

Vol. 10

Friday, 18 July 1947

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<u>Antibiotics in the Treatment of Sinus Infections</u>: During a single decade the indications for sinus surgery have become greatly modified because of the demonstrated ability of the sulfonamides and the antibiotics to alter profoundly the course of many acute and some chronic infections. The majority of acute sinus infections were adequately managed before the introduction of chemotherapy. The main value of the antibiotics and the sulfonamides lies in their ability to control infections resistant to ordinary rhinologic procedures so that surgical measures are either avoided or limited to more simple procedures.

Of the many known antibiotic substances only penicillin, streptomycin and tyrothricin have attained a position of therapeutic importance, but to each of these a specific therapeutic sphere can be assigned on the basis of present knowledge. The antibiotics cannot be regarded as entirely displacing the sulfonamides. In the treatment of some infections the sulfonamides and the antibiotics supplement each other.

Antibiotic therapy is effective only when directed against sensitive micro-organisms. Therefore, whenever possible, sensitivity tests should be made to determine the vulnerability of the pathogen because during the use of antibiotic therapy against resistant bacteria many other therapeutically effective measures are neglected, to the ultimate detriment of the patient.

The antibiotics have proven to be of little or no value in uncomplicated allergy but they have been effectively used against secondary infections complicating the manifestations of allergy of the upper and lower respiratory tracts. Thus, there is reason to expect that bacterial sensitization may sometimes be forestalled in those instances in which infection in an allergic individual can be arrested or eradicated by antibiotic therapy. The prophylactic use of the antibiotics merely to prevent secondary infection cannot as yet be justified because allergic patients are prone to become sensitive to the antibiotic drugs themselves, and this is especially apt to occur when the drug is administered over a long period of time.

Sinus surgery continues to be indicated in the presence of advanced, irreversible tissue change in the nasal passages and sinus cavities, even when attributable to allergic influence alone, and for the reasons generally accepted prior to the introduction of the antibiotics. When secondary infection of allergic tissues takes place, it is less amenable to chemotherapy than is similar infection in otherwise normal tissues. Chronic infection in sinuses containing extensive, irreversible tissue changes due to allergy can rarely be influenced by chemotherapy alone and it eventually demands some form of surgical attack.

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The generally accepted rule that as little surgical intervention as possible should be employed in acute sinus infection has become even more rigid since the introduction of chemotherapy. Exceptions to this rule were formerly conceded in the presence of orbital extension of the sinus infection, bacteremia, or retrograde thrombophlebitis. Timely chemotherapy has eliminated most of these exceptions. Thus, penicillin will rapidly control orbital cellulities of sinus origin, clear the blood stream of viable organisms and impede the progress of intravenous extension of the infection. Once appreciable collections of pus exist, however, drainage must be established in spite of continuous chemotherapy.

The administration of antibiotics in mild and transient sinus infections must be regarded as poor therapeutic practice. It has long been recognized that immunity often fails to be acquired when an infection is promptly controlled by chemotherapy. The prompt arrest of bacterial activity and of the tissue reactions incident to bacterial invasion prevents positive stimulation of immunological responses. As a result, there are frequent recurrences at very short intervals. The tendency to readminister the chemotherapeutic agent at each recurrence seems justified by the success attending its use during the first attack. Under these circumstances, however, repetition of the courses of chemotherapy fails to prevent progressive tissue changes, fosters the development of resistant strains of micro-organisms, and may sensitize the patient to the drug. It is when prolonged, continuous chemotherapy has rendered the pathogen resistant to the drug that infection may spread to previously uninvolved sinuses during the active course of treatment with antibiotics. Because of the interference of chemotherapeutic agents with immunological responses, the concomitant use of autogenous vaccines or lysates deserves serious consideration as a means of avoiding recurrences.

In general, chronic sinus infections are resistant to antibiotic therapy because the drug penetrates with great difficulty those abnormal tissues resulting from repeated or prolonged infection. Tyrothricin lacks the ability to penetrate tissue, and its toxicity in other than surface use renders its value in the treatment of chronic sinus infections highly questionable. Even though penicillin and streptomycin control the chronic infection temporarily, recurrence frequently follows withdrawal of the drug. The action of penicillin is not inhibited by organic matter as is the action of the sulfonamides, but the drug is physically unable to penetrate accumulations of pus containing susceptible pathogens. Under such circumstances surgical drainage is still indicated. Streptomycin actually loses some of its antibacterial property in the presence of body fluids. Thus the tolerance of Gram-positive cocci for streptomycin is increased from four to eight times in body fluids. If the

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clinical and laboratory findings warrant it, both penicillin and streptomycin may be used in resistant cases. The toxic properties of streptomycin are less marked than those of the sulfonamides but greater than those of penicillin. Although streptomycin must be used against penicillin-fast microorganisms, penicillin is the antibiotic of choice against infections susceptible to it.

Because eradication of chronic infections in the sinuses cannot always be accomplished by surgery alone, antibiotic therapy as an adjunct to surgery may play a decisive role. The combined local and intramuscular use of penicillin, after surgical failure, frequently is followed by the disappearance of exudate and viable organisms. Thus far, the most satisfactory results in the management of chronic sinus infections, with advanced irreversible tissue changes, have been obtained by the combined use of surgery and chemotherapy.

In infectious sinus diseases, effective antibiotic therapy during the preoperative period depends upon early and accurate diagnosis (especially bacteriological diagnosis), followed by selection of the antibiotic most lethal to the invading organisms, given in adequate dosage by the most effective route of administration, and over a sufficient period. Because antibiotic drugs can impede or arrest the spread of infection, minimize the occurrence of bacteremia and the toxic effects of an active and overwhelming infection, there results a period during which operation can be delayed and detailed preoperative studies made. During this delay period recovery may occur without surgery.

A sense of false security may be engendered by the prompt therapeutic effects of the sulfonamides or the antibiotics in those sinus infections in which irreversible tissue changes have taken place. Recurrence is the rule when chemotherapy is withdrawn and although the recurrent attacks may appear to subside with resumption of chemotherapy, complete control of the infection is not obtained until surgical measures are employed.

During the period of operation, antibiotics, used locally and systemically, have prophylactic value in the protection of uninfected tissues in the operative field from contamination, the prevention of meningitis, and the control of bacteremia.

Throughout the post-operative period, the antibiotics limit the spread of infection to freshly exposed tissues and tend to shorten the healing period.

Fractures of the paranasal sinuses with a tear of the overlying dura were almost invariably followed by meningitis. The prompt administration of antibiotics has materially reduced the incidence of this complication. When meningitis has already followed such an injury, antibiotic therapy will

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often bring about recovery from the meningitis before any attempt is made to repair the dural defect. In fact, under these conditions, better clinical results have been obtained when dural repair has been delayed until recovery from meningitis has occurred.

Under continuing antibiotic therapy, many fractures of the paranasal sinuses heal by primary union. Bone fragments, if surrounded entirely or even in part by vascular soft tissue, exhibit amazing viability, but those lying free within a sinus cavity require eventual removal. The frequency of sequestrum formation and subsequent surgical removal has been greatly reduced since the introduction of the antibiotics.

The ears and the paranasal sinuses are the most frequent sites of primary foci in meningitis. In the past, surgical drainage of the primary focus has been axiomatic in the treatment of meningitis. Clinical trial has demonstrated that an initial attack of meningitis can be controlled by chemotherapy with or without surgical drainage. The combined use of an antibiotic and a sulfonamide has generally proved to be more effective than a single drug of either group and this is especially true when the pathogen is a pneumococcus. Some workers doubt the value of drainage of primary foci when chemotherapy is used, but a combination of antibiotic and sulfonamide therapy plus eradication of the primary focus appears to give the most consistently permanent result. Even though chemotherapy may not eliminate the need for surgical drainage, its delaying action until the meningitis is controlled is of great value. The primary focus can then be attacked surgically when the results of precision laboratory and roentgenological studies are at hand and the patient has become a better risk for operation.

It has been a common experience to encounter relapsing attacks of meningitis more frequently in sinus infections than in mastoid infections. This alone emphasizes the importance of surgical drainage of a primary focus located in the sinuses. Certainly drainage cannot be safely avoided in the treatment of the relapsing case even though its value may be regarded as questionable during the acute phase of meningitis. Occasionally the full recovery of a patient with relapsing meningitis can be attained with chemotherapy alone, but usually a chronic focus consisting of a formidable collection of pus and sequestra will not remain quiescent indefinitely. Eventually such a focus must be dealt with surgically and especially when reinfection of the meninges coincides with discontinuation of the chemotherapy.

When in the attempt to prevent relapse, surgical drainage of an extradural source of infection produces disappointing results, the failure should not be ascribed to the futility of surgical intervention but rather to incomplete surgical drainage of a single focus or the presence of multiple foci

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which escape recognition. In the presence of an extensive primary focus, surgical intervention cannot be safely disregarded, and the concurrent use of chemotherapy and surgical drainage should be the method of choice.

Osteitis accompanying acute sinus infections is promptly controlled by adequate doses of penicillin, but occasionally the withdrawal of penicillin is followed by reactivation of the osteitis and extension of the infection to the meninges. The meningeal infection usually responds to further penicillin administration thus permitting delay in operation. Surgical intervention has been more often successful when carried out after control of the meningitis.

A feared complication of frontal sinus infections is osteomyelitis. With or without brain abscess, osteomyelitis of the frontal bone has rarely been cured by antibiotic therapy alone. Surgical intervention with maintenance of adequate drainage continues to be imperative. The record of surgery alone is not too brilliant, but the concurrent administration of penicillin, intrathecally and intramuscularly, together with surgical drainage has effected some remarkable recoveries. In spite of the virtues of antibiotic therapy in controlling osteomyelitis of the frontal bone, all necrotic bone must be removed before healing can occur. Although the antibiotics exhibit a peculiar ability to relieve the pain associated with osteomyelitis, their main value lies in the prevention of sequestration and in the arrest of progressive extension to contiguous osseous tissue. The timely use of antibiotics in osteomyelitis secondary to sinus infection has greatly reduced the extent of radical surgery but has not eliminated the need for surgical drainage. (Ann. Otol., Rhin. and Laryng., March '47 - H. P. Schenck)

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Frequency of Encephalitis as a Complication of Measles: Although reports of measles encephalitis are found in the literature prior to the year 1923, it has been only in the last two decades that encephalitis as a complication of measles has seemed to occur in epidemic proportions. It is difficult to determine the exact incidence of measles encephalitis because not all cases of measles are reported and many cases of mild encephalitis may be missed. Stimson stated that this complication usually develops in less than one per thousand cases.

The table shows the incidence of encephalitis in previously reported epidemics of measles and also in this series of cases. There were 10 additional cases of encephalitis at another contagious disease hospital which are not included.

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Author and Year-	Cases of Measles	Cases of Encephalitis	Rate
Top, 1937-1938, Detroit	30,000	2	1:15,000
Gunn and Russel, 1935-1936, London	13,156	5	1:2,600
Peterman and Fox, 1931, Milwaukee	15,001	13	1:1,150
Hoyne, 1938, Chicago	37,831	32	1:1,200
Peterman and Fox, 1938, Milwaukee	27,081	14 -	1:1,900
New York, 1941	79,637	60	1:1,300
Hoyne and Slotkowski, 1946, Chicago	12,846*	20	1:642

\* This figure (January to June), provided by the Chicago Health Department, has been added to the original table.

From January through June of 1946, 307 patients were admitted to the Cook County Contagious Disease Hospital with the diagnosis of measles. Measles encephalitis was diagnosed in 20 (6.5 per cent) of these patients. One hundred and seventy-two patients were under 5 years of age, with 6 instances of encephalitis (3.5 per cent). One hundred and one patients were in the age group of from 5 to 15, with 12 cases of encephalitis (12 per cent). Thirty-four patients were over 15 years of age, and 2 of these had encephalitis (6 per cent). Although Negroes constituted more than one-fourth of the total admissions, all instances of measles encephalitis were among white patients.

Careful analysis of these 20 cases revealed nothing characteristic which would explain the cause of this complication. The authors' observations led them to believe that the intensity of the eruption was of no significance in anticipating the possibility of encephalitis. They found that encephalitis occurred as a complication in patients with a comparatively mild-appearing attack of the disease as well as among those in whom the infection was of an intensive character. Carithers mentioned the theories advanced, and these include "(1) the invasion of the central nervous system by the virus of measles, (2) the invasion of the central nervous system by a neurotropic strain of this virus, (3) an allergic reaction within the central nervous system to this virus, and (4) infection with a virus separate and distinct from the virus of measles." In addition, the authors believe that there may be a constitutional tendency for the cortex to be more vulnerable than usual, and that, when combined with precipitating factors, neurologic manifestations make their appearance.

Clemens reported a case of premeasles encephalitis with neurologic manifestations arising eleven days before the appearance of the typical exanthem. In this series there was 1 instance in which the onset of encephalitis occurred one day prior to the appearance of the eruption. One of the authors had a similar case in 1938. Hamilton reviewed 241 cases and found the average time that elapsed after appearance of the rash before the onset of encephalitic symptoms was 5.2 days as compared with 2.7 days

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in his own series of 44 cases. The average in these 20 cases, when the single instance in which encephalitis developed prior to the eruption is excluded, was 3.4 days. The authors did not observe any case in which encephalitis followed a complete subsidence of the eruption. These facts in themselves suggest that the term "postmeasles" encephalitis, although frequently used, is misleading.

There was considerable variability in the initial symptoms of encephalitis. The types of onset may be divided into two groups, namely, (1) abrupt, convulsions being the presenting manifestation of irritation of the central nervous system, and (2) gradual, with a change in the mental condition varying from lethargy to extreme irritability, with or without convulsions. In 9 of the 20 patients, including a 20 year old woman, there was a history of at least one convulsion prior to admission. The patient who developed convulsions after entering the hospital was a 15 year old girl.

Neurologic findings on physical examination were as variable as symptoms at the onset. Meningeal irritation was manifested in some by nuchal rigidity and positive Kernig and Brudzinski signs. Reflexes were hyperactive, normal, hypoactive, or absent completely. Although paralysis of extremities was not ordinarily observed, one patient did experience paralysis of the lower extremities but eventually regained fully the use of both legs.

Temperature peaks shown by different patients varied considerably. Usually in the course of the illness there was pronounced pyrexia. The highest temperature recorded was 107.4° F. In this particular instance the authors learned that the patient, removed from the hospital prior to recovery, failed to survive. In another case a boy with a temperature of 107° F. eventually made a remarkable recovery. Although this patient was practically comatose for several weeks, his mental condition appeared to be normal when he was discharged from the hospital.

The spinal fluid findings in 16 of the 20 patients are shown in the following table.

		Pandy			Protein, Mg./	Glucose, Mg./	그는 영상 문화되었다.
Number	Appearance	Reaction	!	Cells	100 Ce.	:100 Cc.	Culture
1	Clear and colorless	0		0	£0	120	No growth or contaminated
-)	Clear and colorless	$1 \pm$		100	:30	.50	No growth or contaminated
2	Clear and colorless	0		36	49	72	No growth or contaminated
4	Clear and colorless	2+		400	5:30	.54	No growth or contaminated
5	Clear and colorless	0		15	64	80	No growth or contaminated
6	Clear and colorless			9	49	67	No growth or contaminated
ĩ	Clear and colorless			198	200	59	No growth or contaminated
5	Clear and colorless	0		10	45	101.	No growth or contaminated
9	Clear and colorless	1+		12	74	106	No growth or contaminated
10	Clear and colorless	1 +		250	154	85	No growth or contaminated
11	Clear and colorless	1+		360			No growth or contaminated
12	Clear and colorless	0		- 80			No growth or contaminated
13	Clear and colorless	0		10			No growth or contaminated
14	Clear and colorless	0		7	64	82	No growth or contaminated
15	Clear and colorless	. 2		90	175	59	No growth or contaminated
16	Clear and colorless	0		0	35	10.5	No growth or contaminated

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A high cell count and a pronounced elevation in spinal fluid protein do not necessarily indicate a poor prognosis. One patient with 400 cells and a protein level of 530 mg. made a complete recovery.

In several instances convulsions were present when patients were admitted. The convulsions were controlled with a few drops of chloroform on a mask. To prevent a recurrence, one of the barbiturates was given either as a retention enema or by parenteral injection. Oxygen was used in the presence of dyspnea, tachypnea or cyanosis.

As a rule a lumbar puncture was performed in the examining room, but when the patient was considered too ill this procedure was deferred.

No fast and rigid rule was followed in the administration of fluids parenterally.

Measles convalescent serum in dosages varying from 20 to 100 c.c. was administered intravenously to 7 patients. In one instance 40 c.c. of gamma globulin was given to a patient whose condition was critical. It could not be determined that any beneficial effects resulted from this treatment which was also the experience with measles convalescent serum when used for treatment of encephalitis. Pooled plasma, which is more readily available, was used liberally and repeatedly in almost all cases. The total volume of plasma injected during the acute stage varied from 250 to 1,250 c.c., depending on the severity of the encephalitis. Whole blood, typed and cross matched, was given whenever indicated.

In 3 instances in which the patients remained in a semicomatose condition for more than a week and had a loss of deglutition, tube feedings were instituted. In these patients total protein and albumin-globulin ratio were determined periodically. Amino acids were employed parenterally in the presence of hypoproteinemia. Vitamins were administered empirically.

Occasionally a well padded cast was placed on a spastic extremity to prevent a contracture deformity and physical therapy employed later to assist in the restoration of complete muscular function.

At the time of admission it was difficult to estimate the chances for recovery. Hyperpyrexia and convulsions during the acute stage or even persistence of a semicomatose condition for several weeks were not always associated with a fatal outcome or even permanent damage to the nervous system. In one instance the patient remained in a comatose condition for a month, yet made a complete recovery.

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Of the 20 patients with encephalitis 2 children, each 3 and 1/2 years old, died shortly after admission, having been in the hospital less than twentyfour hours. Another patient, a 15 year old girl, died after being transferred to a private hospital. Including this death in this series, the fatality rate was 15 per cent. Of the remaining 17 patients 16 made a complete recovery, and no mental complications have been noted after a period of one month. One patient, a 2 year old boy, still had some muscular spasticity and incoordination at the time he left the hospital. No further information has been received concerning his progress. The number of hospital days per patient varied from six to fifty with an average of sixteen and one-half days.

<u>Comment</u>. Encephalitis is an early complication of measles and rarely occurs after the rash has disappeared. With respect to age it is much commoner after 5 years than before. Negroes are likely to escape this complication almost entirely.

Even in cases of extremely severe attacks complete mental as well as physical recovery is possible. The fatality rate of 15 per cent for this series is in sharp contrast to a previous report by one of the authors (A. L. H.), in which the fatality rate was more than double this rate and approximately one-third of the survivors had mental or physical defects.

It seems apparent that measles encephalitis is becoming more frequent. This series of 20 cases constitutes an incidence of 1 in 642 on the basis of cases of measles reported in Chicago. Moreover, if 10 additional cases are included, 3 of which were fatal, observed by one of the authors at Municipal Contagious Disease Hospital, then the ratio for 30 patients with encephalitis becomes 1:428 for the reported cases of measles. This is believed to be the highest incidence for measles encephalitis that has been reported. (Am. J. Dis. Child., May '47 - A. L. Hoyne and E. L. Slotkowski)

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<u>Primary Carcinoma of the Liver:</u> Primary carcinoma of the liver is a rare disease. Thirty-one instances of it have been found in 16,303 necropsies at the Mayo Clinic, an incidence of 0.19 per cent. Six of the cases had been reported previously in the literature. The disease occurs most commonly in the Orient and South Africa. A series of reports collected from the literature reveals an incidence of 0.227 per cent among the white-skinned races of Europe and America and an incidence of 0.983 per cent among the Asiatic and African races. This increased tendency of the disease to afflict the latter peoples is believed to be due to the high incidence of schistosomiasis and clonorchiasis among them and to the chronic irritation of the liver caused by these parasitic infections. Primary carcinoma of the liver is a

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disease of older persons. In most of the cases reported upon by the authors, the lesion occurred in the fifth, sixth, and seventh decades of life. In 23 of their 31 cases the disease occurred in males, the sex which usually is more frequently afflicted. The primary carcinomas of the liver arising from hepatic cells are called 'nepatomas," and those arising from bile ductules are called "cholangiomas." Reports of hepatomas in the literature far exceed those of cholangiomas. In 20 of these 31 cases the tumors were hepatomas, and in 11 they were cholangionas. Cirrhosis frequently is associated with primary carcinoma of the liver and undoubtedly is an important causative factor. In 16 (80 per cent) of the 20 cases of hepatoma cirrhosis was associated, but it was present in only 2 (18.2 per cent) of the 11 cases of cholangioma. It is still debatable whether the incidence of primary carcinoma of the liver is any greater in the presence of hemochromatosis than it is when nonpigmentary cirrhosis alone is present. There are no pathognomonic clinical or laboratory signs or symptoms in these cases, and the diagnosis is rarely made before the death of the patient. The most significant symptoms and signs in this series of cases were emaciation, abdominal distention with ascites, abdominal pain, edema of the ankles, jaundice and a palpable abdominal tumor.

Distinction between hepatoma and cholangioma by gross examination is usually difficult and the final diagnosis must be made histologically. The question of multicentric or unicentric origin of these tumors is still debatable, but most authors favor the unicentric origin. In eleven of these 20 cases of hepatoma there was obvious invasion of blood vessels. The early vascular involvement is thought to cause the intrahepatic metastasis so often seen in the presence of hepatoma. Tumorous thrombosis of the inferior vena cava and right auricle may accompany these tumors. In 21 (67.7 per cent) of the 31 cases extrahepatic metastasis was present. Cholangioma as a rule metastasizes earlier and more frequently than does hepatoma. Primary carcinomas of the liver grow exceedingly rapidly, and the prognosis usually is hopeless. Most of the patients die within a few months after the onset of symptoms. Early surgical resection of the liver offers the only chance for cure. (Arch. Int. Med., May '47 - R. M. Hoyne and J. W. Kernohan)

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<u>The Effect of Increased Temperatures on the Therapeutic Efficacy of</u> <u>Penicillin in Experimental Syphilis</u>: It has been shown and reported in a previous communication from the laboratory of the authors that the rate at which the Reiter strain of cultured <u>Treponema pallidum</u> is killed by penicillin <u>in vitro</u> increases with temperature increments throughout the range of from 8° to 40° C. Of an initial inoculum of 10<sup>6</sup> organisms per cubic centimeter exposed to penicillin, an average of 100 per cent remained viable after twenty-four hours at 8° C., 10 per cent at from 22° to 23° C., 1.0 per

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(Not Restricted) cent at from 32° to 33° C., and only 0.02 per cent at from 39° to 40° C. These results were largely independent of the penicillin concentration in the range of from 0.25 to 250 units per cubic centimeter.

The question arises as to whether hyperpyrexia has a similar favorable effect on the therapeutic efficacy of penicillin <u>in vivo</u>, analogous to its effect on the therapeutic efficacy of arsenicals. There is now reason to believe that the percentage of cures obtained with penicillin alone in the treatment of secondary syphilis may be significantly lower than those possible with combined arsenic and bismuth therapy. Similarly, in the treatment of central nervous system syphilis, although penicillin seems to have a definite effect even in those late complications not amenable to arsenicals alone, the therapeutic response is not regular and is often incomplete. Under such circumstances, the effect of induced hyperpyrexia on its therapeutic action is of more than academic interest.

The <u>in vitro</u> results with the cultured nonpathogenic Reiter strain of <u>**T**</u>. <u>pallidum</u> have been confirmed <u>in vivo</u> with pathogenic <u>**T**</u>. <u>pallidum</u>. In the In the treatment of early rabbit syphilis, the therapeutic action of penicillin was strikingly enhanced by a simultaneous increase in body temperature, evidenced by the fact that the effective dose of penicillin was thereby reduced to from one-eighth to one-tenth of its normal level.

The clinical significance of the present experiments is, however, open to question. The combination of fever with penicillin is neither feasible nor desirable for the treatment of early syphilis. Even in those patients who are not cured by penicillin alone, there are other means of supplementing penicillin therapy, such as small doses of mapharsen or bismuth, which do not carry the risk of fever therapy, which do not entail so large an expenditure of professional time and care, and which are practical with mass treatment.

However, the situation is quite different in the case of neurosyphilis, in which penicillin alone may not suffice, and in which the advantages of fever therapy are well recognized. Whether the hyperpyrexia exerts only a single and independent action or serves also to enhance the action of the penicillin, their use in combination may yield results equal to and perhaps exceeding those hitherto obtainable with fever and arsenicals. Penicillin does not interfere with the action of the fever-producing agents ordinarily used (malaria, typhoid vaccine, hypertherm machine), and may thus be given concomitantly with the fever, as it probably should be for maximum efficacy.

Two possible explanations suggest themselves for the effect of high temperatures in reducing the dosage of penicillin required to cure. Either penicillin alone or fever alone may destroy the major portion, but not quite

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all, of the organisms in the infected animal. The simultaneous exposure to the second agent may suffice to destroy the few remaining and otherwise surviving organisms, and thus effect biologic cure. This may involve an additive and possibly a synergistic action between the therapeutic effects of penicillin and of high temperatures on <u>T. pallidum</u> analogous to the demonstrated synergistic action of penicillin and of trivalent arsenicals (oxophenarsine hydrochloride; mapharsen).

The <u>in vitro</u> thermal range studies with <u>T. pallidum</u> and penicillin suggest an alternative explanation. In those experiments, without penicillin, there was a sevenfold increase in the number of viable organisms after twenty-four hours incubation at  $39.7^{\circ}$  C., and the net rate of growth was even greater than that observed at  $37^{\circ}$  C. In the presence of penicillin, however, the organisms died several times faster at the higher temperature. The treponemicidal action of the drug is obviously enhanced at the higher temperature, despite the favorable effect of the latter on the rate of multiplication of the organisms. The favorable therapeutic effect of penicillin <u>in vivo</u> at higher body temperature may therefore be due to a heat-induced more rapid treponemicidal action of penicillin.

It should be emphasized, however, that the latter in vitro experiments involved a saprophytic organism, which is certainly not now <u>T</u>. <u>pallidum</u>, whatever its original identity; the pathogen may be more susceptible to higher temperatures than is the cultured saprophyte. Under such circumstances, the favorable effect of combining penicillin and fever may have a dual basis: (1) an increase in the efficacy of the penicillin itself; and (2) an additive and perhaps synergistic action between the harmful effects of penicillin and of high temperatures on <u>T</u>. <u>pallidum</u>.

The degree to which those observations are applicable to infections other than syphilis will depend on (a) the degree to which the organism is affected by increased temperatures, and (b) the degree to which the bactericidal action of penicillin on the particular organism is enhanced by increasing temperatures in the range of from  $37^{\circ}$  to  $40^{\circ}$  C. This enhanced activity in <u>vitro</u> has been demonstrated in the case of treponemas and staphylococci but has apparently not yet been studied for other pathogens. (Am. J. Syph., Gonor. and Ven. Dis., May '47 - H. Eagle et al.)

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(Not Restricted) <u>Report on Recent Meeting on Streptomycin in the Treatment of Tubercu-</u> <u>losis:</u> A conference on streptomycin was held recently in St. Louis, Missouri. It was attended by seventy-nine physicians, including representatives of the Army, Navy, Veterans Administration, U. S. Public Health Service, National

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Research Council, American Trudeau Society, American Medical Association, and the Pharmaceutical Industry.

Number and Types of Cases of Tuberculosis Reported Upon.

	Number of Patients Treated			
	Full Course 120 Days	61-119 	1-60 <u>Davs</u>	Total
Pulmonary Genito-urinary Bone and Joint Lymph Gland and Sinus	243 13 1 18	123 21 19 39	65 2 21	431 36 20 78
Tracheobronchial and Laryngeal	13	36	20	69
Miliary and Meningitis (surviving)	10 9*	29	18	57 9
Peritonitis (60 days) Pericarditis	8 7*			8 7
Enteritis (60 days) Tongue, Skin, Eye Thoracic Surgery	. 10			10
Prophylaxis (21 days plus)	84			84
(ZI days plus) Total	416	267	126	809

\*The full course in these cases was 60 days instead of the 120 days indicated by the column in which they are placed.

It should be emphasized that the above series .epresents the number of patients treated; the number of lesions would be decidedly greater. Treatment in one hundred of the pulmonary cases was by the Army, and in 37 by the Navy.

<u>Presentation</u>. Cases were reported upon by the Army unit from Fitzsimons, the Navy unit from Sampson, and by 18 study units from Veterans Administration hospitals. X-ray films for all pulmonary cases treated more than 60 days were demonstrated and the changes occurring during treatment were marked on special score sheets by juries of from 8 to 12 observers selected by Doctor Barnwell of the Veterans Administration.

<u>Results.</u> The results in the sinus cases, tracheobronchitis, miliary cases, peritonitis, enteritis and glossitis continue to be quite uniform and remarkable. In laryngitis, the results were less uniform; 2 of the 5 study

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units that reported upon more than 3 cases had found little improvement, especially when the aerosol method was employed. The patients with genitourinary involvement show some symptomatic relief and improvement of lesions in the lower urinary tract. Insufficient data is available to warrant any conclusions concerning lesions of the bone, joint, skin and eye. In the rather chronic type of pericarditis which had been treated the results were unimpressive. The patients with meningitis lived longer than would have been anticipated without streptomycin and an occasional patient "recovered". Only one spread was recorded in the surgical group, and that in a control patient.

Sputum conversion was reported in 32 per cent of 162 cases treated more than 60 days. Relapses occurred in approximately 22 per cent of 120 cases during from 1 to 7 months of post-treatment observation. Extension of disease occurred during treatment in approximately 6 per cent according to the members of the study units, but in 10 per cent according to the juries. Six deaths occurred after more than 2 weeks of intramuscular treatment, 3 due to hemorrhage, 1 to embolism, 1 to thrombophlebitis with gangrene, and 1 to myocarditis. The effect upon proliferative lesions was usually negligible. In 157 cases, reported upon by 7 study units and upon which the statisticians were able to analyze the jurors' opinions, an average of 81 per cent (varying from 46 to 93 per cent) of the exudative lesions were estimated to have been unchanged. In this same group, new lesions (pulmonary for the most part) appeared in 10 per cent. New and old cavities showed improvement (closed, no longer could be seen on the X-ray film, or smaller) in 65 per cent. There was no change in 17 per cent of new cavities and in 29 per cent of old cavities. It was the judgment of all the jurors that similar improvement would "but occasionally," "rarely," or "never" be seen on bed rest alone in 50 per cent of the cases, that it would often be seen in 33 per cent, and that it was the usual result in 17 per cent.

<u>Toxicity</u>. Subjective and objective (caloric test) evidence of vestibular damage occurred in 96 per cent of the patients (in only 30 was it absent). No data were available regarding the permanence of this damage (certainly it lasts for several months) nor as to the degree of disability it would produce. Doctors Fowler and Guild were inclined to regard it very seriously, and in this connection Doctor Fowler showed a very instructive motion picture film. Doctor Hinshaw and others felt that compensatory equilibration was adequate. No deaths were reported which seemed unequivocally due to streptomycin, though one, from renal failure, might have been so looked upon. Signs of toxicity were sufficiently severe in 34 cases (4 per cent) to require cessation of therapy (renal damage in 12, partial deafness in 8 with partial or complete recovery following cessation of treatment, exfoliative dermatitis in 10 of which 3 were mild, neutropenia in 2 which was not impressive, psychosis in 1,

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and hepatitis in 1). The incidence of minor toxicity (skin eruptions, circumoral paresthesias, etc.,) was not recorded.

<u>Development of Resistance</u>. It had been intended to collect reports on this subject from all study units but this was not fully accomplished. Data gathered from the written reports of 6 VA units indicate that <u>Mycobacterium</u> <u>tuberculosis</u> developed an <u>in vitro</u> resistance to more than 20 micrograms per c.c. (usually more than 100) in 39 (63 per cent) of 62 cases in from 60 to 120 days. Initial resistance was 3 micrograms per c.c. or less. It was considered of great importance that this work be extended and made more precise. Also it should be determined whether the resistance thus demonstrated may be accepted as a measure of <u>in vivo</u> resistance to treatment; there is a little evidence that this is the case.

<u>Laboratory Meeting</u>. It was decided that the three large laboratories, sponsored by the National Tuberculosis Association and National Institute of Health, namely, Mr. Steenken's at Trudeau, Doctor Bogen's at Olive View, and Doctor Youmans' at Northwestern University, would run parallel resistance tests with Youmans' and Dubos' media. The results of this experiment will determine which of the two media can be used to greatest advantage and accuracy as a routine laboratory procedure.

It was decided (1) that fewer blood level determinations need be done as a routine, but frequent determinations should be made in those patients who may be having a streptomycin nephropathy; and (2) that a hemolytic strain of <u>Staphylococcus aureus</u>, sometimes spoken of as "staphylococcus SM" and obtainable upon request addressed to the attention of Doctor Welch, Food and Drug Administration, Federal Security Agency, 12 and C Streets, S.W., Washington, D. C., is a better test organism than the <u>Bacillus circulans</u> now being used in most laboratories.

<u>Controls</u>. A discussion of this matter by the entire group disclosed the anticipated divergence of opinion. The study units, being asked whether they could collect cases of patients from previous years with pulmonary lesions "similar" to those they had treated with streptomycin, said they would attempt to do so. The difficulty of collecting such cases with radiological follow-up of six months without collapse therapy was pointed out. This would be impossible for Army, Navy, and several new VA hospitals. No decision was reached on this point.

<u>New Regimens</u>. It was decided that sufficient experience had been gained with the "old" regimen for pulmonary tuberculosis, namely, from 1.8 to 2.0 Gm., given in from 5 to 6 injections per day for 120 days. The following three new regimens were agreed upon and voluntarily adopted:

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 2.0 Gm., 5 injections per day for 60 days (decreasing duration)
 1.0 Gm., 5 injections per day for 120 days (decreasing dose)
 1.0 Gm., 2 injections per day for 120 days (decreasing dose and frequency)

It was agreed that insufficient data had been obtained on genito-urinary, bone and joint tuberculosis to permit a change of regimen.

It was agreed that the 1.8 Gm. dosage should be continued in the thoracic surgery protocol, with a shift to 2.0 Gm. in all future cases when this proves more convenient for hospital personnel.

It was agreed that sufficient evidence had been accumulated to prove that the aerosol method was inferior to the intramuscular route in the treatment of tracheobronchitis and that the former would therefore be abandoned. (This decision presumably applies to laryngitis as well).

Because of the occasional occurrence of signs of local irritation (neuritis and paraplegia) following the intrathecal administration of streptomycin, it was agreed that the daily dose would be decreased from 100 mg. to 50 mg., or to an amount not exceeding 1 mg. per Kg. of body weight.

It was decided to initiate a small pilot study in which streptomycin and promin would be used in conjunction.

The hope was expressed that the next meeting might be held in September. (From notes taken at the meeting)

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<u>Disease of the Nervous System Occurring Among Research Workers on</u> <u>Swayback in Lambs</u>: Swayback is a paralytic disease of newborn and young lambs to which sporadic attention was given by some workers in the Institu of Animal Pathology, Cambridge University, England, from about 1924 to about 1928. Fuller investigations were begun in 1934 in which its pathological nature was established by one of the authors. The disease occurred in many parts of Britain. In certain areas, the incidence in newborn lambs in some years was very high, up to from 70 to 90 per cent. In other areas, it occurred annually but with a very low proportion of cases. The affected lambs were born from apparently healthy parents, mostly from ewes that had been in an "affected area" for more than one year. The disease occurred in either sex, in single lambs, and both of twins or in all three of triplets. There were ataxia and paralysis (progressive except in the mildest cases), the lambs

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either walking with a staggering gait or being completely paralyzed and unable to rise. The pathology is a symmetrical cerebral demyelination and degeneration of the motor tracts, ranging in some cases from unmistakable macroscopic gelatinous softening to others in which the liquefaction process is so severe as to cause a porencephalic-like cavitation extending from pole to pole of the cerebral hemispheres. There was thus some justification for comparing the disease to Schilder's encephalopathy bearing in mind the differences which might be seen in the reaction of the immature brain of the fetal lamb. The enzootic ataxia of lambs in Australia was shown later to have the same pathology. It is now certain that the same condition has occurred in certain parts of Peru, Patagonia and the Argentine under the name of "Renguerra", in New Zealand, and from the descriptions it might well have occurred in Sweden and India, but in none of the other European countries. Schulz informs the authors that in South Africa a disease similar to swayback has been identified in a small coastal strip of the country.

All attempts by the workers at Cambridge to transmit the disease failed. They inoculated emulsions of various organs, various parts of the nervous system, and blood into young healthy lambs of differing ages by almost all routes. Various other workers were all equally unsuccessful in transmitting the condition. The possibility that the disease was a variety of congenital lead encephalopathy was considered by both Innes and Bennetts; in areas where lead has been extensively mined the sheep must have been absorbing the metal in large quantities: the disease, however, also occurred in areas where lead had never been mined. Although this concept was discarded it is still possible that lead may be involved indirectly in connection with the utilization of other trace elements. The next step lay in the observation of Bennetts and Chapman (1937) that the disease could be prevented by giving copper supplements to ewes during pregnancy. These observations were confirmed in England by Dunlop, Innes, Shearer, and Wells. The disease apparently is not a copper deficiency per se because it occurred in areas where the pasture had a normal copper content.

This work on swayback demands consideration from the point of its possible application to the study of human disease. Apart from (1) the very rare occurrence of a Schilder's type of encephalopathy in monkeys, (2) the occurrence of a rare form of demyelinating encephalitis in the moose described by King (1939), and (3) the acute leuco-encephalitis of horses (corn stalk disease) commented upon by Hurst (1940) there is no idiopathic demyelinating disease which occurs in animals with any frequency. The demyelinating diseases occurring in man differ widely but are linked together by the common feature of myelin loss whether focal, perivascular or diffuse. The etiology of all the demyelinating conditions is obscure and attempts to incriminate viruses, bacteria, toxins, allergy, or a vascular mechanism have failed to carry conviction.

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The experimental production of demyelination by a large number of different agents have simply shown that the lesion could be produced by diverse means. It has generally been regarded that demyelination is not a common lesion in encephalitis caused by known neurotropic viruses, and apart from the recent report by Margulis et co-workers, no virus has been isolated from any disease of the demyelinating group. The cause of the post-infective type of demyelinating encephalopathy remains obscure. The observations of Hurst et al. on experimental distemper in dogs in Australia indicated that this virus might underlie the demyelination occasionally found in the so-called post-distemper encephalitis, but this has not been the experience of some workers in England working along the same lines.

Disseminated sclerosis is the only common demyelinating disease in man, and in February 1946 the authors began a study of this disease with the help of specialists in various branches of natural science, including chemists. The problem has been approached from a number of angles including geological, geographical and biochemical, but these studies are not yet complete. However, a new line of approach opened up when it became evident that no fewer than four of the seven principal workers in a swayback research unit have developed disease of the central nervous system which would be diagnosed confidently by any neurologist as disseminated sclerosis. In two the signs have advanced little, if at all, for many years, but in all there has been clear evidence of multiple lesions with remissions and relapses.

It is difficult to escape the conclusion that there is an association between the work on swayback and the development of the nervous disorder. Swayback and disseminated sclerosis are both forms of demyelinating diseases, although it must be stressed that apart from the myelinoclastic lesions the resemblance ceases.

It is not easy to believe that swayback and disseminated sclerosis can have a common etiology, yet while the causes of the demyelinating diseases remain so obscure no possible avenue should be left unexplored.

It may be significant that disseminated sclerosis, like swayback, has a definite geographical distribution. There have been several studies of this subject which indicate that disseminated sclerosis is common in the Scandinavian countries, Germany, Switzerland, France and Britain, but is less common in the Mediterranean countries. Apart from Britain and Sweden no swayback has been reported in any other European country. The coloured races are said to be rarely affected by disseminated sclerosis. Within one country great variations in its incidence are reported, and Bing found the incidence three or four times greater in North than in South Switzerland. South Africa may be an important country from the geographical standpoint for it is

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reasonably certain that the disease very rarely, if ever, affects a South-African born person of European stock. The rarity of swayback (except in one coastal area) in South Africa which is a great sheep-rearing country has been mentioned. It is evident, therefore, that both disseminated sclerosis and swayback have a striking geographic distribution, but there is no clear similarity yet known of by the authors between the distribution of these two diseases except perhaps in South Africa where both are rare. Any attempt therefore to incriminate a common infective agent raises many difficulties including the assumption that the "virus" can only become active under strictly limited circumstances. The authors have no evidence that disseminated sclerosis is unduly frequent in those who handle sheep and mutton.

The fact that trace elements (cobalt, iodine, fluorine, manganese, etc.) have now been proved to be of great physiological importance in man and animals, and in particular that copper is concerned with one demyelinating disease of animals indicates that some attention ought to be paid to the possibility of trace elements being involved in the cause of disseminated sclerosis. It would certainly appear that copper therapy is worth a trial. Some of the affected workers with swayback have themselves tried its effect but with uncertain results, so a study is being made of treatment with copper in other cases of disseminated sclerosis. There is little knowledge regarding the danger of the prolonged administration of copper salts in man, but it may not be without risk. It should be noted that in sheep an excess of copper produces intravascular hemolysis, anemia and jaundice, preceded by a very definite rise in blood copper level.

The authors are not yet able to give the results from copper therapy, but preliminary impressions are not favorable. (Brain, J. Neurol., March '47 - A. M. G. Campbell et al.)

<u>A Case of Pulmonary Anthrax with G-I Tract and Liver Involvement</u>: This report of a case of pulmonary anthrax seen in a man in a Philadelphia hospital is presented to call attention to a disease which is sometimes thought of as limited almost solely to the leather and hide industries and to agricultural regions.

<u>Case Report</u>. A 46 year old white man was hospitalized with a chief complaint of cough and dyspnea of three days' duration. He had been perfectly well until four days prior to admission, when he complained of a mild cough and a feeling of general malaise. Although he did not go to bed, he had fever and a headache, and an increasingly severe productive cough developed, accompanied by ain in the left side of the chest. Slight hemoptysis began before his symptoms became pronounced. The day before admission his temperature

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rose to 102° F., his sputum became blood streaked, and he began to breathe with more difficulty. Twelve hours later he suddenly became much worse. His breathing became labored and fast, he was cyanotic, and he began to bring up large amounts of bloody sputum. He became weak and semiconscious and then was brought to the hospital.

Just prior to his illness he was a china and glassware salesman. Before the war he had been a rug merchant and he had recently been cleaning some new rugs which he had planned to sell.

His temperature was 97<sup>o</sup> F.; pulse rate, 140; respiratory rate, 50; blood pressure, 90 systolic and 50 diastolic.

He was an extremely cyanotic, dyspneic, orthopneic, well nourished man of 46, who coughed continually. From the corner of his mouth ran a brownish red sputum. He was sweating profusely. His skin was cold and clammy. He appeared moribund. The head was normal except for the severe cyanosis. The pupils were widely dilated and did not react to light. There was no nasal discharge or obstruction. The mouth disclosed a dry and coated tongue. The chest showed a lag on the left, and there was dulness to percussion over the left base and in the left axilla. Over this area there was bronchial breathing with many rales. For the remainder, the lung fields were clear. The heart was not enlarged. The sounds were regular, rapid, and strong. The aortic second sound was greater than the pulmonic second sound. There were no murmurs. The pulse was rapid, weak and thready. The liver and the spleen were not felt. The extremities were cyanotic and cold.

The patient was put in an oxygen tent and died two hours after admission. No laboratory work was done.

An autopsy was performed 24 hours after death. The left pleural cavity contained about a liter of clear yellow fluid; the right, approximately 500 c.c. There were numerous enlarged hemorrhagic black mediastinal and hilar lymph nodes, measuring up to 3 cm. in diameter. The pericardium contained about 75 c.c. of clear fluid.

The right and left lungs weighed 540 and 770 Gm., respectively. The right lung was reddish gray, and its pleural surface was smooth and moist. The parenchyma was deep purplish red and poorly aerated. About the hilus and extending upward toward the apex in the mediastinum was a mass of intensely hemorrhagic lymph nodes. The nodes around the hilus appeared to compress the lower branch of the pulmonary artery, practically occluding the lumen. Many of the nodes looked like blood clots, and others

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showed traces of grayish lymphoid tissue. The left lung was heavy. The lower lobe was enlarged and firm. The pleural surface was smooth and deep reddish purple. The entire lobe had a gelatinous and homogeneous blackish red appearance. It contained no air and was friable. The upper lobe was congested and edematous.

The spleen weighed 60 Gm. The capsule was gray and wrinkled The parenchyma was pinkish gray, congested and mushy.

The liver weighed 1,500 Gm. The capsular surface was reddish brown and showed small circumscribed bluish black areas beneath the capsule. These measured approximately 1 cm. in diameter and proved to be small cavities which contained dark clotted blood. The parenchyma was smooth and brownish red.

The external surface of the bowel was smooth and glistening. The gastric rugae were prominent, and numerous small superficial ulcers were noted. These were confined to the lower portion of the body and pyloric vestibule. They were most numerous along the greater curvature. The lesions measured from 0.5 to 1.5 cm. in diameter. Some were flat erythematous plaques; others showed shallow central ulcerated necrotic centers, and still others showed rolled indurated edges with fairly deep ulcerated necrotic centers. All of the lesions were covered with a thick clear gelatinous exudate. Several similar lesions were found in the duodenum, jejunum and ileum. None were found in the large bowel.

The outstanding histologic changes were the marked hemorrhage, congestion, and almost total absence of polymorphonuclear cells, even in the areas of liquefaction necrosis. The preponderance of mononuclear phagocytes laden with hemosiderin in all areas of infection was noteworthy. The blood vessels in this case were not thrombosed. Even the smallest branches were normal. No bacilli were demonstrated in the vessels in sections stained by Goodpasture's technic.

The lower part of the left lung showed a thickened pleura infiltrated with mononuclears. The bronchi were filled with detritus; the mucosa had sloughed away partially to completely. The alveolar walls were thickened, owing to capillary dilatation. The spaces were filled with blood. There was secondary atelectasis, with practically no inflammatory response. Hemosiderin and "heart failure" cells were innumerable. The right lung showed hemorrhage in the alveolar spaces, but the alveolar walls and bronchi appeared much less affected.

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The stomach revealed congestion of the vessels, hemorrhage, necrosis, and edema, with ulceration of the mucosa. Large rod-shaped bacilli were numerous in the ulcer craters and invaded the mucosa in great numbers, extending down to but not into the submucosa. Hemosiderin-laden macrophages were numerous.

The small intestine showed a picture practically identical with that in the stomach except that the hemorrhage was confined to the tips of the villi. Bacilli were countless around the ulcerated areas.

All of the pulmonary hilar lymph nodes examined showed massive hemorrhage, in some cases involving all of the node. There was complete loss of the internal structure, and in some areas, necrotic liquefaction. The nodes were filled with macrophages. The vessels were dilated and congested, but no bacilli were seen.

Cultures of material from the liver, the mediastinal lymph nodes, and the larynx presented a moderate number of colonies of anthrax bacilli. Staphylococci and hemolytic streptococci were isolated in small numbers from the larynx and the liver.

Human anthrax is not rare in the United States. A recent survey of the period from 1939 to 1943 shows a 16 per cent increase of cases of anthrax. The infection occurred in people who had no occupational contact with infected material. One patient was a football player (soil?). Several patients were children; one of these, 10 years old, was resident in a mining location in a state where animal anthrax had been unknown for ten years; this child died of a pulmonary and blood stream infection. Other patients were housewives. Some patients had been gardening; others contracted the disease from tooth brushes, shaving brushes, and a fur coat. Many of these cases were pulmonary in type and fatal.

Anthrax must not be thought of as a disease limited to a few industrial and agricultural areas. Although Pennsylvania has had a large number of cases of anthrax annually because of its tanneries and woolen mills, the present case is a good example to show that anthrax may occur anywhere. (Arch. Path., April '47 - J. S. Cowdery)

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Failure of Artificial Dentures Processed Against Tin Foil Substitutes: The results from a recent investigation of substitute materials for tin foil conducted by Commodore George C. Paffenbarger, DC, USNR, Commander

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George W. Ferguson, DC, USN, and Irl C. Schoonover, Ph.D., at the National Bureau of Standards, has shown these materials to be far inferior to tin foil. These substitute materials, such as calcium alginate, nylon, rubber dam, and other film forming materials, were found to cause surface strain in resin dentures. When even a low grade solvent such as ethyl alcohol comes into contact with a denture processed against a tin foil substitute, the surface strain is released, causing the development of cracks in the denture. Resin dentures processed in molds lined with tin foil are almost always free of detectable surface strain.

The investigators state that none of the tin foil substitutes tested at the National Bureau of Standards have been found satisfactory. They suggest that dental officers wishing to show defects in cured resins or to establish the safety of a tin foil substitute may do so by applying a small amount of methyl methacrylate monomer, ethyl alcohol, or other suitable solvent with a tuft of cotton to a specimen cured against the substitute. After from two to five minutes, when the specimen is viewed by transmitted light, a network of fine, almost invisible lines may appear over the area on which the solvent was applied. (A.D.A. Research Commission Report) (Dental Div., BuMed)

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<u>Short Course in Diseases of the Chest</u>: The Bureau of Medicine and Surgery announces the second Annual Postgraduate Course in Diseases of the Chest, sponsored jointly by the Council on Postgraduate Medical Education and the Illinois Chapter of the American College of Chest Physicians. This course will be given at the Chicago Tuberculosis Sanatorium, from 15 to 20 September 1947. In this course emphasis will be placed on the newer developments in the diagnosis and treatment of the diseases of the chest.

The tuition for the course, which is \$50.00, will be paid for from BuMed training funds. Authorization orders only can be given. No service agreement is required. Requests from interested medical officers are desired by dispatch. (Professional Div., BuMed)

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<u>Training in Otolaryngology</u>: The Bureau of Medicine and Surgery has several vacancies for training in otolaryngology. These vacancies are in naval hospitals and civilian institutions. Requests for this training are desired from medical officers of the regular Navy who are interested in otolaryngology. Applications should be submitted in accordance with <u>Bumed</u> <u>News Letter</u> dated 23 May 1947. Applications may be made by despatch. (Professional Div., BuMed)

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<u>Postgraduate Training in Anesthesiology</u>: The need for trained anesthetists in the Navy persists. Anesthesiology, through widening of its scope with the consequently greater responsibilities attached to its practice, is becoming of increased importance in the Navy and offers special opportunities, particularly for the younger medical officers.

The training furnished for this specialty includes the following:

Basic sciences. Opportunity is afforded for study in the basic sciences with particular emphasis on anatomy, physiology, and pharmacology as they apply to anesthesiology.

<u>Anesthesia</u>. Experience with all the anesthetic agents and methods is provided together with pre- and post-anesthetic medication and care, tracheobronchial aspiration, and the treatment of post-operative complications.

<u>Diagnostic and therapeutic nerve blocks</u>. Blocking of the various nerves, including the sympathetics, as used in determining the site of origin of disturbances of sensation, in the treatment of various medical and surgical conditions, and in assessing the probable value of sympathectomy, etc.

<u>Blood and plasma therapy</u>. The operation of the blood and plasma bank falls within the province of the anesthesiologist whose training fits him as a consultant in special problems involving the need for and use of blood, blood derivatives, and infusion fluids.

<u>Inhalation therapy</u>. Supervision of the supply of oxygen, carbon dioxide, and helium, and the equipment used in their administration.

<u>Resuscitation</u>. The treatment of asphyxia and shock are logically supervised by the anesthesiologist. The use of various methods of artificial respiration, the use of analeptics, the estimation of blood and plasma requirements, and experience in intra-arterial infusion, are among the essentials in this field.

<u>Curare</u>. Experience in the use of curare preparations therapeutically.

Intravenous procaine. As used in such conditions as pruritis, post-traumatic pain, and certain types of arthritis.

Requests for this training are desired from medical officers of the Reserve and regular Navy. Reserve medical officers should include an application for transfer to the regular Navy. Requests should be submitted in accordance with information contained in the <u>Bumed News Letter</u> dated 23 May 1947. (Professional Div., BuMed)

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Reserve Dental Officer Questionnaire: Reserve Dental Officer Data Sheet NAVMED-1163 was mailed to Reserve dental officers on inactive duty in March 1947. Many officers have delayed in completing this form and returning it to the Bureau of Medicine and Surgery (Dental Division). Reports from various naval districts have shown a similar delay on the part of dental officers of the Reserve in replying to questionnaires distributed by them. The failure of Reserve officers to inform the Bureau of Medicine and Surgery and the district commandants of their present address has made it impossible to distribute official information of interest and benefit.

In order to conduct an effective program for dental officers of the Reserve, it is necessary to have certain essential information concerning each officer. Utilization of the advice of all members of the Dental Corps Reserve is desired in formulating plans for the Reserve program. (Dental Div., BuMed)

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Improper Preparation of Dental Records: Many improperly prepared DENTAL RECORDS (NAVMED H-4) are received by the Bureau of Medicine and Surgery. The most frequent error consists of omitting adequate identification, which precludes placing the record in the file jacket of the proper individual.

All dental officers are requested to type the following at the top of the DENTAL RECORD (NAVMED H-4):

- a. Family name in capital letters at the left on the line for "Surname", and file or serial number at the right on the same line.
- b. Given names on the line for "Christian name (s)".
- c. City and state in which born on line "Born. Place".
- d. Date of birth on line "Date".

The date on which the dental examination was made, and the name of the dental officer shall be typed on the line "Date and signature of examining dental officer".

Other detailed instructions for the preparation and handling of the DENTAL RECORD may be found in Section VII, Part II, Chapter 2, of the Manual of the Medical Department, 1945. (Dental Div., BuMed)

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<u>Revised Report of Dental Operations and Treatments</u>: The following is intended to clarify the preparation of the revised NAVMED-K.

1. An initial supply of the new Report of Dental Operations and Treatments, NAVMED-K (Rev. 5-47), has been sent to each dental activity. Additional quantities of this form may be requisitioned, when needed, from the appropriate district publications and printing office, or publications distribution center. Upon receipt of the NAVMED-K (Rev. 5-47) all older issues of this form shall be declared obsolete and destroyed.

2. The instructions for accomplishing this form, in paragraph 5112 Manual of the Medical Department apply, in general, to the revised NAVMED-K. However, until this paragraph can be changed to fully agree with the new NAVMED-K (Rev. 5-47), the following supplemental instructions are effective for the items referred to:

(a) The original shall be submitted to BuMed as soon as possible after the last day of each month.

(b) A separate NAVMED-K (Rev. 5-47) shall be submitted as in (a) for treatment of personnel of the Veterans Administration, Army, Coast Guard, State Department, Foreign Military Services, or similar categories. Such reports shall be marked "VETERANS ADMINISTRATION" or other applicable designation above the heading "REPORT OF DENTAL OPERATIONS AND TREATMENTS" for each category.

(c) A supplemental letter report, in detail, shall be attached to this form whenever emergency dental treatment is accomplished for humanitarian reasons for dependents of service personnel, or other civilians.

(d) An information copy of this form, and all other dental treatment reports submitted to BuMed shall be forwarded to cognizant staff or district dental officers.

3. The NAVMED-K (Rev. 5-47) contains all the dental operations, treatments and other data, which BuMed desires to include for statistical study. Only very unusual cases, operations or treatments should be entered on the lines titled "OTHER". Entries such as silver nitrate, thymol, phenol, etc., which are used in cavities prior to placing restorations, or for other purposes, are parts of operations and treatments and are not desired. These entries should be discontinued. Many dental officers add entries on lines titled "OTHER" which should be included under a title already provided, as for example: aphthous stomatitis and streptococcus stomatitis, which should be entered on the line titled "STOMATITIS". A line for reporting "AMALGAM RESTORA-TIONS POLISHED" is provided under the heading "OPERATIVE DENTISTRY".

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No entry is desired for polishing silicate cement fillings, or other types of restorations.

4. The interpretation is changed for the item: "(A) RECEIVING TREATMENT (on date of this report)" which appears under the heading "TREATMENT SUM-MARY" on the back of NAVMED-K (Rev. 5-47). It is now intended that this entry shall indicate the number of persons who are carried on the books, as being under treatment on the last day of the month. These patients have received dental treatment during the month, are to receive continued treatment, and have not been disposed of under any of the following headings: "(B) ES-SENTIAL TREATMENT COMPLETED", "(C) ALL TREATMENT COMPLETED", or "(D) TREATMENT TERMINATED (all or essential treatment not accomplished)". The interpretation for "(C) ALL TREATMENT COMPLETED" is also changed. This entry should not include the figure for "(B) ESSENTIAL TREATMENT COMPLETED". The figure for "TOTAL PATIENTS TREATED", should be the total of (A), (B), (C), and (D) under "TREATMENT SUMMARY".

5. The entry for the item "DAILY AVERAGE DENTAL OFFICERS ATTACHED DURING MONTH" which appears under the heading "DENTAL PERSONNEL STATISTICS" should be the average number of dental officers attached to the command during the month, for example: If two dental officers were attached for 30 days, another one for 15 days, and another one for 8 days, the daily average would be 2.76 for a 30 day month or 2.67 for a 31 day month, even though one may have been on leave 30 days, and one may have been on the sick list 15 days, and one may have been on temporary additional duty elsewhere for 30 days. An entry should be made under remarks for dental officers who are attached but who are on temporary additional duty elsewhere, for example: 1 D.O. temporary additional duty 30 days. No entry should be made under "REMARKS" for dental officers who are attached for temporary additional duty. Dental officers attached for temporary duty, as compared to those attached for temporary additional duty, should be reported under "DAILY AVERAGE DENTAL OFFICERS ATTACHED DURING MONTH"

6. Entries for new items to be reported in the column entitled "CAL. YEAR TO DATE" should commence with the first NAVMED-K (Rev. 5-47) submitted and should not be retroactive for the calendar year.

7. Because of the importance of NAVMED-K (Rev. 5-47), signatory dental officers are expected to check it carefully for accuracy and completeness before submitting it to BuMed.

8. The entry for the item "TOTAL EXAMINATIONS AND DIAGNOSES" which appears under the "EXAMINATIONS AND DIAGNOSES" section shall be the total of the entries made on the nine lines in this section. (Dental Div., BuMed)

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<u>Eighty-Eighth Annual Meeting of the American Dental Association</u>: The eighty-eighth annual meeting of the American Dental Association will be held in conjunction with the Tenth International Dental Congress at Boston, from 4 to 8 August. This will be the first full scientific meeting of the Association since the 1941 meeting in Houston. It will be the first International Dental Congress since 1934.

The Navy will be represented in the House of Delegates by Rear Admiral Alfred W. Chandler, DC, USN, as Delegate, and Captain Edward A. Hyland, DC, USN, as Alternate. Rear Admiral Chandler is the Assistant Chief of the Bureau of Medicine and Surgery for Dentistry, and the Chief of the Dental Division; Captain Hyland is the District Dental Officer for the First Naval District.

The following naval dental officers have been scheduled to present papers at the meeting:

Captain Clemens V. Rault, DC, USN, "Postgraduate Education in the United States Naval Dental School;" Commander Charles E. Schork, DC, USN, "Neoplasms of the Head and Neck;" and Commander George W. Ferguson, DC, USN, "Tin Foil Substitutes for Use in Processing Acrylics."

It is anticipated that the meeting will be attended by as many naval dental officers as can be spared from their official duties. (Dental Div., BuMed)

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## Public Health Foreign Reports:

Disease	Location	<u>Date</u>	lo. of Cases
Cholera	India, Calcutta	April 6-16, '47 April 27-May 3, '47	433 (125 fatal) 232 (71 fatal)
	Indochina (French), Cochinchina	April 21-30, '47	35 (28 fatal)
	Siam (Thailand), Bangkok	April 13-19, '47	61
Plague China, Fukien Prov., Hweian Egypt, Alexandria		JanFeb. '47 April 29, '47 (date rep.)	255 (71 fatal) 1
	Indochina (French), Annam	April 21-30, '47	14 (11 fatal)

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# Public Health Foreign Reports (Cont.):

Disease	Location	Date	No. of Cases
Plague	Peru Piura Dept., Prov.	April '47	23 (4 fatal)
	of Huancabamba Turkey, Urfa Prov., Akcakale	March '47	10
		April 13-19, '47	2
Smallpox	Belgian Congo China, Formosa,	Mar. 30-Apr. 5, '47	47 (1 fatal)
	Kaohsiung Shanghai	March '47 April 20-26, '47	41 (9 fatal) 133
	Colombia Ecuador Ethiopia	May 11-17, '47 April '47 April '47 Feb. 23-Mar. 8, '47 Mar. 16-22, '47	150 326 (5 fatal) 50 14 3
(alastrim)	Great Britain, Eng. and Wales India, Calcutta Indochina (French) Luxemburg	May 4-24, '47 Apr. 27-May 3, '47 May 1-10, '47 May 10, '47 (date rep.)	16 120 (89 fatal) 136 (40 fatal)
(alastrim)	Niger Territory Venezuela	Mar. 21-31, '47 May 10-17, '47	1 240 (52 fatal) 185 (1 fatal)
Typhus Fever	Colombia Ecuador Eritrea Ethiopia Guatemala Libya, Tripolitania Peru Poland Rumania	April '47 April '47 Mar. 30-Apr. 5, '47 Feb. 23-Mar. 8, '47 Mar. 16-22, '47 February '47 February '47 February '47 March '47 March '47 Mar. 1-18, '47 Feb. 1-Apr. 5, '47	130 (2 fatal) 51 (3 fatal) 42 (1 fatal) 11 20 63 (10 fatal) 18 74 131 19
	Yugoslavia	Apr. 20-26, '47 February '47	5,091 (19 fatal) 1,269 23 (4 fatal)
Yellow Fever	Colombia	Jan. 1-31, '47 March 12, '47 (date rep.	4 (fatal) ) 1 (fatal)
(Pub. Health Re	ps., 23 May: 6, 13 & 20	Tuno (17)	

(Pub. Health Reps., 23 May; 6, 13 & 20 June '47)

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Circular Letter 47-79 24

24 June 1947

(Not Restricted)

To: MedOfCom, All U. S. Naval Medical Department Activities

Subj: Contracts for Personal Services

Ref: (a) NCPI 35, Revision 1.

This letter from the Chief of BuMed states that (1) when an activity determines that a position cannot be filled by full-time Civil Service employment and contract employment is to be requested, (2) such a contract should be executed in accordance with the procedures outlined in reference (a) and forwarded to BuMed well in advance of the effective date in order that the contract may be approved by the Secretary of the Navy and returned prior to the date that the contract employee is to enter on duty, and (3) this type of employment will be approved only when it is not feasible to effect employment through regular Civil Service procedures.

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Circular Letter 47-80

24 June 1947

(Not Restricted)

To: All Naval Hospitals and Hospital Ships

Subj: <u>Rations furnished retired officers and nurses, inactive, while</u> patients in naval hospitals; CASH collection for.

Ref:

- (a) BuMed CirLtr 46-84, dated 27 May 1946, with Encl-1 attached thereto.
  - (b) BuMed CirLtr 44-91, dated 22 May 1944, BuMed Bulletin of CirLtrs, 1945 Edition.
  - (c) Pars. 4132 and 4133, ManMedDept, 1945 Edition.

This letter from the Chief of BuMed states that effective 1 July 1947, charges for subsistence furnished officers, Navy and Marine Corps, retired, inactive, and Nurses, Navy, retired, inactive, as properly reported on lines 35, 36, 37, and 38, Section B, of the Monthly Ration Record, NavMed HF-36 shall be <u>collected locally</u> at the rate specified in the Annual Naval Appropriation Act. Included are instructions governing the establishment of this new procedure, the disposition of monies collected, the method of reporting, the exception to procedure in case of deaths, and the procedure in case of those concerned who are permitted to remain at home during convalescence.

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Circular Letter 47-81

25 June 1947

(Not Restricted)

- To: MedOfCom, U. S. Naval Hospitals; U. S. Naval Medical Supply Depots; National Naval Medical Center, Bethesda, Md.; Naval Medical Center, Guam, M. I.
- Subj: <u>Periodic pav increases of ungraded employees</u>.
- Ref: (a) NCPI 195 (Rev. II).
  - (b) BuMed CirLtr No. 47-52 of 24 April 1947.
  - (c) BuMed CirLtr No. 47-74 of 16 June 1947.

The purpose of this letter from the Chief of BuMed is to provide further clarification of the rules and regulations governing <u>periodic</u> pay increases of ungraded employees.

Circular Letter 47-82

26 June 1947

(Not Restricted)

- To: Commandants Naval Districts (Less 10, 15, and 17); Potomac River • Naval Command; District Directors of Naval Reserve; and District Directors of Training.
- Subj: <u>Vessels or Craft assigned to Naval Districts and River Commands</u> for use in making NAVAL RESERVE TRAINING CRUISES of a local and limited nature; Medical Allowance Requirement.
- Ref: (a) BuMed ltr BUMED-T over QB/L11-3 of 7 Sep 45 to Comdts., ND's (except 10, 14, 15, and 17) and RivComs. - cc to Com-14.

This letter from the Chief of BuMed establishes the allowances for subject vessels or craft and gives instructions for disposition of medical material in excess and for maintenance of the allowances as set.

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Circular Letter 47-83

26 June 1947

(Not Restricted)

- To: Commandants Naval Districts (Less 10, 15, and 17). Potomac River Naval Command.
- Attn: District Directors of Naval Reserve and District Directors of Training.

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Subj: <u>Vessels or Craft assigned to Naval Districts and River Commands</u> for use as NAVAL RESERVE ARMORIES; Medical Allowance Requirement.

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- Refs: (a) BuMed ltr BUMED-4223-CRM:kw over QR/L7-1/L8-2 Serial 8331 of 6/16/47 (enclosure 1 of which cancels and supersedes enclosure (A) of BuPers ltr Pers-427e-MK, Serial 1903-6 of 9/11/46) to All Continental NDs, 14th ND and PRNC.
  - (b) BuMed ltr BUMED-T over QB/L11-3 of 7 Sep 45 to Comdts., ND's (except 10, 14, 15, and 17) and RivComs. - cc to Com 14.

This letter from the Chief of BuMed states that many vessels, being assigned for use as armories, have been previously stripped or partially stripped of medical material, or do not have a complete Medical Commissioning Allowance aboard and directs that upon delivery of subject vessels or craft, excess medical material be removed. Instructions are given for the disposition of the excess material removed and for the maintenance of the allowances in accordance with enclosure 1 of reference (a).

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Circular Letter 47-84

27 June 1947

(Not Restricted)

To: Commandants, Eleventh, Twelfth, and Thirteenth Naval Districts

Attn: District Dental Officer

Subj: <u>District Dental Officer Inspection Reports</u>, Forwarding of Via Western Sea Frontier.

Ref: (a) Par. 1350.4 ManMedDept

1. For the purpose of coordinating Medical Department logistics planning, the District Dental Officer Inspection Reports shall be forwarded via Commander, Western Sea Frontier for endorsement.

--BuMed. C. A. Swanson

Circular Letter 47-85

27 June 1947

(Not Restricted)

To: AlNavStas

Subj: <u>Uniform Charge for Interdepartmental Hospitalization, Fiscal</u> Year 1948.

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## Refs: (a) Director, Bureau of the Budget, ltr., to SecNav, dated 8 October 1946.

- (b) Part IV, Chapter 1, ManMedDept, USN, 1945 Edition.
- (c) Executive Order 9411, dated 23 December 1943.
- (d) ALNAV #142 dated 25 June 1947

This letter from the Chief of BuMed, a copy of which is included in the 30 June <u>Navy Department Bulletin</u>, contains instructions concerning interdepartmental charges, charges for supernumeraries from whom local collection is made, and charges for dependents of Navy and Marine Corps personnel during the fiscal year 1948 for hospitalization within and without the continental limits of the United States. Instructions are also given for the disposition of net earned amounts received locally for hospitalization. Necessary detailed reports of hospitalization of supernumerary patients are to be submitted in accordance with reference (b).

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Circular Letter 47-86

30 June 1947

(Not Restricted)

To: All Ships and Stations

## Subj: <u>NAVMED-171</u> (Venereal Disease Contact Report)

- Refs: (a) Par. 236.3, Line 12, subparagraph (b), MMD.
  - (b) Par. 5120, MMD.
  - (c) Par. 12B6.2, MMD.
  - (d) JtLtr BuMed-BuPers P3-2/ET12(021-40) dtd 25 Mar 1941,
    N.D. Bull. AS&SL Cum. Ed. 1943, 41-2064, Page 1160
    (BuMed CirLtr 41-10)
  - (e) General Order #238

1. Attention is invited to the above references.

2. Many ships and stations are failing to report the serial numbers of NAVMED-171 (Venereal Disease Contact Report) on line 12 of the NAVMED-Fa Card (Statistical Report of Patient), as required by refs. (a) and (b). Of 1000 Fa Cards recently submitted on venereal disease admissions to the sick list, 827 or 82.7 per cent contained no serial number.

3. Many naval activities are not completing NAVMED-171 for each patient admitted to the sick list, as required by refs. (c) and (d). Correct preparation and prompt submission of the Venereal Disease Contact Report is an

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aid in locating infected individuals in the civilian population. A recent report from a State Health Officer stated that 30 per cent of the contacts reported to them were located and that 69 per cent of this number were infected with a venereal disease. This would indicate that approximately one out of every three contacts reported to this State Health Department is located and that for each three located at least two are infected. If more complete information had been submitted on our contact reports, a greater percentage of infectious contacts could have been located by local, state and federal health officials. The reservoir of venereal disease in civilian communities is reduced and this in turn has a marked beneficial effect on the incident of venereal disease in the Navy.

4. It is requested that the venereal disease contact reporting procedures be reviewed and that an effort be made to submit more complete reports.

--BuMed. C. A. Swanson

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Circular Letter 47-87

30 June 1947

(Not Restricted)

To: All Ships and Stations

Subj: <u>BuMed Material Requisitions, NavMed-4 (Rev. 12-46), preparation</u> and submission of.

Ref: (a) BuMed CirLtr 47-33, Navy Department Bulletin of 31 March 1947.

This letter from the Chief of BuMed calls to the attention of all concerned ALNAVSTA #22 (listed by error as ALNAV 22 in <u>Bumed News Letter</u> of 4 July 1947) which reads as follows:

Paragraph 11 (a) BuMed Circular Letter 47-33, <u>Navy Depart-</u> ment Bulletin, 31 March 1947, is modified as follows:

Insert a period after the word "available" in first sentence; delete the remainder of the sentence and substitute for it, "material back-ordered by medical supply depots for shore stations will be furnished as material becomes available without regard for fiscal year in which requisitioned." --SecNav.

--BuMed. C. A. Swanson

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Circular Letter 47-88

30 June 1947

(Not Restricted)

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To: Comdts, All Naval Districts and River Commands

Subj: Venereal Disease Control Officers and Interviewers

Ref: (a) BuMedCirLtr 45-143, BUMED-Y-rw P3-1/P3-2, dtd 8 June 1945; BuMedBull CirLtrs, 1945.

This letter from the Chief of BuMed cancels reference (a) and directs that each naval district and river command strengthen its venereal disease control organization by requiring all activities to (a) appoint an officer for additional duty as Venereal Disease Control Officer, and (b) select Pharmacist's Mates for venereal disease patient interviewing. Instruction for these interviewers should be in the form of a short course in venereal disease patient interviewing given by the District Venereal Disease Control Officer or by such other qualified person or method deemed practicable. Close cooperation must be maintained between the district and all activities within it in regard to venereal disease control. It is the desire of the Bureau that the District Venereal Disease Control Officer make frequent visits to all activities within his district in order that he may become cognizant of conditions and problems therein, and thus give greater assistance to local Venereal Disease Control Officers and Interviewers.

ALNAV 154

3 Jul 1947

(Not Restricted)

## Subj: Navy Owned Radium, report on

All naval medical activities using Navy owned radium for therapeutic purposes or having custody or cognizance of Navy owned radium used in civilian institutions report via air mail prior to 15 July to BuMed, Materiel Division, Brooklyn, all quantities by type on hand 1 July and location thereof.

--SecNav. James Forrestal

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