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Sensitization of Penicillin-Resistant Bacteria: Many investigators have made organisms insensitive to penicillin in vitro, but no methods have yet been published for rendering penicillin-insensitive bacteria sensitive, except by repeated culture. In this study, experiments are presented which show that penicillin sensitivity can be restored to some insensitive bacteria by association with other bacteria or their products.

The original idea was that penicillin sensitivity might depend on the presence of a chemical or physical factor. If this were correct, it might be possible, in certain circumstances, for bacteria short of or devoid of this chemical factor to borrow it from other bacteria possessing it, or it might be that growth in association with a sensitive microbe would alter, in some way, the physical structure.

In choosing the bacteria it seemed wise to start with resistant strains of an organism of which most strains are known to be penicillin-sensitive.

On the assumption that during growth of a penicillin-sensitive organism a chemical substance is produced which might be transferred to, or act on, the resistant strain, the general procedure adopted was to grow the resistant and the sensitive organisms together in mixed culture and then isolate the resistant one and test its sensitivity. The control was provided by subculturing the resistant bacterium in a similar manner and growing it on the same medium but without the sensitive strain.

The experiments showed that some strains of penicillin-resistant staphylococci and streptococci can readily be made sensitive by growing in mixed culture with other organisms, either penicillin-sensitive or penicillin-insensitive. The same change can be induced if the bacterial association occurs in the refrigerator, where growth does not take place. Also, some bacterial autolysates can effect this change. The acquired sensitivity lasts a long time. Four strains of staphylococcus with sensitivity induced by mixed culture with C. diphtheriae kept their newly induced sensitivity unaltered through 22 subcultures in broth.

Todd et al. showed that staphylococci which they had rendered resistant by long exposure to nonlethal doses of penicillin gradually lost their resistance on subculture; but many naturally occurring strains of staphylococci are abnormally resistant to penicillin and retain this property in pure culture for a long time. These naturally resistant strains for the most part produce penicillinase, whereas the strains artificially made resistant do not.

In these experiments twenty strains of resistant staphylococci were used - some penicillinase-producers and some not - and there were seven to which a considerable degree of sensitivity could be restored simply by growing them in association with, or exposing them to the influence of, another organism. Four of these seven strains produced penicillinase and so could be classed as naturally resistant.

It has been assumed that naturally resistant strains retain their resistance permanently in the body; but from the studies carried out it seems clear that when some of such strains grow in association with other bacteria - a condition which often happens in the body - they may lose their resistance. This change has been shown to take place within a few minutes after the bacteria are brought into association with each other, and it is reasonable to assume that such a change can happen in the body.

It is true that up to now only seven out of twenty strains tested have undergone this change, but what happens to one strain will probably happen to another if the right conditions can be found.

Though every attempt should be made to use penicillin so as to avoid the formation of resistant strains, the results of these experiments show that in some strains the process is reversible, and the contention that in the near future all strains of staphylococcus will be resistant to penicillin must be reconsidered.

This study is of a preliminary nature, and only the fringe of the subject has been touched; many possibilities have not yet been examined, and others only incompletely. This work is continuing. (Lancet, 10 Jan '48 - A. Voureka)

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The Treatment of Escherichia Coli and Proteus Vulgaris Infections of the Urinary Tract with a New Sulfonamide (NU-445): A study was made of the effects of a new sulfonamide in chronic infections of the urinary tract. This sulfonamide, 3,4 dimethyl-5-sulfanilamido-isoxazole, was supplied under the designation NU-445 (Hoffmann-La Roche Inc.).

This drug has proved to be effective against Escherichia coli and Proteus vulgaris both in vitro and in vivo (animal experiments) and is distinguished by extremely low toxicity. Another outstanding property of NU-445 is its solubility, which is strikingly greater than that of other commonly used sulfonamides in the pH range of from 5.5 to 6.5.

The experimental compound was administered to 50 consecutive patients with urinary tract infections due to E. coli and/or P. vulgaris. The patients were from the Genito-Urinary Surgical Service of the Beth Israel Hospital in New York and from private practice.

The first 24 patients received 1.5 Gm. q.i.d., which amounted to 6 Gm. per 24 hours. With the exception of 4 cases in which medication had to be discontinued because of toxic symptoms (dermatitis in 2 and nausea in 2), NU-445 was given over periods of time ranging from 6 to 60 days, depending on the response of the patient. Since clinical results in this group fell short of expectations, the total daily dosage for the subsequent 26 patients was increased to 8 Gm., given in 4 equally divided doses. In this group, NU-445 was administered for from

5 to 57 days. In the majority of cases, however, the period of treatment was 12 days or less. Generally, treatment was continued until a bacteriological reversal occurred or until clinical ineffectiveness of the drug became apparent.

For all patients routine urine analyses, complete blood counts and determinations of blood levels of NU-445 were carried out semiweekly. Smears of the urinary sediment were examined at frequent intervals, and, urinary sediments were transferred to blood agar and Endo's medium and inoculated in broth with subsequent study of any bacteriological cultures thus obtained.

The appraisal of clinical results was solely on the basis of bacteriological findings. Cures were assumed if urine cultures remained negative for at least 2 weeks following cessation of therapy. Many patients in whom there was no bacteriological cure were greatly improved clinically, but these were not counted as positive results.

It was shown that E. coli infections responded more readily to NU-445 than P. vulgaris infections and that the increase in the dosage to 8 Gm. was attended by an increase in good results with regard to both types of infections. Thus, in the patients infected with E. coli, there were 7, or 46.6 percent, cures on a daily dosage level of 6 Gm. as compared with 11, or 57.9 percent, when the daily intake was raised to 8 Gm. The incidence of cures was even more strikingly increased with the heightening of the dose in the P. vulgaris infections - 2, or 18.2 percent, cures from 6 Gm., as against 8, or 47.1 percent, from 8 Gm. As has been noted previously with the use of other urinary tract disinfectants, the incidence of bacteriological reversals was greater in those cases in which no form of prolonged drainage, involving a foreign body, was used. In the series presented the percentage of failures was 39 in patients in whom no drainage was employed, whereas it was 78 in those in whom a catheter or a tube was used. Thus, best results were obtained in uncomplicated cases of acute and chronic cystitis or pyelonephritis.

Except for the 2 cases each of dermatitis and nausea mentioned, the large doses of NU-445 used were tolerated without any ill effects. There was no instance of leukopenia nor evidence of deposition of crystals within the urinary tract. In fact, no instance of crystalluria was observed. No concomitant alkali medication was given and fluid intake was not forced. (J. Urol., Jan. '48 - L. Narins)

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The Use of Sulfamylon in Rhinosinusitis: Early in 1946 a study was undertaken of the effects of sulfamylon (a sulfonamide) in infections of the nose and accessory sinuses. Later the combination of sulfamylon and neosynephrin hydrochloride was studied in the same types of cases. To date more than 200 patients have been treated with these preparations.

Sulfamylon is 4-aminomethylbenzenesulfonamide hydrochloride, with a molecular weight of 222.67. It is a white crystalline material which is freely

soluble in water. Its aqueous solutions are weakly acidic, a 1-percent solution having a pH of 5.5 and a 20-percent solution having a pH of 5.1.

Chemically this compound differs from sulfanilamide in that a methylene group has been inserted between the benzene ring and the 4-amino group. Because of the presence of this methylene group in its molecule, the antibacterial activity of sulfamylon is not inhibited by p-aminobenzoic acid, and its mode of action probably differs from that of the commonly used sulfonamides. This has been confirmed by several investigators.

When given orally to dogs, sulfamylon is rapidly deaminated and oxidized in the body to p-carboxy benzene sulfonamide, which is excreted in the urine. The process is rapid, so that for from three to four hours the urine is heavily loaded with the material, but 24 hours after a single dose of sulfamylon, the urine is practically free of the excretion product.

Sulfamylon is effective against both the anaerobes and the aerobes. It is especially effective against infections caused by the group of anaerobic bacteria causing gas gangrene. Brewer showed that a 1-percent solution of sulfamylon was more effective in vitro against the Clostridium welchii, Clostridium chauvoei, Clostridium septicum, Clostridium botulinum, Clostridium histolyticum, Clostridium tetani and Clostridium novyi than comparable concentrations of the sodium salts of sulfadiazine and sulfathiazole. In fact, his investigations showed that although sulfamylon was bactericidal to all the organisms tested, sulfadiazine was active only against Cl. welchii and Cl. novyi, and sulfathiazole against Cl. welchii, Cl. novyi, and Cl. tetani. Furthermore, dilution studies revealed that sulfamylon was effective against clostridia in dilutions as great as 1:25,000 though even a 1:100 dilution of sodium sulfathiazole was comparatively ineffective. Lawrence confirmed these results and stated that sulfamylon is bacteriostatic to anaerobic bacteria in dilutions of from 1:32,000 to 1:64,000, and bactericidal in dilutions of from 1:400 to 1:32,000.

When tested against various aerobic organisms, Brewer found sulfamylon effective against Streptococcus hemolyticus, Streptococcus viridans and Diplococcus pneumoniae, types I, II, and III at dilutions of 1:12,800; whereas it inhibited the growth of Staphylococcus aureus and Pseudomonas aeruginosa (Bacillus pyocyaneus) at dilutions of about 1:1600. It was ineffective against Escherichia coli even in concentrations of 1:400.

Lawrence substantiated these findings and proved that sulfamylon was fully as effective against Str. hemolyticus and D. pneumoniae types I, II, and III as sodium sulfathiazole and considerably more active than sodium sulfadiazine. Sulfamylon was definitely bacteriostatic and bactericidal to Str. viridans and showed some inhibitory action on Str. faecalis, whereas the other sulfonamides gave no suggestion whatever of antibacterial action against these organisms.

The toxicity of sulfamylon has been studied by oral, subcutaneous, and intraperitoneal administration of the drug to mice, and oral administration to

rats, rabbits, and dogs. No albuminuria or hematuria was observed and the results of phenolsulfonphthalein kidney tests were negative. Autopsy revealed no significant gross changes, and histologic study of the kidney, liver, stomach and intestines of dogs was essentially negative.

Studies were carried out to determine the local tolerance of mucous membrane to sulfamylon. Solutions of sulfamylon of 0.1, 0.5, 1.0, and 2.0 percent were tested for possible irritation to the conjunctival mucosa of rabbits, and no evidence of irritation could be found even after repeated applications of the above concentrations. In addition, daily urinary bladder irrigations were performed on rabbits with solutions of sulfamylon ranging in concentrations of from 1 percent to 20 percent. Approximately four hours after the fifth irrigation, the animals were sacrificed, and the bladder mucosa inspected and found entirely normal in every case.

Later, Beyer reported his experience with a mixture of sulfamylon and sulfanilamide (in the proportion of from 1 to 9) as a prophylactic in 60 patients with fresh wounds and as a direct antiseptic in 140 patients with infected wounds. Healing was uneventful in every case. Other reports in the literature have attested to the clinical value of sulfamylon against specific anaerobes in wounds.

Recently, Howes investigated the relative effectiveness and tissue toxicity of streptomycin, sulfamylon, calcium penicillin, parachlorophenol, tyrothrycin, and zephiran in tissue cultures and wounds. He concluded that:

"For local chemotherapy, sulfamylon, 5 percent, seems to be superior to the six other antibacterial substances tested. It possesses the widest range of antibacterial activity and is relatively nontoxic. It is active in the presence of pus and blood and is not affected by changes in the acidity of the environment. It possesses rapid bactericidal activity.... Streptomycin is next best.... Penicillin is placed third.... Tyrothrycin, parachlorophenol, and zephiran have a toxicity which permits their use only on granulating wounds."

It has not been possible to study the systemic effects of sulfamylon on infections in human beings because there is as yet no known chemical method of determining the blood concentration of the drug. All studies have therefore been limited to its use locally in wounds, and now in this study it has been used in the nose and accessory nasal sinuses.

Clinical Investigations. Early in 1946 a clinical investigation of the effects of the local use of sulfamylon in rhinosinusitis was undertaken. Prior to this time solutions of the sodium salts of sulfathiazole and sulfadiazine had been used, as well as a solution of sulfadiazine in ethanolamines, and combined solutions of sodium sulfathiazole with desoxyephedrine. Also, solutions of penicillin had been employed in various concentrations.

The first patients treated with sulfamylon were those with suppurative sinusitis, in which antral irrigation via the natural orifice was followed by

instillation of 1-percent solution of sulfamylon into the affected antrum. The results were excellent, surpassing the results being obtained through use of the other solutions mentioned above.

Later some patients with subacute and chronic suppurative rhinosinusitis were treated locally by repeated atomizer applications of a 1-percent solution of sulfamylon, and the results were also quite encouraging. However, it was often necessary to prescribe a vasoconstrictor for simultaneous use in these cases because sulfamylon has no vasoconstrictor properties.

A combination of 1-percent sulfamylon with 1/4-percent neosynephrin hydrochloride was then made available and was found more useful than the solution containing 1-percent sulfamylon alone. Still later a 4-percent solution of sulfamylon was tried but was not found to be more effective than the 1-percent solution.

In all, sulfamylon was employed in more than 200 cases of rhinosinusitis in 137 patients. In no case of simple coryza ("common cold") was the drug prescribed. Clinical evidence of nasal or sinus suppuration was a prerequisite for use of the drug. Cultures were taken in approximately one half of the cases and revealed the presence of the following organisms: Streptococcus viridans, Staphylococcus aureus (nonhemolytic and hemolytic), Staphylococcus albus (nonhemolytic and hemolytic), Aerobacter aerogenes, Proteus vulgaris, Pseudomonas aeruginosa (Bacillus pyocyaneus), and Diplococcus pneumoniae (types undetermined).

In early acute rhinosinusitis and in cases without antral involvement, the combined solution of 1-percent sulfamylon and 1/4-percent neosynephrin was prescribed for home use by atomizer spray at intervals of from 2 to 4 hours, according to the severity of the case. In children, drops were prescribed according to age.

In cases of antral empyema, irrigation was carried out via the natural orifice (whenever possible) with physiologic sodium chloride solution to cleanse the antrum completely of all visible pus or mucopus. The saline solution was then evacuated by instillation of air, and 1-percent or 4-percent sulfamylon solution was instilled so as to fill the antrum as completely as possible. The cannula was then removed and the patient warned not to blow the nose for several hours. The combined solution of sulfamylon and neosynephrin was then prescribed for home use as a spray at intervals of from two to four hours for 48 hours, when the antrum was again irrigated and sulfamylon solution instilled.

In every case there was marked improvement noted at the time of the second irrigation, and rarely was any pus found on the third irrigation 48 hours later. (In all cases irrigations were done every 48 hours until the antral washings returned clear, and then, in most cases, one more antral irrigation was carried out 48 hours later as a safeguard against recurrence.) There were

three cases of Pseudomonas aeruginosa infection of the nose, and one of the middle ear (in a patient not reported in this series). Sulfamylon definitely reduced the formation of "green pus" but did not promptly eradicate the infection, although the infection in every one of the cases eventually cleared up with persistent treatment with the drug.

In this series there were 53 patients with empyema of the antrum, with or without other sinus involvement when first seen. Of this number, 11 had been treated unsuccessfully by irrigation and instillation of a penicillin solution on at least three occasions at 48-hour intervals. In addition, these patients were taking sulfathiazole orally. In all of these cases there was a prompt response to irrigation with and instillation of 1-percent sulfamylon solution, and in no case were more than three irrigations necessary to clear up the infection. In 13 cases the infection was so severe that sulfathiazole or sulfadiazine was prescribed for oral use simultaneously with the antral irrigations, local chemotherapy with sulfamylon, and vasoconstriction. In no acute case in this series was any surgery of the sinus required, and every patient made an uneventful and prompt recovery.

It is felt that the above statement should be further explained in the light of the author's opinions regarding the treatment of these cases. It is felt that irrigations through the natural orifice should always be done in preference to antral punctures, especially in early cases. At the same time, it is believed that repeated antral irrigations through the natural orifice are not to be recommended, for trauma to the orifice may lead to some degree of stenosis. Therefore, it has been the author's rule to limit antral irrigations through the natural orifices to three or four. If more irrigations are necessary, a large antrum window should be made in the naso-antral wall of the lower meatus of the nose. Radical sinusotomy should never be done in acute cases of sinusitis unless complications arise, or until every effort made to clear up the infection by conservative measures over a period of at least several months proves ineffective. It is noteworthy, then, that since beginning the use of sulfamylon, as described, not a single antrostomy has been performed in any case of acute sinusitis.

In more than 20 cases of chronic suppurative rhinosinusitis of long standing, there was a decided improvement following the prescription of sulfamylon solution as a nasal spray, with or without neosynephrin (as seemed indicated). However, several patients had a prompt recurrence of the infection on stopping the sulfamylon spray, even after four or more weeks of continuous treatment. The majority of these had either refused radical surgery of the sinuses and were being treated conservatively at their own request, or had secondary atrophic rhinitis in which the value of radical surgery was questioned.

No case of drug sensitivity was encountered, even though a number of patients used the drug on several occasions when they suffered repeated attacks of acute sinusitis. The continued use of sulfamylon over a period of ten days or more led to slight secondary injection of the nasal mucosa, but in no case

did allergic or vasomotor rhinitis develop, as is so often seen with the preparations of sodium sulfadiazine with or without desoxyephedrin. Discontinuance of the preparation resulted in prompt recovery of the mucous membrane, so that in 48 hours it appeared normal again. (Ann. Otol., Rhin., and Laryng., Dec. '47 - S. L. Fox)

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Local Use of Sulfamylon (Para-[Aminoethyl]-Benzene Sulfonamide Hydrochloride) in Cases Involving Surgery of the Eye: In the summer of 1946 the author and colleagues experienced considerable trouble with infections due to Pseudomonas aeruginosa (B. pyocyaneus) as secondary contaminants. Although many preparations and various procedures were tried to control the contamination, none proved particularly successful. In one case, Ps. aeruginosa invaded the inside of the eye after an operation for cataract, and the eye was lost.

On 1 October 1946, the author and colleagues began using sulfamylon, which was available in both 1- and 4-percent solutions, buffered with citrate to a pH of 6.5, to irrigate the conjunctival sac and to saturate eye pads used for dressings.

Sulfamylon is a sulfonamide compound with a wide range of antibacterial activity, but, unlike most of these drugs, it is not inhibited by para-aminobenzoic acid. It has, therefore, proved effective in the presence of pus and blood. For example, Beyer treated a series of 60 patients with fresh wounds using the substance (known in Germany as "marfanil") as a prophylactic against infection, and 140 patients with infected wounds using it as an antiseptic. The results were almost uniformly successful, and Beyer concluded that the drug was a valuable aid in the treatment of wounds. More recently, Howes and his associates reported on a comparative study of sulfamylon, calcium penicillin, parachlorophenol, tyrothricin, and zephiran chloride with regard to efficacy, speed of action, and toxicity. For local chemotherapy they found that sulfamylon was superior to the others, that it possessed the widest range of antibacterial activity, and that it was relatively nontoxic.

Since the authors have started using the drug, they have used it in 84 successive surgical cases, and in no instance have they had a case of contamination with Ps. aeruginosa. Moreover, there have been none of the reactions to the drug which had been experienced with other sulfonamide preparations, such as sulfathiazole.

A few of the patients, it is true, had been exposed to the drug for only 3 or 4 dressings, but most of them were patients with cataract who had had dressings changed daily for 7 or 8 days. There were 5 cases of retinal detachment in which dressings were changed every other day. Each new dressing was applied moistened with 1-percent sulfamylon. This treatment was continued for a month after operation. In no instance was there any pain, redness, or irritation

from irrigating the conjunctival sac with 1-percent sulfamylon. The 4-percent solution has not been used for a sufficiently long period to determine whether it also is nonirritating. It appears at present that the 1-percent solution is sufficient to control contaminations with Ps. aeruginosa. (Arch. Ophth., Nov. '47 - W. B. Clark)

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Sulfamerazine Treatment of Pneumonia in Adults: Pneumonia lost many of its terrors with the discovery and development of the sulfonamides, and the results of treatment of this disease are progressively improving. There is, however, a tendency to regard the sulfonamide drugs as superseded by penicillin not only in the severely ill but even in mild conditions in which the former have proved adequate. Needles are never pleasant to the patient or convenient to the attendant. The authors consider that sulfonamide treatment for primary pneumonia in adults is satisfactory in the vast majority of cases, and should be given before the clinical diagnosis is confirmed by bacteriological and radiological studies. Further, they believe that all but the most severe cases in aged or debilitated patients are reduced by this treatment to a two-day fever which can be adequately treated at home. Hospital care, with facilities for fuller investigation and treatment, is needed only for patients who fail to respond rapidly to sulfonamides or who are critically ill or whose condition is otherwise complicated.

Pneumonia commonly occurs without the classical physical signs. The authors maintain that, in the absence of an influenza epidemic, patients complaining of respiratory symptoms are suffering from some measure of lung consolidation if they have a temperature higher than 100° F. (37.8° C.) for more than one day. They have encountered many such patients in whom roentgenograms have shown segmental or central consolidation, and consider that all these should be given the benefit of a full course of a suitable sulfonamide without delay.

It is very desirable to obtain at the outset, and before treatment is started, a specimen of sputum for complete bacteriological investigation. This will give a reliable indication of the causal organism in 70 per cent of cases. Radiological confirmation that resolution is complete, particularly in every patient over 40, is essential. Patients with carcinoma of the bronchus not infrequently exhibit pneumonia, but complete clearing rarely occurs.

The authors do not attempt to prove that any sulfonamide is more successful than penicillin in the treatment of pneumonia although they have reached this conclusion from a small series of cases that are not statistically significant). Sulfonamide therapy is certainly less troublesome, and with the newer preparations there is no need for frequent dosage, with consequent loss of sleep. Toxic effects are minimal. In the Central Middlesex County Hospital, England, patients may be admitted to any medical ward under the care of any of the physicians, so that treatment is that considered best by the physician concerned and

is in no way standardized. By common consent, however, the treatment now used almost invariably is that with sulfamerazine.

Sulfamerazine, a methyl homologue of sulfadiazine, is absorbed more rapidly and excreted more slowly than sulfadiazine. At equal blood levels it is no more toxic than sulfadiazine and is far less so than many of the older preparations. As a result, a single dose of sulfamerazine will produce more quickly a higher blood level of the drug than the same dose of sulfadiazine, and this blood level will be longer maintained. Because it is more soluble than sulfadiazine it presents less risk of urinary obstruction with crystals. The rapid absorption renders parenteral administration almost unnecessary, since an oral dose will produce therapeutic blood levels in two hours, but within four hours the blood levels remain the same as those obtained by equal dosage intravenously. Thus, in comparison with older sulfonamides, smaller doses of sulfamerazine less frequently given will produce and maintain an adequate blood level (from 12 to 15 mg. per 100 ml. of blood). The course that the authors have found satisfactory consists of an initial "loading" dose of 3 Gm., followed in 8 hours by 2 Gm. and then 1 Gm. 8-hourly. The doses can be arranged so that patient and attendant can have an uninterrupted night. With this regimen, a blood level of 15 mg. is reached within four hours. It was found that this level is well maintained throughout treatment. Adequate urinary output must be maintained by giving 6 pints (3.4 litres) of fluid daily, but alkali is not required, since it decreases tubular reabsorption of the drug and therefore increases its loss by excretion.

In the authors' experience the above dosage is always well tolerated, and rapid subjective improvement occurs. The temperature falls to normal in from 24 to 36 hours in most cases and never rises more than 1° F. above normal afterwards. Treatment is continued, according to the severity of the case, for from 48 to 72 hours after the temperature has reached normal, so that in a moderately severe case about five days' treatment (18 Gm. in all) will be needed. No evidence was found that such a dosage produced a reduction in granulocytes in the blood. This agrees with the findings of others who have used somewhat larger doses.

For this investigation the last 189 proved cases of pneumonia at the hospital were studied - that is, those occurring since sulfamerazine became easily available. Criteria of diagnosis were clinical signs, supported by radiological evidence of well-defined consolidation, together with (in most cases) the presence of leucocytosis and the isolation of a causal micro-organism. Cases in which the pneumonia occurred as a terminal event in another mortal illness were excluded. In the series there were 101 males and 88 females. The average age for males was 43.0 years and for females 40.5 years, the extremes of age being 13 and 76 years. Of these 189, 113 were treated with sulfamerazine from the start without a single death; 36 were treated with sulfamezathine (sulfadimethylpyrimidine), with three deaths; and 22 with penicillin, with one death. Combined treatment was given to 12 patients, one of whom died. The remaining cases were so mild that no specific therapy was deemed necessary.

One patient showed on the third day a transient rubelliform rash which faded in spite of further administration of sulfamerazine. In this case, unlike those described by Hall and Spink, there was no relapse of temperature with the eruption.

Two women became confused during treatment. One had had only 7 Gm. and her treatment was changed to penicillin. The other developed a psychotic state only after an adequate course of treatment had been given; the confusion cleared in four days and the pneumonia resolved rapidly. Two cases of drug psychosis have been reported by Flippin, Gefter, Domm, and Clark in 1943, but in both these, because small doses of sulfonamide had been given, the condition may have been due to pneumonia rather than its treatment.

Drug fever occurs with all sulfonamides. Gefter et al. reported it in severe cases, in most of which over 40 Gm. of sulfamerazine had been given. Two cases occurred in this series, the pneumonia responding according to expectation, but fever persisting unexplained until a critical fall after stopping the sulfonamide.

The authors have encountered no serious toxic manifestations in the use of this sulfonamide, and believe them to be excessively rare provided that administration is not too prolonged.

The authors emphasize the need for the radiological demonstration of complete resolution of the pneumonic process and adequate convalescence. (Brit. M. J., 13 Dec. '47 - H. Joules and S. D. V. Weller)

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Studies in Enterococcal Food Poisoning: Although the disease-producing potentialities of the enterococci have long been recognized, evidence for the etiological relationship of these intestinal streptococci to outbreaks of food poisoning has been relatively limited. However, Linden, Turner, and Thom in 1926 reported the isolation of nonhemolytic streptococci from two food poisoning outbreaks caused by cheese. The organism in each case produced experimental diarrhea in cats. One of these strains was identified by Sherman, Smiley, and Niven in 1943 as Streptococcus faecalis. In 1934 Jordan and Burrows recorded the isolation of an alpha streptococcus from a cocoanut cream pie filling which caused food poisoning. The organism, which produced filtrates toxic to monkeys, was identified as Streptococcus faecalis on the basis of carbohydrate fermentations. The authors found that culture filtrates prepared from "greening streptococci" isolated from other sources were not toxic for monkeys. The question of the toxicity of streptococcus culture filtrates is a matter of dispute and has been reviewed by Dolman. Dewberry in 1943 refers to a food poisoning outbreak caused by canned tomatoes in which a heat-resistant streptococcus of "the faecalis type" was present in great abundance and almost in pure culture. In a retrospective study, Sherman et al. found that a total of six strains of nonhemolytic streptococci isolated by others

from an equal number of outbreaks were all Streptococcus faecalis. The present authors have identified as Streptococcus faecalis an alpha streptococcus isolated by Dack in 1939 from turkey dressing. It was also observed by Sherman and his collaborators that almost any laboratory strain of Streptococcus faecalis or of other enterococci could produce diarrhea when fed in pure culture to cats whereas other varieties of nonhemolytic streptococci did not do so.

In the present study, it was found that enterococci (mostly Streptococcus faecalis) were the predominant organisms isolated from the suspected foods in each of four outbreaks of food poisoning. The offending foods were canned evaporated milk, charlotte russe, roast beef, and ham bologna.

The general impression resulting from a study of the literature and the outbreaks reported upon in this paper is that food poisoning may be more commonly caused by enteric streptococci than has been hitherto believed. It is thus somewhat surprising that enterococci have not been more frequently implicated in outbreaks of bacterial food poisoning since they can be readily isolated from raw and pasteurized milk as well as from green Swiss cheese. They are also found on human hands and are the most abundant streptococci of human feces, and in addition, grow at refrigerator temperatures. There are, however, several possible explanations for this fact:

1. There might be the inclination to regard Streptococcus faecalis as a saprophytic organism, the presence of which in suspected foods is considered of little significance.

2. There is an apparent tendency, indicated in reports submitted to the United States Public Health Service, to implicate the staphylococcus as the only possible remaining cause in those outbreaks in which known enteric pathogens are not isolated.

3. In those instances in which bacteriological study of a food poisoning outbreak is limited to a search for the well known enteric pathogens and the staphylococci, absence of these etiological agents often automatically leads to a designation of the outbreak as one of unknown etiology.

4. The failure to use a fairly rigid quantitative technic in the isolation of bacteria from suspected foods may result in misinterpretation of the significance of those organisms which are actually recovered. (Pub. Health Reps., 23 Jan '48 - L. Buchbinder et al.)

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Dog, Fox, and Cattle Rabies in New York State: An epizoötic of rabies has been in progress in New York State since 1943. The unusual features of this prevalence have been the introduction and widespread occurrence of fox and cattle rabies, coupled with a striking drop in the incidence of the disease

in dogs. There is reason to believe that the decline was largely due to the extensive dog vaccination program carried out, and the circumstances offer an excellent opportunity for evaluating the effectiveness of this control measure.

During 1946 rabies was reported in 377 dogs, 308 foxes, and 440 cows, while during the first nine months of 1947 the disease was reported in only 40 dogs but in 218 foxes and 173 cows.

The authors present evidence indicating the value of prophylactic vaccination against rabies in dogs. In 10 counties where 78 per cent of the enumerated dogs were vaccinated, the rabies attack rate in nonvaccinated dogs, following completion of the program, was 15.8 times the rate in vaccinated dogs observed during the same period of time in the same area.

Based on experience gained in sponsoring 24 county control programs, the following general recommendations for the control of rabies in dogs have been presented:

a. It is felt that mass dog vaccination is a valuable adjunct to dog control (adequate confinement of dogs suspected of having rabies and dogs known to have been bitten by rabid animals). However, it is essential that both technics be used.

b. It is suggested that these measures preferably be applied over an area which is at least county-wide. Annual re-vaccination of the dogs in a given county is probably necessary only if rabies continues to exist within the limits of this or adjacent counties.

c. Such control measures should be initiated in advance of the introduction of the disease, when cases are occurring in adjacent counties.

d. The importance of an educational program to implement application of control measures should be emphasized.

e. A well qualified person employed on the state level to promote and supervise the control program is essential.

f. State financial aid to counties for the conducting of dog vaccination clinics has been of great help in New York State.

g. The placing of local authority in the hands of a county advisory committee on rabies, made up of representatives of all groups concerned with the problem, is deemed wise.

h. Emphasis should be placed on the benefits to be derived by the individual dog and his owner from the program, rather than on the legal necessity of complying with the regulations or laws that may apply.

In the experience of New York State, rabies in cattle seems clearly to have been due to the bites of rabid foxes. Fox rabies, and as a corollary, cattle rabies, has spread in a slow radial fashion over a 2-year period.

Control of the fox problem has been attempted by the creation, through trapping, of a zone of fox scarcity surrounding the infected area. Adequate evaluation of this procedure is not as yet possible. (Am. J. Pub. Health, Jan. '48 - R. F. Korns and A. Zeissig)

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Recommended Methods for Rabies Control: A Conference on Rabies held at the University of Pennsylvania, Philadelphia, on 9 April 1947, called by Dr. R. A. Kelser, Chairman of the Special Committee on Rabies of the American Veterinary Medical Association, and attended by representatives of the American Medical Association, the U. S. Public Health Service, the Bureau of Animal Industry of the U. S. Department of Agriculture, U. S. Livestock Sanitary Association, American Animal Hospital Association, American Veterinary Medical Association, and the American Public Health Association, resulted in the series of principles and recommendations presented below. The American Public Health Association's representative, Haven Emerson, M.D., reported them to the Committee on Research and Standards at its meeting on 6 October 1947, and it was voted to publish them in the Journal as recommended methods for a program for the control of rabies in the United States.

The Conference unanimously agreed on the following principles and considerations in connection with such rabies control program as might be undertaken on a national basis:

a. Rabies in the United States is of sufficient importance to make it desirable that the federal government participate in means for its control through cooperation with the several states, contributing funds and personnel.

b. Rabies in man is generally a disease reportable to local and state health authority. Rabies in lower animals should be specifically a disease reportable to public health or other responsible state health authority. It should be reported by states, with place of occurrence specified. Through a central federal agency, the consolidated information should be assembled, analyzed, and distributed to all states, agencies, and individuals having responsibility in a rabies control program.

c. In a program for the control of rabies in the United States prime consideration must be given to: (1) adequate diagnostic facilities, (2) the control of animals capable of transmitting the disease, and (3) mass immunization of susceptible animals, particularly dogs.

Diagnostic Facilities -- To be considered adequate, facilities for the diagnosis of rabies should include not only provision for the microscopic examination

of brain specimens from suspected animals but also means for the inoculation of laboratory test animals. The number and location of laboratories performing services connected with the diagnosis of rabies should be adequate to provide prompt service within reasonable distances. Further, facilities should be provided for maintenance of suspected cases of rabies in lower animals under proper veterinary observation.

Control of Animals (dogs, cats, and wild life) Capable of Transmitting Rabies -- Control measures should include the following:

a. Licensing of all dogs.

b. Proper disposition of ownerless, unwanted, and stray domestic animal pets.

c. As soon as rabies appears in a community, strict control of all dogs should be enforced for whatever period of time may be considered necessary. Dogs should not be permitted to run at large but should be properly confined on their owner's premises and only be permitted away from same when under proper restraint by a responsible individual.

d. Dogs which have bitten persons or other animals, and dogs which are suspected of having rabies, should be confined in a suitable, authorized place under veterinary supervision for a period of not less than 14 days.

e. Dogs known to have been exposed to rabies should be destroyed or kept confined for a period of not less than 6 months.

f. Dogs under 6 months of age, being particularly susceptible and less satisfactorily immunized than older animals, should be confined until the area is certified as officially free of rabies.

g. Adequate provision and facilities for enforcing all regulations and requirements connected with the control program should be made available.

h. The control program should be continued for a period of at least 90 days subsequent to the last reported case of the disease in animals.

i. Should rabies be found to exist in wild life, prompt arrangement should be made for active cooperation with the U. S. Fish and Wild Life Service and the analogous agency of the state involved. In this connection, when rabies has become established in wild species a program for reducing the number of individuals of affected species should be instituted and continued until the disease disappears. Routine brain examinations should be made to determine the incidence of the disease in the wild species and when it has abated.

Mass Immunization -- The vaccination of dogs, combined with other control measures as indicated herein, provides the most satisfactory method for

the prompt control of rabies. Vaccinated dogs, when properly tagged, may be allowed at large 30 days after vaccination. Vaccination should consist of at least one injection of an immunizing dose of an accepted canine rabies vaccine. Evidence indicates that a single 5 ml. subcutaneous injection of an approved vaccine is effective in a mass vaccination program. However, the injection of 3 doses of vaccine in 5 ml. amounts, a week apart, provides greater immunization and should be advised when practical. For permanently reducing the number of susceptible dogs, it should be suggested that dog owners have their dogs immunized annually.

In any rabies control program it is deemed essential that a local (county or municipal) Rabies Advisory Committee be organized to facilitate operational functions and cooperative effort. Further, the Conference agrees that an educational program should be launched by appropriate authorization, representing federal, state, and local agencies, to explain the necessity of control measures, including the efficacy of the rabies vaccines now approved by the U. S. Bureau of Animal Industry and the National Institute of Health. The object of such an educational campaign is to acquaint the public and owners of dogs and other pet animals with pertinent facts concerning rabies and the reasons for and importance of the measures taken for the control and eradication of the malady and the value of specific immunization against rabies. The advisability and desirability of utilizing vaccination not only for the control of the disease during an outbreak, but also in building up and maintaining a relatively highly immune dog population through the annual vaccination of dogs with rabies vaccine should be pointed out.

In view of the essential existing responsibility of the Bureau of Animal Industry of the U. S. Department of Agriculture, the U. S. Public Health Service, and the U. S. Fish and Wild Life Service, this Conference recommends that the function of coordinating a campaign for the control of rabies on a national scale be vested jointly in these three agencies. A plan for accomplishing this on a cooperative basis can undoubtedly be worked out through consultation of representatives of the agencies involved.

The principles and recommendations on which this Conference has agreed should be considered in a rabies control program on a national scale. In general, they are in accord with the procedures recommended by the Subcommittee on Rabies, Committee on Animal Health, National Research Council and the report (now in press) of the Rabies Committee of the New York Academy of Medicine. There are other reports on rabies and its control by various other agencies, and omission of reference to them does not mean that the conclusion of this Conference is or is not in general agreement with them. The Report of the Subcommittee on Rabies of the National Research Council and that of the Rabies Committee of the New York Academy of Medicine happened to be readily available during discussions of the Conference. (Am. J. Pub. Health, Jan. '48)

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Isolation from Wild Bird Mites (Liponyssus Sylviarum) of a Virus or Mixture of Viruses from which St. Louis Encephalitis and Western Equine Encephalomyelitis Viruses have been Obtained: In a previous communication by Reeves, Hammon, Furman, McClure, and Brookman, it was reported that in addition to three strains of western equine encephalomyelitis virus isolated from mites, Liponyssus sylviarum (Canestrini and Fanzago), found in the nest of a yellow-headed blackbird, another virus was isolated which had not yet been identified. Several months of laboratory work, including serial passages through several species of animals and extensive immunological tests, have led to the results summarized in this preliminary paper. The completed studies will be reported elsewhere in detail.

This agent, following isolation in mice and after several serial passages through mice, killed mice, guinea pigs, and chick embryos, but failed to kill guinea pigs which previously had been vaccinated with western equine encephalomyelitis virus. It was not neutralized by hyperimmune western equine serum or by St. Louis or Japanese B encephalitis serum alone, yet a mixture of the three was effective in neutralizing the virus. A complement-fixing antigen prepared from the brains of mice infected with this virus reacted with specific antiserums against western equine, St. Louis, and Japanese B viruses; and antigens prepared from each of these three viruses in turn reacted with the serums from animals immunized against the mite virus. In cross-vaccination tests, however, there was no immunity in either direction in so far as Japanese B virus was concerned.

After 8 serial passages through mice the virus had only the immunological characteristics of St. Louis virus, and it would not kill guinea pigs. After 10 passages through chick embryos it had only the characteristics of a western equine virus.

Two possibilities presented themselves: (1) that this was a simple mixture of two viruses or (2) that it was a stem virus, maintained by mite-to-bird passage, which could develop as either virus after passage in more selective hosts. The first possibility appeared more likely; but the second was challenging and not incredible, since these two viruses have been found so frequently in close association and appear to have the same vectors and vertebrate hosts. There is some further support for the latter possibility in the following results of two experiments. (1) Laboratory mixtures of known strains of these two encephalitis viruses, although not interfering completely in mice, are maintained with great difficulty through two passages. The western equine virus is greatly inhibited, and attempts to recover it beyond the third passage have all failed. (2) Guinea pigs are killed promptly with signs typical of the western encephalitis by a suspension of the brains of mice which die after an inoculation with 100 LD_{50} (third passage through mice) of the mite virus mixed and incubated with an equal volume of undiluted hyperimmune western equine serum. The same suspension of mouse brain which killed normal guinea pigs failed to kill pigs immune to western equine virus. Thus, a high dilution of the mite agent

after 3 passages through mice, mixed with a great theoretical excess of western equine immune serum, still maintained through passage a large amount of the equine-like component.

Until more convincing evidence can be presented that this agent represents a "new" virus, however, it appears to be more appropriate merely to report that a virus, or mixture of viruses, has been isolated from wild bird mites which, after serial passage in the brains of mice, may be identified as a strain of St. Louis encephalitis virus, and that a factor identifiable as the virus of western equine encephalomyelitis is obtained after the agent is passed serially through chick embryos. (Science, 23 Jan '48 - W. McD. Hammon et al.)

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Re Roentgenologic Pulmonary Manifestations of Fatal Histoplasmosis: In recent years, various investigators have suggested that the pathogenic fungus, Histoplasma capsulatum, is the cause of certain instances of calcification occurring within the lungs and mediastinal lymph nodes. Although final proof of this hypothesis is not yet available, the basic significance of the observation as it now stands should not be minimized. Anyone who has attempted to rationalize repeated negative tuberculin reactions in patients with unmistakable roentgenological signs of hilar and parenchymal calcium deposits can best appreciate the implications of this noteworthy contribution.

As additional information is awaited regarding the true role played by Histoplasma capsulatum in the production of clinically unimportant intrathoracic calcium deposits, it is perhaps well to recall that histoplasmosis can be a serious and frequently fatal disease involving the lungs, any or all of the abdominal viscera, the skin, the mucous membranes, the lymph nodes, the bone marrow, and occasionally other portions of the body. Furthermore, the disease appears to be increasing in frequency - at least in certain areas.

Histoplasmosis is notoriously difficult to diagnose by clinical methods, and therefore it is logical to search for some reliable roentgenologic clue which might serve to identify the process more accurately. As pulmonary involvement is such a common manifestation of the disease, the attention is naturally directed toward the roentgenogram of the chest.

Nine patients with histoplasmosis which eventually proved fatal were seen at the University of Michigan Hospital between 1938 and 1946, and 5 of them had definite pulmonary involvement proved by autopsy. Four of these patients have been reported upon elsewhere.

In a supplementary analysis of the roentgenologic pulmonary findings in the five patients with fatal histoplasmosis involving the lungs, it was indicated that the pulmonary changes in histoplasmosis are fully as varied as the clinical

manifestations of the disease. Thus, histoplasmosis belongs to that relatively large group of diseases affecting the lungs in which the roentgenologist must be content to identify the presence of abnormality, to determine its extent, to describe certain features regarding its appearance, and to offer various suggestions regarding its etiology without arriving at a definite diagnosis. The possibility of Histoplasma capsulatum as the etiologic agent of chronic pneumonitis should be particularly mentioned when widespread, coarse, granular, parenchymal lesions are encountered.

Final diagnosis of histoplasmosis depends upon various laboratory procedures all of which are directed toward identification of the causative organism - a yeast-like fungus characteristically found in the cells of the reticuloendothelial system. (Am. J. Roentgenol., Dec. '47 - J. F. Holt)

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Caries Prophylaxis by Obstruction of the Invasion Roads: The author considers it to be established that dental caries is produced by invasion of the teeth by micro-organisms along nonobstructed organic invasion roads, and that whether or not the invasion roads are blocked by calcium deposition from the saliva depends apparently on some unknown quality of the saliva. He states that H. Eggers Lura from Denmark found more than ten different enzymes in the saliva. It appears from the qualities of most of them that their actions are concerned with the biologic cleansing of the mouth. It is probable that those cases of bad breath which have their source in the mouth may be traced back to a poor enzymatic quality of the saliva.

Lura found phosphatase enzymes which govern the process of calcification. These enzymes may be the decisive components of the saliva which determine whether or not the organic invasion roads through the enamel will be open or obstructed. It seems that by the naturally occurring biologic processes such organic invasion roads can be obstructed only by calcium deposition. People who are naturally caries immune are fortunate enough, apparently, to possess saliva of such quality that it has deposited calcium in these invasion roads. This deposition seems to be governed not only by the amount of calcium present in the saliva but also by the enzymatic action of a phosphatase.

The principle of obstruction of the organic invasion roads by calcium deposition from the saliva governed by enzymatic action is apparently similar to that noted in the action of fluorine. Fluorine attracts calcium to a degree far stronger than iron attracts oxygen in the rust-producing reaction. Whenever organic invasion roads are fluorinized by coming in contact with water-soluble sodium fluoride, calcium from the surrounding fluids is attracted and the invasion roads are obstructed to some degree by the formation of water-insoluble calcium fluoride. The production of reliable obstruction by topical application of sodium fluoride is rather difficult. In work on caries prophylaxis, one author carried on experiments with topical application for two years and succeeded in reducing the incidence of caries by only about 30 percent.

The author considers that quick information concerning the ability of a chemical to obstruct the invasion roads is obtained by testing its ability to desensitize sensitive dentine. Sensitivity of dentine and caries susceptibility are based on the same principle. In sensitive dentine the dentinal tubules must be obstructed; in caries prophylaxis the lamellae and the prism sheaths of the enamel must be obliterated. Sensitive dentine may be desensitized by a single impregnation with 10-percent silver nitrate solution precipitated with a saturated calcium, 40-percent zinc chloride solution, which procedure the author and co-workers also use in caries prophylaxis. The 2-percent fluoride solution recommended for topical application in caries prophylaxis has no influence whatsoever on sensitive dentine.

When the dentinal tubules are obstructed by calcium deposition, and, as a result, opaque, nonsensitive dentine is produced, caries resistance is established. Arrested dentinal caries, showing a hard, dark surface, is considered to be based on this principle. The primary consideration in such a condition is not the fact that the surface is polished but that the dentinal tubules are obstructed. Some cavities extend to the pulp in a short time, although others may remain open cavities for decades and not expand. Their walls have become opaque through a process of obstruction of the dentinal tubules with calcium salts. The caries process has been walled off by a barrier of hypercalcification; this can be shown by grenz-ray examination.

If it becomes established that the presence of a certain phosphatase in the saliva determines the ability of the saliva to obstruct the invasion roads by calcium deposition, it will be possible through suitable tests to find out whether or not this enzyme is present in a saliva and thereby indicate the presence, or absence, at that time, of caries-immune conditions. The work of Lura suggests that such a time is not far away.

A number of misunderstandings which have caused considerable confusion should be clarified. Every dentist knows the slogan, A Clean Tooth Never Decays. Parents and dentists often blame children with caries susceptibility for not keeping their teeth as clean as do children with caries immunity. It is argued that the soft deposits on the teeth favor the development of caries. That attitude does not appear to be justified. If the teeth of a caries-susceptible child are impregnated and the child's tooth-brushing habits are not changed, the teeth stay far cleaner. The obstruction of the invasion roads obliterates the footholds for any deposit, and the enamel washed by the saliva appears clean and shiny. Soft deposits do not produce caries; but caries susceptibility, caused by open invasion roads, facilitates the formation of soft deposits.

The significance of the tenacious plaque has been misinterpreted. It was correctly observed that caries-susceptible children may have tenacious plaques. These plaques often stick to the tooth surface so strongly that it becomes necessary to use a scaler in order to remove them, and then they may form again very quickly in the same place. After a few months, a cavity is found in such

a place. It has been explained that plaques caused the formation of caries. The fact is that it is the other way around. Invadable lamellae furnished the foothold for the formation of a plaque, which is fixed to the tooth surface by this foothold. Numerous histologic observations prove the correctness of this statement. If the plaque is removed and the surface is polished, the micro-organisms in the entrance of the lamellae continue to remain intact. By proliferation, they form the plaque again at the same place. On the other hand, by impregnating this place thoroughly and obstructing the lamellae, the formation of a new plaque and the development of caries can be prevented. Thus, it is seen that in the case of the tenacious plaque, the susceptibility to caries, that is, the open entrance to lamellae, is primary, and the formation of the tenacious plaque secondary. In teeth where all entrances to the lamellae are obstructed, no tenacious plaque can develop.

In the same category belongs the sensitivity of some enamel spots to sweets. There is no possibility for enamel to become sensitive. Such sensitivity apparently results from lamellae which are open all the way to the dentine and which rapidly conduct a sugar solution along their path. The change of osmotic tension at the dentinoenamel junction produces sensation. If left alone, a cavity will soon develop in such a place. By impregnation such sensitivity can be removed and caries formation prevented through obstruction of the lamellae.

The development of green stain has the same background. In this condition, green-stain-producing micro-organisms apparently develop in the open entrances of the prism sheaths, mainly. If the green stain is polished away, it often comes back soon because the micro-organisms are not removed from inside the prism sheaths. But if, after removing the stain, the enamel is impregnated, the stain does not reappear. The living place for the micro-organisms has been obliterated.

In order to facilitate the penetration when desensitizing dentine, the tooth is dried with benzoin and then it is moistened with a 1-percent solution of nacconol. In dentine the effectiveness of this process can be ascertained by determining if sensitivity to cold water has disappeared. In experiments during four years, Younger found a reduction of about 90 percent of caries susceptibility. (Am. J. Orthodontics, Dec. '47 - B. Gottlieb)

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Multiple Sclerosis in the Navy: Of the less commonly occurring diseases, there were but 20 cases of multiple sclerosis in the relatively small forces of the Navy during the 8-year period from 1934 through 1941, and of these 20 cases, 11 occurred in 1941 and 9 in the years from 1934 through 1940. During the period from 1942 through 1945 there were 225 cases of disseminated sclerosis reported, resulting in an average annual rate of 2.3 per 100,000 average strength. The incidence rates decreased from 3.0 in 1942 to 2.0 in 1945; for this same period the average number of sick days per case increased rapidly, with an

overall average of 96.7 sick days per case. Of the 225 cases, 77, or 34.2 percent, were considered to have existed prior to entry into the Naval service.

During the war period roughly two thirds of the patients with multiple sclerosis were invalided from the service and most of the rest were returned to duty. Of the 66 patients returned to duty, 20, or 30.3 percent, were subsequently readmitted to the sick list with this same diagnosis.

Past civilian studies have shown that the colored races have rarely been affected. In the Navy and Marine Corps, of the 225 new admissions during the war years, 222 were for the white race and 3 were for the Negro race, resulting in an average annual rate of 2.3 per 100,000 for whites and 0.7 per 100,000 for Negroes. There were no admissions for the brown, yellow, or red (American Indian) races.

Although the largest percentage of the incidence occurred in males, the average annual rate for the females was approximately three times that of the males. Of the 225 new admissions, 210 were for male personnel and 15 were for female personnel. The average annual rate per 100,000 for the male group, however, was 2.2 whereas for the female the rate was 6.5.

The majority of the admissions, 191, or 84.9 percent, occurred in the ages between 20 and 40. The lowest average annual rate occurred in the "19 and under" age group after which there was a gradual increase in the rates up to the 40-44 age group. (Statistics of Navy Medicine, Feb. '48)

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Reports on USN Research Projects:

Physical Analysis of Respiratory Gas Transfer re Carbon Monoxide. One of the problems encountered in dealing with carbon monoxide as an industrial or military hazard, is that of determining a maximum safe exposure time for an individual exposed to a carbon monoxide containing atmosphere. This involves finding out how much carbon monoxide the body can tolerate and how rapidly it is taken up from the ambient air. Forbes, Sargent, and Roughton, and Pace, et al., have recently provided considerable quantitative information on the second aspect of the problem and also have given empirical formulas for the rate of uptake of carbon monoxide by normal individuals. This paper presents an attempt to develop a formula for the prediction of the rate of uptake by the body on the basis of a physical analysis of the absorption process. It is well known that if an individual is exposed to an atmosphere containing carbon monoxide, his blood carboxy-hemoglobin concentration increases with time, linearly at first, but more slowly later as equilibrium is approached. It most often occurs that these equilibrium values are so high as to be dangerous, and it is thus of practical importance to deal primarily with the initial linear portion of the absorption curve.

An approximate formula, $R = \frac{DM_A}{D+M_A} c_o$, for the rate of uptake of carbon monoxide by the body has been derived from a physical picture of the respiratory process and has been shown to agree rather well with the experimental data now available. The rate, R, depends on both the alveolar diffusion coefficient, D, and the alveolar respiratory minute volume, M_A, as well as on the ambient gas concentration, c_o.

The analysis indicates the relevant variables and suggests experimental work which should lead to more complete quantitative understanding of the uptake of carbon monoxide. (Proj. X-417, Rep. No. 12, 9 Sep '47, Nav. Med. Res. Inst., Bethesda, Md. - D. E. Goldman)

A Modification of the Redemann Semi-Micro-Kjeldahl Steam Distillation Apparatus. The Redemann semi-micro-Kjeldahl steam distillation apparatus has been modified. Introduction of standard taper joints, all glass reaction vessels, smaller dimensions, and changes in baffle design facilitate analysis at the micro level. The excellent performance of the modified apparatus in the recovery of from 0.05 to 0.10 mgm. of nitrogen from ammonium sulfate standards has been indicated by representative analyses. The apparatus has been successfully employed in the determination of blood urea nitrogen. Steam distillation of the digestion mixture is possible when sorbitan trioleate (SPAN 85) is used as an antifoam. The method permits duplicate analyses with less than 2-percent error. (NM 007 040, Rep. No. 1, 20 Nov '47, Nav. Med. Res. Inst., Bethesda, Md. - R. L. Burt)

The Construction and Analysis of a Metal Evaporator for Use with the Electron Microscope. Applying the principles set forth by Williams and Wyckoff, a metal evaporator has been constructed to evaporate gold and other suitable substances to aid in the preparation of electron microscope specimens. Analysis of the operation of the metal evaporator showed that a vacuum of less than 0.2 micron of Hg. pressure can be obtained in 44 minutes. Gold evaporated for one minute at 1700° C, at a distance of 10 cm. from the specimen, produces a film of satisfactory thickness (about 16 A.). Electron photomicrographs of Leptospira icterohemorrhagiae showed increased contrast, visibility, detail, and image area. The height of a projection on the specimen is indicated precisely by the length of its shadow. Metal films of any desired thickness can be obtained by calculating suitable filament temperature and evaporation duration. Other uses of the metal evaporator are the study of radiant energy uncomplicated by conduction and convection; and the coating of mica windows with beryllium in order to preserve their transparency to x-rays and to make them conduct an electric current. A single disadvantage of shadowed microscope specimens is apparent, namely, the obscuring of internal detail by the surface film. (NM 000 002, Rep. No. 2, 9 Aug '47, Nav. Med. Res. Inst., Bethesda, Md. - M. Maxfield and C. Levich)

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Photodosimetry Programs in Naval Hospitals: The utilization of nuclear energy has brought the subject of radiological safety to the fore and made it a matter of general concern.

Modern considerations place increasing emphasis on the accumulated quantity of ionizing radiations sustained by persons subject to such hazards in their work. Present naval directives call for the measuring and recording of the amount of ionizing radiations received by personnel working on radioactive material derived from Operation Crossroads. The quantity of ionizing radiations received by exposed personnel at installations of the Atomic Energy Commission is measured and recorded.

Photodosimetry is the principal method by which accumulated dosage is calculated. All x-ray technicians trained at Bethesda are now being given a course of instruction and qualified in this specialty. The Radiation Laboratory, San Francisco, also offers a course of instruction in photodosimetry.

It is felt that the application of photodosimetry by naval medical activities (particularly hospitals), where considerable radiological work is done, should be of great advantage because it will accomplish the following:

Render personnel safety conscious.
Reduce tendency to reckless exposure.
Provide valuable record of actual exposure.
Prevent exposure beyond permissible limits.
Afford valuable training to personnel which will be needed for future developments.

Naval hospitals are encouraged to give all possible consideration to the establishment of a program of photodosimetry in their departments of radiology. A manual of photographic dosimetry is being prepared and should be ready for distribution in the near future.

Further information may be obtained by communicating with the Chief of the Bureau of Medicine and Surgery. (Atomic Defense Div., BuMed)

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Maryland State Dental Law Change: The Secretary of the Maryland State Board of Dental Examiners has advised the Surgeon General that a recent change in the State Dental Law requires that every holder of a license to practice dentistry in Maryland must register annually before April 1st. All communications regarding this matter should be addressed to: Kyrle W. Preis, D.D.S., Secretary, Maryland State Board of Dental Examiners, 700 Cathedral Street, Baltimore 1, Maryland. (Dental Div., BuMed)

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Special Training Duty in Maxillofacial Prosthesis for Reserve Dental Officers: The U. S. Naval Dental School, National Naval Medical Center, Bethesda, Md., will give a special training course in maxillofacial prosthesis to a limited number of Reserve dental officers during the period from 19 April 1948 to 30 April 1948 inclusive. The course of instruction will include the technic for constructing plastic substitutes for lost parts, such as noses and ears. A newly developed technic for making coverings for artificial hands will also be given in this course. (Ocular prosthesis will not be included in this training.)

It is felt that this training will be valuable to the Navy in event of national emergency and that it will give Reserve dental officers an opportunity to serve the civilian population better during peacetime. There are few people trained in this special field.

One Reserve dental officer from each Naval District within the continental limits and one from the Potomac River Naval Command will be accepted for this training. Requests should be submitted to the Commandant of the Naval District in which the officer maintains his official residence.

Final approval of requests and issuance of orders will depend upon the availability of funds. (Dental Div., BuMed)

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Dental Research Through the Office of Naval Research: Of the research projects involving problems related to dentistry that have been submitted to the Office of Naval Research by the various universities and institutions, the following are among those that have been recommended by the Dental Branch of the Medical Sciences Division for approval:

"Dietary and Other Factors Concerned in Mouth and Tooth Deterioration," Cornell University, C. M. McCay, principal investigator.

"Use of Germ-Free Animals in the Study of Dental Caries," University of Chicago, J. R. Blayney, director.

"Recognition and Evaluation of Factors Influencing Micro-Organisms of the Mouth," University of Pennsylvania Dental School, J. L. T. Appleton, principal investigator.

"Study of Dental Casting Materials," University of Michigan, Norris O. Taylor, principal investigator.

"Hormonal Effects on Oral Hard and Soft Tissues," Columbia University, Dr. E. Ziskin, principal investigator.

"Bacteremias Resulting from Tooth Extraction and Scaling," Tufts College, J. P. Lazansky, principal investigator.

"Relation of Vitamin C in Inflammatory Conditions of the Gingivae," Georgetown Dental School, W. C. Hess, principal investigator.

"Anylolytic Activity of Saliva as Related to Dental Caries," Georgetown University Dental School, W. C. Hess and E. Everett, principal investigators.

"Investigation of Salivary Ammonia and Its Relation to Dental Caries and Periodontal Diseases," Western Reserve University, J. P. Muntz, director.

"Influence of Dietary Protein on Dental Caries," Massachusetts State College, Julian O. Holmes, principal investigator.

"Determination of Masticatory Efficiency," Tufts College Dental School, J. T. O'Rourke and R. S. Manly, principal investigators.

For further information concerning the dental program communications may be addressed to the Office of Naval Research, Navy Department, Washington, D. C. (Office of Naval Research)

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OP24B/cj
Serial: 6P24 21 January 1948

To: All Ships and Stations

Subj: U. S. Naval Dental Technicians School, Naval Training Center, Great Lakes, Illinois - Establishment of

1. The following activity is hereby established, under an officer in charge;

U. S. Naval Dental Technicians School
Naval Training Center
Great Lakes, Illinois 7302-270

This activity is under the military command and coordination control of the Commanding Officer, Administrative Command, U. S. Naval Training Center, Great Lakes, Illinois, and is under the management control of the Bureau of Medicine and Surgery.

2. By copy of this letter, the Chief of Naval Personnel is requested to order an officer of the Dental Corps to duty as officer in charge of this activity.

3. Bureaus and offices concerned take necessary action.

--SecNav. John L. Sullivan

Circular Letter 48-7 22 January 1948

To: MedOfCom, NavHosp, St. Albans, N.Y.; Philadelphia, Pa.; Corona, Cal.; Long Beach, Cal.; San Diego, Cal.; Oakland, Cal.; MedOfCom, Medical Supply Depot, Brooklyn, N.Y.; MedOfCom, National Medical Center, Bethesda, Md.

Subj: Work Improvement Program (WIP) in Medical Department Activities, Report on Installation and Progress of.

Refs: (a) NCPI-220 (Rev. 1)
(b) NCPI-220 (Rev. 1, Amend. 3)
(c) NCPI-230
(d) BuMed Cir ltr No. 47-118, 2 Sept 1947

This letter from the Chief of BuMed requests that addressees furnish the Bureau with certain information concerning the work improvement program.

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Circular Letter 48-8 23 January 1948

To: All Holders of the Manual of the Medical Department.

Subj: Advance Change 3-3, Manual of the Medical Department.

Encl: 1(HW) Advance Change 3-3, MMD.

1. The enclosed changes are effective immediately. This advance change shall be recorded on the "Record of Changes" page in the Manual and the individual paragraph changes are to be inserted in their proper places in the text of the Manual. At a later date, these changes will be incorporated in printed page change 3.

--BuMed. C.A.Swanson

Note: Copy of enclosure (9 pages) not reproduced in News Letter-Ed.

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Circular Letter 48-9 23 January 1948

To: Medical Officers in Command, All Naval Hospitals; Senior Medical Officers of Activities having Nurse Corps Officers; Senior Nurse Corps Officers.

Subj: Nursing Service in the Navy.

1. During the First Session of the Eightieth Congress, there was advocated legislation that would grant permanent commissioned status to members of the Nurse Corps of the Army and the Navy. This bill was enacted into law (Public Law 36 - 80th Congress) in accordance with a stated intent by its proponents that this due recognition of the Nursing profession in the Services would result in a greater majority of nurses devoting their efforts to the actual bedside care of the patient.

2. The Bureau appreciates that an unprecedented shortage of nurses has markedly retarded efforts to bring about this very desirable improvement in the employment of Nurse Corps Officers. However, as procurement programs become more effective and an increased number of nurses are available to our medical facilities, it is expected that Nurse Corps Officers below the grade of Lieutenant Commander will be accorded greater opportunity to expend their training and professional skill in actual bedside duties.

3. The primary function of the nurse should be considered in this light and with a full awareness of the nurse's motivation by the highest tenets of her profession, Commanding and Senior Medical Officers and Chief Nurses are enjoined to implement this plan of employment of nurses in as full a measure as may be possible under existing circumstances.

--BuMed. C.A.Swanson

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Circular Letter 48-10 (Not released in time for this issue.)

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Circular Letter 48-11 27 January 1948

To: Commandants, All Naval Districts and River Commands (Less 17th Naval District); Medical Officers in Command, All Naval Hospitals, (Less Brooklyn and Oceanside); Superintendent, U.S. Naval Academy, Annapolis, Maryland.

Subj: Hospital Modernization Program, Cancellation of

Ref: (a) BuMed ltr: BUMED-422-DJC:gs, Serial 4070, dtd 23 Feb 1947.

1. This subject program is hereby cancelled and outstanding requisitions submitted thereunder will be returned for cancellation.

2. Cancellation of the subject program does not in any way affect the established procedure under current budgetary, survey, and requisitioning directives for routine normal replacement of worn out, damaged and obsolete items of equipment which cannot be repaired or modified so as to render satisfactory service.

3. This action is necessitated because of budgetary limitations.

--BuMed. C.A.Swanson

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Circular Letter 48-12 27 January 1948

To: All Naval Activities Having Spectacle Dispensing Units.

Subj: Spectacles, Disposition of; Policy Regarding

This letter from the Chief of BuMed states that in many instances spectacle dispensing units have been unable to effect delivery of completed spectacles to patients. Instructions are given concerning (1) the policy and procedures for providing a more adequate delivery service and (2) the disposition of spectacles presently on hand or accumulated subsequent to this date which cannot be delivered in accordance with (1).

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Circular Letter 48-13 29 January 1948

To: All Ships and Stations

Subj: Photofluorographic Examination of the Chest of Navy and Marine Corps Personnel for the Two-Year Period Ending 1 Oct 1947.

Refs: (a) Par. 21103, MMD.
(b) AlNav #509-46
(c) BuMed CL 47-113

Encls: 1. (HW) Estimated percent of all Navy and Marine Corps personnel having received a routine chest x-ray.
2. (HW) List of stations having photofluorographic equipment.

This letter from the Chief of BuMed states that by analyzing a sampling of approximately 10 percent of the personnel assigned to each ship and station replying to references (b) and (c), the number of Navy and Marine Corps personnel having a routine annual chest x-ray in accordance with reference (a) has been estimated for two successive years. During the period from 15 September 1945 to 15 September 1946, approximately 51 percent of all Naval personnel were examined, and during the period from 1 October 1946 to 1 October 1947, approximately 58 percent were examined. This increase was not as great as had been expected.

All naval districts within the continental United States, with the exception of two, showed an increase in the percentage of personnel examined during the past year, whereas ships and noncontinental stations showed an almost uniform decrease in the percentage examined. This may be explained in part by the lack of photofluorographic facilities outside the United States. It indicates that every effort should be made to insure that a chest X-ray is taken and the results are recorded in the health record in each instance before transferring personnel to ships or to overseas stations for duty.

Photofluorographic units have been assigned to the stations listed in enclosure 2 for examination of personnel of the station and other activities in the vicinity. Those units in naval shipyards and fleet dispensaries are particularly accessible to personnel of ships. Mobile photofluorographic units are available for stations within the United States which have no other access to photofluorographic equipment. Request for assignment of a mobile unit should be made to the Commandant of the Naval District in which the activity is located.

Note: Full copy of letter together with the enclosures appears in the Navy Department Bulletin of 31 January 1948.

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Circular Letter 48-14 30 January 1948

To: All Ships and Stations

Subj: High-School Graduate Training Program, Physical Requirements for

Ref: (a) Recruiting Service Order No. 32-47 (Enclosures A and B).
(b) ALNAV 242-47.

1. The enclosure to reference (a) established physical requirements for high school graduates enlisting to attend certain service schools.

2. The physical requirements for the service schools affected are recapitulated herewith for the information of Medical Department personnel.

3. Requirements:

(a) The physical requirements for enlistment for general service as modified by reference (a) apply in the case of recruit applicants for the following service schools:

> Cooks and Bakers, Electricians's Mates, Machinist's Mates, Machinist's Mates (Shop), Motor Machinist's Mates, Metalsmiths, Yeomen, Storekeepers, Radiomen, Sonar Operators, Optical Primary, Fire Controlmen, Radarmen, Patternmakers, Aviation Fundamental.

(b) The physical requirements for enlistment for general service as modified by reference (b), except that normal color perception is required, apply in the case of recruit applicants for the following service schools:

Electronic Materiel (ETM), Aviation Electronic Materiel (AETM), Hospital Corps School (HA) (CRUITORD 33-47).

(c) The physical requirements for enlistment for general service as modified by reference (b), except that normal color perception and in addition a clean mouth free from disease are required, apply in the case of recruit applicants for the following service school:

Basic Submarine.

4. The foregoing requirements are effective pending promulgation of page changes to the Manual of the Medical Department at a later date.

5. This letter is for information purpose and it is not to be construed as modifying the provisions of reference (a) or of its enclosures.

--BuMed. H. L. Pugh

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ALNAV 9 28 January 1948

Subj: Immunization Requirements

Alnav 8-47 cancelled effective upon receipt General Orders 249 and 252. Refer to Manual Medical Department, Part III, Chapter 5B, Change 2, for immunization requirements.

--SecNav.

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