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Clinical, Functional and Histologic Responses of Fatty Metamorphosis of Human Liver to Lipotropic Therapy: Lipotropic therapy has been a major advance in the treatment of liver cirrhosis. Normally, an adequate supply of lipotropic substances (methionine, choline, and others) permits phosphorylation of neutral fats to phospholipids, in which form fats are more easily transported from the liver to the various tissues of the body. Inadequate supply or utilization of lipotropic substances, due either to faulty nutrition, hepatic injury, or endocrine disturbance, may result in fatty infiltration and eventual cirrhosis of the liver. Most of the experimental work, including that on the relation of lipotropic agents to nutritional cirrhosis, has been performed on animals. In man, the studies on the effect of lipotropic substances have centered chiefly on the therapeutic results in cirrhosis. There have been few studies dealing with the histologic changes occurring in the livers of human patients following lipotropic therapy. The majority of investigators reported favorable response, especially in those subjects having large livers. The recently expanded use of the liver biopsy permitted a histologic evaluation of lipotropic therapy in human fatty livers. The present study concerns itself with a comparison of the clinical, functional, and histologic responses of patients with fatty livers to lipotropic therapy and the problem concerning whether disappearance of fat is associated with histologic, functional, and clinical improvement in patients with fatty livers with and without cirrhosis.

The 15 patients selected for this study had enlarged livers with from moderate to severe fatty infiltration as proved by initial needle biopsy. The patients were divided into two groups. Group I consisted of 5 persons without cirrhosis, the severe fatty changes in the liver being presumably due to disturbed nutrition. Four were chronic alcoholics and one had pellagra. They were essentially asymptomatic, showing no signs of liver disease. Group II consisted of 10 patients with fatty cirrhosis. Most of these presented some of the usual signs and symptoms of cirrhosis such as ascites, jaundice, splenomegaly, spider nevi, and gastro-intestinal disturbance, as well as the laboratory findings of impaired liver function. As shown in the table below, patients

TYPES OF THERAPY (DAILY AMOUNTS)	NUMBER OF CASES	
	Group I—Nutritional Fatty Liver	Group II—Fatty Cirrhosis
1. High protein-high vitamin B complex; CHO 450 Gm.; protein 200 Gm.; fat 80 Gm.; thiamine 50 mg.; vitamin C 500 mg.; nicotinic acid 300 mg.; Brewer's yeast 45 Gm.	1	2
2. Choline Gm. 3; cystine Gm. 3; CHO 450 Gm.; protein 80 Gm.; fat 50 Gm.; thiamine 25 mg.; vitamin C 100 mg.; nicotinic acid 100 mg.; Brewer's yeast 12 Gm.	2	6
3. Methionine Gm. 5; CHO 450 Gm.; protein 80 Gm.; fat 50 Gm.; thiamine 25 mg.; vitamin C 100 mg.; Brewer's yeast 12 Gm.	2	2
Total number cases	5	10
Number of cases with repeat biopsies	2	7
Total number biopsies	9	27

of both groups received either a high protein diet plus considerable vitamin B complex, or a basic diet plus cystine and choline, or the basic diet plus methionine. Although choline plus cystine and methionine may have effects other than lipotropic, in this study only their lipotropic properties were conconsidered.

Prior to institution of therapy all livers showed histologically from moderate to severe fatty changes. The earliest histologic response became evident after 2 weeks of therapy, and in 4 weeks practically all livers showed disappearance or marked diminution of fat. With the disappearance of the fatty globules from the parenchymal cells, increased glycogen storage became evident. The irregularity in size and staining qualities of cytoplasm and nuclei disappeared or became less marked. Regeneration of injured hepatic cells also took place. Of the 7 cirrhotic patients on whom biopsies were repeated, only one showed a decrease in fibrosis and periportal inflammatory activity after treatment. One patient showed no significant change; 5 patients showed no halt in the progression of the mesenchymal reaction. In these 5, Mallory's connective tissue stain revealed an increase and thickening of collagenous fibers extending from the periportal fields into the nearby surrounding parenchyma. Gomori's reticulum fiber stain showed a change in the reticulum pattern in the vicinity of the portal triads. The individual fibers were more closely spaced, much coarser, and showed evidence of sprouting. This indicated new formation of fibers and not mere collapse after reduction of the size of the liver cells due to the disappearance of fat. This increase in connective tissue was associated with a more marked periportal infiltration, consisting chiefly of mononuclear phagocytes, lymphocytes, and occasional polymorphonuclear leukocytes.

No significant difference in the favorable clinical and morphologic responses brought on by the different lipotropic agents was noted in this series. After three weeks of treatment, the patients with the originally asymptomatic nutritional fatty livers remained well clinically. In those with cirrhosis all but 2 claimed to be subjectively improved as evidenced by increased appetite, feeling of well-being, and vigor. Objective improvement, as measured by weight change, reduction in ascites, disappearance of jaundice, and an improved blood picture, was seen in 12 of the 15 patients.

Considering the liver function tests as a whole without regard to individual types, little functional impairment was shown in the group with nutritional fatty livers prior to treatment. In only 16 percent of all 68 tests performed were abnormal ranges found. The greatest abnormalities occurred in the serum alkaline phosphatase, total cholesterol, cholesterol esters, and thymol turbidity tests. After treatment of these patients, all 142 tests, except for the thymol turbidity, showed general improvement.

In the group of patients with cirrhosis, 67 percent of 131 function tests performed were abnormal before treatment, the greatest abnormalities occurring in the cephalin-cholesterol flocculation, thymol turbidity, serum alkaline phosphatase, albumin-globulin ratio, serum bilirubin, and urinary

urobilinogen. After treatment of these patients, only 41 percent of 133 tests performed were abnormal; all tests showed approximately equal improvement except for the thymol turbidity, which showed no change.

A striking finding was the consistent elevation of total cholesterol in both groups of patients after lipotropic therapy. The average increase in the group with nutritional deficiency was 51 mg. per 100 ml., and in the group with cirrhosis, 18 mg. per 100 ml. The cholesterol ester fraction revealed no significant change.

It might be considered that the increase in fibrosis seen in these patients following lipotropic therapy was due to a collapse of the reticulum as a result of loss of fat from liver cells. There are, however, several points which are in favor of the increase in fibrosis being reactive and not due to collapse of the reticulum. First, paralleling the increase in connective tissue there is also an accompanying increase in periportal infiltration. Second, specific fiber stains reveal definite changes in the reticulum pattern. The disappearance of fat without decrease of fibrosis after lipotropic therapy agrees with the findings of Gilman and Beams and the clinical observations of Weir and others in human cirrhosis. Recently, Best's group of workers has shown an apparent decrease in fibrosis in rats after lipotropic therapy. This discrepancy between human and animal experiments may possibly be due to differences in species in the handling of fat. Time as a factor, especially in view of the shorter life span of the experimental animal as compared with man, also must be taken into consideration in that the longest period of histologic check-up in this study was seven months. It is possible that with longer periods of observation, a more favorable response of connective tissue to lipotropic agents might have been obtained. Nevertheless, the clinical implications of progressive fibrosis found histologically in the liver in some patients, coincident with clinical and functional improvement, is important in the evaluation of therapy for cirrhosis. The fact that dietary and lipotropic therapy of cirrhosis has undoubtedly been beneficial from both a clinical and laboratory standpoint does not necessarily mean that such therapy can bring about cure of this chronic disease. It is possible that many of the patients who have shown marked improvement under lipotropic therapy, if followed for a long enough period of time, will be found eventually to succumb as a result of the continued fibrotic process in the liver. The stage of irreversibility in the liver in some patients may occur quite early, even in the fatty stage of cirrhosis. These facts deserve consideration in the evaluation of lipotropic therapy of cirrhosis.

The striking increase in serum cholesterol following lipotropic therapy is consistent with Bloor's findings and hypothesis that cholesterol, as well as phospholipids may play an important role in fatty acid transport. Lack of decrease in the thymol turbidity after therapy may have several possible explanations. It may be due to regeneration still taking place in the liver. Hoagland has postulated that the thymol turbidity may be a measure of regeneration rather than of parenchymal damage. Another possible explanation

is that it may be due to the hypercholesterolemia following therapy, noted in this study. It has been demonstrated that thymol turbidity depends not only on globulin but that it also bears some relation to the serum lipids. In some types of lipemia the thymol turbidity may be increased independently of liver damage. (Am. J. Clin. Path., April '48 - M. Franklin et al.)

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Studies of Urinary Excretion of Methionine by Normal Persons and by Patients Having Liver Disease: The increasing use of methionine in the treatment of diseases in which there is liver damage makes the further study of the metabolism of this essential amino acid necessary. It is particularly important to establish the degree to which ingested synthetic methionine is utilized by the body, especially for comparison of normal persons with patients having parenchymatous damage of the liver.

This report concerns the urinary excretion of added dietary dlmethionine by 6 normal children and 3 adults as compared with that by 7 children and 4 adults of similar age and weight who showed laboratory or clinical evidence of liver disease.

Dl-methionine was given in the form of 0.5 Gm. tablets of "Meonine." For the children aqueous solutions were prepared from chemically pure crystals of the dl-form.

The microbiologic assay for methionine developed by Dunn, adapted for use with oxidized peptone media prepared by the method of Lyman et al., was used for all analyses. The organism used was Lactobacillus fermentii-36, which utilizes both the d- and l-forms of methionine. Titratable lactic acid produced by a standard growth of the organism served as an index of methionine present. Urea, the principal growth-inhibitor (to Lactobacilli) found in urine, was removed by treatment of urine with purified urease.

The results of this study confirm those of Dunn (insofar as methionine is concerned) who, in 1946, when he studied the urinary excretion of 12 amino acids, found values for methionine averaging 2.7 mg. per 24 hours.

In one group of patients suffering from hepatic disease the values for the urinary excretion of methionine showed no significant difference from those found in normal persons. Ingestion of additional methionine in one large dose (3 Gm. to children, 5 Gm to adults) produced both in normal persons and in patients with hepatitis or cirrhosis, a sharp rise in the urinary figures of methionine. However, the total amount excreted was found to be relatively low, and has reached an average of only 10 percent of the supplementary dose of methionine given. Thus, it may be assumed that in persons with abnormal livers, methionine may be utilized apparently to the same extent as in normal persons. It seems that the liver damage must be extensive before significant alteration of urinary excretion of exogenous (or endogenous) methionine can be found.

Slight prolongation of high methionine levels in the urines of patients suffering from hepatic disease would appear to be the only deviation from excretion by normal persons. This difference manifested itself only in the group of adults with their more severe hepatic abnormalities and was not apparent in the group of children suffering from mild hepatitis. Interpretation of this finding must include evaluation of the use of dl-methionine. Although the occurrence of d-amino acids in proteins has been reported, their significance in human metabolism has not been established. Since Lactobacillus fermentii-36 measures both enantiomorphs, the isomeric type of the methionine found in these studies remains to be established. It is not unlikely that the increased post-ingestion values represent renal spillover from a transient hyper-d-methioninemia produced by administration of dl-methionine in amounts greater than physiologic needs. This explanation is supported by finding low basal excretion levels, suggesting that methionine is ordinarily almost completely metabolized, even in patients suffering from hepatic disease.

In severe cirrhosis, the absorption of methionine (solution of crystalline methionine) from the small intestine is slightly impaired, as shown by Machella in the authors' laboratory. It is questionable whether this slight delay in absorption represents a satisfactory explanation for the prolongation of high methionine levels in the urine, extending over several days after the ingestion of one dose.

It is concluded that methionine is well utilized by patients with hepatic disease of mild or moderately severe nature. (Am. J. M. Sc., March '48 - J. E. Wheeler and P. Gyorgy)

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The Treatment of Keloids: Keloids may range in size from a slight thickening of scar tissue and from an area a few millimeters in diameter to tumors as large as an adult fist, or even larger. There may be keloidal bands which cause disfigurement by drawing the soft parts out of position, such as occurs about the mouth or eyelids. Keloids may be red, brown, the normal color of the skin, or even paler than the skin. At times, they are pedunculated. They may be sensitive to pressure. Keloids that have existed for a long time and those that have developed very slowly are likely to be firm and even hard to the sense of touch. Recently developed keloids of comparatively rapid growth are rather less hard to the palpating finger. Telangiectasis may occur before the patient receives any irradiation.

The underlying constitutional cause of the formation of keloids is not known, but the exciting cause is traumatism, and the traumatism is not always some operative procedure. Repeatedly it has been seen that keloids develop on the basis of a small "pimple" which has been scratched by the patient. This occurs especially in the upper sternal region. There must also be some local factor which is active in the etiology, for in the removal of a number of moles from a patient by electrodesiccation, it was noticed that one or more of these

showed hypertrophy when other lesions on the same patient, and apparently of the same character, showed no such hypertrophy. This indicates that the cause is not merely a constitutional one.

Usually the patient with keloids seeks relief because of deformity or for cosmetic reasons, but occasionally he may come for treatment because pain is a prominent symptom. In other cases, keloids may cause actual mechanical obstruction, such as interference with the wearing of shoes, when they occur on the feet.

Keloids are difficult to treat. It requires much patience on the part of both the patient and the physician. So far as is known, the roentgen rays and radium are the only two agents which will arrest the lesion or cause it to disappear, and if these agents are used thoroughly when a scar begins to hypertrophy, there will probably be no need of combining excision or electrosurgery with them. It is because of the frequent neglect of hypertrophied or growing scars that it is necessary again to call attention to these methods of treatment. If the general practitioner, the surgeon and the dermatologist are alert and apply skillfully the roentgen rays and radium to scars that are beginning to show hypertrophy, keloids will cease to be a problem in the field of medicine. Because of the great tendency of recurrence in the wound after excision of the keloid and very generally because the second keloid is larger than the first, the surgeon may feel almost helpless. This helplessness is unnecessary if the surgeon will combine the skillful application of irradiation to the wound after his excision of the keloid.

Generally, in the radiotherapy of keloids the aim should be to produce a progressive atrophy without erythema or destructive effect on the skin or overlying epithelium. The technic will vary considerably with the size or thickness of the keloids, especially in the cases in which the roentgen rays alone are used. The thicker and older keloids will require more irradiation and more filtration and correspondingly a longer course of treatment. In the more recent cases of hypertrophied scars in which the scar tissue is still young, considerably less treatment is necessary, and less filtration, because it is likely to be more superficial.

Immediate treatment is important when the physician can observe any tendency of the scar to hypertrophy. It is true that some scars show a little tendency to hypertrophy and later undergo atrophy and need no treatment, but it is better if such spontaneous recovery is not awaited. If keloids can be treated within a month or two after the hypertrophy has been recognized, the keloidal tendency will be arrested usually by roentgen rays or radium alone. Either of these agents will produce a satisfactory result, and can be used according to the convenience of the radiologist.

The most frequent and the most extensive keloids follow burns. Therefore, the attending surgeon or physician should give special attention to the scars following the healing of extensive burns, for, as is well known, such burns when

associated with keloids lead to contractures, deformities, and distressing appearances.

Even a very small scar undergoing hypertrophy, for example, if it is located on the upper lip or somewhere on a young girl's face, is very important. As soon as this hypertrophy is recognized, one or two treatments with from 80 to 100 percent of an erythema dose confined to the lesion will do no harm and generally will arrest the hypertrophy. This treatment is given with superficial or 125 kv. therapy; if one or two doses do not cause this hypertrophy to disappear, then it should be repeated. It is the authors' practice in such cases to repeat these treatments one or two months apart. In these small lesions, a large dose can be given and in the authors' observation it has not done any harm at any time, and the results have been perfect. Even ordinary scars are benefited and made to disappear if treated early by irradiation.

With this thought in mind, when treating even a small lesion on the face, the authors frequently give a postoperative erythema dose preferably about the time that the lesion is healed. They believe that this helps to prevent any hyperplasia and even makes the scars less prominent.

In all instances, the larger the area involved the less must be the individual dose and the more frequently it should be applied, especially until the tendency to hypertrophy has been arrested; e. g., in treating a lesion on the upper lip, 5 mm. in diameter, it is safe to give from 80 to 100 percent of an erythema dose at once, and to repeat it in a month or two, but if the lesion is 4 or 10 cm. in diameter, it is unsafe to give such large dosage, and it is better to give a 25-percent dose at weekly intervals, or a 50-percent dose at a two-week interval.

The older the keloid the more fibrous tissue has formed, and the more fibrous tissue there is present in a lesion, the less will be the response of the lesion to irradiation. It must not be expected that large and older keloids will disappear following the irradiation without leaving some scarring and atrophy, and perhaps even some telangiectasis. For that reason, it is best to remove the thickened keloid or reduce it to the level of the skin, and then allow it to granulate under control observation, and control postoperative prophylactic treatment.

These older keloids may be removed with the scalpel, by electrosurgical excision, or by electrodesiccation. Because of the general experience that keloids form, especially after burns, it would seem illogical to attempt to remove the lesion by electrosurgery or to destroy or reduce its size by electrodesiccation, but experience has shown that excellent results can be obtained by this means.

When an older keloid is from 2 to 5 mm. in thickness, it seems best to destroy it or reduce it to the skin level by electrodesiccation.

If it is thicker than this, it seems best to remove it either by electrosurgical excision or by excision with the scalpel. Generally, it is impossible to close the wound by sutures. Therefore, after the excision or destruction, the tendency to reformation of the keloid must be controlled by means of irradiation.

The authors have no proof of the value of preoperative irradiation. However, there is abundant proof of the value of irradiation given immediately after operation, for in all their experience they have been able to prevent a recurrence of the keloid by means of postoperative irradiation.

The time for the postoperative irradiation is not definitely established, but the authors know from a very extensive general experience that from 50 to 100 percent of an erythema dose can be given immediately after an operation, or within a few days, and this in no way interferes with the healing of the wound. Therefore, it would seem advisable to give 80 percent of an erythema dose shortly after the operation. At the end of two weeks the scar should be inspected, and the dosage repeated, or after the operative wound has healed if it has been sutured. If the wound is healing by granulation, treatment should be repeated in about two weeks with a 50-percent erythema dose. After that time, an inspection should occur in at least from two to four weeks, and immediate treatment should be given if there is still any tendency to hypertrophy of the scar. Such a method of treatment will do no harm, and will not interfere with the healing of the wound by granulation tissue.

In general, this postoperative treatment is best given by means of the roentgen rays with 1 or 2 mm. of aluminum filtration depending on the thickness of the lesion, and using 125 kv. This will give sufficient depth value with less superficial destruction of the epithelium. The distance should be regulated according to the size and thickness of the lesion, varying from 30 cm. distance for a small lesion 1 or 2 cm. in diameter, and 1 or 2 mm. thickness; or 50 cm. for a larger lesion, varying from 5 to 10 cm. or more in diameter, and 3 mm. or more thick.

When excising a keloid it is inadvisable to make an extensive excision such as would be done with a malignant tumor. The excision can be confined rather closely to the actual outline of the keloid.

In some locations, treatment of keloids is more easily carried out with radium than with roentgen rays, or it may be possible to cross-fire with a combination of roentgen rays and radium. Knox used this method to good advantage in the extensive and deep-seated keloidal masses developing in the cheeks. Radium was placed in the mouth and roentgen rays were applied to the external surface of the cheek.

Flat radium applicators are usually employed when treating a keloid with radium. In all cases the "soft" beta rays should be eliminated by suitable screening. If the lesion is more than 1 or 2 mm. thick, only gamma rays should be used. In general, the advice given relative to the roentgen treatment of

keloid holds for radium when used for the same purpose. A half-strength, glazed, flat element applicator, screened with 0.1 mm. aluminum, may be placed in contact with the keloid for ten, fifteen, or twenty minutes, depending on size, age, and location. Treatments may be repeated about once monthly. Such applications are suitable for superficial lesions. Gamma rays are employed for thick, hard lesions. The flat application (half-strength) may be screened with 1 mm. brass, and 1 mm. aluminum and placed in contact with the lesion for from eight to twelve hours. This may be given in one treatment or in divided doses of one or two hours daily. Tubular applicators, containing 25 mg. element, or 25 mc. radon, and screened with 1 mm. brass, 0.5 mm. silver and 1 mm. aluminum or 0.5 mm. platinum and placed at a distance of 1 cm. or 2.5 cm., may be held over each square inch of surface for from two to six hours. (Am. J. Roentgenol., March '48 - G. E. Pfahler and G. P. Keefer)

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Modern Management of Hyperthyroidism: A knowledge of the fundamentals of hyperthyroidism is essential if the new antithyroid agents are to be used most effectively. The originating factor in hyperthyroidism is not exactly known, but it is suspected that the original stimulus comes from the hypothalamus, which in turn stimulates the anterior pituitary. This in turn produces the thyrotropic stimulating hormone, which results in hyperplasia within the thyroid. From this there follows an excessive synthesis of thyroxin, which results in hyperthyroidism.

Because nerve tracts originate in the hypothalamus, emotional strain has played an interesting and important part in hyperthyroidism. Patients have been known to be thrown into fatal hyperthyroid crises by emotional strain. These emotional states have an unpredictable effect on the thyroid and produce varying degrees of hyperthyroidism. On the basis of metabolic rate studies alone, the activity of the thyroid cannot be measured in terms of predictable fatality. At the Lahey Clinic reactions of extreme severity have been seen in patients with a metabolic rate of 25, and patients with a rate of 90 have been operated upon without undue postoperative reactions. In a group of individuals with apparently equally unstable nervous systems, some become psychotic when hyperthyroidism develops, and others do not. The effects of thyroid activity are more far-reaching than is often considered. For instance, Eggenburger demonstrated that the incidence of goiter in one of the Swiss cantons was 79 percent, and that following the compulsory iodination of all salt to be used for foods, this dropped in ten years to 9 percent; but, in addition, the average height of recruits in this period increased one inch, and the number of harelips, cleft palates, and spina bifida decreased.

All of the generally known effects of thyroid activity are based on the use of iodine by the thyroid, and iodine metabolism is probably the thyroid's major function. Workers at the Lahey Clinic for this reason have been interested in blood iodine studies. In Boston the blood iodine in normal persons, as shown

in 7,000 determinations, is about 7 gamma per 100 c.c. (1 gamma = .001 mg.), and in patients with hyperthyroidism the blood iodine runs from 21 to 100 gamma per 100 c.c. At first the studies concerned the total blood iodine, and the relationship between these values and the state of the hyperthyroidism after Lugol's solution was not understood.

Through improved chemical methods, it is now known that when a patient is given Lugol's solution, although the total blood iodine is raised, actually the protein-bound organic iodine is lowered. When a metabolic rate is lowered by x-radiation, irradiated iodine, subtotal thyroidectomy, or by ligation of the arteries to the gland, the protein-bound iodine, or that fraction of the iodine that is bound in the thyroxin, is lowered, and the patients are improved clinically. From a practical point of view, however, the determination of the protein-bound iodine is of no clinical value in the diagnosis of hyperthyroidism, because the normal amount of blood iodine in a patient in Boston is higher than the normal amount of iodine in a patient in Cleveland, for example. In blood iodine studies, the normal iodine in the patient's environment whether the patient is on a diet rich in iodine and whether he is on medication that contains iodine must be considered. Furthermore, because an iodine determination is a time-consuming task and subject to great error, it is felt that it is of value only for activities that deal with cases of thyroid disease in considerable numbers and are doing experimental work with it. It is not comparable to the basal metabolic rate for routine evaluations.

At the Lahey Clinic it has always been thought that patients with stormy postoperative courses must have an excessive outpouring of thyroxin. It can now be demonstrated by iodine determinations performed about two hours after the operation that there is a prompt rise in the protein-bound iodine, indicating that there is an excessive output of thyroxin. It also can be shown that the arteries going to the thyroid carry less protein-bound iodine than the veins coming from the gland.

If patients who have hyperthyroidism are given antithyroid agents, such as thiouracil, thiobarbital, propylthiouracil, or methylthiouracil, either something happens to the iodine with which the gland manufactures thyroxin or to the process by which iodine is synthesized into thyroxin. The iodine within the gland is in the form of an iodide that must be liberated as free iodine to combine with tyrosine forming diiodotyrosine as an intermediate step in the formation of thyroxin. The antithyroid agents bring about their interference with the liberation of free iodine from the iodide, or obstructing the cooxidase process that goes on in the thyroid acinar cells. If enough of the antithyroid agent is given, synthesis of thyroxin will be stopped, but the thyroxin that is already manufactured will not be affected. No matter how high the metabolic rate is, if one of the antithyroid agents is given long enough, not only is the rate brought to normal, but myxedema can be produced.

There have been some misconceptions about antithyroid agents. There are patients who become iodine-fast and whose metabolic rate will no longer drop; but, there are no patients whose rates will not ultimately drop to normal

if they are given enough of the antithyroid agent and it is not combined with iodine. Every person has a given daily requirement of thyroxin. If the manufacture of thyroxin was stopped completely, the time it would take a metabolic rate to come to normal would depend on how much thyroxin was used each day and how much the gland had stored. The Lahey Clinic has established the following rules which are roughly dependable: In a patient with exophthalmic goiter, or primary hyperthyroidism, on daily doses of from 200 to 400 mg. of propylthiouracil or methylthiouracil, the metabolic rate will drop about one degree a day. In a patient with toxic adenoma the rate will drop about half a degree each day. This difference is due to the fact that the gland in exophthalmic goiter is relatively small and can store thyroxin in only limited quantities; but in a toxic adenoma of large size filled with colloid, which is the vehicle of thyroxin, large amounts of thyroxin can be stored.

Thiouracil and thiobarbital have been largely abandoned because of the high incidence of complications. At the clinic, the complications with the use of thiouracil have been 9 percent, with thiobarbital, 28 percent, and with propylthiouracil, 1.25 percent. Methylthiouracil has not been used long enough to be able to report on it. One problem has been the prevention of agranulocytosis caused by bone marrow depression. Workers at the clinic believe that when a leukocyte count drops to 4,500 or a differential count drops to 45 percent polymorphonuclear leukocytes, it is time to stop the antithyroid agent. It is dangerous to go below these points because following the omission of the agent the leukocyte count will continue to fall for a time.

The thyroid-stimulating hormone of the pituitary gland if uninhibited produces thyroid hyperplasia. Hyperplasia produces an excess of thyroxin, which gives rise to hyperthyroidism. Normally a stimulus from the pituitary gland in the presence of an inadequate amount of thyroxin produces more thyroxin; but, when there is too much thyroxin, its effect on the pituitary gland is to diminish the output of the thyroid-stimulating hormone, and thus the thyroid is in balance. In preparation for surgery, when a patient with hyperthyroidism is given an antithyroid agent, he should get no iodine until near the end of this antithyroid therapy; since the antithyroid agent inhibits the synthesis of thyroxin by reducing the available iodine, the administration of a large amount of iodine puts a greater load on the antithyroid agent. If the patient has had iodine, it takes a little longer to bring his metabolic rate to normal; and, if he has a toxic adenoma and has had iodine, it takes longer still to bring the rate to normal. If a hyperthyroid patient has a metabolic rate of plus 45, it takes about forty-five days on antithyroid therapy to prepare him for surgery; and if he has a toxic adenoma, twice as long. With the present acute shortage of hospital beds, these patients are now given antithyroid agents at home and their leukocyte and differential counts are checked and reported weekly by their family doctors. When these patients are given antithyroid agents and their metabolic rates brought to normal, the histologic picture in the gland is unchanged. For this reason, it has been felt that these agents do not constitute a substitute for surgery. Too many patients who were thought to have permanent remissions

with this treatment are now having recurrences. The length of time the agent is given has nothing to do with whether or not a permanent remission will result. Even propylthiouracil, which is the safest of all the agents, cannot be given over long periods without regularly checking the leukocyte and differential counts. Since the mortality from surgery is low (1,100 patients with toxic goiters, prepared with one of the antithyroid agents, have been operated upon at the clinic with but one death, and that from a coronary thrombosis on the second day), since the incidence of tetany is less than 0.5 percent, since the incidence of recurrent laryngeal paralysis is less than 0.3 percent, and since the incidence of recurrent hyperthyroidism is less than 1 percent, at the Lahey Clinic it is believed that surgery is the safest way of relieving hyperthyroidism.

The clinic is constantly trying to improve the methods of preparing these patients for surgery. It has been found that, if patients prepared with thiouracil alone are operated upon, the glands are so hyperplastic and so friable that bleeding cannot be controlled. They will not hold ties or hemostats, and operation is technically impossible. When these patients are prepared with an antithyroid agent and then the gland is involuted with iodine, these patients are successfully handled. Ten minims of Lugol's solution are given daily for the last three weeks of the preparation period. This does not interfere with the drop in metabolism from the antithyroid agent and completely involutes the gland.

Problems, almost impossible, prior to the time antithyroid agents existed may now be solved. For instance, one of the clinic patients with hyperthyroidism, a 77-year-old woman with a metabolic rate of 44, also had auricular fibrillation, heart failure, and diabetes. When she was given thiouracil, her metabolic rate dropped to 1, and following subtotal thyroidectomy when compensation had been restored, her postoperative pulse rate never exceeded 80. Another example is the psychotic patient whose psychosis has been brought on by hyperthyroidism. He cannot be put in a general hospital because often he will shriek and yell and have to be restrained. The mental hospital, on the other hand, is usually not equipped to manage such a seriously ill patient. He can now be given an antithyroid agent until his metabolic rate is brought to normal, and the psychosis disappears. Then he can be operated on in a general hospital.

How patients with chronic cardiac decompensation can be restored to complete compensation in a week, when, previously, before operation, neither by rest, digitalization, or any of the methods of cardiac management could compensation be restored, is explained simply. Metabolism and circulation rate go hand in hand. At the clinic the circulation rate is determined by introducing decholin in the median cephalic vein and measuring the time interval until it is tasted. When there is a normal metabolic rate, but a heart that is incompetent, that is true cardiac decompensation. When there is hyperthyroidism with an elevated basal metabolic rate and a heart that is capable of producing the compensatory increased circulation rate, that is the average case of hyperthyroidism without heart failure. When, on the other hand, there is

hyperthyroidism with a heart incapable of meeting the demands for an increased circulation rate, that is true thyrocardia. It is by lowering this elevated metabolic rate, either with one of the antithyroid agents or by means of subtotal thyroidectomy, that these patients are put back in cardiac balance.

Although nothing can be done for severe exophthalmos of long standing, if the patient with excessive exophthalmos comes for treatment before there has been a high degree of lid compression and interference with the nutrition of the eye, the eye can be saved and in some cases with a fair cosmetic result. This is done by the neurosurgeon who turns down two small flaps over the frontoparietal area, raises the anterior lobe, loosens the bony orbit, and decompresses the contents of the ocular canal.

The goiters that only extend a little way beneath the clavicle are really not true intrathoracic goiters. In true intrathoracic goiters, most, if not all, of the goiter is in the mediastinum. With rate exceptions these can be removed through the upper thoracic strip, no matter how large they are. The maneuver by which large tumors are removed involves grasping the top of the tumor above the clavicle, cutting a slit in the capsule, and separating it from the pleura. The local effects of intrathoracic goiter are tracheal compression and compression of the venous channel returning blood from the head. In attempting to remove intrathoracic goiters, it is important to introduce a rigid-walled metal intratracheal catheter under local anesthesia. If an intratracheal catheter must be used and the patient is given a general anesthetic in order to introduce the catheter, he can accumulate mucus and choke on the table before a catheter can be introduced. Often the constriction is so low that a tracheotomy cannot be completed in time. An intrathoracic goiter should be suspected in any patient with a goiter that extends behind the clavicle and in which there are dilated superficial thoracic veins readily seen under infrared light.

Apathetic hyperthyroidism, a state not recognized by many doctors who have not had very extensive experience with disturbances of the thyroid, is a low-grade disease, occurring in elderly persons over a period of years, characterized by no activation, no eye signs, and no enlargement of the gland. It is because of the absence of the usual signs of thyroid disease that it is often overlooked. It is associated with a small firm gland, marked myasthenia, and excessive weight loss. This disease should be considered in any patient with an unexplained tachycardia, myasthenia, and weight loss. (From material in the April '48 issue of the Bulletin of the U. S. Army Medical Department and originally presented by Frank Lahey of the Lahey Clinic of Boston at a recent Monthly Medical Meeting, Army Medical Center, Washington, D. C.)

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Epidemic Tinea Capitis, a Public Health Problem: In recent years, outbreaks of ringworm of the scalp in large city areas, especially in the eastern United States, have been repeatedly reported in dermatological and general medical literature.

Ringworm of the scalp is caused by several species of fungi, the most common being the Microsporon audouini and Microsporon lanosum. The M. audouini is capable of causing widespread outbreaks. Other species of fungi causing sporadic cases of tinea capitis are the M. fulvum, Achorion schoenleinii (favus), and other trichophyton organisms.

Ringworm of the scalp is characterized by localized, round scaly patches of alopecia with short broken-off hair. The fungus invades the hair and hair follicle, multiplies, and progresses down the wall of the follicle. Soon large numbers of mycelia form around the hair between it and the walls of the follicle. The mycelia and spores increase and proceed downward in the hair to the point where the hair bulb begins. The hair papilla which is responsible for the reproduction of new hair is never involved in this process. However, the hair will break off at the weakest point, which is the position of greatest parasitic invasion, just a few millimeters above the surface of the scalp. The bottom end of the hair is still infected, and because it remains in the follicle, the infection goes on. As fast as the hair grows upward, it is filled with spores and mycelia. Until some means is used to get the whole hair out en masse, or there is developed a vehicle containing a fungicide that can penetrate into the hair follicle, it is practically impossible to cure this disease.

The spread of infection to other parts of the scalp and to other persons is easily brought about by thousands of parasites on the smallest piece of hair which breaks off and falls on new regions. Infection is readily transmitted from one child to another by the interchange of caps, mufflers, barber shop instruments, backs of subway, and theater seats, etc.

In M. audouini infections, inflammatory reaction occurs in only a small percentage of cases and then is very little. Livingood and others have found that when there is a localized inflammatory reaction manifested by redness, pustular or true kerion reaction, the prognosis for cure by local medication is very good. Tinea capitis caused by the animal-type fungus, which produces an inflammatory reaction of varying degrees responds readily to treatment without the need of such intensive therapy as x-ray epilation. The inflammatory reaction aids in the spontaneous expulsion of the infected hair.

The incubation period of this infection is undetermined, and the period of communicability exists as long as the fungus or its spores can be found at the site of the lesions. Susceptibility in childhood is universal. Reinfection is common and there is no immunity after cure. M. audouini infection, known as the human type, is rare after puberty, but adults as well as children are susceptible to the animal type, M. lanosum, which is transmitted by contact with lesions or hairs from lesions of cats and dogs.

The long course of the disease and the ease with which it is spread make infection with M. audouini a serious one. The cost and time required for treatment, the psychic insults the infected child undergoes, and the long restriction necessarily imposed on his activities are conditions which make early and adequate treatment imperative.

Methods for prevention and control include the early recognition and reporting of the disease. It, like any other communicable disease, requires isolation and early and adequate treatment in each case to prevent spread of the infection to other areas of the scalp and body of the same individual as well as to prevent its spread to other children. Infected children should be excluded from school until recovery, and in institutions the infected should be separated from healthy children. Each child should use a stocking cap or other type of inexpensive head covering which can be destroyed by burning after use. All children under fifteen years of age who have had contact with an infected person should be examined by the Wood's light at regular intervals until it is reasonably certain that they are not infected. Cleanliness of the hair and scalp and education of the parents and school authorities must be maintained on a continual basis.

In the Hagerstown, Maryland, outbreak which started in 1944, a full-time officer of the United States Public Health Service was assigned to work with the deputy State health officer. He remained in charge from August 1944 to November 1945 with a staff assisting him. During that period a total of 8,657 children ranging from 6 weeks to 18 years of age were examined. Five hundred sixty-five (479 boys and 86 girls) were found to be infected. Of the cases among these children only 8 were not due to M. audouini. It was found that over 65 percent of the boys had the infection in the "clipper area." In the treatment program, in which 17 topical remedies were tried, trained personnel carried on intensive, closely supervised care through daily treatments at clinics. The results achieved among the 493 treated at the United States Public Health Service clinic were as follows: (a) 48 were cured by manual epilation with 1 or 2 treatments; (b) 274 were cured by topical application; (c) 126 discontinued treatment before being pronounced cured; and (d) 45 were under treatment at the close of the study period. Salicylanilide ointment 5 percent in carbowax 1500 and copper undecylenate saturated solution in carbowax 1500 were the most effective remedies.

Thallium sulfate for epilation of the hair is not recommended because of the danger of complications. Carrick used copper oleate, undecylenate-undecylenic acid and propionate-propionic acid as fungicides for 171 infected scalps during the period from October 1944 to March 1946 and reported cures in about 41 percent of the total number treated in this manner. Strickler reports that in 64 papercent, or 74 cases of M. audouini scalp infection out of 115, cures were obtained with 3-percent solution of acetic acid in iodine along with a wetting agent.

Criteria for diagnosis should include clinical evidence of the disease, characteristic fluorescence on examination of the scalp with Wood's light, demonstration of the fungi on direct microscopic examination, and in all cases positive culture with identification of the organism.

Criteria for cure should include the absence of clinical evidence of infection, absence of fluorescence when scalp is examined under Wood's light, and negative cultures for ringworm on any scale or any other likely material which can be obtained. Three negative cultures while the patient is under treatment and three negative cultures while without treatment taken at weekly intervals should be sufficient for the cultural requirements. Any equivalent to this requirement would be satisfactory.

Leading dermatologists have continued to stress in their writings the need for organized public health action in the prevention and control of this epidemic disease.

X-ray epilation followed by local therapy under supervision is the recommended treatment by most authors. Local treatment with penetrating liquid vehicles or other penetrating bases should be more widely utilized because x-ray epilation is not the ideal method. Immunological and hormonological methods should also be investigated further.

Lynch emphasized several warning points. Before epilation the use of topical applications is not only a waste of time but also, unless the applications are very mild, the irradiation must be delayed until any reaction has subsided. Inadequate or fractional dosage with x-rays is also to be decried because all these exposures have cumulative and permanent effects and an epilating dose cannot be administered after any considerable amount of previous roentgen treatment has been given. (Pub. Health Reps., 27 Feb '48 - R. K. C. Lee)

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Field Tests with Tick Repellents: The results of preliminary laboratory tests of certain organic materials as tick repellents were published in the Public Health Reports, 8 August 1947 (News Letter, 10 October 1947). Those which showed most promise and were available in sufficient quantity (N-n-butyl-acetanilide, 1-benzyl cyclohexanol-1, 2-phenyl cyclohexanol, benzyl benzoate, dimethyl phthalate, dibutyl phthalate, 6-2-2 mixture, and phthalic acid-hexahydro-diethyl ester) have subsequently been tested under field conditions, with Army cooperation, at Camp Bullis, Tex., June 1947. This area was selected because of the local abundance of the lone star tick, Amblyomma americanum.

Enlisted men from the 32d Medical Battalion, Brooke Army Medical Center, Fort Sam Houston, Tex., served as test subjects.

The data obtained concerned only nymphal and adult ticks, since the larvae were not sufficiently prevalent to provide significant information. Two series of tests were performed.

In the first series of tests, 20 men wearing treated and untreated regulation fatigue uniforms were exposed to heavy tick infestations for approximately 4 hours per day. Sixteen uniforms were treated in pairs, each pair with a different

repellent, and four were left untreated as controls. Freshly laundered garments were impregnated, once only, using a solvent (acetone) with 2 ounces of repellent per uniform. Since trousers were tucked in combat boots, socks were untreated. The test subjects were not told which uniforms were treated and which were untreated.

The second series of tests was, in substance, a repetition of the first, except that a comparison was made of dosages of 1 and 2 ounces per uniform and fewer materials were tested.

As might be expected, under conditions involving variables which could not be eliminated, the results of the tests were not wholly consistent, but none the less were strongly indicative of the relative repellent value of the various materials. Although the effectiveness of all test materials was reduced as a result of aging, wear and other factors influencing their chemical breakdown, this reduction was not constant. Similarly, the difference in the degree of protection from nymphs and adults and at dosages of 1 and 2 ounces, though perceptible, was not constant.

All materials tested gave some degree of protection. From the standpoint of maximum repellency, butylacetanilide and benzyl cyclohexanol consistently rated first and second respectively in all tests.

Only two compounds, butylacetanilide and phthalic acid-hexahydro-diethyl ester afforded complete protection against both nymphal and adult ticks on the first day after impregnation in the first series, and only the former on any subsequent days in both series. Although none of the materials at a dosage of one ounce gave complete protection from both nymphs and adults, butylacetanilide, benzyl cyclohexanol, and phenyl cyclohexanol did give a high degree of protection (more than 90 percent) on several different days.

It was noted (1) that reasonably consistent results were obtained from butylacetanilide throughout both series of tests, (2) that butylacetanilide gave from adequate to excellent protection against both nymphs and adults of Amblyomma americanum at dosages of both 1 and 2 ounces for 10 days of wear, and (3) that the end-point for persistence of its effectiveness was apparently not reached.

The data for the first series of tests suggested that benzyl cyclohexanol and phenyl cyclohexanol, though somewhat inconsistent in performance, were promising. In the second series both chemicals, at a dosage of 2 ounces, were almost equally as effective as butylacetanilide for the first few days of wear, but the effectiveness of benzyl cyclohexanol was greatly reduced after the fifth day and that of phenyl cyclohexanol after the third day.

Phthalic acid-hexahydro-diethyl ester, which showed promise of affording adequate protection up to 3 days, was not available for further testing.

In the first series, benzyl benzoate and dimethyl phthalate, though they gave reasonable protection from nymphs, were quite erratic in their performance against adults, and in the second series, insofar as observed, the results from benzyl benzoate were compatible with those of the first. Both materials in the first tests were more persistent in effectiveness than benzyl cyclohexanol and phenyl cyclohexanol.

Dibutyl phthalate and the 6-2-2-mixture provided insufficient protection and were erratic in performance in all tests.

As noted in an earlier report (loc. cit.) butylacetanilide does not stain fabrics and does not have an objectionable odor. Although no data are available on its toxicity, the related compounds N-n-ethylacetanilide and N-n-propylacetanilide have been tested by the United States Food and Drug Administration and pronounced safe from the standpoint of irritation to the skin. Furthermore, there was no evidence of dermatitis or other objectionable reaction among 29 persons wearing garments or socks impregnated with this compound.

When the impregnation of clothing by use of solvents is not feasible, treatment may be accomplished equally as well, and also more economically, by use of aqueous emulsions. Laboratory tests have shown that 5-percent emulsions of butylacetanilide in 1-percent solutions of sodium oleate, Tween 80, Triton X-500, Triton 720, or Triton 770, or in a 2-percent solution of laundry soap do not break after several weeks standing, and hence are sufficiently stable for practical purposes. Clothing dipped in an emulsion of this concentration takes up the amount of repellent required to provide adequate protection.

Incidental observations suggested that butylacetanilide affords complete protection from the two common (in the U.S.) species of man-infesting chiggers, Eutrombicula alfreddugesi and E. masoni. Although no controlled tests were performed, it was noted that the larvae of these mites when placed on impregnated clothing appeared to be immobilized in from 4 to 10 seconds, often more rapidly than they could be brought into the focus of a lens.

While on a field assignment in western Arkansas, after leaving Camp Bullis, the writer was exposed to moderate populations of all stages of the lone star tick and very heavy chigger populations for 8 days. Only trousers and socks were treated with butylacetanilide. No tick or chigger bites were received during the period. (Pub. Health Reps., 12 Mar '48 - J. M. Brennan)

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Deaths Due to Electric Shock in the Navy and Marine Corps: The prevention of accidental deaths and injuries has always been a primary consideration in the Navy and the subject of considerable study. For the purpose of assembling useful information concerning the various types of persons who died as a result of exposure to electric shock in the Navy and Marine Corps, data from the Form N (Certificate of Death) on these individuals by age group and by occupational group for the war years have been studied.

During the years from 1942 through 1945, there were 199 persons in the Navy and Marine Corps who died as a result of electric shock. Over the 4-year period the highest rates were found in the age group of from 25 to 29, in which the death rate per 100,000 average strength was 2.6. There were no persons over 45 years of age who died as a result of electric shock, and, except for these, the lowest rates occurred among the youngest men, those under 20.

For the officers of both the Navy and Marine Corps the rates were much lower than for the enlisted men of both services. In Marine Corps officers the rate, 1.8 per 100,000 strength, was higher than that in Navy officers, 0.4 per 100,000 strength. However, it should be kept in mind that the numbers of persons involved in both cases were very small. For enlisted men of the Marine Corps the rates were slightly higher, 2.4 per 100,000, than those in the enlisted men of the Navy, 2.2 per 100,000.

Among the enlisted men of the Navy the highest rates occurred in the artificer groups which include the electricians, engine room and fireroom personnel, and "all other" artificers (among which are included carpenters, shipfitters, boilermakers, and metalsmiths). The highest rates occurred among the electricians, with an average annual death rate for the 4-year period of 9.8 per 100,000 strength, followed by "all other" artificers, and engine room personnel.

Of the 199 deaths due to electric shock in the years from 1942 through 1945, the majority occurred at overseas bases and aboard ships. The highest average annual death rate for the period was reported from noncontinental areas, 3.7 per 100,000 strength, with ships reporting a rate of 3.3 and continental Naval districts a rate of 0.7. (Statistics of Navy Medicine for April '48)

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Current Morbidity for Scarlet and Rheumatic Fever in the Navy: In order to know what could be expected in the way of scarlet fever and rheumatic fever in the Navy and Marine Corps during the spring of 1948, seasonal increases for these diseases were studied. Incidence rates for both diseases were assembled from data included in the Monthly Morbidity Report (NavMed-582) for the period from June 1945 through January 1948. All rates are based upon cases taken up as A's (New Admissions), ACD's and AD's (Admitted Contributory Disability and Additional Diagnosis) and EC's (Diagnosis Established or Corrected).

It has been noted that the increases in the early winter months are generally an indication of the severity of the following spring peaks. The January 1948 rates for both scarlet fever and rheumatic fever were lower than the corresponding rates in 1947 and considerably lower than the corresponding rates in 1946, presaging a possible lower peak rate for these diseases this spring than for the 2 previous years. For scarlet fever, the incidence rate

in January 1948 was 0.3 per 1,000 strength as compared with 1.1 a year ago and 8.7 in January 1946. Similarly, the incidence rate for rheumatic fever in January 1948 was 1.1 per 1,000 strength as compared with 1.8 in January 1947 and 3.2 in January 1946. (Statistics of Navy Medicine, April '48)

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Amebiasis and Liver Abscesses in the Navy: During World War II many members of the Armed Forces served in areas in which amebiasis is endemic and under conditions favorable to the acquisition of infection. Despite this, however, the incidence rates for amebiasis, and the liver abscesses (reported as both amebic and other) generally associated with amebiasis were considerably lower during the war period in the Navy and Marine Corps than for the prewar years. From data contained on the Fa card (Individual Statistical Report of Patient) a study has been made of the three diagnoses, (1) amebiasis, (2) abscess, amebic, liver, and (3) abscess, liver (pyogenic) for the years 1936 through 1945. This last diagnosis was included in the study because it was thought that due to the difficulty of demonstrating the presence of Endamoeba hystolytica many cases of amebic abscess of the liver may have been reported as simply liver abscess (pyogenic abscess).

It should be pointed out that although the incidence rates for all three of the diagnoses included in the study were lower during the war years than in the prewar period, because of the long incubation period of the disease and in many cases the mild nature of its symptoms, there may be a reservoir of as yet unreported or unsuspected amebiasis resulting in a possible future increase in the incidence of liver abscesses.

In the ten-year period from 1936 through 1945 there were 1,705 cases of amebiasis reported in the Navy and Marine Corps, 88 cases of amebic abscess of the liver, and 47 cases reported as liver abscess. For all three diagnoses the average annual incidence rates for the prewar period (for the four years from 1936 through 1939) were more than three times as high as those for the four war years; for amebiasis 43.8 per 100,000 strength as against 14.0, for amebic abscess of the liver 2.4 as against 0.7, and for liver abscess 1.6 as against 0.4. Over the ten-year period there were parallel trends for both amebiasis and amebic abscess of the liver. Preliminary data for 1946 have revealed a slight decrease in the incidence rate for amebiasis, with small increases in the rates for the liver abscesses.

Because of the difficulty of demonstrating the causative agent of the disease and the mild nature and frequent masking of its symptoms in many cases, patients who are admitted with another disability are found frequently to have amebiasis while on the sick list; the diagnosis is then changed to amebiasis by reason of its being a concurrent or intercurrent disability. In 1945 the new method of admission AD (Additional Diagnosis) was added to the nomenclature of the Medical Department of the Navy, and of the 676 patients with amebiasis in that year, 216, or 32.0 percent,

were admitted by this method. Preliminary data for 1946 indicate that AD admissions will be even more important, constituting 39.8 percent of the incidence of amebiasis.

The majority of the patients with amebiasis and amebic abscess of the liver were returned to duty. Of the remainder, a large proportion were continued on the sick list for some other disability (diagnosis changed). One half of the patients with the diagnosis, liver abscess, were returned to duty, and the other half were divided equally between "diagnosis changed" and other methods of disposition.

Of the three diagnoses, liver abscess had the highest percent of recurrences, 18.5 percent of the patients having been readmitted.

Concerning mortality, liver abscess was outstanding, 21.3 percent of these cases terminating in death. In view of the generally mild clinical course for amebiasis, only 0.1 percent of the cases of this disease were fatal.

In line with the high fatality rates associated with liver abscesses, the average number of sick days per case for both amebic abscess of the liver and liver abscess were far higher than for amebiasis, an average over the ten-year period of 102.7 sick days per case reported for amebic abscess of the liver and 90.3 for liver abscess as against 35.6 sick days per case for amebiasis.

Over the ten-year period there was one case of amebic abscess of the liver for each 19.4 cases of amebiasis. When the two types of liver abscess are combined, the ratio is reduced to one case of liver abscess for each 12.6 cases of amebiasis. Prior to 1943 the ratios fluctuated considerably from year to year because of the small numbers of cases involved. However, since 1943 there has been an increase in the proportion of cases of liver abscesses in comparison with the cases of amebiasis. Preliminary data for 1946 indicate a further intensification of this trend: a ratio of one case of amebic abscess of the liver for each 13 cases of amebiasis, and for the two types of liver abscess combined, a ratio of one case of liver abscess for each 9 cases of amebiasis. (Statistics of Navy Medicine, April '48)

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Facts About Fatigue: An article from the August, 1947, Industrial Health Bulletin, a Canadian publication, declares that fatigue is an important problem for industry and merits serious attention from management. The health, both physical and mental, of an employee is often the basic cause for fatigue, and therefore it should be the purpose of management to help the worker maintain good health at all times. This can be accomplished by preplacement and periodic medical examinations, health education, and general supervision of workers' health. There are many environmental factors which also contribute to fatigue. among which are adverse temperature, poor illumination, and noise. All of these factors are controllable, and an effort should be made to correct them. Other factors contributing to fatigue are the hours of work, method of work, boredom, and morale of the workers. It is important, too, to remember that each worker has his own personal problems which, by causing mental strain, also enter into the fatigue picture. Along with this, to combat fatigue successfully, it is necessary to take into account not only the hours spent by the worker on the job but also those off the job. (Industrial Hygiene Digest, Jan. '48)

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Trypanosomes of Chagas' Disease in Texas: In an investigation concerning Chagas' disease by A. Packchanian, working at the University of Texas, Galveston, Texas, under contract with ONR , the following progress up to 31 December 1947 has been made:

Three species of blood-sucking insects, Triatoma, were found to be naturally infected with Trypanosoma cruzi in Texas. It was shown that these insects can transmit Tr. cruzi to man and animals. The wood rat, armadillo, and opossum in Texas, proved to be naturally infected with Tr. cruzi.

Methods were developed for liquid and semi-liquid culture of trypanosomes and for slide microscopic identification. (NR-132-161, Quarterly Proj. Summary, 1 Jan '48, ONR, Navy Dept., Washington, D. C.)

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Faster Sharpening of Microtome Knives by the Use of Alumina-Dreft Suspension: It has been found that microtome knives are sharpened very quickly and effectively on a Fanz microtome knife sharpener by using a grinding compound composed of Alumina (Arthur H. Thomas Co., Philadelphia) and Dreft as follows: Alumina #8, 5 Gm.; Alumina #9, 3 Gm.; Dreft, 5 Gm.; and distilled water, 200 c.c. (The amounts are approximations.)

In the sharpening procedure about 20 c.c. of well-shaken Alumina-Dreft suspension is poured on the glass plate of the knife sharpener at the beginning and replenished as needed. It has been found that it is best to make up a fresh suspension before each grinding session. An absolutely smooth glass plate is important.

For a simple touching up of the blade edge, about 2 minutes of sharpening on each side, followed by several periods of sharpening for a few seconds on each side, will be all that is necessary to give a fine, straight, polished edge.

If the edge is badly nicked, correspondingly longer time will be required to obtain a suitable cutting edge. In this case, a total time of about 30 minutes (depending on the hardness of the knife steel) may be required, alternating sides at approximately 5-minutes intervals and checking the edge frequently under the medium-power objective of a microscope. The edge should be finished as described in the preceding paragraph. (Science, 26 Mar '48 - H. Sugiura)

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Naval Medical Research Project Reports: The following is a list of recently completed reports on research projects being carried out by Naval Medical Department activities:

Naval Medical Research Institute, NNMC, Bethesda, Maryland

Project	Report No.	Date	Title
X-418	6	28 Jul 47	The Role of Oxalates in Rat Dental Caries
X-418	7	6 Nov 47	The Role of Oxalates on the Incidence and Extent of Dental Caries in the Cotton Rat Sigmodon Hispidus Hispidus
X-535	12	12 Dec 47	Studies on the Oxygen Consumption of Schistosoma Mansoni
X-535	13	23 Dec 47	Laboratory Tests to Determine the Toxicity of Some Organic Chemicals to the Snail Australorbis Glabratus (Say)
X-535	14	2 Jan 48	On the Demonstration of Hyaluronidase in Cercariae of Schistosoma Mansoni

Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

Project	Report No.	Date	Title
X-759	2	23 Dec 47	Prolonged Survival Time in Guinea Pigs Infected with Clostridium Welchii and Treated with Adrenal Cortical Extract
X-759	3	3 Jan 48	Induction of Alloxan Diabetes in Mice
NM 005 007	1	28 Jan 48	Failure of the Offspring of Mosquitoes Infected with Japanese B Encephalitis to Transmit the Virus
NM 005 007	2	30 Jan 48	Attempts to Establish the Virus of Measles in Laboratory Animals by Mosquito Passage
NM 005 007	3	2 Feb 48	Inability of Mosquitoes to Transmit the Lansing Strain of Poliomyelitis Virus to Mice
NM 005 017	1	12 Jan 48	Notes on the Biology and Control of Mosquitoes at Umiat, Alaska
NM 005 017	2	10 Feb 48	A Taxonomic Treatment of the Mosquitoes of Umiat, Alaska
NM 007 026	1	14 Feb 48	A Colorimetric Method for the Determination of Acetone Bodies in Blood
NM 007 039	1	1 Dec 47	Incidental Finding of Megaloblastic-Like Cells in Bone Marrow of One of Two Swine with Macrocytic Anemia and Achlorhydria
NM 007 039	2	16 Dec 47	Correlation Between the Mean Corpuscular Volume and Reticulocytosis in Phenylhydrazine Anemia in Swine
NM 007 039	3	22 Dec 47	The Lethal Dose of Total Body X-Ray Irradiation in Swine
NM 007 039	4	23 Dec 47	A Method for the Titration of Heparin-Like Substances in Plasma
NM 007 039	5	30 Jan 48	The Acceleration of Plasma Coagulation by Low Concentrations of Heparin

Naval Medical Research Institute, NNMC, Bethesda, Maryland (Cont.)

Project	Report No.	Date	Title
NM 007 039	6	2 Mar 48	The Use of Taka-Diastase and Papain in the Determination of Folic Acid
NM 008 001 X-161	3	19 Jan 48	A Modification of an Applicator Used in Dental Anesthesia Induced by Local Refrigeration
NM 009 003	1	1 Mar 48	Description of a Prosthetic Hand Appliance
NM 011 013	1	5 Jan 48	Photofluorometric Determination of Gallium in Tissues
NM 011 015	3	17 Jan 48	Preparation of Compressed Helium-Oxygen Gas Mixtures
			Summaries of Research (1 July - 31 December 1947)

Medical Research Department, U. S. Submarine Base, New London, Conn.

Color Vision Report	16	6 Oct 47	Proposed Specifications of Red and Green Navy Signal Lights
NM 003-020	1	12 Feb 48	Some Statistical Remarks on the Method of Constant Stimulus Differences
NM 003-021	1	12 Feb 48	Interpretations of Measurements of Auditory Thresholds
NM 003-022 (X-747 (Sub. No. 154))	2	22 Jan 48	Detection Thresholds and Pure Tone Thresholds in Auditory Acuity
NM 003-022 (X-747 (Sub. No. 154))	3	30 Jan 48	Studies on Pitch Discrimination in Masking. II. The Effect of Signal/Noise Differential
NM 003-022	4	31 Mar 48	The Emergence of a Tonal Sensation
NM 003-026	1	30 Jan 48	Pitch Discrimination and Absolute Pitch
NM 003-026	2	10 Feb 48	Suggestions for Constructing Tests of Pitch Discrimination

Medical Research Department, U. S. Submarine Base, New London, Conn. (Cont.)

Project	Report No.	Date	Title
NM 003-036	1	22 Mar 48	Outline and Discussion of Methods for Selection of Submarine Reserve Personnel
NM 006 007 (X-761 (Sub. No. 163))	-	12 Feb 48	The Feasibility of Group Audiometry
Medical Field Research Laboratory, Camp Lejeune, N. C.			
NM 011 005	-	2 Dec 47	A Study of Revised Sights on Garand Rifles
Naval Medical Research Unit #4, U. S. Naval Hospital, Dublin, Georgia			
X-758 (Gen. 167)	-	18 Jan 48	Observations on the Effect of Tonsillectomy and the Administration of Penicillin on Rheumatic and Nonrheumatic Fever Patients
U.S. Naval School of Aviation Medicine and Research, NAS, Pensacola, Fla.			
X-148 (Av-4-3)	20	18 Mar 48	The Effects of Repeated Rotary Acceleration on the Oculogyral Illusion

NOTE: Those interested in seeing copies of the complete reports should address their request to the research activity from which the report originates. Reference may be made to those reports in the same way as to published articles, noting authors, title, source, date, project number, and report number.

Appointment in Dental Corps Now Without the Usual Professional Examinations: Candidates for appointment as lieutenant (junior grade) in the Dental Corps of the U. S. Navy are not now required to present themselves for the extensive professional examinations heretofore required for appointment. The professional examination will now consist of a review of transcripts of scholastic records and other credentials by a board of dental officers in the Navy Department. Candidates will not be required to be present for this review.

Citizens of the United States between the ages of 21 and 32 who possess a degree in dentistry conferred by an accredited dental school and who meet the physical requirements may apply for a commission in the Dental Corps of the U. S. Navy at any time. Civilian dentists and inactive Naval Reserve dental officers who received their appointments subsequent to 31 December 1946 who desire an appointment as lieutenant (jg) in the Dental Corps of the U. S. Navy should submit applications to the nearest Office of Naval Officer Procurement. Naval Reserve dental officers on active duty who received their appointments subsequent to 31 December 1946 and who desire an appointment should submit applications to the Chief of Naval Personnel via official channels. Naval Reserve dental officers (active or inactive) who received their appointments on or prior to 31 December 1946 and who desire entry into the Dental Corps of the regular Navy should make application for transfer.

Candidates will be given physical examinations by boards of medical examiners that have been convened by the Chief of Naval Personnel, and the reports are to be forwarded with the applications for appointment. In the event that such a board of medical examiners is not available in the area of an activity receiving applications for appointment as lieutenant (jg), DC, USN, each candidate is to be physically examined by any medical officer (or officers) present, and the report of the findings (NavMed-Y) in duplicate forwarded with the application for appointment; candidates who are otherwise acceptable will be authorized by the Chief of Naval Personnel to appear before a board of medical examiners prior to delivery of commission. (Dental Div., BuMed)

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Public Relations Begin at Home: Public relations begin at home in any organization. In other words, as long as we have freedom of speech, internal satisfaction and good morale, or internal dissatisfaction and poor morale, will filter out to the public via word of mouth, which is the most effective public relations medium. Therefore, in the interest of favorable public relations, it is essential that an organization work ceaselessly at giving honest and fair consideration to all points of view held by personnel of all levels within the organization. The attainment of fair consideration for all points of view cannot be accomplished simply by assigning the job to some division or branch of an organization and then forgetting about it. It can be aided by such assignment only to a limited extent, but, for its full accomplishment, it must be an accepted attitude and working philosophy of the whole organization.

In the Navy, every man or woman, whether civilian or military, is an important cog in its organization; this cannot be overemphasized. The development of such an understanding, because it creates confidence and stimulates interest throughout all levels, constitutes a sound step in good organization. For, each responsible individual in the Navy who believes in his job will reflect his enthusiasm and confidence to a circle of persons having the same general level of responsibility in walks of civilian life, which will include social, professional, business, and other avenues of activity.

In working toward greater national security, the Navy is now developing military-civilian teamwork at levels of major responsibility - departmentally, in the bureaus, and, in the field as well. This creates an opportunity not only for the development of a greater strength and effectiveness in the Navy itself, but a further increase in the public understanding of and confidence in the Navy.

Belief and interest in the job being done, and just plain liking the place where you work are the grass roots of good public relations. (Public Relations Div., BuMed)

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Training in the Hazards of Nuclear Radiation: The Bureau of Medicine and Surgery announces the availability during the years 1948 and 1949 of training for medical officers and Medical Service Corps officers in the Hazards of Nuclear Radiation. Medical officers from the U. S. Army, U. S. Air Force, U. S. Public Health Service, and the U. S. Navy will be in attendance.

A six months' course will be conducted at the University of Chicago, Institute of Radiobiology and Biophysics, beginning 1 October 1948. This course will consist of didactic and laboratory training concerning the atomic nucleus, properties and measurement of radiations, general radiobiology, health physics, and mammalian radiobiology. BuMed's quota is six places.

A ten months' course is available at the Atomic Energy Project, University of Rochester, Rochester, New York, beginning 30 September 1948. This course consists of didactic and laboratory training in radiation physics and chemistry, instrumentation and monitoring, physical effects of ionizing radiations, pharmacology, and toxicology. BuMed's quota is three places.

Requests are desired from interested medical officers, especially those who have had training in internal medicine or radiology. Requests are also desired from Medical Service Corps officers who have a Bachelor of Science degree in the field of biology.

Applications should be prepared in accordance with the outline in the News Letter dated 23 May 1947, page 22. Each request must contain a signed agreement not to resign during the course and to remain in the Navy for a period of three years upon completion thereof. Requests may be made by dispatch if applicants are assigned to sea or foreign shore duty.

In addition to the courses mentioned above, it is anticipated that there will be other courses available from time to time in the broader phases of the aspects of medicine concerned with nuclear energy. Medical officers and Medical Service Corps officers may obtain further details by addressing the Bureau of Medicine and Surgery, Attention Code 74. (Professional Div., BuMed)

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ALNAV 29 3 April 1948

Subj: Oxophenarsine Hydrochloride, Instructions Concerning

Addressees hereby authorized and directed to survey and destroy all oxophenarsine hydrochloride (mapharsen) JAN Stock No. 1-324-460 and 1-325-155 after it reaches the potency dating shown on the ampule or material showing no potency dating. Reorder as required not to exceed six month's requirements. All recent arsenical reactions occurred in patients receiving outdated or nearly outdated arsenicals. Arsenicals now being issued have a comparatively long potency dating.

--SecNav

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Op24B/cj, Serial 127P24 29 March 1948

To: All Ships and Stations

Subj: Disestablishment of U. S. Naval Hospital, Brooklyn, N. Y.

1. The following activity is disestablished, effective 30 June 1948:

U. S. Naval Hospital
263 Flushing Avenue
Brooklyn 5, New York 3435-174

2. The Commandant, Third Naval District, will effect the reassignment of the functions of the Naval Hospital, Brooklyn, to the Naval Hospital, St. Albans.

3. The Naval Hospital, St. Albans, is assigned as a component of the Naval Base, New York, effective 1 May 1948.

4. Bureaus and offices concerned take necessary action.

--SecNav.

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Circular Letter 48-41 5 April 1948

To: All Ships and Stations

Subj: Monthly Morbidity Report, NavMed 582

1. It is apparent from monthly morbidity reports received in the Bureau that not all personnel completing subject report fully understand the instructions for reporting "Total Patient Sick Days During Month" under Part I. The following comments are intended to amplify the instructions printed on the back of subject form and are related to both Type 1 and Type 2 reports.

2. The figure desired is the number of sick days accumulated by all active duty patients at the reporting activity during the month. For a patient admitted to an activity on 20 March, and disposed of on 15 April, 11 sick days would be accumulated in March and 15 in April, and reported in the totals for the respective months. Only the sick days accumulated during a given month and at an activity are included in that activity's report. Sick days for patients who have been transferred (T) to convalescent leave, will not be included. Sick days accumulated by a patient prior to admission to a given activity will not be reported by that activity.

--BuMed. H. L. Pugh

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Circular Letter 48-42 6 April 1948

To: Naval Hospitals, Naval Dispensaries (Major) Continental

Subj: Pharmacy Services

Encl: 1. (HW) Questionnaire to be completed (Parts I, II, III, & IV).

This letter requests that addressees furnish the Bureau with certain information which will be used in evaluating the present status of pharmacy so that plans may be developed to insure the best possible pharmaceutical support of medical services.

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Circular Letter 48-43 13 April 1948

To: Comdts, ND's (less 10, 15, and 17), and PRNC.

Subj: Vessels or Craft Assigned to Naval Districts and River Commands for Use in Making Naval Reserve Training Cruises of a Local and Limited Nature; Medical Allowance Requirement.

Ref: (a) BuMed Circular Letter 47-82 dated 26 June 1947.

1. Paragraph 1 of reference (a) is hereby modified as follows:

Add sub-paragraph e -

	AMOUNT
e. 9-218-750 First Aid Kit, Medical Officer & Hospital Corpsman.	* 1

Add explanatory note -

* One (1) is authorized in addition to above items for each vessel making seagoing cruises with a Medical Officer aboard. This kit contains narcotics and Officers in Charge of applicable vessels should be advised thereof and instructed to institute necessary safeguarding measures.

--BuMed. H. L. Pugh

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Circular Letter 48-44 14 April 1948

To: All Continental Stations

Subj: NavMed-172, Weekly Morbidity Report; Suspension of

Ref: (a) Par. 35D2, ManMedDept

By this letter, the submission of the Weekly Morbidity Report by shore stations in the continental U. S. is suspended until such time as it may again be required by the Bureau in accordance with reference (a).

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