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INFECTIONS DUE TO STAPH. AUREUS IN A GENERAL HOSPITAL

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Through an invitation extended to me to work in the United States, an opportunity was provided of studying the present clinical significance of lesions in which *Staphylococcus aureus* is found. The investigation was carried out in the New York Hospital, and the time of year chosen was the six months comprising the late autumn, winter, and early spring of 1956-7. It was hoped thereby to include a period of the year when septic conditions were considered to be most prevalent. The object of the study was to discover: (1) the incidence of staphylococcal infections, (2) their relation to antibiotic resistance, and (3) their clinical severity. To get a general picture, recourse was had to contemporary records of the whole of the hospital, exclusive of private patients, while more particular study was made of samples obtained from two-monthly studies on each of the floors devoted to an out-patient surgical clinic, to general surgery (including fractures and plastic work), and to general medicine. For purposes of reference *Staph. aureus* in the hospital records was defined as "a typical pigmented staphylococcal colony which shows haemolysis on a blood agar plate." One should emphasize that there were two sorts of investigation going on at the same time: (1) into the records of the hospital; and (2) from direct personal observations.

Incidence

To obtain the maximum incidence of infections in patients entering hospital, daily assessments were made throughout the six-months period of investigation of both the total number of patients entering and the number admitted specifically for the treatment of an infection. These, however, although exclusive of tuberculosis, were not necessarily staphylococcal; they might be diagnosed as any type of viral or bacterial infection—for example, infectious mononucleosis, infected pilonidal sinus, cellulitis, etc. At the end of the six months the figures thus computed amounted to a total of 11,670 admissions, with 446 (3.8%) patients admitted for treatment of an infection. There was little variation from month to month in the proportion of the total which were included in the infections. The figures are given in Table I, and show that the percentage of patients admitted for treatment of an infection was not high; it could be inferred that the proportion of these patients

suffering from infections due to *Staph. aureus* was considerably lower than 3.8%.

From a study of the bacteriological records it was possible to obtain some idea of the number of infections due to *Staph. aureus* within the hospital. These also were studied daily, records being made of each patient's name, the type of lesion from which he was suffering, and the organism isolated from it. The totals were naturally higher than the totals admitted for treatment of an infection, for they included reports on subsidiary lesions—for example, a patient might be admitted for a neurological disorder and develop a boil on one of his limbs. Also, much the greatest number of records referred to nose and throat swabs, many of which were taken from children as a routine measure on admission, irrespective of whether the children had any condition suspected of being infected within the vicinity of the throat. Thus, of the 680 reports made of cultures from throat swabs of in-patients, only 260 were described in the records as associated with inflamed areas. Only these latter throat cultures were included in the number

TABLE I.—Number and Percentage of Patients Admitted Within the Hospital Diagnosed as Suffering from an Infection

	Total Patients Admitted	Total Patients Admitted for Treatment of Infection	Percentage of Total Admitted with Infection
November, 1956	2,020	73	3.5
December, 1956	1,810	77	4.2
January, 1957	2,224	80	3.6
February, 1957	1,906	67	3.5
March, 1957	2,240	77	3.4
April 1-21, 1957	1,470	72	4.9
Totals ..	11,670	446	3.8

TABLE II.—Number and Proportion of Patients Admitted Who were Suspected of Infection while in Hospital and From Whose Lesions *Staph. aureus* was Isolated

Month	(1) No. of In-Patients with Lesions Suspected of Infection	(2) No. of Patients Whose Lesions Contained <i>Staph. aureus</i>	(3) Percentage of (1) from which <i>Staph. aureus</i> was Grown	(4) Percentage of Total Patients* Admitted Whose Lesions Contained <i>Staph. aureus</i>
November, 1956	344	90	26.2	4.45
December, 1956	672	113	15.2	6.3
January, 1957	791	135	15.4	6.1
February, 1957	690	104	15.0	5.4
March, 1957	646	110	15.3	4.9
April 1-21, 1957	511	70	17.6	4.7
Totals ..	3,654	622	17.0	5.3

*From the Department of Public Health and Preventive Medicine, Cornell University Medical College, with a grant from Messrs. Lederle Laboratories Division, American Cyanamid Co.

* For total patients admitted see Table I.

examined for *Staph. aureus*. The figures for in-patients assessed in this way showed that, of the total of 11,670 patients admitted, a *Staph. aureus* organism was isolated from 622 (approximately 5.3 % of the total), a figure distinctly higher than that obtained from patients infected on admission. Table II gives the figures from which the percentages were derived.

In out-patient surgical clinics the proportion of lesions containing *Staph. aureus* was more than twice as high as that of the inmates of the hospital in general. From 1,551 patients suspected of being infected, *Staph. aureus* was isolated from 624—40% as compared with 17% for all infections within the hospital. It was not possible to gauge what proportion this was of all those admitted to the out-patient surgical clinics, for the method of recording admissions was too complicated for one worker to be able to use in the time available. It is, however, interesting to note that the percentage quoted varied from month to month, being at its highest in December, 1956 (48.7%), and decreasing to its lowest in March to April, 1957 (30.8%).

Special Studies of Incidence

These were necessarily carried out in sequence and cannot therefore be described as strictly comparable. Two months were devoted to each type of clinic, during which time the same investigator examined, among a series of consecutive admissions, every lesion in the clinic suspected of being infected, there being no selection of patients. The criteria of infection were: (1) the presence of redness, swelling, and tenderness of surrounding tissues; (2) the presence of pus or mucopus; or (3) the chronicity of an open wound, such as an ulcer, which had defeated all previous efforts to heal it. If any or all of these conditions were satisfied and it was possible to obtain a specimen, a sample was taken and investigated in a bacteriological unit specially devoted to the investigation. Thus every swab represented a lesion which was suspected of being infected. The results thus obtained were as follows:

Surgical Out-patient Clinic.—Between November 1 and December 30, 1956, 301 patients were seen and 113 were thought to have infections. Although 30 lesions were not examined bacteriologically, of the remaining 83 *Staph. aureus* was present in 70. Thus the incidence of lesions infected with this organism should have lain between 24 and 33% of admissions. A few of the abscesses when first opened were sterile on culture in spite of containing material grossly indistinguishable from pus. These patients had not received antibiotics and the sterility of their contents remains unexplained.

Surgical In-patient Clinic.—During January and February, 1957, 362 patients were admitted to the surgical floors. The number from whom swabs were taken because of suspected infection was 62, but in only 48 of these was *Staph. aureus* isolated—an incidence of 13.3%.

Medical In-patient Clinic.—From March 1 to April 20, 1957, 217 patients were admitted to the medical floors. Those in whom a lesion was suspected of being infected

TABLE III.—Incidence of Lesions, Among Patients Admitted, From Which *Staph. aureus* was Isolated

	Time	Total Admitted	No. with <i>Staph. aureus</i>	Percentage with <i>Staph. aureus</i> of Total Admitted
Whole hospital, in-patients	Nov. 1, 1956–April 20, 1957	11,670	622	5.3
Surgical out-patient clinic	Nov. 1–Dec. 30, 1956	301	70 (+30 or less)	24 to 33
„ in-patient „	Jan. 1–Feb. 28, 1957	362	48	13.3
Medical „ „	Mar. 1–April 20, 1957	217	37	17

numbered 55; *Staph. aureus* was isolated from 37, the incidence during this time being, therefore, 17% of admissions.

For comparison, the figures obtained from the hospital records and from each type of clinic are given in Table III. From this it is seen that a much greater incidence of staphylococcal infections was obtained from direct observation than from the usual methods of examination.

Relation of Staphylococci Found to Antibiotic Resistance

A short and easily applied method of estimating sensitivity was employed, so that a test was also made of the practicability of testing antibiotics before treatment. The staphylococci included were limited to those which were haemolytic, had the ability to ferment mannite, and exhibited coagulase activity against pooled human plasma. Observations were also made on pigment production, but very few among those tested did not produce a yellow colour. The antibiotics tested were those in common use—penicillin, streptomycin, chloramphenicol, oxytetracycline and tetracycline, erythromycin, novobiocin, and, at a later stage, bacitracin. Staphylococci were picked from a surface colony appearing on a blood-agar plate which had been inoculated directly with material from the lesion. The surface of a second blood-agar plate was heavily seeded from this single colony emulsified in saline. "Multidiscs" were then placed directly on the agar surface. Additional multidiscs containing novobiocin, 5 µg. per ml., and bacitracin, 2 units per ml., were also used, but the poor diffusibility of the latter prevented its results from being assessed satisfactorily. The plates were incubated at 37° C.

Strains were considered sensitive when a ring of inhibition approximately 20 mm. in diameter was produced within 24 hours' incubation on a blood-agar plate. Occasionally a few minute colonies would appear, growing on the area of inhibition, but these were disregarded for practical purposes. The figures for each clinic are given in Table IV. It will

TABLE IV.—Numbers of Strains of *Staph. aureus* Found Sensitive to Antibiotics

Clinic	Total Strains Tested	No. Sensitive To						
		Penicillin	Streptomycin	Chloramphenicol	Tetracyclines	Erythromycin	Novobiocin	None
Surgical out-patients	55	20	43	47	35	46	45	0
in-patients	48	8	20	47	16	40	47	0
Medical „	20	5	11	17	8	16	17	0
Totals ..	123	33	74	111	59	102	109	0

be seen that out of 123 strains obtained from the 230 infected lesions found among 880 patients none was found to be resistant to all six antibiotics, and the antibiotics to which most strains were susceptible were those least often used in hospital. Tests for susceptibility to bacitracin were carried out on 60 strains. A well-defined but narrow ring of inhibition was produced with 39 of these.

It is of interest to note that the pattern of resistance during the earliest three months of the study remained nearly uniform; the majority of strains were susceptible *in vitro* to chloramphenicol, erythromycin, and novobiocin, but resistant to penicillin, streptomycin, and the tetracyclines. During February, 1957, however, when erythromycin was used more frequently than before on the surgical in-patient floors, the number of strains found resistant to this antibiotic mounted. In fact, on four occasions when serial cultures were made, beginning before erythromycin treatment, the *Staph. aureus* isolated some days later was found to be resistant to this antibiotic. This finding is in agreement with that of Haight and Finland (1952). It is also of interest that every strain found sensitive to penicillin was also inhibited by every other antibiotic tested.

*Obtained from Consolidated Laboratories Inc. Each multidisc contained 10 µg. per ml., except that for penicillin, whose concentration was 1.5 units per ml.

From Table IV it can be seen that penicillin-sensitive strains were isolated in a greater proportion of the total obtained from surgical out-patients than from the in-patients on either the surgical or medical floors. The out-patients were a mixture of those coming direct from outside and those referred to the clinic after having received treatment within the hospital. It was hoped that, by analysing only those cultures made from freshly opened lesions, some light might be thrown on the incidence of penicillin-susceptible strains in patients who had not been treated in hospital. The results, however, indicated little, for not only was the number small (14) but the staphylococci isolated were evenly distributed between strains susceptible and those insensitive to penicillin.

Clinical Significance of *Staph. aureus* in Lesions

From the bacteriological records of the hospital it could be found what type of lesion was most commonly associated with the bacterium in question and from which the staphylococcus was most commonly isolated in pure culture. A survey of cultures made from sputa, throat swabs, infected eyes, abscesses, infected bursal fluid, extremities, sinuses, stools, dermatitis, cellulitis, omphalitis, infected ulcers, wounds (operative and accidental), and from biliary drainage, ani, vaginae, and cervixes, showed clearly that there were certain conditions in which *Staph. aureus* was most often found alone. Table V gives these types of lesions and the frequency with which *Staph. aureus* was isolated from them.

In contradistinction to the figures in Table V the number of times *Staph. aureus* was found alone in cultures from throat swabs or blood was very much lower. 1,418 throat

TABLE V.—*Infected Conditions in Which Staph. aureus Predominated*

Type of Lesion*	Total	No. with Pure Cultures of <i>Staph. aureus</i>	No. with Mixed Infections Including <i>Staph. aureus</i>	No. Infected But With no <i>Staph. aureus</i>	No. in Which No Growth was Obtained
Boils, abscesses, and carbuncles ..	228	144	23	41	20
Cellulitis ..	15	11	1	2	1
Infected extremities ..	88	44	27	16	1
Infected eyes (mainly anterior chambers)	84	31+13†	9+6†	9	16
Infected wounds ..	171	63	43	50	15

* The different categories are mutually exclusive.

† These figures denote the number of times *Staph. albus* was isolated.

swabs were cultured, and, though *Staph. aureus* was found in these 645 times, it grew in pure culture nine times only. Similarly, a low proportion of *Staph. aureus* was found among 396 blood cultures; from these staphylococci were isolated 20 times and from the living body 10 times only.

Severity of *Staph. aureus* Infections

It was only possible to adjudge the seriousness of these infections from direct observation. For this purpose the special studies provided the best means of estimating how much damage was associated with *Staph. aureus*. In none was the organism isolated from the blood. Apart from this the studies bore out the findings of the bacteriological records in the type of lesion expected to be associated with *Staph. aureus*; most were superficial lesions such as boils, stitch abscesses, pulp infection, or paronychia. Often a post-operative sinus would appear as an outlet for material which looked brown and grumous, and might easily be ascribed to the breaking down of a haematoma. Staphylococci were almost always associated with these, but it was extremely difficult to assess their potentiality for harm. Wounds with such sinuses, for prophylactic reasons, were usually opened down to the underlying fascia for their entire length so as to enable easier egress of the infected fluid. Though the wound looked unpleasant, its healing was progressive and the patients suffered no systemic effect after its opening.

Other conditions in which *Staph. aureus* was found included dermatitis, pressure sores, chronic ulcers, compound fractures, otitis, infected glands, and cellulitis when it had reached a stage at which fluctuant areas could be incised. A number of such cases were seen which subsided under antibiotic therapy well before this stage; their bacteriology then had to remain in doubt. *Staph. aureus* accompanied by other organisms was also found in sputa of patients suffering from pneumonitis following bronchitis, carcinoma, or chronic conditions such as bronchiectasis. It was thus not possible to ascribe any part of the patient's illness to this organism alone. Conditions from which it was isolated in pure culture gave some idea of its pathogenicity. In pure culture it was undoubtedly associated with the presence of creamy pus, as, for instance, the purulent exudate from a chronic empyema sinus, abscess cavities, and exposed bone. The severity of these infections in terms of danger to life was not great, nor could necrotic tissue be excluded as the origin of the pus. There were, however, three very ill patients whose cases require more detailed description.

One patient, with rheumatoid arthritis, whose abscess developed about her hip-joint after injections of cortisone, had fever so long as the pus, containing penicillin-resistant staphylococci, was enclosed, but, once opened, the abscess cavity ceased to cause her disturbance except while it was being packed. She received no antibiotics during the period of observation owing to previous allergic reactions to them.

A second patient who entered hospital was operated on for removal of an iliac thrombosis. In spite of this, gangrene steadily ascended her limb till successive amputations ended in a disarticulation at the hip. *Staph. aureus* was repeatedly isolated from her gangrenous tissues, but there was no frank suppuration or evidence of inflammation. Her vascular condition seemed sufficient reason to account for her serious condition.

A third patient died. She entered hospital at the age of 80 for treatment of diverticulitis by resection of her gut in the ileocaecal region. Owing to the persistence of symptoms, a further resection of the sigmoid was performed, and a gastrostomy. A subtotal gastrectomy was later undertaken owing to much bleeding from the gastro-intestinal canal and the presence of multiple ulcers on her stomach surface. Death eventually supervened, but, though a *Staph. aureus* had earlier been isolated from a rash round one of her wounds, there was no sign of peritonitis until necropsy, when perforation of her colon was also observed. *Proteus vulgaris* had been found in the abdominal wound connected with the gastrostomy, and after she had died it was isolated, together with *Staph. aureus*, from her peritoneal cavity, blood, and lungs. Thus, though *Staph. aureus* was present in the pathological foci, death could not with certainty be ascribed to it alone.

Discussion

In considering the findings reported here one should remember that this was primarily a clinical investigation. Barring those from whom routine nose and throat cultures were made, patients were first examined, and only after some type of infection had been diagnosed were specimens sent for bacteriological examination from any inflamed and accessible area. The ubiquitous presence of staphylococci (Blowers, Mason, Wallace, and Walton, 1955; Howe, 1954, 1956; Hare and Thomas, 1956; Shooter, Taylor, Ellis, and Ross, 1956; Shooter, Griffiths, Cook, and Williams, 1957) would not necessarily account for their appearance in these lesions. Inasmuch as the special studies bore out the findings obtained from the hospital records, it may be as well to mention that every care was taken not to contaminate the culture swab by contact with the patient's skin.

Thus it would seem fair to associate *Staph. aureus* with the types of infection described here, if not definitely to attribute them to its presence. The irritation caused by a tight suture, for instance, could readily cause a stitch abscess or some ulceration without any demonstrable presence of *Staph. aureus*. Was its presence therefore to be considered as causal when the two were found together? In the same way, when post-operative haematoma eventually found their way to the surface and began to exude

through a sinus, some doubt must be cast on the assumption that this could be attributed to the presence of *Staph. aureus*. Nevertheless, though little clinical evidence of serious pathogenicity could be seen in the staphylococci, susceptible or insusceptible to the antibiotics used in the patients' therapy, their presence in greater proportion among patients while in hospital than when entering (5.3% as compared with less than 3.8%) indicates that these same patients were not free from risk of superimposed infection. For example, a patient with a necrotic pulp infection with osteitis, whose culture when first examined revealed only a Gram-negative rod, was admitted for further surgery, and, in spite of the administration of erythromycin, four days later a *Staph. aureus* was cultivated from the wound.

It was not a function of the investigation to examine the opportunities for added infection which arose in this hospital, but it was observed that, so far as arrangements on the different floors were concerned, risk from infection by contact or through air currents was reduced to a minimum by having no more than four patients to a ward, the provision of washing facilities for dressers and others in each ward, and the covering of sterile instruments and towels, which were wrapped separately for each dressing. Nurses seldom touched the dressings, which were left to the interns, who had been instructed in a no-touch technique. Since the incidence of *Staph. aureus* in lesions found on the medical floors was higher, in the special study, than on the surgical in-patient floors, added infection could not be attributed reasonably to faulty dressing technique.

Apart from the presumptive evidence of added infection within the hospital, other points of interest arise from this survey. None of the staphylococci included in the special studies was persistently resistant to every antibiotic against which it was tested. It would seem, therefore, to be to the advantage of the patient, when culture of his lesion reveals a pure growth of staphylococcus, to test its susceptibility to antibiotics. Though not infallible, the tests have shown a fair correlation between sensitivity *in vitro* and clinical response (Rodger, Branch, Power, Starkey, Gregory, Murray, and Harrop, 1956). Such tests when carried out with multidiscs on blood agar can give an answer within eight hours to two days, according to whether the test is done on the primary or on a subculture. This does not seem a long time to wait. In the meantime the medical attendant prescribes an antibiotic till he learns from the result of the test that he is confirmed in his choice or that another is more suitable.

From the appearance of the staphylococcal infections in the special study it was difficult to believe that they were of serious import. When dealt with effectively by antibiotic therapy at their earliest sign or by surgery when pus had collected, the period of convalescence was mainly occupied in progressive healing. This applied to those incisions in which no other secondary infection took place.

No mention has been made here of neonatal staphylococcal infection, staphylococcal infection of lungs and bronchi, or of enterocolitis. The first may be a primary infection, the infant having as yet developed little immunity to bacterial invasion; thus it may succumb to an organism of relatively low virulence (Beaven and Burry, 1956; Wysham, Mulhern, Navarre, LaVeck, Kennan, and Giedt, 1957). In the reports obtained during the six months' survey at the New York Hospital there were none in which *Staph. aureus* was cultured in pure growth from either sputa or faeces. Yet severe infections of lungs and intestinal canal are attributed to the staphylococcus—for example, the pneumonias described by Hausmann and Karlish (1956) and the diarrhoeas by Cook, Elliott, Elliot-Smith, Frisby, and Gardner (1957), and by Turnbull (1957). In considering the origin of such serious conditions one should take into account that, when "other pathogens" are also present, or where little or slow response is made to administration of an antibiotic to which the staphylococcus isolated is sensitive, one's attribution of the disease in question to the staphylococcus can be called in question. In any event, as

infections by *Staph. aureus* do not lend themselves to the fulfilment of all of Koch's postulates, every care should be taken to exclude any other factor in the pathogenesis of the lesion being studied.

From this point of view attention should be drawn to the fact that a high proportion of the patients specially studied had other debilitating conditions predisposing to infection, such as diabetic gangrene, carcinoma, acute pancreatitis, paraplegia, multiple injections of cortisone, arteriosclerosis, or other vascular conditions obliterating the blood supply to a part. If these were not present, their age, often 65 to 85 years, militated against the patients' resistance to bacterial invasion. These conclusions are in conformity with the opinions expressed by McDermott (1956a, 1956b).

Summary

Of 11,670 patients admitted to the New York Hospital during the six months between November 1, 1956, and April 20, 1957, 3.8% were admitted for treatment of some kind of infection, the inference being that those whose infections were staphylococcal comprised a still smaller proportion of the total admitted.

During their stay in hospital, 5.3% of these patients suffered from an infection from which *Staph. aureus* was isolated. From comparison of these percentages it is assumed that many of these infections were acquired in hospital. The incidence of staphylococcal infections within the hospital remained fairly uniform from month to month, but among surgical out-patients it was at its height in December, 1956, and January, 1957.

A special study carried out in consecutive patients over three periods, each of two months, on the surgical out-patient, surgical in-patient, and medical in-patient floors supported these conclusions and showed that none of the staphylococcal strains isolated from 123 patients were persistently resistant to each of seven antibiotics against which they were tested.

When *Staph. aureus* was the only organism cultured from infected lesions and the patient did not suffer from some condition predisposing to infection, there was little evidence that, effectively treated, these conditions had serious consequences.

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