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# Antibiotic-Resistant Staphylococci

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CONTENTS

PAGE

I. EPIDEMIOLOGICAL STUDIES ON ANTIBIOTIC-RESISTANT STAPHYLOCOCCI . . . . . 174 - 190

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II. MEDICAL SCHOOL NEWS . . . . . 191

III. WEEKLY CALENDAR OF EVENTS . . . . . 192 - 197

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# I. EPIDEMIOLOGICAL STUDIES ON ANTIBIOTIC-RESISTANT STAPHYLOCOCCI

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## 1. Introduction: The Rising Incidence of Antibiotic-Resistant Strains

Microbial resistant to antibiotics is relative and interpretations of this phenomenon have undergone changes, since the beginning of the antibiotic era in 1941-42 when penicillin was first used. This is probably due to the larger doses now used, and a refinement of methods of administration. For example, in 1942 Spink et al[1] reported a study of the in vitro action of penicillin against 67 strains of staphylococcus which had been isolated prior to the use of penicillin and reported that "8 of the strains or approximately 12% were found to be quite resistant, requiring 0.4 units to 0.8 units of penicillin before growth was completely inhibited." This statement has often been quoted to mean that 12% of the strains were penicillin-resistant before penicillin was used in the therapy of staphylococcal infections. At the present time a susceptibility of strains of staphylococci to such low concentrations of penicillin would be interpreted as meaning that the organisms were sensitive to the antibiotic and the concentrations would be well within that which could be obtained with adequate doses of penicillin.

The boundaries of resistant have not been well defined and precise standard values have not been adopted in order to express susceptibility or resistance of a micro-organism to antibiotics. All strains of bacteria possess some measurable degree of resistance to antibiotics, but for practical application in therapy, arbitrary criteria for the delineation of degrees of resistance can be stated. For this purpose strains of staphylococci can be classified as follows: sensitive, inhibited by 1.0 unit or microgram of anticiotic per ml.; moderately resistant, inhibited by 1.0 to 10.0 units or micrograms per ml., and resistant, inhibition by more than 10.0 units or micrograms per ml.

There have been numerous reports emphasizing the increasing frequency with which antibiotic-resistant staphylococci were being encountered in infections of hospitalized patients. These studies, which have been reported by different investigators from medical centers in many parts of the world, are summarized in Table Ia. Initial observations on the susceptibility of staphylococci, which were isolated prior to the advent of penicillin in therapy, revealed that there were no strains resistant to 1.0 unit of penicillin per ml.[1,2] In 1942 Rammelkamp and Maxon[3] sounded a note of warning when they reported increased resistance to penicillin in four strains of staphylococci isolated from patients during the course of penicillin therapy for localized infections. The increasing incidence of penicillin-resistant strains was reported by others and by 1945 the percentage of strains from hospitalized patients which were resistant to one unit of penicillin ranged from 13% to 57%.[4-7] In one hospital the percentage of resistant strains was reported to be 14.1% in 1946, 38% in 1947 and 59% in 1948.[10] From 1951 to 1953 the percentage ranged from 64.7% to 80.0%.[8,20-24]

In contrast to the rising incidence of penicillin-resistant strains of staphylococci, which have been isolated from hospitalized patients, there has been no associated rise in the incidence of resistant strains obtained from outpatients and individuals unassociated with hospitals. The reported results of studies in the latter group are listed in Table Ib. The incidence of penicillin-resistant strains obtained from outpatients has varied from 0 to 36%.

Studies of cultures of Micrococcus pyogenes isolated from the upper respiratory tract of apparently healthy personnel in hospitals are listed in

Table I

Incidence of Penicillin-Resistant Strains of *Micrococcus pyogenes*

| Year | Authors | Country | Per Cent Resistant | Reference |
|---|---|---|---|---|
| a. Hospitalized Patients | | | | |
| Prior to 1942 | Spink et al | U.S.A. | 0 | (1) |
| Prior to 1942 | North and Christie | Australia | 0 | (2) |
| 1944 | Rantz and Kirby | U.S.A. | 21.0 | (4) |
| 1945 | Bondi and Dietz | U.S.A. | 13.9 | (5) |
| 1945 | Gallardo | U.S.A., India | 12.9 | (6) |
| 1945 | Plough | U.S.A. | 36.6 | (7) |
| 1946 | Boe and Vogelsang | Norway | 15.9-54.5 | (8) |
| 1946 | Blair et al | U.S.A. | 8.8 | (9) |
| 1946 | Barber and Whitehead | England | 14.1 | (10) |
| 1947 | Barber and Whitehead | England | 38.0 | (10) |
| 1948 | Barber and Whitehead | England | 59.0 | (10) |
| 1949 | Summers | England | 50.0 | (11) |
| 1949 | Beigelman and Rantz | U.S.A. | 56.0 | (12) |
| 1949 | Forbes | England | 68.4 | (13) |
| 1949 | Martyn | England | 55.5 | (14) |
| 1949 | Rountree and Thomson | Australia | 53.0 | (15) |
| 1949 | Berger | Austria | 19.0-40.0 | (16) |
| 1949 | Nichols and Needham | U.S.A. | 68.0 | (17) |
| 1950 | Spink | U.S.A. | 55.0 | (18) |
| 1950 | Cairnes and Summers | England | 78.0 | (19) |
| 1951 | Boe and Vogelsang | Norway | 68.0 | (8) |
| 1951 | Rountree | Australia | 80.0 | (20) |
| 1952 | Finland and Haight | U.S.A. | 75.0 | (21) |
| 1952 | Rountree and Thomson | Australia | 64.7 | (22) |
| 1953 | Dowling et al | U.S.A. | 69.0 | (23) |
| 1953 | Miyahara et al | U.S.A. | 76.0 | (24) |
| b. Out-Patients | | | | |
| 1948 | Barber and Whitehead | England | 29.4 | (10) |
| 1949 | Barber et al | England | 0.0 | (25) |
| 1949 | Summers | England | 24.0 | (11) |
| 1949 | Forbes | England | 12.5 | (13) |
| 1949 | Rountree and Thomson | Australia | 4.0 | (15) |
| 1951 | Thomson and Schwabacher | England | 20.0 | (26) |
| 1951 | Vogelsang | Norway | 3.9 | (27) |
| 1952 | Birnstingle et al | England | 16.0 | (28) |
| 1952 | Linsell | England | 18.6 | (29) |
| 1952 | Rountree and Thomson | Australia | 36.0 | (22) |
| 1953 | Dowling et al | U.S.A. | 25.0 | (23) |
| c. Hospital Staff | | | | |
| 1949 | Barber et al | England | 83.0 | (25) |
| 1949 | Rountree and Thomson | Australia | 32.0 | (15) |
| 1949 | Rice and Lonargan | U.S.A. | 30.0 | (30) |
| 1951 | Rountree and Barbour | Australia | 32.1 | (31) |
| 1953 | Dowling et al | U.S.A. | 85.0 | (23) |

Table Ic. From 1949 to 1953 the incidence of resistant strains from this group has varied from 30% to 85%. These results are similar to those obtained from studies of strains isolated from infected hospitalized patients, and indicate a possible epidemiological relationship in the strains from the two groups. It can be concluded from these reports that a high incidence of penicillin-resistant strains of staphylococci now exists in the nares and pharynges of members of hospital staff, and in infections of hospitalized patients. There is a lower incidence of similar strains inhabiting the nasopharynx of individuals in out-patient groups.

Observations on the incidence of strains of staphylococci resistant to streptomycin are presented in Table II. As in the case of penicillin, no resistant strains were encountered when this antibiotic was first introduced.[13,32] However, the incidence of resistant strains increased rapidly during the years from 1949 to 1953. By 1950 Spink[18] found 98% of strains studied at the University of Minnesota Hospitals to be resistant to 1 mcgm. of streptomycin per ml. Rountree and Thomson[22] in studying material from out-patients found only 10.8% of strains to be resistant to streptomycin in 1952.

Table II

Incidence of Streptomycin-Resistant Strains of Micrococcus pyogenes

| Year | Authors | Country | Per Cent Resistant | Reference |
|---|---|---|---|---|
| a. Hospitalized Patients | | | | |
| 1948 | Barber et al | England | 0.0 | (32) |
| 1949 | Forbes | England | 0.0 | (13) |
| 1949 | Martyn | England | 3.7 | (14) |
| 1949 | Rountree and Thomson | Australia | 16.5 | (15) |
| 1950 | Spink | U.S.A. | 98.0 | (18) |
| 1951 | Rountree | Australia | 45.0 | (20) |
| 1953 | Miyahara et al | U.S.A. | 37.0 | (24) |
| b. Out-Patients | | | | |
| 1952 | Rountree and Thomson | Australia | 10.8 | (22) |
| c. Hospital Staff | | | | |
| 1949 | Rice and Lonargan | U.S.A. | 0.0 | (30) |

Reported results of studies with chlortetracycline (aureomycin) are shown in Table III. In 1949 no strains of chlortetracycline-resistant strains were found in either hospitalized patients or members of the personnel of hospitals.[17,30,33,35] There then followed an increase in the number of more resistant strains until 1953, when 78% of strains found in hospitalized patients and 64% in a hospital staff were resistant to this antibiotic.[23] On the other hand, the incidence of chlortetracycline-resistant strains has not

exhibited a similar increase in out-patients. The range of resistant strains in out-patients has been from 2% to 19%.[23,28,34]

The incidence of antibiotic-resistant strains of M. pyogenes isolated from patients at the Minneapolis General Hospital has been investigated for

Table III

Incidence of Chlortetracycline-Resistant Strains

of Micrococcus pyogenes

| Year | Authors | Country | Per Cent Resistant | Reference |
|---|---|---|---|---|
| | a. Hospitalized Patients | | | |
| 1949 | Schneierson | U.S.A. | 0.0 | (33) |
| 1949 | Nichols and Needham | U.S.A. | 0.0 | (17) |
| 1950 | Spink | U.S.A. | 60.0 | (18) |
| 1950 | Schneierson | U.S.A. | 4.5 | (33) |
| 1951 | Schneierson | U.S.A. | 20.0 | (33) |
| 1952 | Finland and Haight | U.S.A. | 25.0 | (21) |
| 1953 | Miyahara et al | U.S.A. | 21.0 | (24) |
| 1953 | Dowling et al | U.S.A. | 78.0 | (23) |
| | b. Out-Patients | | | |
| 1951 | Anderson | England | 19.0 | (34) |
| 1952 | Birnstingle et al | England | 4.0 | (28) |
| 1953 | Dowling et al | U.S.A. | 2-12 | (23) |
| | c. Hospital Staff | | | |
| 1949 | Needham and Nichols | U.S.A. | 0.0 | (35) |
| 1949 | Rice and Lonargan | U.S.A. | 0.0 | (30) |
| 1952 | Clark et al | England | 60.0 | (36) |
| 1953 | Dowling et al | U.S.A. | 64.0 | (23) |

the years 1951 through 1953.[37] A summary of the strains of staphylococci which were found to be resistant in vitro to over 50 units or micrograms of antibiotic per ml. is found in Table IV. Sixty-two and five-tenths per cent of the strains studied in 1951, 57.2% in 1952 and 67.7% in 1953 were not inhibited by 50 units of penicillin per ml. Streptomycin-resistant strains increased from 48% in 1951 to 65.3% in 1953. With oxytetracycline (terramycin), there was an increase from 38% in 1951 to 47.5% in 1952, and to 62.7% in 1953. Results with chlortetracycline (aureomycin) have been similar to those with oxytetracycline.

The data in regard to chloramphenicol (chloromycetin) is quite different from that of the other antibiotics. There has been a decrease in the number

of chloramphenicol-resistant strains since 1951. This decrease was associated with a reduction in the use of this antibiotic in 1951. The number of strains which were resistant to 50 mcgm. per ml. decreased from 25% in 1951 to 2.5% in 1952, and to 0.65% in 1953. Of all strains of staphylococci which were studied at the Minneapolis General Hospital in 1953, 95% were inhibited in growth by 12.5 mcgm. per ml.

Table IV

Staphylococcus aureus isolated from infections at Minneapolis General Hospital

| | 1951 | 1952 | 1953 |
|---|---|---|---|
| | Resistant to >3.1 units or micrograms per ml. | | |
| Bacitracin | 10% | 11.5% | 7.8% |
| Neomycin | 0 | 25.0 | 4.5 |
| Erythromycin | - | 0 | 21.0 |
| Carbomycin | - | 0 | 20.9 |
| | Resistant to >50 units or micrograms per ml. | | |
| Penicillin | 62.5% | 57.2% | 67.7% |
| Streptomycin | 48.0 | 48.8 | 65.3 |
| Oxytetracycline | 38.0 | 47.5 | 62.7 |
| Chlortetracycline | 23.0 | 33.2 | 62.7 |
| Chloramphenicol | 25.0 | 2.5 | 0.65 |

A summary of the strains which were resistant to 3.1 mcgm. per ml. of the other antibiotics is also found in Table IV. Approximately 10% were found to be moderately resistant to bacitracin each year. There has been a rising number of strains resistant to erythromycin. In 1952 all strains that were studied at the Minneapolis General Hospital were sensitive to 3.1 mcgm. of erythromycin per ml. But in 1953, 21% of all strains examined were observed to be resistant to this concentration. The majority of these resistant strains required from 200 to 400 mcgm. of erythromycin per ml. for inhibition of growth. Carbomycin has not been used extensively, but every strain of staphylococcus that has exhibited resistance to erythromycin in this study, has also been resistant to carbomycin in similar concentrations. Cross resistance is evident between these two antibiotics.

It is apparent from studies carried out during the last decade at the University of Minnesota, and elsewhere, that the incidence of antibiotic-resistant strains of staphylococci is directly related to the quantities of antibiotics that are being administered to a hospital population. As each antibiotic is extensively employed in therapy, the incidence of resistant strains of staphylococci rises for that antibiotic. If the use of an antibiotic is curtailed, as with chloramphenicol, the incidence drops. This correlation of antibiotic-resistance with the quantities of antibiotic being used is unique for the staphylococcus only, and is particularly applicable to hospital populations in large centers.

2. Epidemiology of Staphylococcal Infections

A knowledge of the mechanisms involved in the spread of these bacteria is important because prevention of infection by these highly resistant strains must be attempted. The primary reservoir of pathogenic staphylococci is the human nasopharynx. The carrier rate of coagulase-positive staphylococci in the general population has been reported to be 25 to 50%, whereas in hospital personnel the carrier rate is reported to be 50 to 75%.[22,25,31,38,39] Nasal carriers are usually skin carriers of the same strains.[39,41]

The mechanism by which staphylococci invade wounds from nasal carriers is not clearly understood. It has been reported that contamination of the air with staphylococci in the dust from the clothing and bed clothes of carriers is of more significance than the transfer of staphylococci by droplets from the nasopharynx.[42,43] Surgical wounds may possibly be contaminated by surgeons when small puncture holes of the gloves permit accumulated perspiration containing staphylococci to ooze into the tissues.[44] The incidence of antibiotic-resistant strains of staphylococci found in hospitalized patients is roughly proportional to the duration of time spent in the hospital. This was reported by Cairnes and Summers,[19] who found a group of hospitalized patients to possess antibiotic-resistant strains in 25% of the cases on the first day, 52% from the second to the seventh day and 68% after the eighth day. Rountree and Barbour[31] studied the carrier rate of 127 nurses during the first 16 weeks of their training and observed an increase in the carrier rate from 52.6% to 71.4%, and in the penicillin-resistant carrier rate from 4.3% to 32.1%. Lepper et al[45] reported an increase from 0 to 75% of erythromycin-resistant staphylococci among members of a hospital staff during a five-months period when the drug was employed frequently in treatment of patients. The incidence of infected surgical wounds has been recently reported to be increasing by Howe,[46] who stated that the rate of infection of clean wounds after operation gradually increased from 1.24% in 1949 to 4.66% in 1953 on the house service at the Massachusetts Memorial Hospitals despite the prophylactic use of antibiotics. This was attributed to an abnormally high penicillin-resistant carrier rate in the hospital personnel and patients.

Bacteriophage typing of staphylococci has contributed much to the study of the epidemiology of staphylococcal infections. A predominance of Group III phage patterns of staphylococci isolated from infections caused by antibiotic-resistant strains encountered in hospitals, indicates the selection of a specific group of staphylococci having the property of resistance.[47-49]

### 3. The Origin of Antibiotic-Resistant Staphylococci in Infections

In an attempt to determine the origin of antibiotic-resistant staphylococci in infections, cultures were isolated from 23 patients at the Minneapolis General Hospital in 1953.[50] All the patients selected in this study developed infections from erythromycin-resistant strains.

All cultures were studied for bacteriophage lysis as a typing procedure. The methods of bacteriophage typing described by Williams and Rippon[51] and Blair and Carr[52] were used. This consisted of placing each of 34 bacteriophages in specified dilutions on an agar plate which had been heavily inoculated with a culture. If a strain was not lysed with any of the diluted bacteriophages it was re-examined with undiluted bacteriophages. The pattern of lysis obtained determined the type of strain being examined.

In discussing the results of bacteriophage typing of cultures, the patients are divided into four groups.

(1) Group I. No change occurred in the bacteriophage type of staphylococcus during therapy, but erythromycin resistance developed. Table V

Table V

Studies of M. pyogenes Isolated

Before and After Therapy with Erythromycin

| Patient No. | Before Treatment | | | After Treatment | | |
|---|---|---|---|---|---|---|
| | Source | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml.) | Source | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml) |
| 6 | Blood | 47/53/75/77 | 0.75 | Blood | 53/77 | 400.0 |
| 13 | Blood | 7 | 0.75 | Blood | 7 | 50.0 |
| 15 | Blood | $VA_4$ | 0.38 | Wound | $VA_4$ | 12.5 |

shows the results with cultures from three patients from whom sensitive strains were isolated prior to therapy with erythromycin and the subsequent emergence of erythromycin-resistant strains after therapy with this antibiotic. The bacteriophage type of the staphylococcus remained the same in each case. In these three patients it may be postulated that the erythromycin selected out the resistant cocci contained in the invading population of staphylococci, resulting in survival of the resistant cells, and suppression of the sensitive organisms.

(2) Group II. A change occurred in the bacteriophage type of staphylococcus during therapy and the cultures isolated after therapy were resistant to erythromycin. Table VI shows the results in three patients in which the erythromycin-resistant strains isolated following therapy were of different bacteriophage types from the sensitive

Table VI

Studies of M. pyogenes Isolated

Before and After Therapy with Erythromycin

| Patient No. | Before Treatment | | | After Treatment | | |
|---|---|---|---|---|---|---|
| | Source | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml.) | Source | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml) |
| 1 | Blood | 44A<br>$6/47/VA_4$ | 0.38<br>0.38 | Blood | $VA_4$<br>6/31A<br>53 | 400<br>200<br>200 |
| 10 | Wound | 47/47C/54/75 | 0.38 | Wound | 53 | 400 |
| 12 | Blood | $VA_4$ | 0.38 | Skin Infection | 53 | 400 |

strains isolated prior to therapy. In all three cases, the staphylococci which were highly resistant to erythromycin were of type 53. This strain was present in the environment of the hospital. It is concluded that these three patients were infected with erythromycin-sensitive strains which were eliminated during therapy, and then the original invading strains were replaced by resistant organisms as a result of cross infection.

(3) Group III. No cultures were isolated prior to therapy; erythromycin-resistant strains were isolated during or after therapy with erythromycin. In six patients erythromycin was used in therapy, and staphylococci which were highly resistant to erythromycin, were isolated after treatment was begun. These results are presented in Table VII. Since no cultures were obtained prior to therapy, it was impossible to compare bacteriophage types of individual strains. Most of the strains were of type 47 or 53, the types frequently found in hospital environments and which are reported to show increased resistance to antibiotics.

Table VII

Studies of M. pyogenes Isolated During Therapy with Erythromycin

| Patient No. | Source of Culture | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml.) |
|---|---|---|---|
| 5 | Sputum | 53 | 400 |
| 8 | Sputum | 47/47C/53/75/77 | 50 |
| 18 | Throat | 47 | 400 |
| 20 | Wound | 47/54 | 200 |
| 21 | Wound | 47 | 200 |
| 23 | Stool | Nontypable | 200 |

(4) Group IV. Erythromycin-resistant staphylococci were isolated from infections in patients who had been treated with antibiotics other than erythromycin. Eleven patients did not receive erythromycin but were treated with other antibiotics. In most cases treatment consisted of combinations of penicillin, streptomycin and one of the tetracycline compounds. The results of studies of the cultures isolated from this group of patients are presented in Table VIII. Seven of the eleven cultures were lysed by bacteriophage type 53 and three by type 47. This is additional evidence of cross infection occurring in hospitalized patients.

It can be concluded from the study of these patients that infections with erythromycin-resistant staphylococci occur as a result of (a) the emergence of resistant staphylococci from the original sensitive strain by a process of selection and (b) cross-infection by strains which are already resistant to the antibiotic.

4. A Comparative Study of Antibiotic-Resistant Staphylococci in Different

Table VIII

Studies of M. pyogenes Isolated from

Patients Who Were Not Treated with Erythromycin

| Patient No. | Source of Culture | Bacteriophage Type | Erythromycin Sensitivity (Mcgm. per ml.) |
|---|---|---|---|
| 2 | Blood | 53 | 400 |
| 3 | Wound | 53 | 400 |
| 4 | Wound | 53 | 400 |
| 7 | Wound | 53 | 400 |
| 9 | Blood | $VA_4$/31/53/54 | 400 |
| 11 | Leg Ulcer | 47/$VA_4$/54/75 | 100 |
| 14 | Wound | 47/54/75 | 400 |
| 16 | Pleural Fluid | 53 | 400 |
| 17 | Wound | 47/53/54/75 | 400 |
| 19 | Wound | 47 | 400 |
| 22 | Infected Bartholin Cyst | Nontypable | 400 |

Environmental Groups

The alarming increase in antibiotic-resistant staphylococci is being encountered in various medical centers, and in patients at the University of Minnesota Hospitals, prompted a comparative study of coagulase-positive strains, isolated from different environmental groups, with regard to antibiotic resistance and bacteriophage types.

(1) Methods of Study

(a) Isolation of Staphylococci

Cultures for staphylococci were obtained from the nasopharynges of 208 individuals on the surgical services of the University of Minnesota Hospitals in January 1954. The group consisted of physicians, nurses, nurses' aids and orderlies. During the same month similar cultures were obtained from 200 individuals in the out-patient clinic who had not been hospitalized or treated with antibiotics for at least the preceding six months. The third group consisted of 96 strains isolated from septic infections in 66 in-patients on the surgical service and were collected from July 1, 1953, to January, 1954.

All cultures were inoculated on human blood-agar, and trypticase soy or thioglycolate broth, and isolates were made from these media. All cultures of staphylococci were examined for

coagulase activity by employing human plasma with the slide and test-tube techniques.

(b) Susceptibility to Antibiotics The technique described by Waisbren[53] employing serial dilutions of antibiotics in broth was used to test the in vitro susceptibility of all strains of coagulase-positive staphylococci to antibiotics. Susceptibility was determined for each strain with the following antibiotics: penicillin, streptomycin, chlortetracycline, oxytetracycline, chloramphenicol, bacitracin and erythromycin.

(c) Determination of Bacteriophage Groups of Strains The patterns of lysis of all the cultures by bacteriophages were determined as described previously. The types were divided into groups according to the following classification:* Group I, phages 29, 52, 52A, 79; Group II, phages 3A, 3B, 3C, 55; Group III, phages 6, 7, 42E, 47, 53, 54, 70, 73, 75, 77; and Group IV, phage 42D. Strains of staphylococci were designated as members of groups according to the pattern of lysis. In some cases overlapping occurred to such degrees that strains were designated as intermediate members of groups.

(2) Results

Staphylococci were isolated from 85.6% of the members of the hospital staff and 74% of the group in the out-patient. Coagulase-positive staphylococci were obtained from 68 (32.7%) of the hospital staff and 41 (20.5%) of the out-patients. These data are presented in Table IX.

The results of tests for in vitro susceptibility of all coagulase-positive strains from the three environmental groups are compared in Table X.

(a) Penicillin Approximately 41% of the strains obtained from the hospital staff and from the septic infections of patients were resistant to 1000 units of penicillin per ml., and only 19.1 and 5.2% respectively were sensitive to 1.0 unit per ml. In contrast to this high degree of resistance, 60.9% of the strains from

Table IX

Staphylococci Isolated

From Hospital Personnel and Out-Patients

| Group | Number of Persons | Total Strains | | Coagulase-Positive Strains | | |
|---|---|---|---|---|---|---|
| | | No. | Per Cent | Total | Per Cent of Persons | Per Cent of Strains |
| Hospital Personnel | 208 | 178 | 85.6 | 68 | 32.7 | 38.2 |
| Out-Patients | 200 | 148 | 74 | 41 | 20.5 | 27.7 |

* This classification was suggested in January 1954 by the subcommittee on Bacteriophage Typing of Staphylococci of the International Committee on Bacteriological Nomenclature and employs 19 strains of bacteriophage (54).

Table X

Results in Percentage of *In Vitro* Susceptibility of *M. pyogenes*, Isolated from Different Groups, to Antibiotics in Units or Micrograms per Ml.

| Group | 0.1-1.0 | 1.0-10 | 10-100 | 100-500 | 500-1000 | >1000 |
|---|---|---|---|---|---|---|
| **Penicillin (Units per Ml.)** | | | | | | |
| Staff | 19.1 | 2.9 | 29.4 | 7.3 | | 41.1 |
| Inpatients | 5.2 | 3.1 | 8.3 | 33.3 | 9.3 | 40.6 |
| Outpatients | 60.9 | 7.3 | 21.9 | 9.7 | | |
| **Streptomycin (Mcgm. per Ml.)** | | | | | | |
| Staff | | 25.0 | 26.4 | 2.9 | | 45.5 |
| Inpatients | | 7.2 | 13.5 | 1.0 | | 78.9 |
| Outpatients | | 70.7 | 29.3 | | | |
| **Chlortetracycline (Mcgm. per Ml.)** | | | | | | |
| Staff | 54.4 | 7.3 | 19.1 | 19.1 | | |
| Inpatients | 3.1 | 21.8 | 70.8 | 4.1 | | |
| Outpatients | 85.3 | 14.7 | | | | |
| **Oxytetracycline (Mcgm. per Ml.)** | | | | | | |
| Staff | 47.0 | 14.7 | 10.2 | 27.9 | | |
| Inpatients | 8.3 | 13.5 | 46.8 | 30.2 | 1.0 | |
| Outpatients | 75.6 | 24.4 | | | | |
| **Chloramphenicol (Mcgm. per Ml.)** | | | | | | |
| Staff | | 92.6 | 7.3 | | | |
| Inpatients | 23.9 | 71.5 | 3.1 | 2.1 | | |
| Outpatients | | 97.5 | 2.5 | | | |
| **Bacitracin (Units per Ml.)** | | | | | | |
| Staff | 32.3 | 67.7 | | | | |
| Inpatients | 22.9 | 73.9 | 3.1 | | | |
| Outpatients | 9.4 | 90.6 | | | | |
| **Erythromycin (Mcgm. per Ml.)** | | | | | | |
| Staff | 97.0 | | | | 1.5 | 1.5 |
| Inpatients | 91.6 | 1.1 | 1.1 | 1.1 | 3.1 | 2.0 |
| Outpatients | 100.0 | | | | | |

the out-patients were sensitive to 1.0 unit per ml.

(b) Streptomycin The greatest degree of resistance to streptomycin was demonstrated by strains isolated from infections in hospitalized patients. Approximately 79% of these strains were not inhibited by 1000.0 mcgm. per ml. Of the strains from the hospital staff 45.5% were resistant to 1000.0 mcgm. per ml. All strains from the out-patients were inhibited in a range of 1.0 to 100.0 mcgm. per ml., with 70.7% occurring in a therapeutic range of 1.0 to 10 mcgm. per ml.

(c) Chlortetracycline (Aureomycin) Staphylococci isolated from the septic infections of hospitalized patients revealed the highest incidence of resistance since 75% required 10.0 to 500.0 mcgm. per ml. for inhibition. Of the strains from the hospital staff 54.4% were susceptible to 0.1 to 1.0 mcgm. per ml. All strains from the out-patients were inhibited by 10.0 mcgm. or less per ml., and 85.3% were susceptible in a range of 0.1 to 1.0 mcgm. per ml.

(d) Oxytetracycline (Terramycin) The results with oxytetracycline were similar to those obtained with chlortetracycline. Of the strains from in-patients, 77% required 10 to 500 mcgm. per ml. for inhibition of growth. There were 47% of the strains from hospital personnel which were sensitive in a range of 0.1 to 1.0 mcgm. per ml., and 39% required 10 to 500 mcgm. per ml. for inhibition. Strains which were most sensitive were from the out-patients, 75.6% being sensitive to 0.1 to 1.0 mcgm. per ml., and all strains were susceptible to 10.0 mcgm. per ml.

(e) Chloramphenicol (Chloromycetin) This antibiotic has been used to a limited degree at the University of Minnesota Hospitals. This is reflected in the similarity of results in all three environmental groups. Over 90% of the strains from the hospital staff and the out-patients were susceptible to 1.0 to 10.1 mcgm. per ml. In the in-patient group 23.9% were susceptible to 0.1 to 1.0 mcgm. per ml.

(f) Bacitracin This antibiotic has been used parenterally and topically in a few cases of septic infections in this hospital. Results in each group were similar in that all strains were inhibited in a range of 0.1 to 10.0 mcgm. per ml. with the exception of 3.1% of the strains obtained from infections of in-patients that required 10.0 to 100.0 mcgm. per ml. for inhibition.

(g) Erythromycin (Ilotycin) A high incidence of susceptibility of strains from all groups was exhibited for erythromycin. One hundred per cent of the strains from out-patients, 97% from the hospital staff and 91.6% from infections of patients were inhibited by 0.1 to 1.0 mcgm. per ml. Approximately 3% and 5% of the strains from the staff and in-patients, respectively, required over 500.0 mcgm. per ml. for inhibition of growth.

(3) Bacteriophage Types of Staphylococci Isolated from Different Environmental Groups

As can be seen in Table XI, the strains of staphylococci isolated from out-patients were distributed throughout all groups. In contrast there was a predominance of Group III strains among the cultures obtained from the members of the hospital staff and the in-patients. Group III contained the strains of increased antibiotic resistance. The number of strains in Groups I and II from the hospital staff and in-patients was much less than the percentage of strains in these groups in the out-patients. These findings are in agreement with previous reports that antibiotic-resistant strains of staphylococci are in bacteriophage Group III.

Table XI

Table XI

The Incidence of Phage Groups of Staphylococci Isolated from Different Environmental Groups

| Bacteriophage Group | Staff | Inpatients | Outpatients |
|---|---|---|---|
| I | 7.3 | 1.0 | 17.0 |
| II | 8.7 | 2.0 | 21.9 |
| III | 52.9 | 56.2 | 19.5 |
| IV | | | 2.4 |
| I and III | 5.9 | | 9.7 |
| I and IV | 1.4 | | |
| N. T. | 23.5 | 40.6 | 29.2 |

5. Discussion

It is evident from other published reports, from the findings at the University Hospitals and at the Minneapolis General Hospital, that strains of staphylococci recovered from individuals outside of a hospital or who have not received an antibiotic differ from those obtained from patients in a hospital and from hospital personnel. A high percentage of the former are susceptible to the action of antibiotics, whereas "hospital" strains possess considerable resistance to most of the antibiotics. Bacteriophage typing confirms the finding that the appearance of resistant staphylococci is a property of certain strains, occurring most frequently among the Group III phage types. Resistance to each antibiotic is roughly correlated with the quantities of antibiotics used.

It can be concluded that antibiotic-resistant strains predominate in the hospital environment as a result of a selective process of antibiotic action. These resistant strains are carried by patients and by members of the hospital personnel. Highly resistant strains infect wounds, cause pneumonea, genito-urinary tract infections and, in some cases, septicemia ensues with often fatal results.

There is great need for an awareness of the nature and magnitude of this problem. The ubiquity of the pathogenic antibiotic-resistant strains of staphylococci in the hospital environment indicates the need for prophylactic measures to prevent cross infections of patients and the establishment of the carrier state in members of the hospital staff.

6. Conclusions

(1) There has been an increasing incidence of antibiotic-resistant strains of staphylococci in the nasopharynges of individuals who are closely associated with the environment of hospitals and in septic infections which occur in patients during hospitalization.

(2) The incidence of antibiotic-resistance of strains is roughly proportional to the quantity of an antibiotic used in a hospital.

(3) The incidence of antibiotic-resistant strains in the general population that is not associated with hospitals is much less than in hospital personnel.

(4) Infections with antibiotic-resistant strains occur as a result of two mechanisms: (a) the emergence of resistant strains from more sensitive strains by a given antibiotic selecting out resistant cocci, thus permitting their survival and multiplication, and (b) cross-infection by strains which are previously resistant to antibiotics.

(5) Antibiotic resistance is a property of certain strains of staphylococci, the majority of these strains being in bacteriophage Group III.

(6) Vigilance in aseptic technique to prevent cross infections of patients and the carrier state in the hospital personnel is necessary as measures of prevention.

The authors wish to express their appreciation for the many individuals who cooperated in these investigations. Miss Mae Collin of the Laboratories at the Minneapolis General Hospital aided in the studies at that institution. Dr. Ernest Reiner participated in the collection of strains of staphylococci from hospital personnel and from the out-patient group. Stanley Shapiro assisted in the typing of strains with bacteriophage. All of the personnel in the Bacteriology Laboratories of the University Hospitals were most helpful in the isolation of staphylococci from patients. We are indebted to Dr. O. H. Wangensteen and the surgical staff for cooperating in every way in the epidemiological studies conducted on their service.

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## II. MEDICAL SCHOOL NEWS

### Coming Events

November 22 - 24 Continuation Course in Fractures for General Physicians
December 2 - 4 Continuation Course in Obstetrics for Specialists

* * *

### Continuation Course

The University of Minnesota will present a continuation course in Obstetrics for Specialists at the Center for Continuation Study from December 2 to 4, 1954. The guest faculty will include Dr. Curtis J. Lund, Professor and Head, Department of Obstetrics and Gynecology, University of Rochester Medical School; and Dr. Ralph A. Reis, Professor, Department of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. The course will be presented under the general direction of Dr. John L. McKelvey, Professor and Head, Department of Obstetrics and Gynecology, University of Minnesota Medical School.

* * *

### Faculty News

Dr. Jerome T. Syverton, Professor and Head, Department of Bacteriology and Immunology, his wife, and their two daughters, spent two months in Europe. Dr. Syverton participated in The Third International Congress for Poliomyelitis held in Rome from September 6 to 10, and visited laboratories in Italy, France, the Netherlands, Denmark, and England.

Dr. Newell R. Ziegler, Director of the Blood Bank, attended the annual meetings of the American Association of Blood Banks in Washington from September 12 to 15.

The Department of Bacteriology and Immunology was recently host to two distinguished visitors: Dr. Eero Mustakallio, Dean and Professor of Bacteriology, Turku University Medical School, Turku, Finland; and Dr. Igor Tamm, Associate Member, Rockefeller Institute for Medical Research and Associate Physician, Hospital of the Rockefeller Institute, New York. During his visit to the University Dr. Tamm gave a lecture on "Intracellular Development of Viruses."

On September 29, Dr. Robert Wise, Assistant Professor, Department of Medicine, gave a lecture at the Squibb Institute for Medical Research in New Brunswick, New Jersey.

Dr. R. Dorothy Sundberg, Associate Professor, Department of Anatomy, and Hospital Hematologist, attended the International Congress of Hematology in Paris, France, from September 6 through 12. She presented two papers entitled "Osteoblasts and Ostoclasts in Films of Bone Marrow" and "Granulomatous Lesions in the Bone Marrow."

Miss Ruth Hovde, Assistant Professor of Medical Technology, assumed office as President of The American Society of Medical Technology at its meetings in Miami in June, 1954.

Miss Elaine Duerr, Instructor in Medical Technology, has been awarded an American Cancer Society Fellowship for the study of exfoliative cytology under Dr. John R. McDonald, Mayo Clinic, and will be on a three-month leave of absence.

III. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
WEEKLY CALENDAR OF EVENTS

Physicians Welcome

November 22 - 27, 1954

Monday, November 22

Medical School and University Hospitals

| | |
|---|---|
| 9:00 - 9:50 | Roentgenology-Medicine Conference; L. G. Rigler, C. J. Watson and Staff; Todd Amphitheater, U. H. |
| 9:00 - 10:50 | Obstetrics and Gynecology Conference; J. L. McKelvey and Staff; W-612, U. H. |
| 10:00 - 12:00 | Neurology Rounds; A. B. Baker and Staff; Station 50, U. H. |
| 11:30 - | Tumor Conference; Doctors Hitchcock, Zimmermann, and Stenstrom; Todd Amphitheater, U. H. |
| 12:15 - | Obstetrics and Gynecology Journal Club; Staff Dining Room, U. H. |
| 12:30 - 1:30 | Physiology Seminar; Effective Physical Activity on Body Composition; Josef Brozek; 214 Millard Hall. |
| 1:30 - 2:30 | Pediatric-Neurological Rounds; R. Jensen, A. B. Baker and Staff; U. H. |
| 1:30 - 3:30 | Dermatology Hospital Rounds; H. E. Michelson and Staff; Dermatology-Histopathology Room, M-434, U. H. |
| 4:00 - 6:00 | Anesthesiology Conference; F. H. Van Bergen and Staff; Room 100, Mayo Memorial. |
| 4:30 - | Public Health Seminar; Heart Disease Around the World; Ancel Keys; 15 Owre Hall. |
| 4:30 - | Pediatric-Medicine Infectious Disease Rounds; Station 33, U. H. |
| 5:00 - 6:00 | Physiology-Surgery Conference; Todd Amphitheater, U. H. |
| 5:00 - 6:00 | Urology-Roentgenology Conference; C. D. Creevy, O. J. Baggenstoss and Staff; Eustis Amphitheater. |

Ancker Hospital

| | |
|---|---|
| 8:00 - 9:00 | Pediatrics Contagion Rounds; L. R. Critchfield; Contagion 5. |
| 8:30 - 10:30 | Medical and Surgical Chest Conference; Dr. Gehlen and Staff; Auditorium. |
| 10:00 - 12:00 | Surgery Grand Ward Rounds; Begin Floor E4. |
| 11:00 - 12:00 | Medicine Resident Rounds. |
| 11:00 - 12:00 | Pediatric Rounds; Harry Orme; Contagion 1. |
| 12:30 - 2:30 | Surgery Out-Patient Clinic; Room 8. |
| 2:00 - 3:00 | Routine EKG Interpretation; Dr. Sommers and House Staff; Medical Record Library. |
| 2:30 - 3:00 | Discussion of Problem Case; Auditorium. |

## Monday, November 22 (Cont.)

Ancker Hospital (Cont.)

3:00 - 4:00 Surgery Journal Club; Classroom.

3:00 - 4:00 Lectures on Electrocardiography; Ben Sommers; Auditorium.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Richard Raile; Station K.

10:30 - 12:00 Medicine Rounds; Thomas Lowry; Station F.

11:00 - Orthopedic and Fracture Rounds; Drs. John Moe and Arthur Zierold; Station B.

11:00 - Pediatric Seminar; Erling Platou; Classroom, Station M.

12:30 - Surgery Grand Rounds; Dr. Zierold, Station E.

1:30 - 2:30 Tuberculosis Conference; J. A. Myers; Station M.

2:00 - Pediatric Rounds; Stations I and J.

Veterans Administration Hospital

9:30 - Infectious Disease Rounds; Drs. Hall, Zinnemann and Middlebrook.

1:30 - Cardiac Conference; Drs. Smith, Berman, Hoseth, Simonson, Swerdlow, Shapiro, and J. Brown; Conference Room, Bldg. I.; Rounds immediately following conference.

## Tuesday, November 23

Medical School and University Hospitals

9:00 - 9:50 Roentgenology-Pediatric Conference; L. G. Rigler, Irvine McQuarrie and Staffs; Eustis Amphitheater, U. H.

12:30 - 1:20 Pathology Conference; Autopsies; J. R. Dawson and Staff; 104 Jackson Hall.

12:30 - Bacteriology and Immunology Seminar; Nature and Function of Reserve Food Particles; Del Rose Dubbs; Evidence for Mitochondria and Their Possible Function; Marvin Field; 1050 Mayo Memorial.

12:30 - Anatomy Seminar; Studies of Experimental Cirrhosis in the Rat; F. W. Hoffbauer; 226 Jackson Hall.

3:30 - Pediatric Seminar; Problems in the Laboratory and Clinical Diagnosis of Non-Paralytic Poliomyelitis; Paul Ellwood; 1450 Mayo Memorial.

4:00 - 5:00 Pediatric Rounds on Wards; Irvine McQuarrie and Staff; U. H.

4:30 - 5:30 Clinical-Medical-Pathological Conference; Todd Amphitheater, U. H.

5:00 - 6:00 X-ray Conference; Subject to be announced; Erik Husfeldt, Copenhagen; Eustis Amphitheater, U. H.

Ancker Hospital

8:00 - 9:00 Pediatric Rounds; Edward Strem; Contagion 1.

8:00 - 10:00 Visiting Staff Rounds.

Tuesday, November 23 (Cont.)

Ancker Hospital (Cont.)

9:00 - 12:00 Practical Diagnostic Clinic; Harry Orme; Out-Patient Department.

11:00 - 12:00 Medical X-ray Conference; Auditorium.

4:00 - 5:00 Medical-Pathological Conference; W. F. Mazzitello; Auditorium.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Elizabeth Lowry; Station J.

9:30 - 10:30 Obstetrics and Gynecology Staff Rounds; William P. Sadler and Staff; 301 Harrington Hall.

10:00 - Psychiatry Grand Rounds; R. W. Anderson, Station H.

10:00 - Cardiac Rounds; Paul F. Dwan; Classroom, Station I.

11:30 - 12:30 Neurology-Neurosurgery Conference; Classroom, Station M.

12:30 - 2:30 Dermatology Rounds on Clinic; Carl W. Laymon and Staff.

12:30 - ECG Conference; Boyd Thomes and Staff; 302 Harrington Hall.

1:00 - Tumor Clinic; Drs. Eder, Coe, and Lipschultz; Classroom.

3:30 - Pediatric-Psychiatry Rounds; Jack Wallinga; Station I.

Veterans Administration Hospital

7:30 - Anesthesiology Conference; Surgical Conference Room, Bldg. 43.

8:30 - Hematology Rounds; Drs. Hagen and Wexler.

8:30 - Surgery Journal Club; Conference Room, Bldg. I.

9:30 - Surgery-Pathology Conference; Conference Room, Bldg. I.

10:30 - Surgery-Tumor Conference; D. Ferguson and J. Jorgens.

1:00 - Review of Pathology, Pulmonary Tuberculosis; Conference Room, Bldg. I.

1:30 - Combined Medical-Surgical Chest Conference; Conference Room Bldg. I.

2:00 - 2:50 Dermatology and Syphilology Conference; H. E. Michelson and Staff; Bldg. III.

4:00 - Thoracic Surgery Problems; Conference Room, Bldg. I.

5:30 - Physiology Seminar; Surgical Conference Room, Bldg. 43.

Wednesday, November 24

Medical School and University Hospitals

8:00 - 9:00 Roentgenology-Surgical-Pathological Conference; Paul Lober and L. G. Rigler; Todd Amphitheater, U. H.

11:00 - 12:00 Pathology-Medicine-Surgery-Pediatrics Conference; Todd Amphitheater, U. H.

12:30 - 1:20 Radio-Isotope Seminar; Lloyd McLean; Betatron Room in Cobalt Underground Section, U. H.

Wednesday, November 24 (Cont.)

Medical School and University Hospitals (Cont.)

1:30 - 3:00 Pediatric Allergy Clinic; Albert V. Stoesser and Lloyd Nelson; W-211, U. H.

3:30 - 4:30 Dermatology Clinical Seminar; F. W. Lynch; 3rd Floor Conference Room, Heart Hospital.

4:30 - 5:50 Dermatology Seminar; 3rd Floor, Conference Room, Heart Hospital.

5:00 - 6:00 Residents Lectures; Cardiac Operations; C. Walton Lillehei; Todd Amphitheater, U. H.

5:00 - 5:50 Urology-Pathological Conference; C. D. Creevy and Staff; Eustis Amphitheater, U. H.

5:30 - 7:30 Dermatology Journal Club and Discussion Group; Hospital Dining Room.

7:30 - 9:30 Dermatology Seminar; Review of Interesting Slides of the Week; Robert W. Goltz; Todd Amphitheater, U. H.

Ancker Hospital

8:30 - 9:30 Clinico-Pathological Conference; J. Noble; Auditorium.

9:00 - 10:00 Contagion Rounds; L. R. Critchfield; Contagion 5.

11:00 - 12:00 Medicine Resident Rounds.

1:30 - 2:30 Pediatric Rounds; Ray Anderson, Contagion 1.

3:30 - 4:30 Pediatric Surgery Conference; Harry Orme and I. D. Baronofsky; Auditorium.

Minneapolis General Hospital

8:30 - 9:30 Obstetrical and Gynecological Grand Rounds; William P. Sadler and Staff; Station C.

9:30 - Pediatric Rounds; Henry Staub; Station I.

10:30 - 12:00 Medicine Rounds; Thomas Lowry and Staff; Station D.

12:15 - Pediatrics Staff Meeting; Classroom, Station I.

1:30 - Pediatric House Staff Seminar; Erling Platou; Station I.

1:30 - Pediatric Rounds; Erling Platou; Classroom, Station I.

Veterans Administration Hospital

8:30 - 10:00 Orthopedic X-ray Conference; E. T. Evans and Staff; Surgical Conference Room, Bldg. 43.

8:30 - 12:00 Neurology Rehabilitation and Case Conference; A. B. Baker.

9:00 - Gastro-Intestinal Rounds; Drs. Wilson, Zieve, Ferguson, Brakel, Konig and Swenson.

10:30 - Psychosomatic Conference; C. K. Aldrich; 7th Floor, Bldg. 43.

12:30 - Medical Journal Club; Doctors' Dining Room.

12:30 - X-ray Conference; J. Jorgens; Conference Room, Bldg. I.

Wednesday, November 24 (Cont.)

Veterans Administration Hospital (Cont.)

1:30 - 3:00 Metabolic Disease Conference; Drs. Flink and Latts.

3:30 - Urology Pathology Slide Conference; Dr. Gleason; Conference Room, Bldg. I.

7:00 - Lectures in Basic Science of Orthopedics; Conference Room, Bldg. I.

Thursday, November 25 (HOLIDAY)

Friday, November 26

Medical School and University Hospitals

8:00 - 10:00 Neurology Grand Rounds; A. B. Baker and Staff; Station 50, U. H.

9:00 - 9:50 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:30 - 11:50 Medicine Rounds; C. J. Watson and Staff; Todd Amphitheater, U. H.

10:30 - 1:50 Otolaryngology Case Studies; L. R. Boies and Staff; Out-Patient Department, U. H.

11:00 - 12:00 Vascular Rounds; Davitt Felder and Staff Members from the Departments of Medicine, Surgery, Physical Medicine, and Dermatology; Eustis Amphitheater, U. H.

11:45 - 12:50 University of Minnesota Hospitals Medical Staff Meeting; Progress in Otology; Lawrence R. Boies; Powell Hall Amphitheater.

1:00 - 2:50 Neurosurgery-Roentgenology Conference; W. T. Peyton, Harold O. Peterson and Staff; Todd Amphitheater, U. H.

1:30 - 2:30 Dermatology Grand Rounds; Presentation of Cases from Grouped Hospitals (University, Ancker, General and Veterans) and Private Offices; H. E. Michelson and Staff; Eustis Amphitheater, U. H.

2:30 - 4:00 Dermatology Hospital Rounds; H. E. Michelson and Staff; Begin at Dermatological Histopathology Room, M-434, U. H.

3:00 - 4:00 Neuropathological Conference; F. Tichy; Todd Amphitheater, U. H.

4:30 - 5:20 Ophthalmology Ward Rounds; Erling W. Hanson and Staff; E-534, U. H.

5:00 - Urology Seminar and X-ray Conference; Eustis Amphitheater, U. H.

Ancker Hospital

8:00 - 9:00 Pediatric Rounds; Edward Strem; Contagion 1.

11:00 - 12:00 Contagion Rounds; Harry Orme; Contagion 5.

3:00 - 4:00 Medical-Surgical-Pathological Conference; Auditorium.

4:00 - 5:00 Medical Journal Club; Conference Room, E5.

4:00 - 5:00 X-ray Surgery Conference; Auditorium.

Minneapolis General Hospital

9:30 - Pediatric Rounds; Elizabeth Lowry; Station J.

10:30 - Pediatric Surgical Conference; Tague Chisholm and B. Spencer; Classroom, Station I.

Friday, November 26 (Cont.)

Minneapolis General Hospital (Cont.)

12:00 - Surgery-Pathology Conference; Drs. Zierold and Coe; Classroom.

1:00 - 3:00 Clinical-Medical Conference; Thomas Lowry; Classroom, Station M.

1:30 - Pediatric Contagion Rounds; L. Wannamaker; Station K.

Veterans Administration Hospital

10:30 - 11:20 Medicine Grand Rounds; Conference Room, Bldg. I.

12:30 - Urology X-ray Conference; X-ray Department.

1:00 - CPC Conference; Conference Room, Bldg. I.

2:00 - Chest Pathology Follow-Up Conference; E. T. Bell; Conference Room, Bldg. I.

Saturday, November 27

Medical School and University Hospitals

7:45 - 8:50 Orthopedic X-ray Conference; W. H. Cole and Staff; M-109, U. H.

9:00 - 9:30 Pediatric Grand Rounds; Eustis Amphitheater, U. H.

9:00 - 11:50 Medicine Ward Rounds; C. J. Watson and Staff; Heart Hospital Amphitheater.

9:15 - 10:00 Surgery-Roentgenology Conference; L. G. Rigler, J. Friedman, Owen H. Wangensteen and Staff; Todd Amphitheater, U. H.

10:00 - 11:30 Surgery Conference; Todd Amphitheater, U. H.

10:00 - 12:50 Obstetrics and Gynecology Rounds; J. L. McKelvey and Staff; Station 44, U. H.

Ancker Hospital

8:30 - 9:30 Surgery Conference; Auditorium.

9:30 - 11:00 Medicine Grand Ward Rounds.

Minneapolis General Hospital

8:00 - Urology Staff Conference; T. H. Sweetser; Main Classroom.

9:00 - Psychiatry Grand Rounds; R. W. Anderson; Station H.

9:30 - Pediatric Rounds on all Stations; R. B. Raile.

11:00 - 12:00 Medical X-ray Conference; O. Lipschultz, Thomas Lowry and Staff; Main Classroom.

Veterans Administration Hospital

8:00 - Proctology Rounds; W. C. Bernstein and Staff; Bldg. III.

8:30 - Medical X-ray Conference; Conference Room, Bldg. I.