writer greatly prefers, however, the following:

**Systematic Analysis.**—1. Reduce the calculus to a fine powder and pour over it some water and finally dilute hydrochloric acid in a beaker. Warm gently half an hour, or longer, on the water bath. Then allow to cool and filter.

2. Treatment of the residue. It seldom happens that the calculus is completely soluble in the weak acid. A residue usually remains which may contain uric acid, xanthin, calcium sulphate, and remains of organized matter. To prove the xanthin treat the residue with warm *dilute* ammonia and filter. The filtrate contains the xanthin if it is present. Acidify it with nitric acid and add a small amount of silver nitrate solution. This produces a flocculent precipitate which dissolves by warming, and crystallizes on cooling in bunches of fine needles.

In the residue free from the xanthin look for calcium sulphate by extracting with water and applying the usual tests. This solution may contain uric acid which is recognized by evaporation and crystallization after adding a little hydrochloric acid. In the final residue some uric acid may be also present. Dissolve in alkali, reprecipitate with hydrochloric acid, and examine any crystals which may form under the microscope.

3. Treatment of the hydrochloric acid solution. This may contain calcium oxalate, cystin, the phosphates and possibly some xanthin. Look for the last in a small portion of the solution. Make this portion alkaline with ammonia, add a few drops of calcium chloride solution, filter if a precipitate forms and treat the filtrate with ammoniacal silver nitrate solution. In presence of xanthin a flocculent precipitate forms.

Dilute the remaining and larger portion of the hydrochloric acid solution with twice its volume of water, add enough ammonia to give a strong alkaline reaction and then acetic acid to restore a weak acid reaction. By this treatment phosphates are held in solution, while calcium oxalate, if present, precipitates. Therefore allow the mixture to stand half an hour and then filter off any precipitate which appears. This precipitate may contain cystin as well as calcium oxalate. Cystin may be dissolved by pouring ammonia on the filter, and on evaporating the ammoniacal solution is obtained in form suitable for microscopic examination.

The residue free from cystin is dried and heated to redness on platinum foil. This treatment converts calcium oxalate into carbonate. Place the foil in a beaker and add some dilute acetic acid; an effervescence shows the carbonate. To the clear solution add next some ammonium oxalate which gives a white precipitate of calcium oxalate, if the latter metal is present.

Next look for phosphates and bases in the acetic acid solution obtained after filtering off cystin and calcium oxalate. More calcium may be present, in excess of that combined as oxalate, which may be recognized by adding a little solution of ammonium oxalate. If a precipitate forms treat the whole of the liquid with ammonium oxalate, after warming on the water bath, allow to stand an hour

and filter. Concentrate the filtrate to a small volume, transfer to a large test-tube and add enough ammonia to produce an alkaline reaction. If a precipitate now appear it must consist of magnesium phosphate, showing both magnesium and phosphoric acid present in the original. If no precipitate appear, magnesium is absent, but phosphoric acid may still be present. To find it divide the ammoniacal liquid into two portions. To one add a few drops of magnesia mixture (white precipitate), and to the other add nitric acid in slight excess, and then a few drops of ammonium molybdate reagent (yellow precipitate). Both tests must be successful. *Ammonium* salts are recognized by heating the original powdered calculus with pure potassium hydroxide solution; odor of ammonia and reaction on red litmus paper (turned blue) in the fumes.

*Sodium* and *potassium* are recognized by treating solution of the powdered calculus in hydrochloric acid with pure ammonia and a little ammonium carbonate in excess. Let precipitate settle and filter. Evaporate to dryness in a platinum dish, and heat residue strongly to drive off all ammonium salts.

## PRESERVING AND MOUNTING URINARY SEDIMENTS.

The method of the late Dr. Charles Heitzmann was to add to the thickest sediment (which now can be easily obtained by use of the centrifuge) a few drops of a strong chromic acid solution. Let stand a week, then gradually add a little chemically pure glycerine day after day for three or four days. Let stand for a few days more until all water has evaporated, then mount without any addition, clean, and surround with asphalt. The exact amounts of the chromic acid and glycerine used must be learned by practice.

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## TABLES.

The following tables will save time in figuring. The table at the top gives figures more in accordance with the writer's observations in each case. The table at the bottom, unless otherwise specified, is based on English standards which the writer finds are in excess of American. In many cases a deduction of even 25 per cent. from the upper table (per cent. of normal average) may be made with closer approximation to American standards in health. Example: Table 1:—1360 c.c. is given as average normal for an American, but not infrequently we find 950 c.c. voided in 24 hours by healthy males, so that care must be taken not to assume figures above 75 per cent. in the upper tables as indicating necessarily anything abnormal. Figures less than 50 per cent. of normal in the upper tables are usually significant of disease if the condition is permanent and the weight, diet and exercise are average.

## TABLE I.

QUANTITY OF URINE IN 24 HOURS.

| | MALES. | | | FEMALES. | | |
|---|---|---|---|---|---|---|
| | Fluid-ounces. | Cubic centimeters. | % normal av'ge. | Fluid-ounces. | Cubic centimeters. | % normal av'ge. |
| A | 46. | 1360 | 100 | 37. | 1100 | 100 |
| | 43. | 1290 | 95 | 34.83 | 1045 | 95 |
| | 40.83 | 1225 | 90 | 33. | 990 | 90 |
| | 38.5 | 1155 | 85 | 31.16 | 935 | 85 |
| | 36.33 | 1090 | 80 | 29.33 | 880 | 80 |
| | 34. | 1020 | 75 | 27.5 | 825 | 75 |
| B | 31.66 | 950 | 70 | 25.66 | 770 | 70 |
| | 29.5 | 885 | 65 | 23.83 | 715 | 65 |
| | 27.16 | 815 | 60 | 22. | 660 | 60 |
| | 25. | 750 | 55 | 20.16 | 605 | 55 |
| | 22.66 | 680 | 50 | 18.33 | 550 | 50 |
| C | 20.33 | 610 | 45 | 16.5 | 495 | 45 |
| | 18.16 | 545 | 40 | 14.66 | 440 | 40 |
| | 15.83 | 475 | 35 | 12.83 | 385 | 35 |
| | 13.66 | 410 | 30 | 11. | 330 | 30 |
| | 11.33 | 340 | 25 | 9.16 | 275 | 25 |
| D | 9. | 270 | 20 | 7.33 | 220 | 20 |
| | 6.83 | 205 | 15 | 5.5 | 165 | 15 |
| | 4.5 | 135 | 10 | 3.66 | 110 | 10 |
| | 2.33 | 70 | 5 | 1.83 | 55 | 5 |
| | 1.16 | 35 | 2½ | 0.83 | 25 | 2½ |
| | 0 | 0 | 0 | 0 | 0 | 0 |
| AI. | 50 | 1500 | 100 | 40 | 1200 | 100 |
| | 55 | 1650 | 110 | 44 | 1320 | 110 |
| | 60 | 1800 | 120 | 48 | 1440 | 120 |
| AII. | 65 | 1950 | 130 | 52 | 1560 | 130 |
| | 70 | 2100 | 140 | 56 | 1680 | 140 |
| | 75 | 2250 | 150 | 60 | 1800 | 150 |
| AIII. | 80 | 2400 | 160 | 64 | 1920 | 160 |
| | 85 | 2550 | 170 | 68 | 2040 | 170 |
| | 87 | 2625 | 175 | 70 | 2100 | 175 |
| AIV. | 90 | 2700 | 180 | 72 | 2160 | 180 |
| | 95 | 2850 | 190 | 76 | 2280 | 190 |
| | 100 | 3000 | 200 | 80 | 2400 | 200 |
| Etc. | 125 | 3750 | 250 | 100 | 3000 | 250 |
| | 150 | 4500 | 300 | 120 | 3600 | 300 |
| | 175 | 5250 | 350 | 140 | 4200 | 350 |
| | 200 | 6000 | 400 | 160 | 4800 | 400 |
| | 225 | 6750 | 450 | 180 | 5400 | 450 |
| | 250 | 7500 | 500 | 200 | 6000 | 500 |
| | 275 | 8250 | 550 | 220 | 6600 | 550 |
| Etc. | 300 | 9000 | 600 | 240 | 7200 | 600 |
| | 325 | 9750 | 650 | 260 | 7800 | 650 |
| | 350 | 10500 | 700 | 280 | 8400 | 700 |
| | 375 | 11250 | 750 | 300 | 9000 | 750 |
| | 400 | 12000 | 800 | 320 | 9600 | 800 |
| | 425 | 12750 | 850 | 340 | 10200 | 850 |
| | 450 | 13500 | 900 | 360 | 10800 | 900 |
| | 475 | 14250 | 950 | 380 | 11400 | 950 |
| | 500 | 15000 | 1000 | 400 | 12000 | 1000 |

Quantities between 1360 and 1500 or 1100 and 1200 are accepted as normal.

## TABLE II.

### RATIO OF DAY URINE TO NIGHT URINE.

The author having collected his urine for the 24 hours, day and night, separately, during 28 successive days, found the lowest ratio of day to night to be 1.7 to 1, the highest 7 to 1. On 12 days out of the 28 the ratio was 3 to 1. On 4 days the ratio was between 2 and 3 to 1. On only 3 days was it below 2 to 1, and on 8 days it was from 4 up to 7 to 1. I have, therefore, adopted 3 to 1 as a basis on which to reckon percentage.

DESCENDING SCALE.

| | Per cent. | | Per cent. |
|---|---|---|---|
| 3 to 1 | 100 | 1.50 to 1 | 50 |
| 2.85 to 1 | 95 | 1.35 to 1 | 45 |
| 2.70 to 1 | 90 | 1.20 to 1 | 40 |
| 2.55 to 1 | 85 | 1.05 to 1 | 35 |
| 2.40 to 1 | 80 | 0.90 to 1 | 30 |
| 2.25 to 1 | 75 | 0.75 to 1 | 25 |
| 2.10 to 1 | 70 | 0.60 to 1 | 20 |
| 1.95 to 1 | 65 | 0.45 to 1 | 15 |
| 1.80 to 1 | 60 | 0.30 to 1 | 10 |
| 1.65 to 1 | 55 | 0.15 to 1 | 5 |

## TABLE III.

### TOTAL SOLIDS IN THE URINE.

Conversion of grains to grammes and relation to normal averages for a weight of 145 pounds. (See also page 32.)

| DESCENDING SCALE. | | | ASCENDING SCALE. | | |
|---|---|---|---|---|---|
| Grains. | Grammes. | Per cent. | Grains. | Grammes. | Per cent. |
| 899. | 58. | 100 | 899. | 58. | 100 |
| 854.05 | 55 1 | 95 | 943.95 | 60.9 | 105 |
| 809.10 | 52.2 | 90 | 988.9 | 63.8 | 110 |
| 764.15 | 49.3 | 85 | 1033.85 | 66.7 | 115 |
| 719.2 | 46.4 | 80 | 1078.8 | 69.6 | 120 |
| 674.25 | 43.5 | 75 | 1122.75 | 72.5 | 125 |
| 629.30 | 40.6 | 70 | 1168.7 | 75.4 | 130 |
| 584.35 | 37.7 | 65 | 1213.65 | 78 3 | 135 |
| 539.4 | 34.8 | 60 | 1258.6 | 81.2 | 140 |
| 494.45 | 31.9 | 55 | 1303.55 | 84.1 | 145 |
| 449.5 | 29. | 50 | 1348.5 | 87. | 150 |
| 404.55 | 26.1 | 45 | 1393.45 | 89.9 | 155 |
| 359.6 | 23.2 | 40 | 1438.4 | 92.8 | 160 |
| 314.65 | 20.3 | 35 | 1483.35 | 95.7 | 165 |
| 269.7 | 17.4 | 30 | 1528.3 | 98.6 | 170 |
| 224 75 | 14.5 | 25 | 1573.25 | 101.5 | 175 |
| 179.8 | 11.6 | 20 | 1618.2 | 104.4 | 180 |
| 134.85 | 8.7 | 15 | 1663.15 | 107.3 | 185 |
| 89.9 | 5.8 | 10 | 1708.1 | 110.2 | 190 |
| 44.95 | 2.9 | 5 | 1753.05 | 113.1 | 195 |
| 22.475 | 1.45 | 2½ | 1798. | 116. | 200 |
| . . . | . . | . . | 2022.75 | 130.5 | 225 |

## TABLE IV.

UREA IN GRAINS PER FLUID OUNCE AND GRAMMES PER LITER.

| | MALES. | | | FEMALES. | | |
|---|---|---|---|---|---|---|
| | Grains per fluid-ounce. | Grammes per liter. | % of normal av'ge. | Grains per fluid-ounce. | Grammes per liter. | % of normal av'ge. |
| | 10.09 | 21.50 | 100 | 8.924 | 19.00 | 100 |
| | 9.56 | 20.42 | 95 | 8.478 | 18.05 | 95 |
| A | 9.008 | 19.35 | 90 | 8.003 | 17.10 | 90 |
| | 8.589 | 18.28 | 85 | 7.585 | 16.15 | 85 |
| | 8.007 | 17.10 | 80 | 7.139 | 15.20 | 80 |
| | 7.571 | 16.12 | 75 | 6.692 | 14.25 | 75 |
| | 7.068 | 15.05 | 70 | 6.246 | 13.30 | 70 |
| | 6.566 | 13.98 | 65 | 5.800 | 12.35 | 65 |
| B | 6.059 | 12.90 | 60 | 5.354 | 11.40 | 60 |
| | 5.556 | 11.83 | 55 | 4.908 | 10.45 | 55 |
| | 5.049 | 10.75 | 50 | 4.162 | 9.50 | 50 |
| | 4.546 | 9.68 | 45 | 4.015 | 8.55 | 45 |
| | 4.036 | 8.60 | 40 | 3.560 | 7.60 | 40 |
| C | 3.532 | 7.52 | 35 | 3.123 | 6.65 | 35 |
| | 3.332 | 6.45 | 30 | 2.919 | 5.70 | 30 |
| | 2.527 | 5.38 | 25 | 2.231 | 4.75 | 25 |
| | 2.019 | 4.30 | 20 | 1.784 | 3.80 | 20 |
| | 1.517 | 3.23 | 15 | 1.338 | 2.85 | 15 |
| D | 1.009 | 2.15 | 10 | 0.892 | 1.90 | 10 |
| | 0.507 | 1.08 | 5 | 0.445 | 0.95 | 5 |
| | 0.256 | 0.54 | 2½ | 0.225 | 0.48 | 2½ |
| | 10.821 | 23.04 | 100 | 10.427 | 22.2 | 100 |
| | 11.362 | 24.192 | 105 | 10.948 | 23.31 | 105 |
| AI. | 11.904 | 25.344 | 110 | 11.47 | 24.42 | 110 |
| | 12.445 | 26.496 | 115 | 11.991 | 25.53 | 115 |
| | 12.986 | 27.648 | 120 | 12.512 | 26.64 | 120 |
| | 13.527 | 28.8 | 125 | 13.034 | 27.75 | 125 |
| | 14.068 | 29.952 | 130 | 13.555 | 28.86 | 130 |
| | 14.609 | 31.104 | 135 | 14.076 | 29.97 | 135 |
| AII. | 15.150 | 32.256 | 140 | 14.598 | 31.08 | 140 |
| | 15.691 | 33.408 | 145 | 15.119 | 32.19 | 145 |
| | 16.232 | 34.56 | 150 | 15.640 | 33.3 | 150 |
| | 16.773 | 35.712 | 155 | 16.162 | 34.41 | 155 |
| | 17.314 | 36.864 | 160 | 16.683 | 35.52 | 160 |
| AIII. | 17.856 | 38.016 | 165 | 17.205 | 36.63 | 165 |
| | 18.397 | 39.168 | 170 | 17.726 | 37.74 | 170 |
| | 18.938 | 40.32 | 175 | 18.247 | 38.85 | 175 |
| | 19.479 | 41.472 | 180 | 18.769 | 39.96 | 180 |
| | 20.020 | 42.624 | 185 | 19.290 | 41.07 | 185 |
| AIV. | 20.561 | 43.776 | 190 | 19.811 | 42.18 | 190 |
| | 21.102 | 44.928 | 195 | 20.333 | 43.29 | 195 |
| | 21.643 | 46.08 | 200 | 20.854 | 44.4 | 200 |
| | 24.349 | 51.84 | 225 | 23.461 | 49.95 | 225 |
| Etc. | 27.054 | 57.6 | 250 | 26.068 | 55.5 | 250 |
| | 29.760 | 63.36 | 275 | 28.675 | 61.05 | 275 |
| | 32.465 | 69.12 | 300 | 31.281 | 66.6 | 300 |
| | 35.171 | 74.88 | 325 | 33.888 | 72.15 | 325 |
| Etc. | 37.876 | 80.64 | 350 | 36.495 | 77.7 | 350 |
| | 40.582 | 86.4 | 375 | 49.102 | 83.25 | 375 |
| | 43.287 | 92.16 | 400 | 51.709 | 88.8 | 400 |

## TABLE V.

UREA IN GRAINS AND GRAMMES PER 24 HOURS.

| | MALES. | | | | FEMALES. | | | |
|---|---|---|---|---|---|---|---|---|
| | Grains. | Gram's. | Approx. | % | Grains. | Gram's. | Approx. | % |
| A | 410.75 | 26.50 | 27 | 100 | 312.75 | 20.50 | 21 | 100 |
| | 390.29 | 25.18 | 25 | 95 | 301.94 | 19.48 | 19 | 95 |
| | 369.675 | 23.85 | 24 | 90 | 285.975 | 18.45 | 18 | 90 |
| | 349.215 | 22.53 | 23 | 85 | 270.165 | 17.43 | 17 | 85 |
| | 328.60 | 21.20 | 21 | 80 | 254.20 | 16.40 | 16 | 80 |
| | 307.83 | 19.88 | 20 | 75 | 238.39 | 15.38 | 15 | 75 |
| B | 287.525 | 18.55 | 19 | 70 | 222.425 | 14.35 | 14 | 70 |
| | 267.065 | 17.23 | 17 | 65 | 206.615 | 13.33 | 13 | 65 |
| | 246.45 | 15.90 | 16 | 60 | 190.65 | 12.30 | 12 | 60 |
| | 225.99 | 14.58 | 15 | 55 | 174.84 | 11.28 | 11 | 55 |
| | 204.875 | 13.25 | 13 | 50 | 158.875 | 10.25 | 10 | 50 |
| C | 184.915 | 11.93 | 12 | 45 | 143.065 | 9.23 | 9 | 45 |
| | 164.30 | 10.60 | 11 | 40 | 127.10 | 8.20 | 8 | 40 |
| | 143.84 | 9.28 | 9 | 35 | 111.29 | 7.18 | 7 | 35 |
| | 123.225 | 7.95 | 8 | 30 | 95.325 | 6.15 | 6 | 30 |
| | 102.765 | 6.63 | 7 | 25 | 79.515 | 5.13 | 5 | 25 |
| D | 82.15 | 5.30 | 5 | 20 | 63.55 | 4.10 | 4 | 20 |
| | 61.69 | 3.98 | 4 | 15 | 47.74 | 3.08 | 3 | 15 |
| | 41.075 | 2.65 | 3 | 10 | 31.775 | 2.05 | 2 | 10 |
| | 20.46 | 1.32 | 1 | 5 | 15.965 | 1.03 | 1 | 5 |
| | 10.23 | 0.66 | ⅔ | 2½ | 8.215 | 0.53 | ½ | 2½ |

| | Grains. | Grammes. | Per cent. | Grains. | Grammes. | Per cent. |
|---|---|---|---|---|---|---|
| AI. | 514.6 | 33.2 | 100 | 412.3 | 26.6 | 100 |
| | 540.33 | 34.86 | 105 | 432.915 | 27.93 | 105 |
| | 566.06 | 36.52 | 110 | 453.53 | 29.26 | 110 |
| | 591.79 | 38.18 | 115 | 474.145 | 30.59 | 115 |
| | 617.52 | 39.84 | 120 | 494.76 | 31.92 | 120 |
| | 643.25 | 41.5 | 125 | 515.375 | 33.25 | 125 |
| AII. | 668.98 | 43.16 | 130 | 535 99 | 34.58 | 130 |
| | 694.71 | 44.82 | 135 | 556.605 | 35.91 | 135 |
| | 720.44 | 46.48 | 140 | 577.22 | 37.24 | 140 |
| | 746.17 | 48.14 | 145 | 597.835 | 38.57 | 145 |
| | 771.9 | 49.80 | 150 | 618.45 | 39.90 | 150 |
| AIII. | 797.63 | 51.46 | 155 | 639.065 | 41.23 | 155 |
| | 823.36 | 53.12 | 160 | 659.68 | 42.56 | 160 |
| | 849.09 | 54.78 | 165 | 680.295 | 43.89 | 165 |
| | 874.82 | 56.44 | 170 | 700.91 | 45.22 | 170 |
| | 900.65 | 58.10 | 175 | 721.525 | 46.55 | 175 |
| AIV. | 926.28 | 59.76 | 180 | 742.14 | 47.88 | 180 |
| | 952.01 | 61.42 | 185 | 762.755 | 49.21 | 185 |
| | 977.74 | 63.8 | 190 | 783.37 | 50.54 | 190 |
| | 1003.47 | 64 74 | 195 | 803.985 | 51.87 | 195 |
| | 1029.2 | 66.40 | 200 | 824.6 | 53.2 | 200 |
| AV. | 1157.85 | 74.7 | 225 | 927.675 | 59.85 | 225 |
| | 1286.50 | 83. | 250 | 1030.75 | 66.5 | 250 |
| AVI. | 1415.15 | 94.3 | 275 | 1134.825 | 73.15 | 275 |
| | 1543.80 | 99.6 | 300 | 1236.9 | 79.8 | 300 |

Those examining urine in Chicago and vicinity will find the figures in the upper half of the page far more common than those in the lower.

## TABLE VI.

(*a.*)

### URIC ACID RELATIVE TO WATER.

DESCENDING SCALE.

| MALE PATIENTS. | | | FEMALE PATIENTS. | | |
|---|---|---|---|---|---|
| Grains per fluid oz. | Grammes per liter. | Per cent. | Grains per fluid oz. | Grammes per liter. | Per cent. |
| 0.173 | 0.37 | 100 | 0.191 | 0.407 | 100 |
| 0.164 | 0.35 | 95 | 0.181 | 0.386 | 95 |
| 0.155 | 0.33 | 90 | 0.172 | 0.366 | 90 |
| 0.147 | 0.31 | 85 | 0.162 | 0.345 | 85 |
| 0.138 | 0.296 | 80 | 0.153 | 0.325 | 80 |
| 0.129 | 0.277 | 75 | 0.143 | 0.305 | 75 |
| 0.121 | 0.259 | 70 | 0.133 | 0.285 | 70 |
| 0.112 | 0.24 | 65 | 0.124 | 0.264 | 65 |
| 0.103 | 0.22 | 60 | 0.115 | 0.244 | 60 |
| 0.095 | 0.20 | 55 | 0.105 | 0.224 | 55 |
| 0.086 | 0.185 | 50 | 0.095 | 0.203 | 50 |
| 0.077 | 0.166 | 45 | 0.086 | 0.183 | 45 |
| 0.069 | 0.148 | 40 | 0.076 | 0.163 | 40 |
| 0.060 | 0.129 | 35 | 0.066 | 0.142 | 35 |
| 0.052 | 0.111 | 30 | 0.057 | 0.122 | 30 |
| 0.042 | 0.092 | 25 | 0.047 | 0.102 | 25 |
| 0.034 | 0.074 | 20 | 0.038 | 0.08 | 20 |
| 0.026 | 0.055 | 15 | 0.028 | 0.06 | 15 |
| 0.017 | 0.037 | 10 | 0.019 | 0.04 | 10 |
| 0.008 | 0.018 | 5 | 0.009 | 0.02 | 5 |
| 0.004 | 0.009 | 2½ | 0.004 | 0.01 | 2½ |

In this table the average of Parkes is chosen, since it is lower than that of Yvon-Berlioz. But in order to make the average for female patients, the ratio of male to female in the Yvon-Berlioz average is taken.

(*b.*)

ASCENDING SCALE.

| | | | | | |
|---|---|---|---|---|---|
| 0.232 | 0.500 | 100 | 0.255 | 0.550 | 100 |
| 0.244 | 0.525 | 105 | 0.267 | 0.577 | 105 |
| 0.255 | 0.550 | 110 | 0.280 | 0.605 | 110 |
| 0.267 | 0.575 | 115 | 0.293 | 0.632 | 115 |
| 0.278 | 0.600 | 120 | 0.306 | 0.660 | 120 |
| 0.290 | 0.625 | 125 | 0.319 | 0.687 | 125 |
| 0.302 | 0.650 | 130 | 0.331 | 0.715 | 130 |
| 0.313 | 0.675 | 135 | 0.344 | 0.742 | 135 |
| 0.325 | 0.700 | 140 | 0.357 | 0.770 | 140 |
| 0.336 | 0.725 | 145 | 0.369 | 0.797 | 145 |
| 0.348 | 0.750 | 150 | 0.382 | 0.825 | 150 |
| 0.359 | 0.775 | 155 | 0.395 | 0.852 | 155 |
| 0.371 | 0.800 | 160 | 0.408 | 0.880 | 160 |
| 0.383 | 0.825 | 165 | 0.420 | 0.907 | 165 |
| 0.394 | 0.850 | 170 | 0.433 | 0.935 | 170 |
| 0.406 | 0.875 | 175 | 0.446 | 0.962 | 175 |
| 0.418 | 0 900 | 180 | 0.459 | 0.990 | 180 |
| 0.429 | 0.925 | 185 | 0.472 | 1.017 | 185 |
| 0.441 | 0.950 | 190 | 0.484 | 1.045 | 190 |
| 0.452 | 0.975 | 195 | 0.497 | 1.072 | 195 |
| 0.464 | 1.000 | 200 | 0.510 | 1.100 | 200 |
| 0.522 | 1.125 | 225 | 0.573 | 1.237 | 225 |
| 0.580 | 1.250 | 250 | 0.637 | 1.375 | 250 |
| 0.638 | 1.375 | 275 | 0.701 | 1.512 | 275 |
| 0.696 | 1.500 | 300 | 0.765 | 1.650 | 300 |
| 0.754 | 1.625 | 325 | 0.828 | 1.787 | 325 |
| 0.812 | 1.750 | 350 | 0.892 | 1.925 | 350 |
| 0.870 | 1.875 | 375 | 0.956 | 2.062 | 375 |
| 0.928 | 2.000 | 400 | 1.020 | 2.200 | 400 |

## TABLE VII.

### (*a.*)

TOTAL URIC ACID IN 24 HOURS.

DESCENDING SCALE.

| MALE PATIENTS. | | | FEMALE PATIENTS. | | |
|---|---|---|---|---|---|
| Grains. | Grammes. | Per cent. | Grains. | Grammes. | Per cent. |
| 8.600 | 0.555 | 100 | 8.17 | 0.527 | 100 |
| 8.170 | 0.527 | 95 | 7.76 | 0.501 | 95 |
| 7.740 | 0.499 | 90 | 7.35 | 0.474 | 90 |
| 7.310 | 0.472 | 85 | 6.94 | 0.448 | 85 |
| 6.880 | 0.444 | 80 | 6.54 | 0.422 | 80 |
| 6.450 | 0.416 | 75 | 6.13 | 0.396 | 75 |
| 6.020 | 0.388 | 70 | 5.72 | 0.370 | 70 |
| 5.590 | 0.361 | 65 | 5.31 | 0.343 | 65 |
| 5.160 | 0.333 | 60 | 4.90 | 0.316 | 60 |
| 4.730 | 0.305 | 55 | 4.49 | 0.290 | 55 |
| 4.300 | 0 277 | 50 | 4.08 | 0.263 | 50 |
| 3.870 | 0.250 | 45 | 3.67 | 0.237 | 45 |
| 3.440 | 0.222 | 40 | 3.27 | 0.211 | 40 |
| 3.010 | 0.194 | 35 | 2.86 | 0.184 | 35 |
| 2.580 | 0.166 | 30 | 2.45 | 0.158 | 30 |
| 2.150 | 0.139 | 25 | 2.04 | 0.132 | 25 |
| 1.710 | 0.111 | 20 | 1.63 | 0.105 | 20 |
| 1.290 | 0.083 | 15 | 1.23 | 0.079 | 15 |
| 0.860 | 0.055 | 10 | 0.82 | 0.053 | 10 |
| 0.430 | 0.028 | 5 | 0.40 | 0.026 | 5 |
| 0.021 | 0.014 | 2½ | 0.02 | 0.001 | 2½ |

### (*b.*)

ASCENDING SCALE.

| | | | | | |
|---|---|---|---|---|---|
| 9.30 | 0.60 | 100 | 8.80 | 0.57 | 100 |
| 9.76 | 0.63 | 105 | 9.24 | 0.59 | 105 |
| 10.23 | 0.66 | 110 | 9.68 | 0.62 | 110 |
| 10.69 | 0.69 | 115 | 10.12 | 0.65 | 115 |
| 11.16 | 0.72 | 120 | 10.56 | 0.68 | 120 |
| 11.62 | 0.75 | 125 | 11.00 | 0.71 | 125 |
| 12.09 | 0.78 | 130 | 11.44 | 0.74 | 130 |
| 12.55 | 0.81 | 135 | 11.88 | 0.77 | 135 |
| 13.02 | 0.84 | 140 | 12.32 | 0.79 | 140 |
| 13.48 | 0.87 | 145 | 12.76 | 0.82 | 145 |
| 13.95 | 0.90 | 150 | 13.20 | 0.85 | 150 |
| 14.41 | 0.93 | 155 | 13.64 | 0.88 | 155 |
| 14.88 | 0.96 | 160 | 14.08 | 0.91 | 160 |
| 15.34 | 0.99 | 165 | 14.52 | 0.94 | 165 |
| 15.81 | 1.02 | 170 | 14.96 | 0.97 | 170 |
| 16.27 | 1.05 | 175 | 15.40 | 1.00 | 175 |
| 16.74 | 1.08 | 180 | 15.84 | 1.03 | 180 |
| 17.20 | 1.11 | 185 | 16.28 | 1.05 | 185 |
| 17.67 | 1.14 | 190 | 16.72 | 1.08 | 190 |
| 18.13 | 1.17 | 195 | 17.17 | 1.11 | 195 |
| 18.60 | 1.20 | 200 | 17.60 | 1.14 | 200 |

## TABLE VIII.

PHOSPHORIC ACID IN GRAINS PER FLUID OUNCE AND GRAMMES PER LITER.

| | MALES. | | | FEMALES. | | |
|---|---|---|---|---|---|---|
| | Grains per fluid-ounce. | Grammes per liter. | Per cent. | Grains per fluid-ounce. | Grammes per liter. | Per cent. |
| AI. | 1.174 | 2.5 | 100 | 1.127 | 2.40 | 100 |
| | 1.117 | 2.38 | 95 | 1.070 | 2.28 | 95 |
| | 1.058 | 2.25 | 90 | 1.014 | 2.16 | 90 |
| A | 1.004 | 2.13 | 85 | 0.958 | 2.04 | 85 |
| | 0.939 | 2.00 | 80 | 0.901 | 1.92 | 80 |
| | 0.883 | 1.88 | 75 | 0.845 | 1.80 | 75 |
| B | 0.821 | 1.75 | 70 | 0.789 | 1.68 | 70 |
| | 0.765 | 1.63 | 65 | 0.732 | 1.56 | 65 |
| | 0.704 | 1.50 | 60 | 0.676 | 1.44 | 60 |
| | 0.648 | 1.38 | 55 | 0.66 | 1.32 | 55 |
| | 0.587 | 1.25 | 50 | 0.563 | 1.20 | 50 |
| C | 0.530 | 1.13 | 45 | 0.507 | 1.08 | 45 |
| | 0.469 | 1.00 | 40 | 0.450 | 0.96 | 40 |
| | 0.413 | 0.88 | 35 | 0.394 | 0.84 | 35 |
| | 0.352 | 0.75 | 30 | 0.338 | 0.72 | 30 |
| | 0.295 | 0.63 | 25 | 0.281 | 0.60 | 25 |
| D | 0.234 | 0.50 | 20 | 0.225 | 0.48 | 20 |
| | 0.178 | 0.38 | 15 | 0.169 | 0.36 | 15 |
| | 0.117 | 0.25 | 10 | 0.112 | 0.24 | 10 |
| | 0.061 | 0.13 | 5 | 0.059 | 0.12 | 5 |
| | 0.032 | 0.07 | 2½ | 0.028 | 0.06 | 2½ |
| | 0 | 0 | 0 | 0 | 0 | 0 |
| A | 0.986 | 2.1 | 100 | 0.939 | 2.0 | 100 |
| | 1.035 | 2.205 | 105 | 0.986 | 2.1 | 105 |
| | 1.083 | 2.31 | 110 | 1.030 | 2.2 | 110 |
| | 1.134 | 2.415 | 115 | 1.080 | 2.3 | 115 |
| AI. | 1.183 | 2.52 | 120 | 1.127 | 2.4 | 120 |
| | 1.233 | 2.625 | 125 | 1.174 | 2.5 | 125 |
| AII. | 1.282 | 2.73 | 130 | 1.221 | 2.6 | 130 |
| | 1.331 | 2.835 | 135 | 1.268 | 2.7 | 135 |
| | 1.380 | 2.94 | 140 | 1.315 | 2.8 | 140 |
| | 1.430 | 3.045 | 145 | 1.362 | 2.9 | 145 |
| | 1.479 | 3.15 | 150 | 1.409 | 3.0 | 150 |
| AIII. | 1.528 | 3.255 | 155 | 1.456 | 3.1 | 155 |
| | 1.578 | 3.36 | 160 | 1.503 | 3.2 | 160 |
| | 1.627 | 3.465 | 165 | 1.55 | 3.3 | 165 |
| | 1.676 | 3.57 | 170 | 1.596 | 3.4 | 170 |
| | 1.726 | 3.675 | 175 | 1.643 | 3.5 | 175 |
| AIV. | 1.775 | 3.78 | 180 | 1.690 | 3.6 | 180 |
| | 1.824 | 3.885 | 185 | 1.737 | 3.7 | 185 |
| | 1.874 | 3.99 | 190 | 1.784 | 3.8 | 190 |
| | 1.921 | 4.095 | 195 | 1.831 | 3.9 | 195 |
| | 2.003 | 4.2 | 200 | 1.878 | 4.0 | 200 |
| | 2.220 | 4.725 | 225 | 2.113 | 4.5 | 225 |
| | 2.465 | 5.25 | 250 | 2.348 | 5.0 | 250 |
| Etc. | 2.712 | 5.775 | 275 | 2.583 | 5.5 | 275 |
| | 2.950 | 6.3 | 300 | 2.818 | 6.0 | 300 |
| | 3.205 | 6.825 | 325 | 3.053 | 6.5 | 325 |
| | 3.452 | 7.35 | 350 | 3.287 | 7.0 | 350 |
| Etc. | 3.698 | 7.875 | 375 | 3.522 | 7.5 | 375 |
| | 3.90 | 8.4 | 400 | 3.757 | 8.0 | 400 |

*Note:*—In the writer's experience the lower half of this page is of little value. When the figures exceed 2.40 or 2.5, which is rare, calculate by dividing the figure found by 2.4 or 2.5.

## TABLE IX.

PHOSPHORIC ACID IN GRAINS PER 24 HOURS AND GRAMMES.

| | MALES. | | | FEMALES. | | |
|---|---|---|---|---|---|---|
| | Grains. | Grammes. | Per cent. | Grains. | Grammes. | Per cent. |
| A | 49.60 | 3.20 | 100 | 40.30 | 2.60 | 100 |
| | 47.12 | 3.04 | 95 | 38 285 | 2.47 | 95 |
| | 44.64 | 2.88 | 90 | 36.27 | 2.34 | 90 |
| | 42.16 | 2.72 | 85 | 34.255 | 2.21 | 85 |
| | 39.68 | 2.56 | 80 | 32.24 | 2.08 | 80 |
| | 37.20 | 2.40 | 75 | 30.225 | 1.95 | 75 |
| B | 35.72 | 2.24 | 70 | 28.21 | 1.82 | 70 |
| | 32.24 | 2.08 | 65 | 26.195 | 1.69 | 65 |
| | 29.76 | 1.92 | 60 | 24.18 | 1.56 | 60 |
| | 27.28 | 1.76 | 55 | 22.165 | 1.43 | 55 |
| | 24.80 | 1.60 | 50 | 20.15 | 1.30 | 50 |
| C | 22.32 | 1.44 | 45 | 18.135 | 1.17 | 45 |
| | 19.84 | 1.28 | 40 | 16.12 | 1.04 | 40 |
| | 17.36 | 1.12 | 35 | 14.105 | 0.91 | 35 |
| | 14.88 | 0.96 | 30 | 12.09 | 0.78 | 30 |
| | 12.40 | 0.80 | 25 | 10.075 | 0.65 | 25 |
| D | 9.92 | 0.64 | 20 | 8.06 | 0.52 | 20 |
| | 7.44 | 0.48 | 15 | 6.045 | 0.39 | 15 |
| | 4.96 | 0.32 | 10 | 4.03 | 0.26 | 10 |
| | 2.58 | 0.16 | 5 | 2.015 | 0.13 | 5 |
| | 1.24 | 0.08 | 2½ | 1.085 | 0.07 | 2½ |
| AI. | 49.6 | 3.2 | 100 | 40.3 | 2.6 | 100 |
| | 52.08 | 3.36 | 105 | 42.315 | 2.73 | 105 |
| | 54.56 | 3.52 | 110 | 44.33 | 2.86 | 110 |
| | 57.04 | 3.68 | 115 | 46.345 | 2.99 | 115 |
| | 59.52 | 3.84 | 120 | 48.36 | 3.12 | 120 |
| | 62.00 | 4.00 | 125 | 50.375 | 3.25 | 125 |
| AII. | 64.48 | 4.16 | 130 | 52.39 | 3.38 | 130 |
| | 66.96 | 4.32 | 135 | 54.405 | 3.51 | 135 |
| | 69.44 | 4.48 | 140 | 56.42 | 3.64 | 140 |
| | 71.92 | 4.64 | 145 | 58.435 | 3.77 | 145 |
| | 74.4 | 4.80 | 150 | 60.45 | 3.9 | 150 |
| AIII. | 76.88 | 4.96 | 155 | 62.465 | 4.03 | 155 |
| | 79.36 | 5.12 | 160 | 64.48 | 4.16 | 160 |
| | 81.84 | 5.28 | 165 | 66.495 | 4.29 | 165 |
| | 84.32 | 5.44 | 170 | 68.51 | 4.42 | 170 |
| | 86.80 | 5.6 | 175 | 70.525 | 4.55 | 175 |
| AIV. | 89.28 | 5.76 | 180 | 72.54 | 4.68 | 180 |
| | 91.76 | 5.92 | 185 | 74.555 | 4.81 | 185 |
| | 94.24 | 6.08 | 190 | 76.57 | 4.94 | 190 |
| | 96.72 | 6.24 | 195 | 78.585 | 5.07 | 195 |
| | 99.20 | 6.40 | 200 | 80.6 | 5.2 | 200 |
| Etc. | 111.60 | 7.20 | 225 | 90.675 | 5.85 | 225 |
| | 124.00 | 8.00 | 250 | 100.75 | 6.50 | 250 |
| | 136.40 | 8.80 | 275 | 110.825 | 7.15 | 275 |
| | 148.80 | 9.60 | 300 | 120.9 | 7.80 | 300 |
| Etc. | 161.20 | 10.40 | 325 | 130.975 | 8.45 | 325 |
| | 173.60 | 11.20 | 350 | 141.05 | 9.10 | 350 |
| | 186.00 | 12.00 | 375 | 151.125 | 9.75 | 375 |
| | 198.40 | 12.80 | 400 | 161.2 | 10.40 | 400 |

## TABLE X.

RATIO OF UREA TO PHOSPHORIC ACID.

| (Yvon-Berlioz.) | Per cent. | (Parkes.) | Per cent. |
|---|---|---|---|
| 8. to 1 | 100 | 10. to 1 | 100 |
| 7.6 to 1 | 95 | 10.5 to 1 | 105 |
| 7.2 to 1 | 90 | 11.0 to 1 | 110 |
| 6.8 to 1 | 85 | 11.5 to 1 | 115 |
| 6.4 to 1 | 80 | 12.0 to 1 | 120 |
| 6.0 to 1 | 75 | 12.5 to 1 | 125 |
| 5.6 to 1 | 70 | 13.0 to 1 | 130 |
| 5.2 to 1 | 65 | 13.5 to 1 | 135 |
| 4.8 to 1 | 60 | 14.0 to 1 | 140 |
| 4.4 to 1 | 55 | 14.5 to 1 | 145 |
| 4.0 to 1 | 50 | 15.0 to 1 | 150 |
| 3.6 to 1 | 45 | 15.5 to 1 | 155 |
| 3.2 to 1 | 40 | 16.0 to 1 | 160 |
| 2.8 to 1 | 35 | 16.5 to 1 | 165 |
| 2.4 to 1 | 30 | 17.0 to 1 | 170 |
| 2.0 to 1 | 25 | 17.5 to 1 | 175 |
| 1.6 to 1 | 20 | 18.0 to 1 | 180 |
| 1.2 to 1 | 15 | 18.5 to 1 | 185 |
| 0.8 to 1 | 10 | 19.0 to 1 | 190 |
| 0.4 to 1 | 5 | 19.5 to 1 | 195 |
| 0.2 to 1 | 2½ | 20.0 to 1 | 200 |
| | | 22.5 to 1 | 225 |
| | | 25.0 to 1 | 250 |

## TABLE XI.

RATIO OF UREA TO URIC ACID.

40 to 1 is normal according to Yvon-Berlioz and 33 to 1 according to Haigs. The writer believes that, when the clinical instruments are used for urea and the Heintz process for uric acid, anything below 40 to 1 must be regarded as indicating relative excess of uric acid. 50 to 1 may be taken as normal.

## TABLE XII.

RATIO OF UREA TO SALTS.

| Urea. | Salts. | Per cent. | Urea. | Salts. | Per cent |
|---|---|---|---|---|---|
| 0.85 | 1 | 100 | 1.33 | 1 | 100 |
| 0.8075 | . . | 95 | 1.396+ | . . | 105 |
| 0.765 | . . | 90 | 1.463 | . . | 110 |
| 0.7225 | . . | 85 | 1.529+ | . . | 115 |
| 0.68 | . . | 80 | 1.596 | . . | 120 |
| 0.6375 | . . | 75 | 1.662+ | . . | 125 |
| 0.595 | . . | 70 | 1.729 | . . | 130 |
| 0.5525 | . . | 65 | 1.795+ | . . | 135 |
| 0.51 | . . | 60 | 1.862 | . . | 140 |
| 0.4675 | . . | 55 | 1.928+ | . . | 145 |
| 0.425 | . . | 50 | 1.995 | . . | 150 |
| 0.3825 | . . | 45 | 2.061+ | . . | 155 |
| 0.34 | . . | 40 | 2.128 | . . | 160 |
| 0.2975 | . . | 35 | 2.194+ | . . | 165 |
| 0.255 | . . | 30 | 2.261 | . . | 170 |
| 0.2125 | . . | 25 | 2.327+ | . . | 175 |
| 0.17 | . . | 20 | 2.394 | . . | 180 |
| 0.1275 | . . | 15 | 2.46+ | . . | 185 |
| 0.085 | . . | 10 | 2.527 | . . | 190 |
| 0.0425 | . . | 5 | 2.593+ | . . | 195 |
| 0.02125 | . . | 2½ | 2.66 | . . | 200 |
| . . . | . . | . . | 2.992+ | . . | 225 |
| . . . | . . | . . | 3.325+ | . | 250 |
| . . . | . . | . . | 3.657+ | . . | 275 |
| . . . | . . | . . | 3.99 | . . | 300 |

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