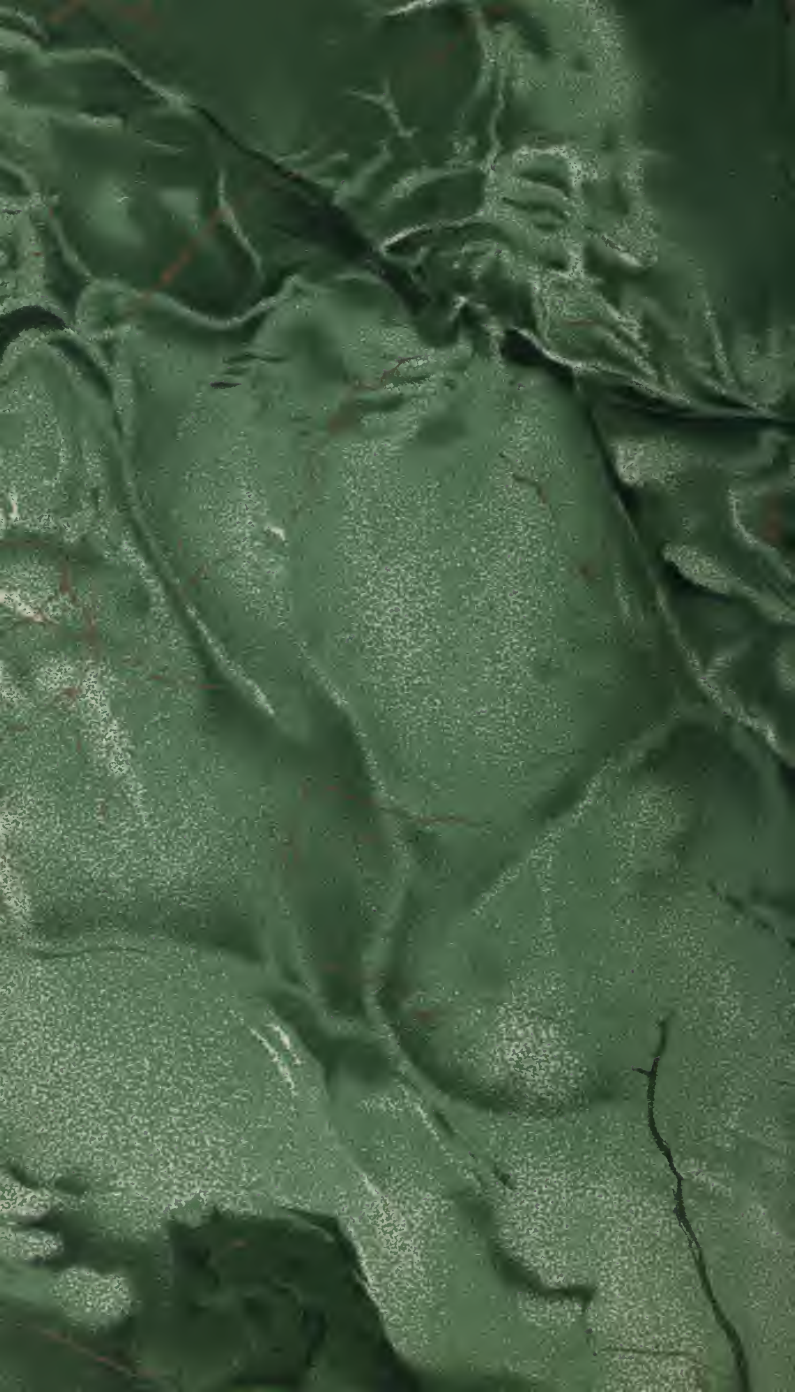

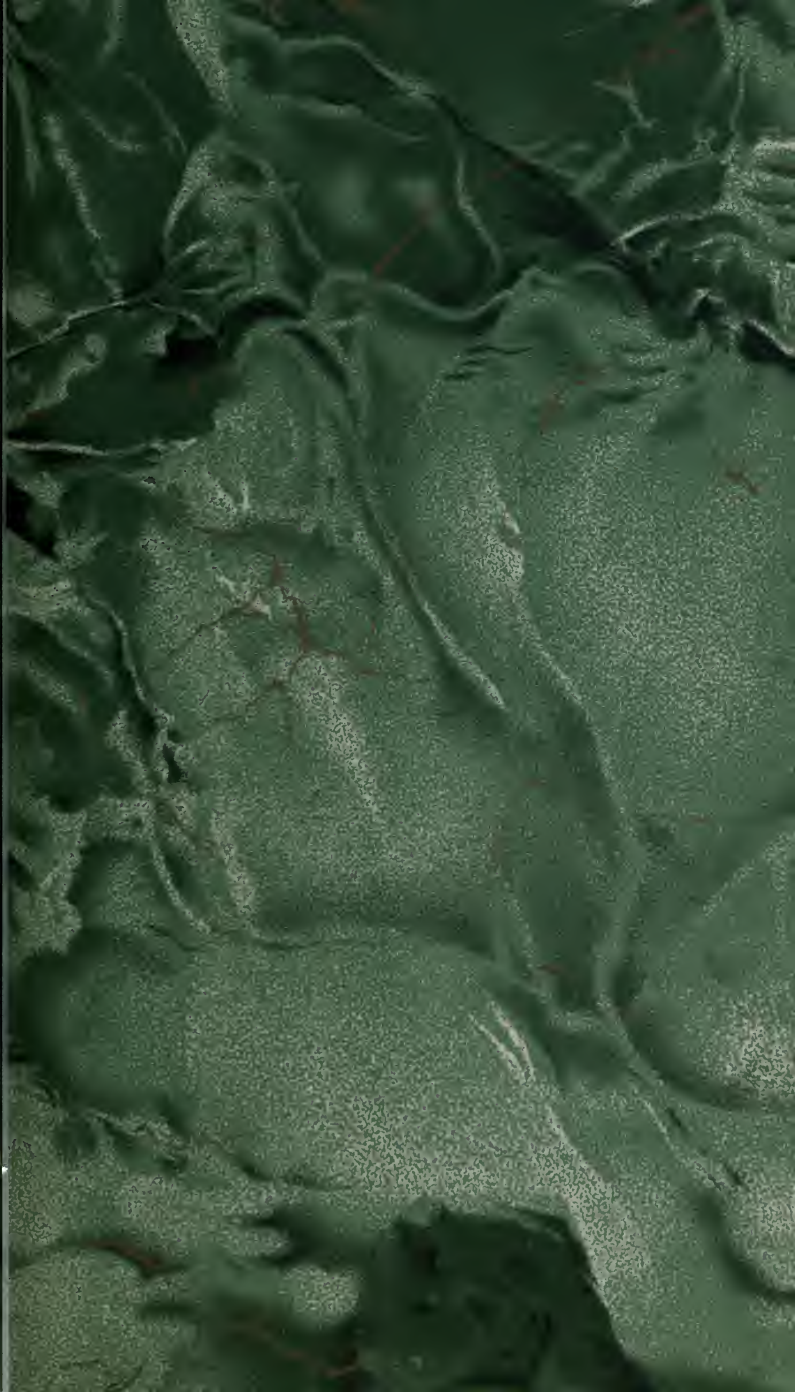

American Medical Assoc
Council on Pharmacy
& Chemistry

ANNUAL REPRINT OF THE REPORTS

OF THE

COUNCIL ON PHARMACY AND CHEMISTRY

OF THE

AMERICAN MEDICAL ASSOCIATION

FOR 1922

WITH THE

COMMENTS THAT HAVE APPEARED
IN THE JOURNAL

Press of
American Medical Association
Five Hundred and Thirty-Five North Dearborn Street
CHICAGO
1923

PREFACE

This volume—the Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association—contains the reports of the Council that have been adopted and authorized for publication during 1922. It includes reports of the Council previously published in THE JOURNAL, along with such editorial comments as have accompanied them. In addition, the volume contains reports of the Council which, because of their lesser importance, were not published in THE JOURNAL, and which as a matter of record are included here. That the Council's official reports may be made available to physicians, chemists, pharmacologists and others interested in medicine, the Council authorized publication of this volume.

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REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY

ADALIN-LUMINAL TABLETS NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

The Winthrop Chemical Company, Inc., markets Adalin-Luminal Tablets, each tablet containing adalin, 5 grains, and luminal, ¼ grain.

Adalin and luminal having previously been accepted for New and Nonofficial Remedies, the Winthrop Chemical Company requested acceptance of this tablet, stating: ". . . this was introduced by us at the suggestion of a number of prominent physicians who had found it of particular service in the treatment of various neuroses and the moderate types of insomnia." It was not stated just why a number of physicians were led to suggest the combination of adalin and luminal presented by the tablets, nor did the firm present any evidence for the value of the combination. There is no evidence that these two similarly acting hypnotics, when administered together, have any effect other than that of the sum of the two components. Hence this combination of two hypnotics in fixed proportions is irrational and tends to the use of a larger dose of hypnotics than would be used if administered separately; i. e., it tends to the prescribing of adalin and luminal without proper consideration of their respective dosages. Therefore the use of this combination is dangerous.

The Winthrop Chemical Company was informed that this combination of adalin and luminal in fixed proportions would be held irrational and therefore inadmissible to New and Nonofficial Remedies (Rule 10) unless the superiority of this combination was established by acceptable evidence. The firm did not present such evidence and accordingly Adalin-Luminal Tablets were declared inadmissible.

ANTIBERIBERI VITAMIN CONCENTRATE-METZ

Preliminary Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 13, 1923, p. 106

The Council has authorized publication of the following report on the experimental status of Antiberiberi Vitamin Concentrate-Metz.

W. A. PUCKNER, Secretary.

The Metz Laboratories, Incorporated, have requested the acceptance for New and Nonofficial Remedies of Antiberiberi Vitamin Concentrate-Metz. The firm has supplied adequate information in regard to the process whereby the product is obtained, and has presented evidence to show that the potency of the product is controlled by adequate animal tests. The firm, however, has presented no proof to indicate that the product is of value therapeutically in human beings, and hence it cannot be admitted to New and Nonofficial Remedies.

The Metz Laboratories frankly admit that there is no evidence to show that Antiberiberi Vitamin Concentrate-Metz is of value in the treatment of human disease. The firm wishes only to make available to students and investigators of nutrition a product which is claimed to be antineuritic (antiberiberi) when fed to pigeons. It increases the food intake of rats fed on substance deficient in vitamin B and caused increased weight, but not to the same extent as does the vitamin B (according to McCollum's nomenclature). The product is offered without therapeutic claims and no dosage is given excepting for pigeons. It is made available as a scientific article for investigation and trial.

The Council believes that, from a scientific standpoint, Antiberiberi Vitamin Concentrate-Metz is suitable for study, suitable for animal experiments and for controlled experiments on man.

For the preparation of Antiberiberi Vitamin Concentrate-Metz, freshly pressed brewers' yeast (from dark beer) is extracted according to the method described by Casimir Funk (*J. Physiol.* **45**:75, 1912) except that mercuric chlorid is used before, instead of after, the phosphotungstic acid, and that instead of silver nitrate another silver salt is used. The extract is tested on pigeons to determine its power to check and cure avian polyneuritis, and on rats to determine its relative freedom from the fraction which promotes the growth of yeast (Funk and Dubin, *J. Biol. Chem.* **48**:437, 1921). The vitamin extract is diluted with sucrose so that 0.065 gm. (1 grain) shall represent the antineuritic potency of 10 gm. of freshly pressed brewers' yeast. Approximately, the finished preparation contains ⅛ grain of the vitamin extract and ⅞ grain sucrose.

Antiberiberi Vitamin Concentrate-Metz is marketed in the following forms:

Antiberiberi Vitamin Concentrate-Metz Powder: 0.065 gm. (1 grain) represents the antineuritic potency of 10 gm. of freshly pressed brewers' yeast.

Antiberiberi Vitamin Concentrate-Metz Tablets: Each tablet represents the antineuritic potency of 10 gm. of freshly pressed brewers' yeast.

Antiberiberi Vitamin Concentrate-Metz Ampules, 1 c.c.: an aqueous solution of Antiberiberi Vitamin Concentrate-Metz, containing in 1 c.c. the antineuritic potency of 10 gm.

of freshly pressed brewers' yeast. This solution is stated to retain its potency for at least six weeks.

Antiberiberi Vitamin Concentrate-Metz is not claimed to be identical in effect with vitamin B in the sense of McCollum's nomenclature, but rather with the antiberiberi vitamin as first described by Funk (*J. Physiol.* **45**:75, 1912). Funk's attempt was directed to the isolation of a substance that would cure beriberi and particularly its analogue, avian polyneuritis. Subsequent investigators (Hoskins, Osborne, Mendel, McCollum et al.) found that yeast extract and many other food derivatives keep (or maintain) rats, mice and other animals eating and growing if the other components of the diet are adequate. These also prevented and cured avian polyneuritis. The Metz Laboratories claim that the Antiberiberi Vitamin Concentrate-Metz stimulates the growth of rats pronouncedly although not to the same extent as the vitamin B (according to McCollum's nomenclature). Whether the antineuritic factor is identical with the "yeast effect" (McCollum B factor) in growing rats is debated. Funk claims that the rat factor for growth contains something more than the antineuritic—that is, the conventional yeast B is a mixture, one of which (D) is essential for yeast. This likewise is debated.

APROTEIN AND APROTINE NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 18, 1922, p. 1786

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

Aprotein and Aprotine are casein preparations marketed as "the foremost tissue and body builders," by The John Norton Co., Columbus, Ohio.

Aprotein.—This preparation (formerly designated Diaprotein No. 2, Granulated Food Casein) is described in the advertising issued by The John Norton Co. (formerly the Diaprotein Co.) as:

"A scientifically, specially prepared granulated casein precipitated from fresh, skimmed milk, concentrated to a high degree."

Though stated to be simple casein, it is designated as a "compound food" which is "readily soluble."

In the information sent the Council by the Diaprotein Co. the product was alleged to have the following composition:

Moisture	8.42
Fat	0.45
Protein	81.47
Ash	5.90
Sugar (lactose)	3.72

Analysis of the submitted specimen showed that it contained *three times* as much fat as claimed and but *one-fourth* as much sugar. The product was not soluble in any ordinary sense. Its high ash and low acidity suggested the presence of combined or occluded calcium.

Aprotein is inadmissible to New and Nonofficial Remedies because, (1) though claimed to be casein, its composition does not agree with that of a good dietetic casein and was not found to have the composition claimed for it and (2) it is not only irrational but also a hindrance to therapeutics to market a well-known substance like casein under a fanciful name.

Aprotine.—In the information sent the Council, this preparation is designated "a sodium-calcium caseinate derivative" prepared by precipitating an acid calcium caseinate from skimmed milk by addition of acid, washing the precipitate, mixing it with sodium bicarbonate and drying. While the term "sodium-calcium caseinate derivative" suggests that Aprotine is a definite sodium-calcium caseinate, the following sets of analyses, furnished by the manufacturer to show the limits of variation in the composition of the product prove it to be a decidedly indefinite mixture:

	SPECIMEN A Per Cent.	SPECIMEN B Per Cent.
Moisture	10.83	8.42
Fat	4.64	0.43
Lactose	Trace	3.78
Nitrogenous matter	76.78	81.47
Ash	7.75	5.90
Total	100.00	100.00

In the advertising furnished the Council, Aprotine is not designated sodium-calcium caseinate derivative, but is claimed to be "granulated casein." In an advertising pamphlet, under "Aprotine Analysis" appears the analysis given for "Specimen B" in the table just given. From this one would infer that Aprotine always has the composition indicated by this analysis, whereas the information furnished the Council made it perfectly plain that the product is a most variable one.

Furthermore, a comparison of the "Aprotine Analysis" in the advertising pamphlet with the statement of composition of Aprotein which was furnished the Council suggests that these two preparations are the same:

	APROTINE Per Cent.	APROTEIN Per Cent.
Protein	81.47	81.47
Lactose	3.78	3.72
Fat	0.43	0.45
Ash	5.90	5.90
Moisture	8.42	8.42
Total	100.00	99.96

In the advertising is the description:

"APROTINE. Compound food. A concentrated form of nourishment which has proven a very satisfactory and effective body builder and restorer, and is foremost in the replacing of tissue elements, which have been destroyed through illness or otherwise."

It is recommended:

"In any wasting disease, such as tuberculosis, anemia, faulty assimilation. For anyone taking a great deal of exercise. For expectant and nursing mothers, and before and after an operation. For lack of vitality and malnutrition, APROTINE taken in either liquid or solid food, will noticeably increase the strength and vitality."

These recommendations suggest that Aprotine is possessed of therapeutic properties whereas its effects will not differ from those obtained from cottage cheese. It is absurd to suggest that the administration of casein is indicated in anemia, lack of vitality and malnutrition or to advise the consumption of Aprotine rather than of good food for "anyone taking a great deal of exercise."

Aprotine is inadmissible to New and Nonofficial Remedies because (1) the statements made in regard to its composition are indefinite and misleading, (2) the therapeutic claims are unwarranted and (3) there is no evidence to indicate that this casein preparation presents an improvement over casein-N. N. R.

BARIUM SULPHATE FOR ROENTGEN-RAY WORK

Report of the Council on Pharmacy and Chemistry

Abstracted in The Journal A. M. A., Nov. 11, 1922, p. 1687

The Council has adopted the report of the American Medical Association Chemical Laboratory on Barium Sulphate for Roentgen-Ray Work that follows and directed that the revised tests and standards be included in New and Nonofficial Remedies, 1923.

W. A. PUCKNER, Secretary.

In consideration of the increasing use of barium sulphate in roentgen-ray work, the Council decided to describe barium sulphate for roentgen-ray work in New and Nonofficial Remedies. The description which appears in New and Nonofficial Remedies, 1917, was prepared after consulting interested manufacturers. This description has appeared in subsequent editions of New and Nonofficial Remedies with but minor changes.

A firm which manufactures barium sulphate for roentgen-ray work criticized the test for this substance, which limits the amount of permissible phosphate.

The firm stated that in the manufacture of barium sulphate for roentgen-ray work it has been the aim to supply an article of as high a degree of purity as is commercially obtainable and that the test which it employs to limit the amount of soluble barium salts is more stringent than that prescribed in New and Nonofficial Remedies. The firm stated that, though its product was free from objectionable impurities and equal to that of other brands on the market, it was confronted with the difficulty that its product, when tested by the New and Nonofficial Remedies standards, appears to contain acid-soluble barium salts. The firm urged that the phosphate test be omitted, in that it shows a noticeable reaction for phosphate when barium phosphate is totally absent, but when nonpoisonous and unobjectionable phosphates, such as calcium phosphate, were present.

The manufacturer submitted the tests which were used for the control of barium sulphate for roentgen-ray work. These included the test for soluble barium salts and also the following test for the fineness (fluffiness) of the product:

> Introduce 15 Gm. of the material into a 50 cubic centimeter glass-stoppered cylinder and add sufficient water, so that, after thoroughly agitating the mixture, it has a total volume of 50 Cc. After this mixture has stood for ten minutes, the upper or aqueous layer should not exceed 5 Cc.

The objection to the phosphate test appeared well founded, and the proposed revision of the text for soluble barium salts and the "fluffiness" test worthy of consideration; therefore, the A. M. A. Chemical Laboratory drew up a tentative revision of the N. N. R. standards which omitted the phosphate test and included the more sensitive barium test and the "fluffiness" test. It submitted this revision to those firms whose brands of barium sulphate for roentgen-ray work had been admitted to New and Nonofficial Remedies.

In general, the replies which were received indicated that the firms were ready to accept the more stringent test for barium salts, other than barium sulphate, and also the "fluffiness" test. One firm, however, definitely objected to the latter test on the ground that users of barium sulphate in roentgen-ray laboratories had found difficulty in preparing suspensions with a too "fluffy" product. Some of the firms did not favor omission of the phosphate test on the ground that appreciable amounts of insoluble phosphate, such as calcium phosphate, should not be permitted in barium sulphate, and two firms recommended the adoption of a test limiting the water and acid soluble material in barium sulphate. For the latter test, the argument was advanced that, under the present N. N. R. standards, large quantities of foreign salts are permitted.

Since one firm held that a "fluffy" barium sulphate had proved unsatisfactory, inquiry was made of a representative

group of roentgenologists as to whether they considered it desirable that barium sulphate be required to be in a finely divided physical condition. Inquiry was also made as to the brands which had been found satisfactory.

In general, the twenty-eight replies which were received held that barium sulphate should be in as fine a state of subdivision as possible. However, many of the replies held that extreme fineness was not essential. This was emphasized by the enumeration of the brands that had been used with satisfaction. One correspondent stated that a medium fineness was to be preferred and that difficulty had been experienced in the use of a very fine powder. Another correspondent stated that a powder passing a forty mesh sieve was satisfactory, and another that a product was acceptable so long as it did not clog up an enema tube (containing no particles larger than a grain of wheat). Several objected to the high price charged for some of the very finely divided products. The following is the reply of a prominent roentgenologist:

> We have used barium sulphate from various manufacturers, and have found little difference, except as to price. For example, some manufacturers label their barium sulphate, "Specially prepared for x-ray purposes," and boost the price three or four hundred per cent. For the last ten years we have used ————————'s chemically pure barium sulphate. It has always proved entirely satisfactory. Other things being equal, I think that perhaps the barium sulphate which remains longest in suspension would be most desirable. To sum up, I would answer your first question by saying that it is not essential for the barium sulphate to be any more finely divided that it is in the various brands that we have used. Second, all brands were found to be satisfactory.

From the replies of the users of barium sulphate, it appears that the fluffiness test is not essential. It has the objection that a powder containing a small proportion of very fine material will respond favorably to the test, even though it contains a relatively large proportion of coarse particles.

The replies also make it clear that the phosphate test (which makes a product containing a negligible amount of calcium phosphate inadmissible) is unnecessary. The adoption, in its place, of a test which shall require reasonable freedom from foreign salts, along with tests which shall guarantee freedom from water soluble and acid soluble barium salts and freedom from heavy metallic salts, such as those of lead, would appear adequately to insure a barium sulphate for roentgen-ray work which is of acceptable quality and which can be produced at a reasonable price.

The revised tests and standards for barium sulphate which were drawn up on the basis of the available evidence were submitted for criticism to the firms whose brands of barium sulphate for roentgen-ray work stand admitted to N. N. R. In consideration of the replies received, the laboratory recommends the adoption of the following tests and standards for

barium sulphate for roentgen-ray work, in place of those now in New and Nonofficial Remedies:

BARIUM SULPHATE FOR ROENTGEN-RAY WORK.—**Barii Sulphas Roentgenographicus.**—Barium sulphate freed from soluble barium salts.

Barium sulphate for roentgen-ray work is a fine white odorless, tasteless and relatively light powder, free from grittiness, and is insoluble in water and organic solvents as well as in aqueous solutions of acids and of alkalies.

Mix 0.5 Gm. of barium sulphate for roentgen-ray work with 2 Gm. each of anhydrous sodium carbonate and anhydrous potassium carbonate; heat the mixture in a crucible until fusion is complete; treat the resulting fused mass with hot water, and then filter. Acidify a portion of the filtrate with hydrochloric acid; add 1 Cc. of barium chloride solution; a white precipitate forms (*sulphate*). Dissolve a portio nof the well washed residue in acetic acid and add 1 Cc. of potassium chromate solution; a yellow precipitate forms (*barium*). Dissolve another portion of the well-washed residue in a smal lamount of hydrochloric acid; place a drop of the solution on the loop of a clean platinum wire, and ignite in a nonluminous flame; a green color is imparted to the flame (*barium*).

Boil 10 Gm. of barium sulphate for roentgen-ray work with 100 Cc. of hydrochloric acid, 1 per cent., for ten minutes, and add sufficient water to restore the original volume. Cool the mixture and filter through a paper which has been washed previously with the diluted hydrochloric acid, returning the first portions if necessary until a perfectly clear filtrate is obtained. Evaporate 50 Cc. of the filtrate to dryness on the water bath; add 2 drops of hydrochloric acid, U. S. P., and 10 Cc. of hot water; filter through a hydrochloric acid washed filter; wash with 5-10 Cc. of hot water, and evaporate the filtrate to dryness in a tared dish on the water bath. The residue, when dried to constant weight at from 100 to 110 C. should not be more than 0.3 per cent. (*limit of water and dilute acid soluble nonvolatile material*). Treat the residue with 10 Cc. of water; filter the solution through a hydrochloric acid washed filter and add 0.5 Cc. of diluted sulphuric acid to the filtrate; no turbidity should develop within one-half hour (*soluble barium salts*).

Boil 5 Gm. of barium sulphate for roentgen-ray work with 50 Cc. of diluted acetic acid. Filter while hot and saturate the clear filtrate with hydrogen sulphide; no turbidity or coloration should be formed (*heavy metals*).

Triturate 2 Gm. of barium sulphate for roentgen-ray work with 5 Cc. of concentrated hydrochloric acid, then add 10 Cc. of a freshly made, saturated solution of stannous chloride; no dark coloration occurs within one-half hour (*arsenic*).

BERBERIN HYDROCHLORID OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report:

W. A. PUCKNER, Secretary.

Berberin hydrochlorid was admitted to New and Nonofficial Remedies, 1910, with the statement under "Actions and Uses" that, given by mouth it acts like other bitter drugs and that it has been used as a bitter tonic for diarrhea and the vomiting of pregnancy, and as a febrifuge.

During the years that berberin hydrochlorid has been on the market, no clear indications of its use have developed. As a bitter tonic, it is replaced with advantage by the liquid preparations of bitter drugs that are official.

Since the continued inclusion of berberin hydrochlorid in New and Nonofficial Remedies may lead to an erroneous estimate of its usefulness, the Council directed the omission of this drug and the accepted brand of it on the ground that it is essentially useless and therefore detrimental to the best interests of medicine and the public. As a matter of record, the description which appeared in New and Nonofficial Remedies, 1922, is appended:

BERBERINE HYDROCHLORIDE.—**Berberinae Hydrochloridum.**—$C_{20}H_{17}NO_4HCl+2H_2O$.—The Hydrochloride of an alkaloid obtained from *Hydrastis canadensis, Berberis vulgaris* and other plants.

Actions and Uses.—Given by mouth, berberine hydrochloride acts like other bitter drugs in the stomach. Very large doses, although not fatal, cause diarrhea, tremor, general weakness, low blood pressure (from depression of vasomotor center and of cardiac muscle), rapid pulse (depression of vagus endings) and quickened respiration. Recovery is slow. Nephritis may be present. Subcutaneous injection kills by paralysis of respiration, with symptoms of asphyxia and paralysis. This drug has been used as a bitter tonic, for diarrhea, and the vomiting of pregnancy, and as a febrifuge.

Dosage.—From 0.06 to 0.3 Gm. (1 to 5 grains). As much as 20 grains has been taken without obvious effect other than a loose stool.

Berberine hydrochloride occurs as bright yellow, acicular crystals or amorphous powder. It is slightly soluble in alcohol, to which it imparts a deep yellow color. It is soluble in 300 parts of cold water, but dissolves more easily in hot water.

An aqueous solution of berberine or its salts treated with chlorine or bromine water produces a blood-red color. Bromine water in excess precipitates the reddish brown berberine tetrabromide hydrobromide—$C_{20}H_{17}NO_4.Br_4HBr$, which is converted by washing with alcohol, or heating to 100 C., to the yellow-brown berberine dibromide hydrobromide $C_{20}H_{17}NO_4.Br_2.HBr$. Ammonium sulphide precipitates from an alcoholic solution of berberine hydrochloride the polysulphide $(C_{20}H_{17}NO_4)_2H_2S_5$, which crystallizes in brown black needles. Berberine solutions, even if very dilute, when treated with potassium iodide solution yield a yellow precipitate of berberine hydroiodide.

BI-OXO-DYN NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 25, 1922, p. 1867

The Council has authorized publication of the following report.

W. A. Puckner, Secretary.

Bi-Oxo-Dyn is put out by "Bi-Oxo-Dyn," Savannah, Ga. According to the information furnished the Council by W. F. Kennedy, Jr., who states that he is the originator and maker of this product, the quantitative composition of Bi-Oxo-Dyn is:

"Bismuth Hydroxide.....14 per cent.
"Iodine ..... 2 per cent.
"Dioxide (Borated) ($H_2O_2 + H_3BO_3 + H_2C_4H_4O_4$).....½ to 1 per cent.
"Menthol .....3¾ grains to ounce
"Hydrastine .....½ gr. to ounce
"Petrolatum .....*q. s.*, to ounces 1"

The following statement bearing on the composition of Bi-Oxo-Dyn appears on the trade package:

"Bi-Oxo-Dyn. Iodized petroleum of Bismuth Dioxide and Iodine. Chloral, 3 per cent., Iodine, 2 per cent., Dioxide (non-toxic)."

Relative to the iodin content it is claimed that Bi-Oxo-Dyn "is an iodized petroleum of 2 per cent. iodine. . . ." With reference to the dioxid constituent of the preparation, the advertising circular declares that the "Di-Oxide that enters into Bi-Oxo-Dyn is identical with Hydrogen Di-Oxide. This valuable Di-Oxide is in turn borated." The following statement with reference to the dioxid said to be contained in the product is given in a letter sent by W. F. Kennedy, Jr., to the Council: ". . . the Dioxide that is used as the antiseptic in Bi-Oxo-Dyn is obtained from Hydrogen Dioxide (Strong Sol.) treated with Anhydrid; this is in turn borated."

From the various claims submitted it is to be inferred that Bi-Oxo-Dyn contains 2 per cent. of free (elementary) iodin and 0.1 per cent. of hydrastin, 3 per cent. of chloral hydrate, 14 per cent. of bismuth hydroxid, 1 per cent. of menthol in a petrolatum base, and from ½ to 1 per cent. of a compound of succinyl peroxid and boric acid.

The A. M. A. Chemical Laboratory reports that Bi-Oxo-Dyn contains no free iodin but that it contains combined iodin in the form of iodid ions. The presence of hydrogen peroxid or other peroxids could not be demonstrated. If present, their amounts must be minute. Since it is known that peroxids, particularly hydrogen peroxid and succinyl peroxid, are unstable in the presence of organic matter, the presence of peroxids in a mixture of the character of Bi-Oxo-Dyn would not be expected. In a circular addressed to "Physicians Who Think" Bi-Oxo-Dyn is designated as a "Urethral Bland—Rectal Lubricant" and it is stated:

"Bi-Oxo-Dyn is of inestimable value for injecting into the inflamed urethra and is recommended in specific urethritis and uterine hemorrhage and painful chordee."

In this circular instructions are given for the use of this indefinite, complex and irrational hodgepodge in:

"Urethritis (Acute and Chronic), Prostatorrhea—Prostatis (Acute or Chronic), Cystitis—Vaginitis (Male or Female), Fistulas, Piles, Orchitis, Epidymitis, and Bubo."

The Council declares Bi-Oxo-Dyn inadmissible to New and Nonofficial Remedies because (1) the statements of its composition are indefinite, misleading and incorrect; (2) the therapeutic claims are unwarranted; (3) the name is not descriptive of the composition of the product and is misleading, and (4) Bi-Oxo-Dyn is a complex, irrational mixture, the marketing of which is detrimental alike to the interests of the public and of scientific medicine.

BLAUDULES

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

Blaudules are marketed by the Wm. S. Merrell Company with the statement that they correspond to pills of ferrous carbonate U. S. P. in ferrous carbonate strength but to be made up with an "Oily excipient and enclosed in soft gelatin capsules with exclusion of air to prevent oxidation."

The following statement in regard to this proprietary modification of a pharmacopeial article is made in the Blaudule advertising: "The only drawback to the use of Pills of Ferrous Carbonate has been the fact that the ferrous carbonate changes rapidly to the ferric salt when exposed to the air because of oxidation." "In order to overcome this difficulty experiments were conducted in the Merrell Laboratories in order to devise a form of providing the ferrous carbonate which would overcome the difficulty of oxidation and at the same time furnish a satisfactory product for administration. These experiments resulted in the preparation of Blaudules."

However, while the Merrell Company claims that Blaudules present "a new and convenient form of supplying fresh Ferrous Carbonate" and that the official pills deteriorate rapidly, oily suspensions of ferrous carbonate were on the market in 1914 and further a study of the subject in the A. M. A. Chemical Laboratory demonstrated that in fact the asserted rapid deterioration of ferrous carbonate pills did not occur. The Council in 1915 declared Frosst's Blaud Capsules, claimed to represent freshly precipitated ferrous carbonate incorporated with castor oil, inadmissible to New and Nonofficial Remedies (Reports of Council on Pharmacy and Chemistry, 1915, p. 164).

In the same year a report from the Association's Chemical Laboratory (The Quality of Commercial Blaud's Pills, *The Journal A. M. A.*, April 17, 1915, p. 1344) demonstrated that the pills of ferrous carbonate on the market had not deteriorated to any considerable extent through oxidation. The result of this examination refuted the commonly assumed instability of ready made Blaud's pills; further, the examination demonstrated that the various proprietary preparations, including the gelatine encapsulated oily suspensions showed no advantage over the ordinary, official, pill of ferrous carbonate.

The Council declared the product Blaudules inadmissible to New and Nonofficial Remedies because it represents an unessential modification of an official article marketed under a proprietary name and with claims of originality and superiority that are unwarranted.

BUTYN

Report of the Council on Pharmacy and Chemistry

From the original report in The Journal A. M. A., Feb. 4, 1922, p. 343

The following report was presented to the Council on Pharmacy and Chemistry by the Committee on Local Anesthesia of the Section on Ophthalmology of the American Medical Association. The Council considered the report and authorized its publication.

W. A. PUCKNER, Secretary.

Council on Pharmacy and Chemistry of the American Medical Association—Gentlemen:

At your request the committee secured some samples of butyn, a new local anesthetic, which the manufacturers, the Abbott Laboratories, provided, and submitted it to animal experimentation and clinical trial. These experiments were begun several months ago by the individual members of the committee, and up to the present time seem to have been sufficiently extensive and conclusive to justify the report herewith submitted.

Though the committee was supplied with samples of powdered butyn, it was thought best to follow the suggestions of the manufacturers and experiment with a 2 per cent. solution, and later, under appropriate precautions, use solutions of great concentration. Accordingly, this report, except where otherwise noted, applies to results as obtained with the 2 per cent. solution.

In accordance with your suggestion, we recorded our observations as follows: anesthesia, including onset, depth, penetration and duration; side actions, including immediate and late irritation, changes in pupil diameter, vascularity, intra-ocular pressure, desiccation of cornea and other side

actions; toxic systemic effects, and comparative value in ophthalmic work, including major as well as minor operations. Under these various headings our observations are as follows:

ANESTHESIA

Repeated trials indicate a striking rapidity of anesthetic action, as indicated by the fact that one minute after one instillation of a 2 per cent. solution of butyn in the eye, surface anesthesia is sufficient to permit of touching the cornea or removing superficially placed foreign bodies without discomfort. This surface anesthesia lasts from fifteen to twenty minutes, when, in the average case, it begins to subside. Occasionally the anesthesia has been noted for from twenty-five to thirty minutes. The depth of anesthesia produced by one instillation is not sufficient for operations, or for even the removal of deeply embedded foreign bodies in the cornea. It is, however, sufficient for the painless extraction of superficially placed foreign bodies, the application of irritating astringents, and the determination of intra-ocular pressure with the tonometer. When the number of instillations is increased, there is a marked increase in the depth, degree and duration of the anesthesia.

For operative work the committee has followed the plan generally used when cocain is the anesthetic employed, which consists in four instillations, three minutes apart, the operative work to be begun from five to ten minutes after the last instillation. This method resulted in the production of an anesthesia deep enough and complete enough for all of the commoner major operations on the eye, with the exception of enucleation, which up to the present time has not been performed under butyn anesthesia by any member of the committee. The height of anesthesia appears to be secured at about five to eight minutes after the fourth instillation of the anesthetic, and its duration is from twenty to thirty minutes in the average case, though frequently lasting much longer, and in a few instances even the surgical anesthesia has lasted for nearly an hour.

SIDE ACTIONS

One instillation of a 2 per cent. solution of butyn almost invariably produces a mild hyperemia of the conjunctiva. This hyperemia is not noticeably increased by subsequent instillations of the anesthetic. It is controlled readily by epinephrin solution, or may be averted by combining epinephrin with the butyn. When epinephrin is not employed, the hyperemia gradually disappears in from thirty to sixty minutes. The hyperemia seems to be more marked and of longer duration in diseased eyes, even though the active stage of disease has passed.

Butyn solutions do not affect the pupil diameter in any way, and produce no change in the intra-ocular pressure. There also is no desiccation or disturbance in the nutrition of the cornea, so far as has been determined. We also are of the

opinion that butyn solutions do not deteriorate rapidly, even when exposed to air and light, nor is their anesthetic efficiency impaired by boiling.

TOXIC SYSTEMIC EFFECTS

In beginning the use of butyn, we were confronted with the statement of the Research Committee of your Council to the effect that butyn is two and one-half times more toxic than cocain when injected hypodermically into albino rats, and that the lethal dose of butyn when injected intravenously into cats is about equal to that of cocain. One member of our committee, Dr. H. M. Langdon, in conjunction with Dr. Herbert Fox, director of Pepper Clinical Laboratory of the University of Pennsylvania, has conducted some animal experiments with a view to determining the toxicity of butyn, and the result of those experiments confirmed those of the Research Committee of your Council. The manufacturers state that their animal experiments substantiate these findings.

However, in no instance, including the hundreds of times that butyn has been used by the members of the committee for minor as well as major operations on the eye, as well as in operative work in the nose and throat, have the slightest systemic toxic manifestations been noted. Following the report that surgeons and dentists had freely used butyn for surface and infiltrative anesthesia with no toxic results, some of the members of the committee have used butyn in paste and in concentrated solutions as a topical application for operative work in the nose as well as in the eye, with no evidence of toxic effects. The committee, in comparing the effects on animals and men, is inclined to believe, as suggested by Professor Sollmann of your Research Committee, that there may be (1) differences in absorbability from mucous membranes; (2) different ratio of toxicity in man and animals, and (3) different frequency of idiosyncrasies. It is probable that if butyn is used as extensively as cocain, there will be cases of toxic effects reported, and then it is a question to decide whether the symptoms are due partly to psychic causes, to idiosyncrasy, or to error in using more of the drug than required to produce the desired effect.

COMPARATIVE VALUE IN OPHTHALMIC WORK

In the use of butyn as a local anesthetic, cocain is used as a comparison, and our committee is unanimous in the opinion that butyn for purely surface anesthesia for minor operations is superior to cocain for the reason that it acts more quickly, fewer applications are required, there are no objectionable side actions, such as dilatation of the pupil or desiccation of the cornea, and the anesthesia is more profound. For producing surface anesthesia for the removal of foreign bodies from the eye, the application of irritating astringents, estimating the intra-ocular pressure with the tonometer, or for any

of the minor operative procedures, butyn solutions seem to be very useful

For major operations, particularly those requiring opening of the eyeball, such as iridectomy and cataract extraction, the technic usually employed in obtaining a cocain anesthesia is employed in obtaining butyn anesthesia. The use of a 2 per cent. solution of butyn results in a more profound anesthesia than is obtained with a 4 per cent. solution of cocain, and without any objectionable side actions. For operations on the extrinsic muscles of the eyeball the results are equal to those obtained with cocain, though the committee believes that a solution stronger than 2 per cent. may be preferable.

INFILTRATION ANESTHESIA

In view of our understanding that butyn might prove quite toxic, we did not at first use butyn for the production of infiltration anesthesia, and only recently have we undertaken some experimental work, using both 0.5 and 1 per cent. solutions for the purpose. While our experience is limited, up to the present time we have had very satisfactory results. A 0.5 per cent. solution of butyn has been injected rather freely into the tissues for the purpose of doing advancements of the extrinsic muscles of the eyeball, for the opening of abscesses in the orbit and the appendages, and as an adjunct in operations in which the eyeball is opened. In the few cases in which this has been tried, a deep and satisfactory anesthesia has been secured. A more comprehensive report covering infiltration anesthesia with butyn will be made later, and will form a part of the committee report to be presented before the Section on Ophthalmology of the American Medical Association.

BUTYN IN NOSE AND THROAT WORK

The chairman of the committee has used butyn solutions as a routine for several months in nose and throat work, and the results, in brief, are considered worthy of being a part of this report, as they bear directly on the question under consideration.

The recognition of the fact that the nasal mucous membrane possesses greater area and increased absorbing surface, as compared to the conjunctiva, made it advisable to begin with weak solutions and use smaller amounts until the toxicity in the average human being could be determined. Therefore, at first one application of butyn in 1 per cent. solution was made over small areas within the nose, and tests for anesthesia were made subsequently at intervals of from one to three minutes. These tests indicated a mild surface anesthesia produced within one minute. Later these tests were extended to include surface anesthesia sufficient for everything pertaining to an examination, including the use of applicators and eustachian catheters, as also for the allaying of discomfort occasioned by the use of astringents

or escharotics. Finally, butyn in 5 per cent. solution was employed as a routine in producing anesthesia for all of the major intranasal operations.

As butyn produces no ischemic effects, there is no shrinking of tissues following its use; hence the condition of the intranasal tissues remains approximately the same except for the anesthesia. This is a valuable feature in those cases in which a portion or all of a turbinate is to be removed. When combined with epinephrin, butyn in 5 per cent. solution produces an anesthesia sufficient for all of the major intranasal operations, including submucous resection of the septum, turbinotomies and intranasal operations on the accessory sinuses. Not only is the anesthesia very satisfactory, but up to the present time not the slightest toxic effects have been noted in the hundreds of operative cases in which the anesthetic has been used. Among these cases are thirty-eight consecutive submucous resections of the septum and twenty-six consecutive intranasal operations on the nasal accessory sinuses.

The technic employed in obtaining anesthesia has been similar to that employed in obtaining anesthesia from cocain, except that the butyn has not been used in greater concentration than 5 per cent. solutions. The anesthesia lasts from thirty to forty minutes.

EXCEPTIONS

In comparing butyn anesthesia with cocain anesthesia, the committee has discovered that occasionally a patient seems to be immune to complete local anesthesia from butyn employed in either 2 or 5 per cent. solution. These cases are relatively few. The failure to secure complete local anesthesia in this very limited number of cases may be due to psychic disturbances or a highly neurotic temperament, or perhaps to a peculiar idiosyncrasy which makes the patient, in a measure, intolerant to the anesthetic effect of the drug.

SUMMARY OF CLINICAL RESULTS

The committee now has a detailed record of clinical experiences with butyn in the performance of several hundred major operations on the eye and the nose and throat. These include cataract extraction, iridectomy (including that done for the relief of glaucoma), trephine operation, magnet extraction of foreign bodies, tenotomy and advancement of the ocular muscles, pterygium operations, removal of cysts and other tumors from the eyeball or lids, grattage, and a few cases of plastic surgery of the lids including the correction of entropion and ectropion. As yet no enucleations have been performed under butyn anesthesia, but we believe that such an operation may be performed very satisfactorily.

Local anesthesia is put to the best test when used for operations which involve cutting the iris or extrinsic muscles of the eyeball. The committee, December 1, had a record of thirty-nine cataract extractions combined with iridectomy,

twenty-three iridectomies for glaucoma or as preliminary to cataract extraction, twenty-one capsulotomies and iridotomies, and eight muscle advancements, all satisfactorily done under butyn anesthesia. Aside from this there were a large number of other eye operations requiring less profound anesthesia which were performed satisfactorily under butyn.

In nose and throat surgery, butyn anesthesia has been used in practically all of the major intranasal operations, including submucous resection of the septum, turbinotomies, opening of accessory sinuses (including exenteration of the ethmoid cells), tonsillectomy and adenectomy, in all numbering nearly 200 cases.

In practically all of these cases, including nose and throat as well as the eye, the anesthesia has been very satisfactory, and the few exceptions are considered exceptions such as might occur under any local anesthetic. Two per cent. solutions of butyn were used for nearly all of the eye operations, whereas 5 per cent. solutions were used in most of the nose and throat operations. If more extended experience confirms out present belief that there is little cause for apprehension concerning toxic effects from the judicious use of butyn, then a 5 per cent. solution may be the strength of concentration preferred in some of the major operations in which profound local anesthesia is desirable and has heretofore been sometimes difficult to secure.

A detailed report of each and every one of our cases would extend this report to an unnecessary length, but will be submitted if deemed either advisable or necessary.

CONCLUSIONS

The results of the clinical and experimental use of butyn seem to justify the committee in arriving at the following conclusions:

1. It is more powerful than cocain, a smaller quantity being required.
2. It acts more rapidly than cocain.
3. Its action is more prolonged than that of cocain.
4. According to our experience to date, butyn in the quantity required is less toxic than cocain.
5. It produces no drying effect on tissues.
6. It produces no change in the size of the pupil.
7. It has no ischemic effect and therefore causes no shrinking of tissues.
8. It can be boiled without impairing its anesthetic efficiency.

Respectfully submitted,

ALBERT E. BULSON, JR., Fort Wayne, Chairman.
WILLIAM ZENTMAYER, Philadelphia.
EDGAR S. THOMSON, New York City.
H. MAXWELL LANGDON, Philadelphia.
HARRY S. GRADLE, Chicago.

CALCIUM PHENOLSULPHONATE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has voted to omit calcium phenolsulphonate (sulphocarbolate) and the accepted brands of this product from New and Nonofficial Remedies and has authorized publication of the following statement.

W. A. PUCKNER, Secretary.

In 1911 a subcommittee of the Council reported:

"The phenolsulphonates (sulphocarbolates) are probably not very valuable as therapeutic agents. Calcium phenolsulphonate has little to recommend it over the official sodium phenolsulphonate and it may be held as an unnecessary duplication of an official substance. Yet its provisional inclusion in New and Nonofficial Remedies is recommended, since it contains two radicals (the calcium and the phenolsulphonic) often given in certain conditions and it may, for that reason, be found to have some advantages over sodium phenolsulphonate."—(Report of Council on Pharmacy and Chemistry, 1911, p. 44.)

In accordance with the recommendation of its subcommittee, the Council voted to admit calcium phenolsulphonate to New and Nonofficial Remedies and accepted those brands which complied with the Council's rules and the standards which were adopted. In the N. N. R. description of calcium phenolsulphonate, it is stated that the salt has the actions and uses of other phenolsulphonates (sulphocarbolates) and that it is believed by some to be an intestinal antiseptic, but that most pharmacologists regard the antiseptic powers of the phenolsulphonates as feeble. Since the acceptance of calcium phenolsulphonate in 1911, no acceptable evidence for the therapeutic value of the phenolsulphonates appears to have been published. The use of phenolsulphonates has proved disappointing and, as a result has been discontinued. Because of this decreasing estimate of the value of phenolsulphonates, the subcommittee on scope decided to omit sodium phenolsulphonate and zinc phenolsulphonate (the two salts now official) from the edition of the U. S. Pharmacopeia which is now in process of preparation. (Tenth Revision of the United States Pharmacopeia, E. Fullerton Cook, Chairman, *Am. J. Pharm.*, February, 1922, p. 103).

The following statement, which appears in the United States Dispensatory, Ed. 20, p. 1035, under Sodii phenolsulphonas U. S., concisely indicates the present status of the phenolsulphonates:

"The phenolsulphonates or sulphocarbolates, as they are commonly called, were introduced into medicine with the idea of obtaining the antiseptic action of carbolic acid in a nontoxic form, for it is well known that the combination of sulphuric acid with phenol destroys its toxicity; but it has been shown by Withers that the phenolsulphonates are not possessed of any antiseptic power. The claim which has been made that they are decomposed in the intestinal tract with the liberation of phenol is not supported by any scientific evidence and seems *a priori* improbable. There is neither sufficient clinical nor scientific evidence for the value of this drug in medicine. Sodium phenolsulphonate is, however, still employed as an intestinal antiseptic."

In consideration of the fact that the extended use of the phenolsulphonates in medicine has failed to demonstrate their therapeutic value, the Council directed the omission of calcium phenolsulphonate and the accepted brands from New and Nonofficial Remedies. The Council directed that, as a matter of record, the description of the drug which appears in the 1922 edition of N. N. R. be transferred to the Council Reports.

CALCIUM PHENOLSULPHONATE. — **Calcii Phenolsulphonas.**—Calcium Sulphocarbolate. — $[C_6H_4(OH)SO_3]_2Ca$. The neutral calcium salt of paraphenolsulphonic acid.

Actions and Uses. — Calcium phenolsulphonate has the actions and uses of other phenolsulphonates (sulphocarbolates). It is believed by some to be an intestinal antiseptic, but most pharmacologists regard the antiseptic powers of the phenolsulphonates as feeble.

It may be prescribed in diarrhea and in diseased conditions in which it is believed that there is an undue amount of intestinal putrefaction.

Dosage.—The average dose is 0.5 Gm. (8 grains).

Calcium phenolsulphonate occurs as a white, or faintly pinkish-white, almost odorless powder, having an astringent, bitter taste. At high temperatures the salt chars, emits inflammable vapors having an odor of phenol, and finally leaves a residue of calcium sulphate. The salt is easily soluble in water and in alcohol.

An aqueous solution of the salt (1: 100) should assume a pale violet color on the addition of ferric chloride solution. An aqueous solution of the salt (1: 100) should not respond to the time-limit test for *heavy metals* prescribed by the United States Pharmacopeia. An aqueous solution of the salt (1: 100), acidified with a few drops of diluted hydrochloric acid, should give no immediate turbidity after the addition of 1 Cc. of barium chloride solution (limit of *sulphate*). If dried to constant weight at 100 C., the salt should not lose more than 2 per cent. of its weight (absence of an undue amount of *water*) If from 0.5 to 1 Gm. of the salt is dried to constant weight at 100 C., the dried substance slowly ignited in an uncovered crucible (care being taken that the contents be freely exposed to the air). the residue cooled, moistened with sulphuric acid and again heated until the weight becomes constant, the residue will amount to not less than 35 per cent., nor more than 36 per cent. of the weight of the dried substance.

COLLENE NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Dec. 23, 1922, p. 2181

The Council has authorized publication of the following report which declares Collene not acceptable for N. N. R. because its composition is not correctly declared and because the therapeutic claims made for it are unwarranted.

W. A. PUCKNER, Secretary.

Collene (Collene Laboratories, Inc., New York) is said to be a solution in distilled water of 0.05 per cent. colloidal silver. The silver is claimed to be in the metallic state. The distinctive features of Collene as advertised are: (1) its colloidal nature, (2) the fineness and uniformity of the colloidal particles, (3) the absence of toxic effects and of a tendency to produce argyria, (4) its high potency in inducing increase of leukocytes and (5) its power to penetrate human tissues 3/16 of an inch. Collene is recommended:

"For all purulent infections of the skin and mucus membrane as Conjunctivitis, Pharyngitis, Gingivitis, wounds, abrasions, etc., as a dressing; for Post-operative Sinuses, Cystitis, Colitis, Endocervicitis, chronic and acute, acute endometritis, Gonorrhea as an injection one-half to full strength; intravenously for general infections as Pyaemia, Purulent Endocarditis, pneumonia and post-partum infections."

These briefly are the salient points advanced in the claims for Collene. Many sweeping statements are made of superiority and therapeutic value but they are based on no adequate evidence. Before a product can be pronounced the "best" of all silver germicides, it must have been subjected to rational and controlled experiments involving other germicidal silver compounds. Collene can hardly be asserted "uniformly superior" to other germicides until such experiments have been conducted. Neither can a product be said to have its place established in the treatment of disease until there is acceptable evidence to that effect. The unwarranted recommendation of Collene for intravenous injection illustrates the case in point. Injection of "Colloidal silver" caused "a great increase of leukocytes even up to 100 per cent. or more." Provided Collene were a colloidal silver preparation it might produce leukocytosis, but even if it were colloidal, the evidence available hardly warrants the claim that "Collene should be found remarkably effective" in certain fevers, and much less the statement that it can be "safely used intravenously" in these fevers. Aside from the general misleading tenor of the advertising, the Council found, when it took up the consideration of Collene, discrepancies between facts and claims.

The first point is that of composition. The Collene Laboratories claimed 0.05 per cent. of colloidal silver while the Council's examination showed that, in effect, the silver content of Collene was not colloidal but ionic.

Naturally this fact—aside from its bearing on the Council's requirement that a correct declaration of composition must be made—brought up two points of importance: (1) the part of the antiseptic power of Collene that is due to ionic silver and (2) the plausibility of the claim for "non-toxic effect" made in the face of Collene's ionic silver content. Certainly the ionic silver content indicates that the antiseptic effect of Collene is of similiar origin to that of silver nitrate and not to its alleged colloidal nature. In view also of the ionic silver present, the nontoxic effects are inherently improbable.

Instead of being "acid free," Collene has a slight acidity (a P_H of 5.2) which may be responsible in some measure for its irritant effect on sensitive tissues.

The claims for penetration of $\frac{3}{16}$ of an inch were based on experiments made on agar and the results were applied to the human tissues. These claims were later retracted by the company.

These findings of the Council were sent to the Collene Laboratories, Inc., and it asked time for the reconsideration of its claims. After a lapse of more than six months, the company offered a new report. This report presented no specific evidence on the questioned points; the letters sent from physicians were irrelevant or at best failed to indicate that any "rigidly controlled experiments" such as the Council had said were necessary had been performed. A few revisions, such as abandoning the penetration claim, were made, but on the whole they were not comprehensive enough, since the fundamental contentions in the Council's report were left untouched.

The Council declared Collene not acceptable for New and Nonofficial Remedies (1) because its composition is not correctly declared and (2) because of the extravagant and misleading tenor of the advertising.

CULTURE-LAC OMITTED FROM N. N. R. AND OPTOLACTIN NOT ACCEPTED

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 13, 1923, p. 127

The Council has authorized publication of the following reports.

W. A. Puckner, Secretary.

Culture-Lac

"Culture-Lac" is described in New and Nonofficial Remedies, 1922, as a culture of *Bacillus bulgaricus* manufactured by the Geck Laboratories, New York. The Special Pharmacal Products Co., Inc., Buffalo, N. Y., has advised the Council that it now owns and manufactures Culture-Lac. The product now marketed, however, is not the preparation described in New and Nonofficial Remedies as Culture-Lac but is said to be a culture containing *Bacillus acidophilus* and *Bacillus bulgaricus*.

In the advertising of Culture-Lac issued by the Special Pharmacal Products, Inc., it is stated:

"Owing to the difference of opinion of the medical profession as to the therapeutic value of the *Bacillus acidophilus* and the *Bacillus bulgaricus*, this laboratory, considering that the types were similar, also that both thrived in the same medium, decided to combine them and by so doing overcome any further objection."

This is not a valid reason for the sale of a mixture of *B. acidophilus* and *B. bulgaricus*. On the contrary, it is essential to therapeutic progress and in the interest of sound therapy that these two bacilli should be administered independently of each other.

The Council has decided that, on the basis of the present available evidence, preparations of *B. acidophilus* may be considered for admission to New and Nonofficial Remedies. In order, however, that an early estimate of the value of the bacillus as a therapeutic agent may be gained, the Council will admit such preparations only on condition that they are marketed under a properly descriptive name. Furthermore, the Council will not consider for acceptance any preparation containing *B. acidophilus* in admixture with other organisms unless acceptable evidence is presented to warrant the mixture.

In the advertising for the new Culture-Lac it is asserted:

"In considering divergent opinion as to whether the *Bacillus acidophilus* or the Bulgarian bacillus is the more active as intestinal antiputrefactives, it must be remembered that the fact has been thoroughly established by Metchnikoff and many other investigators, that functioning independently or both acting together when administered in combination, have marked therapeutic force."

This is an unwarranted therapeutic claim. The therapeutic use of *B. acidophilus* is distinctly in the experimental stage. Although there is evidence that the administration of sour milk products is at times beneficial, the theories advanced by Metchnikoff are entirely unsupported by scien-

tific evidence, and no one subscribes seriously to these opinions at the present time.

The Council directed that the Culture-Lac of the Geck Laboratories be omitted from New and Nonofficial Remedies because it is off the market. The Council declared the Culture-Lac of the Special Pharmacal Products Co., Inc., inadmissible to New and Nonofficial Remedies (1) because there is no acceptable evidence to show that the administration of a mixture of *B. bulgaricus* and *B. acidophilus* is rational; and (2) because the preparation is marketed with unwarranted therapeutic claims.

Optolactin

Optolactin is the proprietary, nondescriptive name applied by Fairchild Bros. and Foster to a tablet said to contain mixed cultures of the *B. bulgaricus* A and *B. acidophilus*. In the advertising the following reason for the marketing of this mixture is offered:

"This product, Optolactin, will enable those who attach a special importance to the *Bacillus acidophilus* to try it in combination with bacilli already well known. . . . And those who already use the *Bacillus bulgaricus* may employ this mixed culture with the assurance that Optolactin has all the qualities of the *Bacillus bulgaricus* of the Fairchild culture and with such new and important properties as may be derived from the inclusion of the *Bacillus acidophilus*."

Here, again, it must be emphasized that this is not a valid reason for the combination. In the interest of therapeutic progress and sound therapy it is essential that these two bacilli should be administered independently of each other.

In the circular which accompanies the trade package of Optolactin it is stated that *B. bulgaricus* "has now acquired a place in therapeutics for the purpose for which proposed by Metchnikoff and his colleagues, with his theory of auto-intoxication, disease resulting therefrom, and the ingestion of these bacilli in combating it." In consideration of the fantastic and erroneous statements which appear in the lay press about "auto-intoxication" and the endless ills said to result therefrom, this statement is likely to lead to the ill-advised use of Optolactin by the public.

The Council declared Optolactin inadmissible to New and Nonofficial Remedies (1) because there is no acceptable evidence to show that the administration of a mixture of *B. bulgaricus* and *B. acidophilus* is rational; (2) because the name is not descriptive of the composition of the preparation; and (3) because the circular accompanying the package is likely to lead to the ill-advised use of Optolactin by the public.

DIPHTHERIA ANTITOXIN SERUM (BURROUGHS, WELLCOME AND COMPANY) OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

The Council was informed that Burroughs, Wellcome and Co., does not have a license for the importation into the United States of biologic products as required under the federal law entitled "An act to regulate the sale of viruses, serums, toxins, and analogous products in the District of Columbia, to regulate interstate traffic in said articles and for other purposes."

As a condition for the acceptance of a biologic product for New and Nonofficial Remedies, the Council requires that its sale in the United States shall be authorized by the U. S. Treasury Department. Since Burroughs, Wellcome and Co., was no longer licensed to sell its Diphtheria Antitoxin Serum, a brand of unconcentrated diphtheria antitoxin, the Council directed the omission of this product from New and Nonofficial Remedies.

"ESTEROL" NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Dec. 16, 1922, p. 2102

The Council has authorized publication of the following report, declaring "Esterol" (Frederick Stearns & Co.) inadmissible to New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

"Esterol" is the proprietary and nondescriptive name under which the firm of Frederick Stearns & Co. markets benzyl succinate. Benzyl succinate has been proposed as a substitute for benzyl benzoate on the ground that, being insoluble in water, it is almost tasteless and does not produce the gastric discomfort which benzyl benzoate is said, at times, to cause.

As might be expected from its composition, benzyl succinate has the action of benzyl esters, as has been determined by Macht (*Proc. Soc. Exper. Biol. & Med.* **38**:177, 1921) and also reported by Bye (*J. Indust. & Engin. Chem.*, March, 1921, p. 217). The available evidence does not permit judgment of the value of benzyl succinate as compared with that of benzyl benzoate. Thus while Nielsen and Higgins (*J. Lab. & Clin. Med.* **6**:388, 1921; **7**:69, 1921) have reported that in alkaline solution the succinate is hydrolyzed more rapidly than the benzoate, clinical trials carried out by Macht (*loc. cit.*) indicated that its action is milder than that of

benzyl benzoate, probably because its insolubility retarded its absorption. The evidence was such as to warrant the admission of benzyl succinate to New and Nonofficial Remedies (THE JOURNAL, Sept. 24, 1921, p. 1023), but with the caution that its actual value remains to be determined.

The proprietary brand of benzyl succinate sold as "Esterol" is inadmissible to N. N. R. because it violates the principles and rules that govern the acceptance of articles as follows:

1. Proprietary names for medicinal articles are recognized only if the Council deems the use of such exclusive names to be in the interest of public welfare. In consideration of the benefits which may come from the discovery of a therapeutic agent, the Council concedes to the person or firm that by right of discovery controls such a product, the right to name it. If the discovery that a previously known substance has therapeutic value is deemed of sufficient importance, the Council may recognize a proprietary name for such a substance if the name be applied by the person who makes the discovery. Benzyl succinate was described in the literature about fifty years ago by Zana and Guareschi (*Gazz. Chem. Ital.* **2**:256). The therapeutic value of benzyl esters was first reported on by D. I. Macht (*J. Pharmacol. & Exper. Therap.* **2**:419, 1915). Hence Stearns & Co. are neither the discoverers of the product nor of its therapeutic properties, and therefore the Council cannot recognize the proprietary name Esterol applied to it by Stearns & Co.

In presenting their brand of benzyl succinate to the Council, Stearns & Co. argued for the recognition of the proprietary name Esterol on the ground that they first determined the therapeutic value of benzyl succinate and first made it available to the medical profession. This would commit the Council, however, to recognize the many benzyl esters described in the literature, all of which would merely present a way of obtaining the action of the benzyl radical. Thus unendurable confusion would be caused by the application of a number of uninforming names applied to the various benzyl esters which might be put out and which so far have not been studied as to their therapeutic effects, for the reason that the benzyl effect is obvious from the make-up of the compound. To prevent this confusion, the Council has admitted benzyl succinate to New and Nonofficial Remedies, has provided tests and standards for the control of the product, and will accept brands of the product only on condition that they are marketed as benzyl succinate (to which may be appended the name or the initials of the firm which markets it).

2. The label of the trade package contains recommendations for the use of Esterol in dysmenorrhea, asthma, colic, and hiccup, and thus advertises it indirectly to the public.

The Council declares Esterol (Frederick Stearns & Co.) ineligible for admission to New and Nonofficial Remedies because the name is in conflict with the provisions against the application of proprietary names to unoriginal articles and because it is advertised indirectly to the public.

EUCODIN AND EUSCOPOL OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

Eucodin and Euscopol are marketed by J. D. Riedel Aktiengesellschaft, Berlin, Germany (Riedel and Co., New York, agents).

Eucodin is methylcodein bromid. It was introduced as a substitute for codein, especially in coughs.

Euscopol is optically inactive scopolamin hydrobromid. It was introduced as a substitute for the official scopolamin hydrobromid with the claim that it is less active in checking secretions, dilating the pupil, etc.

When the period for which those two products had been accepted was about to expire in 1919, Riedel and Co., New York, were informed that the Council wished to receive evidence for the claim that Eucodin "stimulates secretion" and for the claim that Euscopol "is milder than ordinary scopolamin because of the absence of other alkaloids." In reply Riedel and Co. stated that they were not advertising these products and that the claims which the Council had questioned would be omitted when they resumed advertising or issued new circular matter. In consideration of this agreement, the Council continued these products in New and Nonofficial Remedies for a further period of three years.

When in June, 1922, Riedel and Co. was asked to send in the advertising now used for Eucodin and Euscopol, circulars were sent in which were identical with those which formed the basis of the Council's objections in 1919. The Council directed the omission of Eucodin and Euscopol from New and Nonofficial Remedies because they are marketed with claims that lack confirmatory evidence and because it appears that during the years that these products have been available no substantial evidence of their therapeutic usefulness had accumulated.

FLUMERIN, THE DISODIUM SALT OF HYDROXYMERCURIFLUORESCEIN

Preliminary Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Sept. 9, 1922, p. 897

The Council has authorized publication of the following statement on the experimental status of flumerin, the disodium salt of hydroxymercurifluorescein.

W. A. PUCKNER, Secretary.

A report on "Flumerin—A New Mercurial for the Intravenous Treatment of Syphilis," was read before the Section on Dermatology at the recent meeting of the American Medical Association by Edwin C. White, J. H. Hill, Joseph Earle Moore and Hugh H. Young. Flumerin is said to be the disodium salt of hydroxymercurifluorescein. The authors have requested the Council to consider flumerin with a view to its eventual admission to New and Nonofficial Remedies.

The Council considered the evidence presented in the report by Dr. White and his collaborators and recommended its publication in THE JOURNAL. In addition to the evidence presented in the paper, Dr. White supplied the Council with a specimen of flumerin, together with tests and standards for the identification and control of the product.

The A. M. A. Chemical Laboratory has made a preliminary examination of the product and of the chemical information furnished. It considers the evidence for the identity of the substance correct and the proposed tests for its identification and control acceptable.

The animal experiments reported by White, Hill, Moore and Young indicate that flumerin is less toxic than mercuric chlorid, mercuric benzoate, mercuric cyanid or mercuric succinimid and that it produces typical mercury effects when given intravenously to rabbits. The experiments indicate that the drug is effective in eradicating experimental syphilis in rabbits in doses that are well tolerated and which cause little or no injury to the kidneys of these animals.

The clinical trials carried out by White, Hill, Moore and Young appear to give proof of the value of flumerin as an antisyphilitic drug. In primary, secondary and tertiary syphilis, the therapeutic effects of the drug were shown to be the resolution of lesions and the abatement of positive blood Wassermann reactions. As the investigators caution: "The number of cases treated is sufficient to demonstrate that this mercurial is of value, but is too small to permit the allocation of the drug to a definite place in the therapy of syphilis." In consideration of the lack of clinical evidence, the investigators wisely announce: "It is not available for general distribution, and, for the present at least, permission will not be granted for its commercial manufacture."

The available evidence for the therapeutic value of flumerin is thus far limited to the report mentioned. Obviously, confirmation of the work there reported is necessary before more than a tentative acceptance can be accorded. However, flumerin is a definite chemical of nonsecret composition. This, together with the evidence presented in the publication referred to, may warrant its clinical trial in selected cases. Nevertheless, it is recognized that its therapeutic status is in the experimental stage.

The Council has deferred acceptance of flumerin for New and Nonofficial Remedies until proof has been furnished that the product is a useful addition to the list of mercury compounds for use in the treatment of syphilis, and until it is on the market.

GALYL

Report of the Council on Pharmacy and Chemistry

Abstracted in The Journal A. M. A., Nov. 11, 1922, p. 1706

The Council has authorized the publication of the following report.

W. A. PUCKNER, Secretary.

In 1918, Geo. J. Wallau, Inc., acting as United States distributor for Galyl (manufactured by A. Naline, Garenne, France), requested the Council to consider the product.

At that time, Galyl was stated to be tetrahydroxydiphosphoamino diarsenobenzene, and its molecule was said to be made up of two arsphenamin molecules linked by means of two phosphorus groups (—PO.OH—). It contained 35.3 per cent. of arsenic and 7.5 per cent. of phosphorus. The product was insoluble in water, and, for use, had to be dissolved by means of sodium carbonate. Galyl was claimed to be less toxic than arsphenamin, of quicker action on spirilla and of equal therapeutic value.

The U. S. agent did not supply the Council with the information which was required to determine the identity, purity and strength of Galyl; hence the Council postponed the consideration of the product until this information had been submitted.

Later, Wallau, Inc., advised the Council that the composition of Galyl had been changed. The new Galyl was stated to contain only about 18 per cent. of arsenic and to be a sodium salt of the old Galyl, obtained by precipitating a solution of the old Galyl "by means of a solution of sodium hydrosulphite." This compound, according to information submitted, was presumed to be linked with five molecules of sodium sulphite.

It was admitted that the laboratory work on Galyl had all been done with the old product; but it was stated that the toxicity of the new product was lower than that of the old Galyl, and that "hundreds of thousands of injections were given in the French and British armies, without a recorded fatality, and the clinical and serological results were so satisfactory that it was adopted as one of the standard treatments."

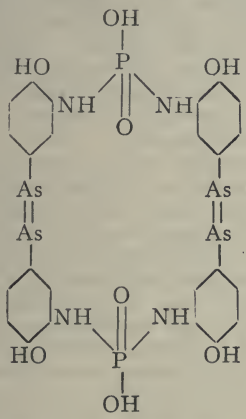
As no tests of a satisfactory nature were furnished, whereby the composition and uniformity of the product might be determined, the A. M. A. Chemical Laboratory was asked to investigate the new Galyl with the idea of devising suitable tests if the product seemed to be what it was claimed to be. (At this time the U. S. Patent Office had issued a patent for the manufacture of old Galyl base; also the U. S. Public

Health Service, on the basis of animal experiments, had authorized the importation of the new "Galyl.")

The investigation made in the Association's Chemical Laboratory presented evidence that either the new Galyl did not have the composition ascribed to it in the advertising matter issued by Wallau, Inc., or that it would not have this composition at the time it is administered.

The following is the report of the A. M. A. Chemical Laboratory:

About two and a half years ago, Galyl was being considered by the Council, at which time it was believed to have the following formula:



The amount of arsenic was stated to be about 35.3 per cent. It was sold in boxes containing two ampules. One contained the Galyl; the other contained a so-called serum (sodium carbonate solution).

Shortly after this time, however, the arsenic content was reduced to about 18 per cent., and subsequent correspondence brought out the fact that "Galyl sodium base" is sold. This form has been licensed by the U. S. Public Health Service under the name "phospharsenamine." It is directly soluble in water and is sold both as a powder and in a concentrated solution ("intramuscular"). In the circular which has been recently passed on by the Council, it is stated: "The newer form of Galyl is a sodium salt of Galyl-base obtained by precipitating a solution of the latter by means of a solution of sodium hydrosulphite. This sodium salt has a formula $C_{24}H_{16}Na_6O_8N_4P_2As_4.5SO_3Na_2$."

In considering this formula, it would seem that the compound does not possess a definite linkage between the sulphite and arsphenamin groups similar to that of the sulphur group

in neoarsphenamin (to which the manufacturers refer as an example). If there is a union, then there are two too many H atoms in the formula. It is likely that the arsenic content is "diluted" to from 18 to 20 per cent. simply by the mechanical incorporation of sodium sulphite. As evidence of the latter point, when Galyl was precipitated out of solution by acetic acid and washed free from sulphurous acid, it did not then respond to the test for sulphur as does neoarsphenamin (see test in N. N. R.).

In working out a suitable test for the phosphorus group, there were evidences that, when solution of the drug Galyl was effected, sodium phosphate was formed. Thus, when a fresh solution of Galyl was treated with magnesia mixture, considerable phosphate was removed (which contained no arsenic), while the arsenic compound and some phosphorus compound remained in the filtrate. The amount of phosphate which would be removed by magnesia mixture progressed as the solution of Galyl stood. From a solution of Galyl, thirty hours old, all of the phosphorus was removed by the addition of magnesia mixture.

When a fresh solution of Galyl was acidified with acetic acid, using methyl red as indicator, phosphorus, in about equal amounts, was found in the filtrate and precipitate, although most of the arsenic was in the precipitate.

The solution of Galyl responds to practically all the tests in N. N. R. for sodium arsphenamin, except that there is present both sulphite (SO_3^{--}) and phosphate (PO_4^{---}) ions. (These tests, however, are mainly those characteristic of the arsphenamin base.) Carbon dioxide does not precipitate the arsphenamin compound when passed through the solution (1:100). This is probably due to the presence of sodium phosphate. It was found that a very small amount of sodium phosphate, added to a solution of sodium arsphenamin, prevents the precipitation of arsphenamin when a vigorous stream of carbon dioxide was passed through the solution. As the manufacturer states, considerable sugar is present.

CONCLUSIONS

The experiments indicate that the sodium salt of diphosphodiarsphenamid ("Galyl sodium base"), if present, is easily hydrolyzed to sodium phosphate and sodium arsphenamin. The manufacturer has presented no proof that a linkage between sodium sulphite and Galyl base exists; on the contrary, the experiments reported herewith disprove any such linkage as occurs in neoarsphenamin (to which the manufacturer refers as a parallel case). When the dry content of the ampule is dissolved in water, either it is partly decomposed into sodium phosphate and sodium arsphenamin, or the original product contains, as such, some sodium arsphenamin and a considerable proportion of free phosphate. In either case, the injection would probably be of a mixture of

phospharsenamin (if any is present),[1] sodium arsphenamin, sodium phosphate, sodium sulphite and sugar.

In December, 1921, this report was sent to the Galyl agent, in duplicate, to facilitate its transmission to the French manufacturer.

In transmitting the report, it was pointed out that if, as the report indicates, (1) Galyl is a mixture containing diphosphodiarsphenamid ("old Galyl"), sodium sulphite and sugar, which decomposes in solution yielding sodium arsphenamin, or that (2) Galyl does contain the sodium salt of diphosphodiarsphenamid (mixed with sodium sulphite), which in solution decomposes by hydrolysis into sodium arsphenamin and sodium phosphate, then a radical revision of the advertising claims for Galyl is in order. It was further explained that in such instance the Council might also require evidence that the administration of Galyl possesses advantages over the administration of sodium arsphenamin.

Nothing has been received from the agent or the manufacturer to offset the findings of the chemical report.

On the contrary, the work has been essentially confirmed by other investigators, as is evident from the following abstract which appeared in *Chemical Abstracts:*

Arsenobenzenes: Galyl—Its Formula and Composition.—"The 'Galyl' (A) prepared by M. Naline does not correspond to the chemical formula usually given for A and is not of constant composition, as it is very easily alterable. One sample contained, in addition to the glucose stated on the label, 3 per cent. of sodium chlorid, 12 per cent. of sodium carbonate and 18 per cent. of sodium hydrosulphite. Instead of being neutral as claimed, it was alkaline to both phenolphthalein and litmus. The toxicity of A is of about the same order as that of the other arsenobenzenes investigated by de Myttenaere.[2]

"Galyl" or Tetrahydroxydiphosphamino Diarsenobenzene.—"Two commercial samples of 'Galyl' assayed 18.4 and 22.45 per cent., respectively, of arsenic instead of 35.04 per cent. and 32.9 per cent., which are percentages for the acid compound and the sodium salt, computed on the basis of the published formulas. From these and other published results of a like nature, it is concluded that 'Galyl' is not a definite chemical entity and that each lot manufactured should be assayed for arsenic at the factory and the true percentage stated on the label."[3]

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1. From these experiments, Galyl might be considered equivalent to this. The old base of Galyl—diphospho diarsphenamide—is adjusted to from 18 to 20 per cent. of arsenic by the mechanical incorporation of sodium sulphite, which serves both as a preservative and a solvent for the base. About 40 per cent. of sugar is also mixed with these substances to aid in causing more ready solution.

2. De Myttenaere, F.: Bull. Acad. roy. de méd. de Belg. **1**: 249-256, 1921; abstr. in Chem. Abstr., Nov. 10, 1921, p. 3724.

3. Dulière, Walter: J. de pharm. **3**: 837, 1921; abstr. Chem. Abstr., March 10, 1922, p. 786.

June 20, 1922, Wallau, Inc., advised in reply to an inquiry from the Council, that no reply to the report had been received from the manufacturer, although this had been asked for repeatedly. Wallau, Inc., state that this information would be sent to the Council when received, and that, pending final action on Galyl by the Council, no new advertising material was being put out but that orders for Galyl were being filled.

The failure of the manufacturer of Galyl to present evidence controverting the findings of the Association's Chemical Laboratory is presumptive evidence that Galyl does not have the composition claimed for it. This conclusion is supported by the evidence of independent investigators.

In the absence of evidence to the contrary, it must be concluded that the composition of Galyl has not been correctly declared (Rule 1) and that the therapeutic claims are unwarranted, since they ascribe to Galyl a composition which it does not appear to possess (Rule 6). Further, since the evidence indicates that the administration of Galyl amounts to the administration of sodium arsphenamin, its use under another name than sodium arsphenamin, and with deceptive claims for its composition, is irrational and a detriment to rational therapy.

Accordingly, the Council declared Galyl inadmissible to New and Nonofficial Remedies.

HAELEPRON TABLETS NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 22, 1922, p. 319

The Council has adopted the following report declaring Haelepron Tablets inadmissible to New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

Haelepron Tablets are made by Bodenstein and Gaslinsky, Berlin, Germany, and sold in the United States by the Haelepron Sales Co., New York. The following nonquantitative statement of the composition of Haelepron Tablets appears on the trade package:

"Haemaglobin, Lecithin, Calc. Lact., Protein vegetab., Ferr. sacch., Ferr. pyrophos."

A similar statement appears in the advertising except that here the preparation is said to contain "Protein animal and vegetable," and instead of one calcium salt, "Calc. Lact.," and two iron salts, "Ferr. sacch., Ferr. pyrophos," being

claimed the presence of two calcium salts, "calcium lactate" and "calcium saccharate," and one iron salt, "pyrophosphate of iron," is declared.

In the information sent the Council, the following report of an analysis of Haelepron Tablets is given:

"Water 8.86, Nitrogen (Protein) 48.10, Ether Extract (Fat) 7.08, Mineral Salts (calcium lactate saccharate Pyrophosphate of Iron) 10.61, Cellulose 1.93, Extractive substance (non-nitrogenous and not cellulose) 23.42."

In the circular it is claimed: "The Protein substances are chiefly blood albumin (Haemoglobin) besides the proteids of Milk, Egg and certain plants. And the mineral residue consists altogether of a variety of lime and iron salts." According to the Haelepron Sales Co., this indefinite mixture is "Indicated whenever nutrition impaired, in nervous conditions and dysemias." The indiscriminate use of the tablets is suggested by the declaration that they are "tolerated by everyone" and their use does not "interfere with . . . other medicines taken simultaneously."

The Council finds Haelepron Tablets inadmissible to New and Nonofficial Remedies because (1) their composition is indefinite and semi-secret, (2) the recommendations for their indiscriminate use are unwarranted, (3) the name is not descriptive of their composition and (4) they are an irrational and useless combination which can have little if any effect on the conditions for which they are recommended.

KALAK WATER NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

Kalak Water is an artificial mineral water sold by the Kalak Water Company, Inc., New York. In 1917, it was found inadmissible to New and Nonofficial Remedies because of the absurd and false claims that were made for it. This action was taken after the proprietor promised to withdraw the advertising circular referred to in the Council's report, but had insisted on its claims on the whole. The Council's report declared that a few grams of sodium bicarbonate daily would have equal therapeutic value with Kalak Water.

At the request of the Kalak Water Co., Inc., the Council has again considered the eligibility of Kalak Water for New and Nonofficial Remedies, based on the advertising claims that are now advanced for it. As a result of this reexamination, the Council has authorized publication of the report which follows, again declaring the product inadmissible to New and Nonofficial Remedies.

W. A. Puckner, Secretary.

Kalak Water, according to the report of an analysis contained in the advertising of the Kalak Water Company, Inc., is an alkaline saline water solution of the following composition:

Total solids at 100 deg. C	5048.8 parts per million
After ignition at red heat	4964.8 parts per million
Difference—carbon dioxid	84.0 parts per million
Di-sodium phosphate (anhydrous)	122.6 parts per million
Potassium chlorid	117.5 parts per million
Sodium chlorid	606.0 parts per million
Sodium carbonate	3655.1 parts per million
Calcium carbonate	475.7 parts per million
Magnesium carbonate	58.3 parts per million
	5035.2 parts per million

Kalak Water is recommended in the advertising for conditions known to be accompanied by acidosis. Its use is proposed specifically for toxaemias of pregnancy, normal pregnancy, anesthesia, scarlet fever, typhoid, colds, influenza, pneumonia, cystitis, and diabetes mellitus. The claim is made that, as a means of combating acidosis, the usual custom of prescribing sodium bicarbonate is inadequate because several other important bases are withdrawn from the body.

Inspection of the contents of Kalak Water leads to the conclusion that the efficiency of the preparation is not great. Sodium acid-phosphate occurs in the amount of 0.12 gm. per liter, whereas on an ordinary diet the excretion of phosphorus oxid (P_2O_5) is from 3.0 to 5.0 gm. The amount of potassium chlorid is 0.11 gm. per liter, while the daily excretion of potassium is equivalent to 3.0 gm. of potassium oxid (K_2O) daily. Sodium chlorid is so commonly taken that neither the sodium nor the chlorid ion can have much therapeutic significance in this case. The amount in the water is small, only 0.6 gm. per liter. The sodium bicarbonate constitutes the largest percentage of the salts in the preparation, amounting to nearly 6.0 gm. per liter, and this would constitute a very small dose if used for combating severe acidosis. Calcium carbonate is present in amounts of 0.4 gm. per liter, while the daily intake of calcium (Ca) is from 1 to 1.5 gm. There is about 0.06 gm. of magnesium carbonate in the water, while the daily intake is about 0.5 gm. From the standpoint of replacing these mineral constituents, the preparation is not of great significance, even if up to four liters are given as recommended for the severe cases of acidosis.

In the Kalak Water advertising, the therapeutic uses of alkalis have been culled from the literature. Although no great objection can be made to the individual abstracts, the impression is conveyed that acidosis is very prevalent and ordinarily very serious. While it is true that calcium and magnesium under certain conditions of laboratory experiments reduce "the swelling of edematous colloids," application of this phenomenon to biology is not clear.

In reference to the use of Kalak Water in colds, influenza, and pneumonia for maintaining a high alkaline reserve, it is stated that "authorities believe that this favors phagocytosis, increases immunity, and hastens convalescence." This claim is hardly warranted. The use of alkalis in nephritis has only a limited value and must be used with more knowledge than there appears in the advertising. As for lessening the production of "acetone bodies," alkali by itself is known to increase their excretion temporarily at least, but they technically circumvent the issue by combining alkali with "a proper diet."

A reprint on "Anesthesia and Acidosis" by Sanders contains statements that must be taken with reserve.

A proposed advertising pamphlet, submitted in the form of a galley proof contains a summarization that is much above the average, but it is not particularly critical, and, of course, Kalak Water is recommended for acidosis of any variety and by inference names the diseases given at the beginning of this report.

The claims advanced in the present advertising for Kalak Water are moderate, but Kalak Water cannot have any great therapeutic significance, and, as a whole, the claims advanced for it constitute unwarranted therapeutic recommendations.

The Council declared Kalak Water inadmissible to New and Nonofficial Remedies because: (1) the therapeutic claims are unwarranted (Rule 6); (2) the name is not descriptive of the composition (Rule 8); and (3) the use of a solution of sodium bicarbonate containing many other ingredients of questionable utility is not conducive of rational therapy (Rule 10).

KALNITE NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The report on Kalnite which follows was sent to the Abbott Laboratories for consideration. In reply the firm wrote that it is not now producing nor selling the product. In order that the consideration of Kalnite may become a matter of record, the Council directed publication of the report.

W. A. PUCKNER, Secretary.

Kalnite was presented to the Council by Sharp and Dohme with the claim that it was composed of potassium nitrate 90 parts and a new double salt of potassium nitrate and aluminum nitrate 10 parts. The A. M. A. Chemical Laboratory analyzed the preparation (Reports A. M. A. Chemical Laboratory, 1921, "Does Kalnite Contain Potassium Aluminum Nitrate?") and reported that there was no evidence that it contained a double salt of potassium nitrate and aluminum nitrate as claimed, and also that it did not contain the amount of aluminum nitrate required by the formula. Subsequently

the Abbott Laboratories requested the Council to consider Kalnite. The Abbott Laboratories advised the Council that it had acquired the right to the trademarked name Kalnite from Sharp and Dohme. In its presentation the Abbott Laboratories did not support the claim advanced by Sharp and Dohme that Kalnite contains a new compound, potassium aluminum nitrate. According to the Abbott Laboratories, Kalnite consists of 90 parts of potassium nitrate and 10 parts of material containing 30.7 per cent. of aluminum nitrate and 43.5 per cent. of potassium nitrate so that the final material contains from 2.9 to 3.2 per cent. of aluminum nitrate and from 94.0 to 96.0 per cent. of potassium nitrate.

Kalnite is presented for the treatment of pyogenic infections, particularly chronic osteomyelitis. It is used in the form of poultices, the vehicle recommended is rolled oats, although kaolin, saw dust, cellulose, bran, etc., may be used. Rolled oats is sterilized for two hours in an autoclave under fifteen pounds pressure. A poultice of uniform consistency is made with boiling water, and Kalnite added in the proportion of 13 grains to an ounce of dry oats. This mixture is applied directly to the skin, well beyond the limits of the affected area, and covered with some water proofing material, in order to retain the moisture.

It is claimed that this procedure stimulates bacterial growth and produces an acute reaction in the chronic infections, until it is cured spontaneously by the normal resisting powers that the body possesses. Certain experiments are reported to show that Kalnite in culture media promotes the growth of bacteria. It is further claimed that this method of treatment stimulates osteogenesis, causes keloid scars to slough away, and aids open wounds to heal with the formation of the minimum amount of scar tissue. The statement is made that pain in osteomyelitis is relieved within a few days to a week by the use of Kalnite, as described above, by causing autolysis and liquifaction of the infiltrated tissues. While it is impossible to refute by direct evidence some of the claims made, the claims may be considered extraordinary in the light of existing experience and knowledge. It is difficult to understand how a mixture of aluminum nitrate and potassium nitrate applied externally can produce the effect stated. That a certain quantity of the salts may be absorbed is understandable, but the mechanism of stimulating osteogenesis is less comprehensible. It is possible that the stimulation to bacterial growth which is claimed for the salts may be responsible for the entire effect, but even this explanation can scarcely be considered wholly plausible.

As evidence of the therapeutic value of Kalnite, a report of the treatment of between two and three hundred cases of chronic infections and chronic osteomyelitis has been presented to the Council. In appraising these case records and radiographs, the advice of surgeons and a specialist in radiography have aided considerably in the conclusions reached. The cases from the clinical standpoint are not deemed to be

very different from what is frequently seen in similar conditions, where the usual therapeutic procedures are employed, i. e., adequate surgical drainage, irrigation and ordinary surportive measures. Careful examination by the roentgenologist failed to confirm some of the author's optimistic results. In several instances when the process was pronounced cured, there was evidence of simply a quiescent stage of the process. Exacerbations of chronic osteomyelitis are well known. On two occasions, the Council has been informed by surgeons of unquestioned professional ability, that cases had come to their attention, where, in their opinion, serious injury to the patient had resulted from the use of the Kalnite treatment in preference to good surgery.

From the evidence submitted, it is considered that the use of Kalnite in the treatment of pyogenic infections and osteomyelitis is irrational. In consideration of the lack of acceptable evidence for the value of Kalnite, the Council held its use irrational and therefore did not admit Kalnite to New and Nonofficial Remedies.

LEUKOCYTE EXTRACT OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report which announces omission from New and Nonofficial Remedies of leukocyte extract and the accepted brand, Leukocyte Extract-Squibb.

W. A. PUCKNER, Secretary.

Leukocyte extract was admitted to New and Nonofficial Remedies in 1915. At that time the reports of its use, though not conclusive, indicated that the preparation might have therapeutic value.

The following statement appears in New and Nonofficial Remedies, 1921: *"Actions and Uses.*—Leukocyte extract is believed to increase the immunizing power of the organism into which it is injected. It is said to be useful as an aid to the action of specific serums or antitoxins and vaccines. It is claimed to be useful by itself in cases in which the correct bacteriologic diagnosis of the infection cannot be obtained. Its use is still in the experimental stage."

To determine whether or not leukocyte extract might be included in New and Nonofficial Remedies, 1922, the Council obtained the statements of ten physicians who, in the belief of the Council, are competent to render expert opinions on the questions involved.

Six of the physicians reported that they had had no experience with leukocyte extract; and some of these expressed the view that they had seen no work that would induce them to use the preparation.

One physician who has given much study to the action of leukocyte extract expressed the opinion that leukocyte extract is harmless and, like other proteins, calls forth the reaction after injection which gives rise to increased leukocytes in the circulation. He believes that it may alter the blood enzyme curve at the time, but he knows of no experimental evidence curve at the same time, but he knows of no experimental evidence in support of this opinion. He believes that it has some value and does not do any harm but he is in doubt regarding its being superior to other forms of nonspecific foreign serum or protein injection.

Another physician recognized as competent to express an opinion on foreign protein therapy, though he had not used leukocyte extract, believed from a consideration of the literature on the subject, that the results were those obtained from the injection of foreign protein, and could see no reason to claim that leukocyte extract possesses any more value than any other foreign protein.

One consultant reported that he had used leukocyte extract; but he believed that doses sufficient to produce leukocytosis caused such violent reactions that the use of this preparation should be abandoned.

One had used leukocyte extract in a few cases of erysipelas with what he thought were distinct beneficial results, but had found the injections painful. He had used the extract in some cases of pneumonia, but without apparent effect.

These replies indicate that a group of representative physicians in this country either have had no experience with leukocyte extract and have for various reasons believed it unnecessary to employ it, or, in a few instances, have employed it without any definite beneficial effects. The opinion, therefore, of a group of representative physicians from all parts of the country does not warrant the use of leukocyte extract or is actually opposed to it.

In consideration of these opinions, the Council directed the omission from New and Nonofficial Remedies of the chapter devoted to leukocyte extract and rescinded the acceptance of the brand of this product now in New and Nonofficial Remedies.

LIPOIDAL SUBSTANCES (HOROVITZ) NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 25, 1922, p. 600

The Council has authorized publication of the following report declaring Lipoidal Substances (Horovitz) inadmissible to New and Nonofficial Remedies because its composition is essentially secret and because the curative claims made for it are unsubstantiated and, therefore, unwarranted.

W. A. Puckner, Secretary.

In the advertising of the Horovitz Biochemic Laboratories Co. (A. S. Horovitz, president) we read:

"Horovitz proves by careful paralled investigations of normal and of pathological tissues, both in addiction disease and in other diseases, that in patients suffering from narcotic addiction disease there is an inactivity of the lymph-glands due to the use of the drug and that the system is not supplied with the necessary fats." "Horowitz further found that the lipoidal content of the cerebro-spinal system varies in strict accordance with the pathological processes introduced by infection or by alkaloids. Furthermore, he has found that the lipoids of various other organs, as well as those of the nervous system, may be extracted and consumed by the administration of narcotic alkaloids."

It is further stated in the advertising that:

"After a long and very careful research investigation Dr. Horovitz worked out a method of rational treatment for narcotic addiction disease which involves the restoration of the lipoids, which have been lost through the action of the drug, and of the toxins, by means of a combination of lipoidal substance from various plant lipoids in the form of a sterile solution. This preparation not only replaces the lipoids lost by the tissues, but also protects the nerve tissues from attacks by the toxins elaborated during the use of narcotics, and, this by detoxicating the tissues, brings about permanent freedom from the craving of narcotics, instead of the temporary relief afforded by other methods of treatment."

The "combination of lipoidal substance of various plant lipoids" which was worked out by Horovitz, the Horovitz Biochemic Laboratories offer as "Lipoidal Substances." This preparation is supplied in ampoules said to contain 1 c.c. of solution. The treatment with "Lipoidal Substances" consists, first, in the complete withdrawal of the narcotic; second, in free catharsis; and third, in the intramuscular injection of the preparation. The initial dose is given as 8 to 12 minims repeated with increase of 3 to 4 minims every three hours during the first day. On the second, third and fourth day 16 minims is to be given twice a day and "from the fifth day until the medication is stopped (usually 28 to 35 days) it will be necessary usually to give but 1 injection of 16 minims each day."

In a request for the admission of its preparation to New and Nonofficial Remedies, the Horovitz Biochemic Laboratories Co. stated:

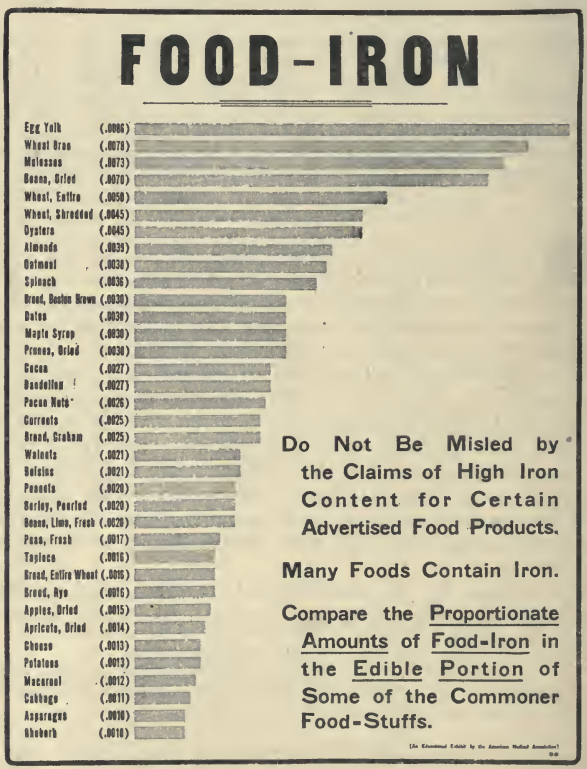
"The composition of Lipoidal Substance is (*a*) Lipoids of plant origin, (*b*) Vitamines (water soluble) of plant origin, (*c*) Non-specific plant proteins, (*d*) Preservatives—None."

While the communication abounded in generalities, it gave neither the identity nor character of the lipoids, of the vitamins nor of the nonspecific protein, nor their quantities or methods for their control. The firm presented no evidence that the injection of "Lipoidal Substances" produced any effect other than by suggestion. Also, while a long list of

references to publications bearing on lipoids was submitted (many of which had no bearing on the subject under consideration) there was no reference to the work of Horovitz quoted in the firm's advertising.

After examining the information which had been submitted, the Council requested the manufacturer to supply:

1. Information as to the character (identity) of the several ingredients contained in the preparation that it marketed, the amount of each ingredient so far as known and the method used for their control.



Photographic reproduction (greatly reduced) of one of the Educational Posters prepared by the Propaganda Department. In the original these posters measure 22 by 28 inches. This one is published for the purpose of offsetting to some degree the misleading claims made by the exploiters of certain advertised food products relative to the amount of food-iron such products contain.

2. Evidence that the administration of "Lipoidal Substances" is of value in the treatment of drug addiction.

3. Evidence for the claims that the "researches" of Horovitz have proved that "in patients suffering from narcotic addiction disease there is an inactivity of the lymph-glands . . . and the system is not supplied with the necessary fats" and that "lipoidal content of the cerebro-spinal system varies in strict accordance with the pathological processes introduced by infection or by alkaloids" and that "the lipoids of various other organs as well as those of the nervous system, may be extracted and consumed by the administration of narcotic alkaloids."

The Horovitz Biochemic Laboratories replied that the requested information would be supplied in about *two weeks.* At the expiration of *three months* the promised information and evidence had not been received; neither had any reports to show the value of the treatment come to the attention of the Council. The Council, accordingly, declared "Lipoidal Substances" (Horovitz Biochemic Laboratories) inadmissible to New and Nonofficial Remedies because the composition is essentially secret and because the curative claims are unsubstantiated and unwarranted.

LIQUID MIXED FOODS OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

In 1907 the Council examined the market supply of the so-called liquid mixed or predigested medicinal foods (*Jour. A. M. A.,* May 11, 1907, p. 1612; Reports of Council on Pharmacy and Chemistry, 1905-1908, p. 63). As result of this examination the Council reported that these were solutions containing as their essential constituents small amounts of protein substances and carbohydrate preserved by alcohol or glycerin or both, and that their value depended on the protein and carbohydrate contained in them. It was found that none of the preparations examined contained sufficient food material to maintain normal nutrition. To obtain a minimum requirement of calories (1,500 calories in 24 hours), from 700 to 1,000 c.c. of these medicinal foods would be required, even if the alcohol contained in them were considered to have food value. In many cases the alcohol contained in these quantities was sufficient to keep a patient in an alcoholic stupor continually.

In view of the considerable use of these liquid predigested foods, the Council decided to admit them to New and Nonofficial Remedies provided they met certain requirements and were marketed in conformity with the Council's rules. These requirements provided:

1. No liquid medicinal or predigested food shall be accepted which contains less nutritive value, exclusive of alcohol and glycerin, than milk.

2. At least one fourth of the nutritive value of the food, exclusive of alcohol and glycerin, shall reside in the nitrogenous matter.

3. The label shall bear a statement whether the peptones and proteoses are produced by enzymes or otherwise.

4. No package or advertising matter of any character shall bear representations which lead the physician to believe that a food contains more nutrients than it actually does, or that it alone can sustain life for a limited period, if the dose advised contains less than 100 calories, exclusive of alcohol and glycerol, per diem dose.

Few preparations on the market came up to the standards. Most of the preparations depended for their effects—real or imagined—chiefly on the high percentage of alcohol which they contained and the extravagant claims that were made for them. New and Nonofficial Remedies, 1922, contains but three Liquid Mixed Foods.

Liquid Peptonoids.—A fluid medicinal food prepared from beef, milk and wheat, containing 17.9 per cent. of alcohol by volume. The nutritive value, derived from the protein digestion products and carbohydrate, maltose, lactose and dextrin, exclusive of alcohol, of 500 gm. of liquid peptonoids corresponds approximately to 410 calories, of which 107 are furnished by protein and 285 by carbohydrate.

Manufactured by The Arlington Chemical Co., Yonkers, N. Y.

Panopepton.—A fluid medicinal food prepared from beef and wheat containing 19.7 per cent. of alcohol by volume. The nutritive value, derived from the protein digestion products, of 500 gm. of panopepton corresponds approximately to 472 calories, of which 132 are furnished by protein and 340 by carbohydrate.

Manufactured by Fairchild Bros. and Foster, New York.

Enemose.—A sterile liquid prepared from beef and wheat, especially designed for colonic alimentation. The nutritive value of 500 gm. of enemose corresponds approximately to 1,190 calories of which 250 are furnished by proteins and 940 by carbohydrates.

Manufactured by Fairchild Bros. and Foster, New York.

At the annual meeting of the Council in 1921 the question of the continued recognition of liquid mixed foods was considered. On the recommendation of its committee on medicinal foods, the Council voted to omit this class of prepara-

tions when the period for which they stood accepted should have expired, on the ground that their usefulness in present day dietal therapy lacks substantiating evidence.

At the 1922 meeting of the Council the question of deleting the liquid mixed foods from New and Nonofficial Remedies was again considered. The Council reaffirmed its decision to delete this class of preparations and, since the period of acceptance expired with the close of 1922, directed that at that time Liquid Peptonoids (Arlington Chemical Co.), Panopepton (Fairchild Bros. and Foster) and Enemose (Fairchild Bros. and Foster) be omitted from New and Nonofficial Remedies, because the claims advanced for these preparations and the rationality of their use has not been substantiated by recent evidence (Rules 6 and 10).

LUETIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the statement below explaining the omission from New and Nonofficial Remedies of Leutin-Mulford and of the general article on Luetin Vaccination for the Diagnosis of Syphilis.

W. A. Puckner, Secretary.

The period for which Luetin-Mulford stood accepted expired with the close of 1921.

In January, 1922, the H. K. Mulford Co. was advised that the committee in charge of Leutin-Mulford had gained the impression that the Luetin test has proved of little value and that, before making recommendation to the Council with regard to the continued inclusion in New and Nonofficial Remedies of the article "Luetin Vaccination for the Diagnosis of Syphilis" and the reacceptance of Luetin-Mulford, the Committee would like to receive evidence for the value of Luetin. The Mulford Company was reminded of this inquiry in March, and again in May, but the requested evidence was not received.

In consideration of the failure of the Mulford Co. to submit the requested evidence and of the report of Alderson (*Archives Syphilology,* May, 1922) that the market supply of Luetin is of doubtful value, the committee recommended that Luetin-Mulford and with it, the general article on "Leutin Vaccination for the Diagnosis of Syphilis" be omitted from New and Nonofficial Remedies.

The Council adopted the report of the committee and directed the omission from New and Nonofficial Remedies of Luetin-Mulford and of the general article on Luetin. It directed that the general article on "Leutin Vaccination for the Diagnosis of Syphilis" which appeared in New and Nonofficial Remedies, 1922, p. 319, be transferred to the Council Reports as a matter of record.

LUETIN.—Luetin is an extract of the killed cultures of several strains of *Spirochaeta pallida,* the causative agent of syphilis.

Actions and Uses.—When injected into the skin, luetin provokes no reaction in normal individuals except a very small erythematous area at, and around, the point of injection. In certain cases of syphilitic infection, a reaction occurs consisting of papules which may become pustules. When the reaction takes the papular form, a large reddish indurated papule (usually from 7 to 10 mm. in diameter) makes its appearance in from twenty-four to forty-eight hours and slowly increases for four or five days, after which the inflammatory process begins to recede. The color of the papule gradually becomes dark bluish-red. The induration disappears within two weeks, as a rule.

In the pustular form, after the fourth or fifth day, the inflammatory process increases in intensity and the papules become vesicular and later purulent. The pustules rupture spontaneously and the defect caused by the escape of the pustular content becomes quickly covered by a crust that falls off within a few days. A small induration sometimes remains for a few weeks or often months, leaving a small keloid after healing.

In the torpid type of syphilis, the site of injection fades to an almost invisible point within from three to four days, so that it may be erroneously considered a negative reaction. After ten days, or even longer, the spot suddenly begins to enlarge and goes through the same stages as seen in the pustular type.

Luetin is employed for the diagnosis of syphilis. It is of use in the examination of tertiary cases, but rarely gives a positive reaction in the primary cases or in untreated secondary cases. In patients who are under treatment by mercury or arsphenamine, the reaction is frequently positive even in cases which fail to give a positive Wassermann reaction.

Dosage.—The amount of luetin to be injected for one test is 0.07 Cc. The material should be properly diluted and injected into, but not under, the skin. A site should be selected on the skin of the upper arm, cleansed and sterilized and the injection made as described.

NITRONINE NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report which declares Nitronine inadmissible to New and Nonofficial Remedies.

In the report it is stated that the product, when received, was found by the A. M. A. Chemical Laboratory to contain

less than 15 per cent. of the claimed amount of nitrous ether. When advising the American Pharmacal Co. of the rejection of Nitronine, the Council informed the company that when reassayed after twenty weeks, the specimen was found to contain less than 3 per cent. of the claimed amount of nitrous ether.

W. A. PUCKNER, Secretary.

Nitronine is put out by the American Pharmacal Co., Sturgis, Mich. It is stated to contain in each fluidrachm: Spirit of nitrous ether 12 minims, cinchonidine sulphate 1⅓ grains, salicin ⅓ grain, fluidextract of hydrastis 1 drop, aromatic sulphuric acid 1 drop, fluidextract of veratrum ½ drop, distilled water sufficient.

Although it is well known that spirit of nitrous ether is prone to decompose when mixed with water or with many organic substances, the Nitronine label gives no indication that the mixture may decompose on keeping. A specimen of Nitronine sent to the Council was examined in the A. M. A. Chemical Laboratory a few days after it was received. When assayed in a nitrometer by means of potassium iodide and sulphuric acid, the amount of nitrogen liberated indicated less than 15 per cent. of the claimed amount of nitrous ether. According to the American Pharmacal Co., Nitronine is indicated in "febrile conditions due to the toxins of infection or contagion which are evolved in Influenza, Feverish Colds, Pneumonia, Malaria Fever, Dengue, Typhoid and Typhus Fevers, Scarlet Fever and Measles." The firm declares that the use of the preparation is indicated in "febrile conditions" and assures us that "the treatment may be commenced upon the appearance of fever without waiting to determine the specific type of infection," thus inviting the routine and ill-considered use of the mixture.

As regards the action of this mixture of cinchonidine sulphate, salicin, veratrum, goldenseal and aromatic sulphuric acid with indefinite amounts of spirit of nitrous ether, the proprietors tell us "The preparation may be relied upon to effect the results mentioned in a superior degree when properly administered where indicated." This means that when the patient recovers under Nitronine treatment—or in spite of it—the preparation must be given the credit; where it does not effect the desired results in a "superior degree," it evidently was not "properly administered" or was not "indicated" and the physician who prescribed Nitronine will have to shoulder the blame.

The extent to which physicians are justified in taking their therapeutic instruction from the American Pharmacal Co. may be judged from the following which appears in a circular that is wrapped with the trade package of Nitronine: "Vomiting of dark green or yellowish matter during treatment indicates the proper action of the remedy in eliminating the toxins or poisonous matter. . . ."

The Council finds Nitronine inadmissible to New and Nonofficial Remedies because: (1) its composition is indefinite; (2) the therapeutic claims made for it are unwarranted; (3) the name is not descriptive of composition, and (4) it is a complex and irrational mixture the use of which hinders the practice of medicine.

PITUITARY ANTERIOR DESICCATED-G. W. CARNRICK CO.

PITUITARY BODY-G. W. CARNRICK CO.

PITUITARY POSTERIOR DESICCATED-G. W. CARNRICK CO.

OVARIAN SUBSTANCE-G. W. CARNRICK CO.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

The G. W. Carnrick Co. requested acceptance for New and Nonofficial Remedies of the following products and of tablets thereof: Pituitary Anterior Desiccated, Pituitary Body, Pituitary Posterior Desiccated, and Ovarian Substance. The firm stated that no advertising for these products was issued and that the literature used to present them to the profession was contained in its house organ, The Metabolist, and consisted entirely of articles abstracted from current medical publications.

While from the firm's statement it was to be assumed that no therapeutic claims were advanced for the products, the trade circular, The Successful Treatment of Asthenic Conditions, which has been widely circulated, contains statements bearing on these products. Some of these are unwarranted by the present state of our knowledge, thus: "When thyroid is given in small doses in hypoadrenia, the suprarenal glands are excited to increased function." "The normal adult whose adrenals function normally is relatively resistant to infection." These claims are made the basis for the recommendation of mixtures of glands, namely, Hormotone and Hormotone Without Postpituitary, already reported on unfavorably by the Council (J. A. M. A., Aug. 16, 1919, p. 549). However, they are prejudical to the rational use of the simple gland preparation under consideration.

The firm's advertising material tends to create the belief that the whole trend of public opinion is toward pluriglandular therapy. Therefore, acceptance by the Council of the simple preparations would constitute in effect a means of advertising the irrational fixed stock pluriglandular mixtures of the Carnrick Company.

STERILE SOLUTION IRON CITRATE (GREEN), STERILE SOLUTION MERCURY BICHLORIDE (THE INTRA PRODUCTS CO.) NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

The Intra Products Co., Denver, Colo., markets Sterile Solution Iron Citrate (Green) "for hypodermic or intramuscular use" for use in chlorosis and anemia, and Sterile Solution Mercury Bichloride "for intravenous use."

The Council voted not to accept these preparations for the following reasons:

Sterile Solution Iron Citrate (Green): No evidence has been presented that iron citrate (Green) is superior in any way to the well known iron and ammonium citrate, and hence the Council reaffirms its previous decision (Reports of the Council on Pharmacy and Chemistry, 1914, p. 145) that iron citrate (Green) and preparations of it are inadmissible to New and Nonofficial Remedies; further, there is no evidence that the hypodermic or intramuscular administration of iron possesses any advantage over the simpler method of oral administration.

Sterile Solution Mercury Bichloride: The Council has previously denied recognition to an intravenous solution of mercuric chlorid on the ground that more experience of the effects made under controlled conditions is needed before the intravenous use of mercuric chlorid can be approved (*The Jour. A. M. A.*, April 16, 1921, p. 1120). No evidence has been presented in this direction and hence this preparation is not admitted.

TETHELIN NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report on Tethelin. When this report was sent to the Mulford Co. for consideration, prior to its publication, the firm replied that the product would not be marketed after the present stock is exhausted.

W. A. PUCKNER, Secretary.

In 1916, T. Brailsford Robertson announced the isolation from the anterior lobe of the pituitary gland of cattle of a product or principal which affected favorably the growth of animals. Robertson named this product Tethelin. He patented his discovery and assigned the patent to the University of California. The university in turn, licensed the H. K. Mulford Co. to manufacture and market the preparation.

In consideration of the claim that Tethelin might be used to accelerate growth and that it stimulated wound repair, the product attracted much attention. Because of the inquiries which the Council had received, the Council took up the consideration when the product was placed on the market for the use of physicians.

The following report based on the published reports and the advertising issued by the Mulford Co. was submitted to the Council by the referee of the committee to which the product has been assigned:

"Tethelin is claimed to have two properties which may be of interest to physicians: it is claimed (1) to promote certain phases of growth (2) to hasten the healing of wounds. The experiments under (1) seem to have been made exclusively upon mice (except for effects upon tumors apparently in rats and mice). The effects upon growth are complicated; at one phase, there is stated to be a 'marked retardation' of growth 'followed by acceleration of the latter portions of the third growth cycle.' However interesting these results may be, they furnish no clue as to how the substance could be used in therapeutics; in fact, the circular contains no suggestion of how advantage could be taken of this property or in what conditions it might be utilized. The referee does not think that at present the Council need consider the growth promoting action of the substance; the Council could give no hint of how it could be used therapeutically. From a practical point of view more emphasis is placed upon (2): the influence of Tethelin upon the healing of wounds. Interesting experiments have been reported upon the effect of the substance upon the healing of wounds in mice, but from the clinical standpoint only six cases of its use are reported—a number insufficient to permit of the drawing of satisfactory conclusions. It is recommended that consideration of Tethelin be postponed pending the submission (1) of evidence that advantage may be taken clinically of its growth promoting actions, (2) of further and more conclusive evidence of its influence upon the healing of wounds."

This report was adopted by the Council and sent the Mulford Company in October, 1918. The Mulford Company replied that it had carried out no experiments with Tethelin and that the Council's request for evidence had been forwarded to the University of California and to Dr. Robertson.

Since the adoption in 1918 of its report holding the evidence for the therapeutic value of Tethelin insufficient to permit its admission to New and Nonofficial Remedies, the Council has received or learned of no reports which tended to establish its value. On the other hand, feeding experiments carried out at the institute of Physiology in University College, London (Drummond, J. C. and Cannon, R. K., Tethelin, the alleged growth controlling substance of the anterior lobe of the pituitary gland, *Biochem. J.*, 16, 53 (1922) failed to demonstrate that the oral administration of the anterior lobe substance had any effect on the growth of test animals. In

consideration of the lack of evidence for the therapeutic usefulness of Tethelin, the Council concluded the consideration of the product and declared it inadmissible to New and Nonofficial Remedies.

THERAPEUTIC RESEARCH INTO THE CLINICAL FIELD OF YEAST PREPARATIONS

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Oct. 14, 1922, p. 1354

The Council has adopted the following report and has authorized its publication. W. A. Puckner, Secretary.

The Council, at its meeting of March, 1921, directed its Therapeutic Research Committee to determine the advisability of undertaking a clinical study of the usefulness in therapy of yeast preparations. Accordingly, the chairman of that committee drew up a provisional plan which proposed to utilize the easily observable phenomena of growth, appetite and laxative effects as cumulative indices of all action and to record these under a variety of normal and pathologic conditions. The plan was submitted to the members of the committee and to others, with a request that they express their views: first, as to whether such an investigation would be likely to justify the effort; second, as to the plan itself, and, third, as to those who should be asked to participate.

The responses indicated considerable interest in the subject. They were rather evenly divided as to the desirability of the investigation, and predominantly skeptical as to the probability of positive results. That is, most of the correspondents doubted the usefulness of yeast in clinical conditions; but about half thought that the question should be investigated in some such manner as was proposed in the plan. The others inclined to the opinion that the results would probably be inconclusive, at least to the advocates of yeast therapy; and that the trials should be begun, if at all, on a very restricted scale.

Since the plan was drafted, Prof. A. L. Daniels has reported experiments on babies and older children, with entirely negative or with unfavorable results. A. F. Hess also had previously published similar, negative data. Since persons of the actively growing age would be most likely to show improvement in growth, the Therapeutic Research Committee concluded not to extend the observations to other groups; nor did a repetition of the investigations of Daniels and Hess seem, to the committee, necessary. The chairman of the committee, therefore, recommended to the Council that the investigations along the lines proposed be not inaugurated, on the ground that, in the light of present knowledge, there does not seem to be a deficiency of growth

vitamin under conditions existing in America, even when the growth demands are most active.

In advising against the proposed investigations of yeast preparations, the chairman of the committee pointed out that this does not entirely dispose of the question of yeast therapy, for several other fields of usefulness are hypothetically conceivable:

A. For individuals living on extraordinary diets of especially low vitamin content: The investigation of this field would need to await more knowledge as to the actual existence of such conditions. The correspondence indicates that no such group has been recognized in this country, with the possible exception of dietary faddists, in whom neurotic factors are likely to be inherent in such degree as to make them difficult subjects for study.

B. As a laxative: There is no doubt that living yeast does act as a laxative, and as such may be useful for subjects afflicted with habitual constipation and its progeny. This much may be granted *a priori;* and it does not seem worth while carrying the subject further at this time, since no plan has suggested itself by which to determine whether it should be preferred to other laxatives.

C. To increase resistance in some other manner: This is too indefinite to be considered seriously for clinical investigation, until the conditions in which it is supposed to act are more sharply defined, or until it is based on animal experiments.

The chairman reported that, as a result of the information obtained, he had come to these conclusions:

1. Apart from the occasional imported cases of beriberi, vitamin deficiency is not a recognized or diagnosable clinical entity in this country.

2. With ordinary diets, yeast does not have any effect on growth, even of babies and children.

3. The one effect of yeast that has been definitely established is the laxative effect. This may be useful in chronic constipation but no direct method is at present available for determining its advantages or disadvantages in comparison with other laxatives. Critical observations in the course of ordinary practice may perhaps furnish some hints at a future time, especially when objective observations are not so much hindered by the psychic influence of commercial propaganda.

For these reasons, the further investigation of the problematic usefulness of yeast in clinical conditions would not be worth the effort and expense.

The report of the Therapeutic Research Committee and the replies to the committee's inquiries were submitted to the Council.

At its meeting in March, 1922, the Council considered the report of its Therapeutic Research Committee and agreed to

the recommendation that the plans for the investigation of yeast preparations be abandoned for the present. The Council directed that the committee's report and the replies which had been received be submitted to those who had previously advised the Council in this matter, with the inquiry whether, in their opinions, the plans should be continued or abandoned. The Council directed that the replies be referred to the committee responsible for the yeast preparations proposed for admission to New and Nonofficial Remedies, with instructions to make final recommendations to the Council.

The replies received were, in general, against a clinical study of yeast preparations under the auspices of the Therapeutic Research Committee of the Council on Pharmacy and Chemistry. The committee therefore, recommended that the Council's decision to abandon, for the present, the plans for the investigations of yeast preparations be allowed to stand and that, as a matter of record, this report be authorized for publication. The Council adopted the recommendations and extended a vote of appreciation to those who had aided in the consideration of the important questions involved.

THROMBOSINE NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

Consideration of Thrombosine was requested by the Peek Chemical Works, New York (acting as agents for the Swiss manufacturer). When the report which appears below was sent to the Peek Chemical Works, this firm wrote that the Council's report was being forwarded to its principals and that the Peek Chemical Works was not interested in the merchandising of the product under the circumstances. The Council postponed consideration of Thrombosine to await the communication of the Swiss manufacturer. No reply, however, was received, and hence the Council authorized publication of its report.

W. A. Puckner, Secretary.

Thrombosine, claimed to be "A physiological remedy for allaying haemorrhage" is manufactured by A. H. Boller and Company, Zurich, Switzerland. In the advertising it is stated that Thrombosine is "obtained by bringing coagulo-active lipoids into conjunction with certain by-products generated during the assimilation of albumen." In reply to a request for a more definite statement of the composition of Thrombosine, the following statement relative to the method of preparation of Thrombosine was furnished the Council:

"0.1 g Lecithin are heated with a mixture of 0.1 g alkali gallates and 0.1 g Peptone 'Witte' whilst adding 25 ccm. 96% alcohol in a porcelain pot in a water bath, the mixture being stirred all the time, until all the alcohol be evaporated and a homogenous viscous mass remains. This is again

dissolved in 100 ccm. physiological saline solution and filled in ampoules. After the sterilization of the ampoules the preparation is immediately ready for use. Through this procedure the lipoids combine with the alkali gallates as well as with the peptone 'Witte,' whereby the haemolitic propensities of the alkali gallates are entirely lost."

Thrombosine is supplied in the form of a solution and is recommended to be used by local application and by intramuscular injection. According to the advertising, the use of Thrombosine "Bolco" is especially recommended in cases of "obstinate hemorrhage of every kind, particularly when it occurs in parts of the body that are difficult of access (pulmonary haemorrhage in tuberculosis, haemorrhage from the stomach or bowels, traumatic haemorrhage from internal organs, haemorrhage occurring in gynaecological and Midwifery cases, etc.)."

In consideration of his extensive investigations of preparations advocated as hemostatics, the Council requested Dr. P. J. Hanzlik, Professor of Pharmacology at Stanford University Medical School, to determine the probable efficacy of Thrombosine for the purpose for which it is recommended. Dr. Hanzlik tested the alleged thromboplastic action of Thrombosine *in vitro* as compared with that of kephalin and physiological solution of sodium chlorid as controls. The following is Dr. Hanzlik's report:

Methods: Two methods were used: (1) The method described in New and Nonofficial Remedies, and (2) that used by Hirschfield and Klinger for "Thrombosine" (*Deutsch. med. Woch.,* 1915, No. 52). The method of Hirschfeld and Klinger was carried out at room temperature and also at 38 C. with oxalate beef instead of goat or sheep plasma as follows: Serozyme was prepared by the addition of calcium chloride to oxalate beef plasma. When coagulation was complete, the coagulum was squeezed by a pair of forceps, and the fluid portion, which constituted serozyme, was separated and used in the tests. Next, two series of dilutions of the cytozymes (Thrombosine and Kephalin) were prepared, using normal saline (0.9 per cent. NaCl) as control. Dilutions of the two cytozymes were made as follows: (1) Undiluted Thrombosine or 2 per cent. Kephalin; (2) equal parts of cytozyme (Thrombosine or Kephalin) and normal saline; (3) 1 part of cytozyme to 4 parts of normal saline and (4) 1 part of cytozyme to 16 parts of normal saline. One c.c. each of the above dilutions of the cytozymes was placed in 4 test tubes. A fifth test tube in each series contained normal saline, making in all 10 test tubes with both products. Then 0.1 c.c. of serozyme and 3 drops of 1 per cent. calcium chlorid solution were added to each test tube, and the whole was allowed to stand for 15 minutes. At the end of this time, 1 c.c. of diluted oxalate beef plasma (prepared by mixing 4 c.c. of normal saline, 1 c.c. of 1 per cent. of sodium oxalate

and 1 c.c. of oxalated beef plasma) was added to each tube and the mixtures shaken and allowed to stand at room temperature. A similar set of mixtures was prepared and immersed in a beaker of water at 38 C. Coagulation was observed at interval of 30 seconds, using the test of complete invertability as the end point of complete coagulation.

Of the two methods, that described in New and Nonofficial Remedies is simpler and more convenient, requiring fewer reagents, than the method advised by Hirschfeld and Klinger. All told, 12 trials were made with "Thrombosine" and Kephalin with the two methods. The "Thrombosine" was sent to the Council by the Peek Chemical Works. Kephalin was prepared freshly in the laboratory from sheep brains.

Results: The results obtained are presented in the accompanying table.

COMPARATIVE ACCELERATION OF COAGULATION OF OXALATE BEEF PLASMA BY KEPHALIN,[1] "THROMBOSINE"[2] AND PHYSIOLIGICAL SOLUTION OF SODIUM CHLORID

N. N. R. Method (Coagulation Time in Minutes)				
Agent	Expt. 1	Expt. 2	Expt. 3	Expt. 4[4]
N. S.[3] (control)	3½	3½	3½	
Kephalin (2% in N. S.)	1	½	5/12	7
Thrombosin (whole)	30+ (P)	20	5+ (P)	10+ (P)

Hirschfeld & Klinger Method (Coagulation Time in Minutes)				
Agent (cytozyme)	Undiluted	Dilution, equal part with N. S.	Dilution, 1 in 4 parts of N. S.	Dilution, 1 in 16 parts of N. S.
At Room Temperature				
N. S. (control)	5+ (P)			
	20+ (P)			
Kephalin (2% in N. S.)	10+ (P)	5½+ (P)	4½	4½
Thrombosine	26+ (P)	26+ (P)	end of 26, no coagulation	end of 26, no coagulation
At 38 C.				
N. S. (control)	15+ (P)			
Kephalin (2% in N. S.)	12+ (P)	5⅛	2	2
Thrombosine	8+ (P)	24 (P)	42 (soft clot)	42 (P)
	60+ (P)	60 (P)		90

1. The Kephalin used was freshly prepared from sheep brains according to Howell's method.

2. The "Thrombosine" used was obtained from freshly opened ampoules labelled as follows: "Boleo A, op. 13. Made by A. H. Boller and Co. Chem. Works, "Hardau," Zurich, Switzerland. 5 c.c.". 6 different ampoules all labeled the same way were used.

3. N. S. = 0.9 per cent. NaCl.

4. In this experiment old plasma and serum were used.

(P) Means partial coagulation as indicated by the presence of few strands of fibrin floating on or near the surface, the remaining portion of the mixture being fluid, though usually cloudy.

+ Used in place of sign meaning "greater than."

Discussion: The results obtained by the two methods of testing agree in the same direction and may be discussed together. The most efficient accelerator of coagulation was kephalin, next in order was normal saline and least efficient was "Thrombosine." Complete coagulation by "Thrombosine" occurred only twice out of the twelve trials that were made. The remaining mixtures containing this agent showed only partial coagulation as indicated by the presence of few floating strands of fibrin near the surface of each mixture. Complete gelatinization did not occurr and the test tubes could not be inverted without loss of contents. The same was true of normal saline, undiluted kephalin and kephalin diluted equal parts (with N. S.) with the Hirschfeld-Klinger method. However, partial coagulation by both normal saline and these two dilutions of kephalin occurred in ⅕ to ½ the time of that by "Thrombosine."

This was even more true of normal saline and kephalin when tested by the N. N. R. method and of the lower dilutions (1:4 and 1:16) of kephalin by the Hirschfeld-Klinger method. Using the N. N. R. method, 2 per cent. kephalin was found to be at least 40 times, and normal saline at least six times, as active as undiluted "Thrombosine." The coagula produced by kephalin and normal saline were firm and the test tubes could be inverted without loss of contents.

On the other hand, "Thrombosine" caused partial (perhaps doubtful coagulation in the majority of the four experiments that were performed with the N. N. R. method. Complete coagulation occurred in one test tube only (Expt. 2).

Using the Hirschfeld-Klinger method, kephalin was found to be a better accelerator when diluted to 4 and 16 parts of normal saline, respectively, than the higher concentrations that were used. On the other hand, "Thrombosine" appeared to exhibit the opposite tendency, though irregularly. That is, higher concentrations seemed to favor acceleration of the partial coagulation that took place. However, in the two sets of experiments that were performed, namely, at room temperature and at 38 C., kephalin was the only agent that caused complete coagulation of the oxalate plasma and this occurred in all trials much sooner (roughly, 1/20 to ⅕ the time) than the partial coagulations produced by "Thrombosine" and normal saline. Therefore, it is obvious, from these results, that kephalin is far superior to "Thrombosine" as an accelerator of coagulation when tested by the Hirschfeld-Klinger and N. N. R. methods, and normal saline is certainly superior to "Thrombosine" when tested by the N. N. R. method, and possibly also by the Hirschfeld-Klinger method.

In view of the totally negative results obtained with "Thrombosine" as an accelerator of plasma coagulation *in vitro*, there was no object in testing its hemostatic activities *in vivo*. In fact, "Thrombosine" as a hemostatic may be regarded as totally worthless, since even kephalin, whose

thromboplastic activity *in vitro* is established, is doubtful. In this connection, it may be stated that the method of testing the hemostatic activity of "Thrombosine" employed by Hirschfeld and Klinger has been shown to be unreliable, since repeated bleeding alone progressively shortens the coagulation time of blood.

Conclusions: (1) As compared with fresh kephalin and normal saline, "Thrombosine" is totally inactive as an accelerator of coagulation of oxalate beef plasma *in vitro* when tested by the method of Hirschfeld and Klinger and that described in N. N. R.

(2) Accordingly, the marked acceleration of coagulation claimed for "Thrombosine" by the manufacturers, and by Hirschfeld and Klinger for goat and sheep plasma *in vitro,* are not sustained.

(3) Consequently, its hemostatic activities may also be regarded as negligible, since even kephalin, whose thromboplastic activity *in vitro* is established, is doubtful.

In consideration of Dr. Hanzlik's findings which contravert the claims made for Thrombosine—the Council voted that the product be not accepted for New and Nonofficial Remedies on account of conflict with Rule 6 (Unwarranted Claims) and 10 (Useless Articles).

VACHER-BALM NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. Puckner, Secretary.

Vacher-Balm (E. W. Vacher, Inc., New Orleans) is an ointment stated to contain menthol, 5 per cent. and eucalyptus oil, 1.5 per cent., in a base composed of petrolatum and paraffin. According to the label on the trade package Vacher-Balm is: "For CATARRH, spasmodic Croup and PAIN, reduces superficial inflammation and helps to prevent infection." In a circular accompanying the package the use of Vacher-Balm is recommended "For Rheumatism, Insect Bites or Other Pain, Corns or Bunions. Catarrah, Hay Fever, Headache (Nervous), Cold In Head, Croup (Spasmodic) Cough, Asthma, Non-diphtheritic Sore Throat, Toothache, Piles." Its internal use for colic is also advised. On a card it is asserted that, if used in time, Vacher-Balm will abort boils.

The Council declared Vacher-Balm inadmissible to New and Nonofficial Remedies because 1, it is advertised indirectly to the public (Rule 4), 2, the claims made for it are exaggerated and unwarranted (Rule 6), and 3, the name of this pharmaceutical mixture of established drugs is not descriptive of its composition (Rule 8).

WHOOPING COUGH BACTERIN NO. 44 (PERSSON) SEPSIS BACTERIN NO. 40 (PERSSON) RHEUMATIC ANTIGEN NO. 38 (PERSSON) GONOCOCCUS ANTIGEN NO. 35 (PERSSON) NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

Acceptance for New and Nonofficial Remedies of the following "mixed" vaccines of the Persson Laboratories, Mt. Clemens, Mich., was requested by the Persson United States Distributing Company, General Distributors for the U. S.:

Whooping Cough Bacterin No. 44 (Persson): Containing killed Bordet-Gengou bacilli, Pfeiffer's influenza bacilli, catarrhalis micrococci, pneumococci and streptococci.

Sepsis Bacterin No. 40 (Persson): Containing killed streptococci, pneumococci and colon bacilli.

Rheumatic Antigen No. 38 (Persson): Containing pneumococci, streptococci, and colon bacilli.

Gonococcus Antigen No. 35 (Persson): Containing killed gonococci, colon bacilli and staphylococci.

The Council accepts a biologic product representing two or more organisms for inclusion in New and Nonofficial Remedies only if there is satisfactory evidence that its therapeutic use is rational. No evidence was presented to the Council to indicate that the mixtures represented by Whooping Cough Bacterin No. 44 (Persson), Sepsis Bacterin No. 40 (Persson), Rheumatic Antigen No. 38 (Persson), and Gonococcus Antigen No. 35 (Persson) are rational; hence the Council voted not to accept them for N. N. R.

YEAST PREPARATIONS AND VITAMIN B CONCENTRATES

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., April 15, 1922, p. 1146

The Council has adopted the following principles as a guide in the consideration of yeast preparations and vitamin B concentrates for New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

1. The claim that deficiency of vitamin B and diseases resulting therefrom are common conditions in the United States is not at this time supported by adequate acceptable evidence.

2. The claim that yeast preparations or extracts are, in principle or in general, essentially more effective or more practical or more available means of administering vitamins than the commonly available vitamin-containing foods is not at this time supported by adequate acceptable evidence. (Any claims for superiority made for such products proposed for inclusion in New and Nonofficial Remedies must be presented in detail and passed on specifically by the Council.)

3. The claim that therapy with yeast or yeast preparations has as yet more than an experimental status is not at this time supported by adequate acceptable evidence.

Preparations for which such claims are made, directly or by implication or in one-sided quotations, in advertisements or letters or by salesmen, cannot be admitted to or retained in New and Nonofficial Remedies.

YEAST PREPARATIONS

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 8, 1922, p. 135

At its 1922 meeting, the Council directed that a general article, giving the present status in medicine of yeast and yeast preparations, be prepared. A committee was appointed for the purpose. This committee submitted to the Council the report which appears below, with the recommendation that its publication in THE JOURNAL and its subsequent inclusion in N. N. R. be authorized. The Council adopted the report of the committee, and, accordingly, the article, Yeast Preparations, appears below. W. A. PUCKNER, Secretary.

Yeast and preparations from it have long been used both externally and internally in medicine. Yeast, as commonly understood, is the ordinary brewer's or baker's yeast, consisting of the minute unicellular organism *Saccharomyces cerevisiae*. These cells have long been characterized by their power to convert certain sugars into products of fermentation, a reaction in which enzymes present in the yeast are concerned.

So-called dried yeast is usually obtained by filtering off the yeast cells grown on extracts of malted grains; they are completely or partially dried and may, or may not, contain a considerable admixture of starchy substance. Lately, preparations of relatively uncontaminated dried yeast have been marketed. Some of the dried yeast preparations are intended to retain their fermentative power. In others this has been destroyed by the process of desiccation. The so-called compressed yeast sold in freshly prepared form, usually with some admixture of a starchy substance to give it a suitable texture, will retain its fermentative activity for several days

when kept at a low temperature. To what extent other microorganisms are likely to contaminate the commercial yeast preparations is not generally known.

Actions and Uses.—Since fermenting liquids, if concentrated enough, have been assumed to have a bactericidal action, yeast has been proposed for use as a bactericide in the treatment of infections of the superficial tissues. Its application for this purpose has, however, been practically abandoned, although there are traditional accounts as to the healing properties of fresh yeast applied to open wounds. As yeast is one of the richest sources of vitamin B, which has recently come into prominence as a hitherto unrecognized food component essential to nutritive well-being and widely distributed in common foods, yeast and preparations derived therefrom have been widely extolled of late as sources of this vitamin whenever there may be indications for its therapeutic use. The latter are still so indefinite, aside from rather exceptional instances, such as beriberi, and the opportunities to obtain vitamin B through the customary foods entering into the dietary of man are so abundant that the special demand for the yeast vitamin seems to be limited relatively at the present time. At all events, the alleged curvative or tonic value of special vitamin B bearing products has been emphasized through widespread advertising to an extent unjustified by available evidence. The beneficial effect of products containing vitamin B on animals subsisting on a diet deprived of this food factor is truly remarkable; but this fact, attested by laboratory observations, should not be interpreted to mean that there is a widespread avitaminosis in this country or that the need for vitamin, other than in exceptional cases, cannot readily be supplied through simple dietary measures. The therapeutic aspects of the vitamin problem are still in the experimental stage.

The ingestion of yeast in liberal portions is known to produce a laxative effect. In some cases, particularly in young children, such use of yeast has been followed by intestinal distention, doubtless attributable to fermentative gas production by the surviving yeast cells. There is, however, a preponderance of evidence regarding the advantageous use of yeast as a mild laxative. Aside from the objectionable possibility just referred to, there are no serious contraindications. Whether the laxative action of yeast is due to the survival of the living cells and some product of their reaction in the intestine or to a chemical component of yeast which may also be present in dead cells is not clear at present. Yeast has often been recommended for internal administration because of its supposed beneficial effects on furuncles, acne, etc. Its adherents assert that it is almost a specific. Many, if not most, clinicians doubt this remarkable effect, which may, after all, be expected from any anticonstipation agent. Whether yeast or its products can provoke a leukocytosis likewise remains undemonstrated. Many of

the conditions for which yeast and yeast preparations have been recommended therapeutically are so variable in their clinical course and so likely to show improvement without special treatment that the elaborate claims made in regard to yeast therapy for somewhat indefinite disorders must be largely discounted. It is not clear to what extent, if at all, live cultures of yeast may be used to change the intestinal flora, if, indeed, such a reaction becomes desirable in many of the conditions for which yeast is commonly used.

Concentrated liquid extracts of yeast (which are rich in vitamin B) have long been used as substitutes for meat extracts in making bouillons and soup stocks, and it is asserted that meat extract is sometimes adulterated with yeast. Yeast vitamin concentrates have been prepared from extracts of yeast by a variety of methods.

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