that stagnation and infection in the diverticula may have been the most important factor in producing the small-intestinal dysfunction.

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ANTIBIOTIC SENSITIVITY SPECTRA THEIR USE IN INVESTIGATING EPIDEMICS

BY

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Staphylococcal infections in hospital wards are the cause of considerable morbidity and mortality, and for many years bacteriologists have been devising methods to facilitate the detection of sources of infection. One of the difficulties has always been the fact that coagulase-positive staphylococci are commonly found in the upper respiratory tract and skin of apparently healthy people, and it is not practicable to eliminate all of these. "Unless the epidemic strain has some special characteristic, it is impossible to decide whether, for instance, a carrier of the species concerned is to be incriminated. It is here that the definition of individual 'types' within species has been found so valuable" (*Lancet*, 1947). Serological typing and phage-typing were used by Allison and Hobbs (1947) in their brilliant investigation of neonatal infections. Phage-typing has indeed been a new and successful weapon in tracing the sources of wound infections, but it requires some experience, and it is not used by many routine laboratories. When we were faced with investigation of an epidemic of wound infections in our surgical wards* it was thought that antibiotic sensitivity patterns might help to determine the cause of the trouble.

Investigation

Between September 12 and 24, 1953, five patients developed wound abscesses seven to ten days after an elective operation. The pus from the wounds yielded pure cultures of *Staphylococcus pyogenes*, and these infections appeared to be confined to patients operated on by one surgical team.

Nose and throat swabs were taken from all the nursing staff in the theatre and wards (22 in all), from the anaesthetist, and from two members of the surgical team. (The third member of the surgical team was away for three weeks when this investigation was started, but he had been present at all the operations done on the cases that became infected.) Coagulase-positive staphylococci were found in over half of the nursing staff. It was thus most desirable to determine whether all these staphylococci belonged to the same strain. Sensitivities to penicillin, streptomycin, chloramphenicol, chlortetracycline ("aureomycin"), and oxytetracycline ("terramycin") were determined with standard pads of these antibiotics on blood-agar plates, and three different patterns were obtained from the nursing staff (see Table I). Although the organisms derived from the

wounds all gave the same pattern (Table II), this did not coincide with any of the patterns derived from the nursing staff. The pattern, however, did coincide with that derived from organisms obtained from the nose and conjunctivae of

TABLE I.—*A, B, and C are Antibiotic Sensitivity Patterns of Strains of Staph. pyogenes Obtained from the Nursing Staff. All Coagulase-positive Staphylococci Derived from Them Belonged to One of these Three Strains*

Antibiotic	A	B	C
Penicillin	++	—	—
Streptomycin ..	+	+	+
Chloramphenicol ..	+	+	+
Aureomycin	+	+	+
Terramycin	+	+	—

++ = Very sensitive, + = sensitive, — = resistant.

TABLE II.—*Sensitivity Spectra of Strains of Staph. pyogenes Obtained from the Pus of the Patients (D), and the Nose and Conjunctivae (E and F Respectively) of the Missing Member of the Surgical Team*

Antibiotic	D	E	F
Penicillin	—	—	—
Streptomycin ..	—	—	—
Chloramphenicol ..	—	—	—
Aureomycin	+	+	+
Terramycin	+	+	+

+ = Sensitive; — = resistant.

the missing member of the surgical team (Table II), who had just returned from his holiday at this stage of the investigation. (While on holiday he had suffered from acute blepharitis and conjunctivitis.) Intensive antibiotic therapy was given and his infection was eradicated. There have been no further staphylococcal wound infections in the wards of his surgical team. It should be added that none of the patients operated on while he was on holiday developed staphylococcal wound infections.

Discussion

The value of *in vitro* sensitivity tests in the treatment of infections is still a somewhat controversial subject. The same can be said of our views on the action of antibiotics in their role as antibacterials. The most widely accepted and most plausible theory seems to be the one which ascribes to the antibiotics a power of interfering with some enzyme system which is essential either for bacterial survival or for their multiplication. Where a species of micro-organism displays great variations in sensitivity to an antibiotic, such as, for instance, *Staph. pyogenes*, the organisms that are sensitive would rely for survival or multiplication on some enzyme system which is interfered with by the antibiotic—for example, by poisoning, competition, or blocking—and the ones that are resistant either do not require this enzyme system or have developed an alternative one. It would seem to be a reasonable assumption that a variant strain of one species relies in its metabolism on the same or similar enzyme systems. Antibiotic sensitivity patterns may therefore be useful in tracing strains of bacteria and in finding sources of infection. The determination of antibiotic sensitivity spectra is a simple procedure that can be carried out in routine bacteriological laboratories, and if it can be relied upon to separate different strains of a species of micro-organism this should provide a useful screening test for sources of infection.

The absence of further wound infections after eliminating virulent organisms from the eyes and respiratory tract of a member of the surgical team is, it is felt, strong evidence that he indeed was the source of infection, as is the fact that none of the patients operated on during his absence developed staphylococcal wound abscesses. Antibiotic sensitivity patterns suggested that the staphylococci in the wounds and in his nose were the same strains, and thus showed us where to find the cause of our trouble and how to deal with it.

Phage-typing was carried out on some of the cultured strains by the Staphylococcal Reference Laboratory, Colindale. This showed that staphylococci with different sensitivity patterns were of different phage types and that those with the same patterns were of the same phage types (Table III). That there is a close analogy between phage

TABLE III.—*Phage Patterns of Staphylococci Obtained from the Nursing Staff (A, B, C), the Infected Wounds (D), and the Surgeon (E and F)*

Phage Patterns	A	B	C	D	E	F
Diluted	52A v.w.	—	—	—	—	—
Undiluted	52/52A/79	73+	29+	75+W	75+W	75+W

type and antibiotic sensitivity is also suggested by investigations on penicillin-resistant strains and their phage types (Selbie, 1953). In the case of erythromycin- and carbomycin-resistant staphylococci there would appear to be no correlation between antibiotic resistance and phage type (Hobson, 1954), although the author does not state whether the phage type was checked after the development of antibiotic resistance.

Sensitivity spectra, using penicillin, streptomycin, chloramphenicol, and the tetracyclines, certainly seem to be of use in the determination of strains of staphylococci, and they were of considerable value in rapidly tracing the source of wound infection in this instance.

I wish to thank Mr. Weait and Mr. Oke, who did most of the technical work and played a vital part in this investigation, Mr. D. Morris and his surgical team for asking for this investigation to be carried out and for supplying the specimens of pus, and Dr. W. F. Hamilton for permission to publish. Dr. R. E. O. Williams of the Streptococcus and Staphylococcus Reference Laboratories very kindly did the phage-typing.

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Medical Memoranda

Two Cases of Favism in Israel

Favism is an acute febrile haemolytic anaemia caused by an unknown factor present in *Vicia fava*, the broad-bean. The disease is contracted by ingestion of the fruit, leaves, roots, stem, or flowers of this plant. It has been said that even the pollen can give rise to the condition. The toxic factor is resistant to weather and heat, and is transmitted via the milk of both the cow and the nursing mother.

No age is exempt, but favism occurs chiefly in children, and males are affected more than females. Some hereditary factor may be present, as the condition has been seen in Israel only among the Oriental population—the Sephardic and Yemenite Jews and the Arabs. So far no authentic case has been reported in the European or Ashkenazi communities. There is a definite seasonal incidence. Most of the cases occur in spring, during February, March, and April, when the broad-bean blossoms. Favism has an affinity with two other haemolytic anaemias—namely, Bagdad spring anaemia and the acute febrile haemolytic anaemia of Lederer. The former, an acute haemolytic anaemia, occurs in Bagdad during a few weeks in the spring, and is said to be due to an allergic reaction to contact with flowers (*Verbena hybrida*) and young fruits. Lederer's anaemia, which gives rise to a similar clinical picture, is said to be due to an allergic response to the streptococcus, the pneumococcus, or the dysentery bacillus. It occurs chiefly in children. The following two cases of favism occurred in Beerva, a Yemenite village situated some nine kilometres from Acre in Western Galilee, Israel.

CASE 1

A boy aged 12 suddenly fell ill on the night of April 17, 1952. At 7 p.m., after supper, he felt sick and vomited twice. Up to that time he had been perfectly well. A little later he passed a small amount of "bloody" urine and felt very faint; at about 9.30 p.m. he had a fit (probably due to acute central anoxia). Some relatives obtained transport and called me, and I reached his bedside at 10.15 p.m. The boy was shocked, very pale, and semicomatose. Ocular and tendon reflexes were present and brisk, but there was no plantar response. The limbs were twitching spasmodically. There was no neck rigidity. He was sweating profusely and the extremities were cold. The pulse was small and thready, with a rate of 140 a minute, and the tongue dry and coated. There were no abnormal signs in the chest. The liver was palpable two fingerbreadths below the costal margin, but the spleen could not be felt. Rectal temperature was 100.4° F. (38° C.). The urine was of a deep port-wine hue, and almost opaque against the light. There was no history of malaria or intake of any drugs. The only positive fact in the history was that the patient, like everyone else in the village, had been eating broad-beans for the past two weeks.

After receiving 2 ml. of nikethamide intramuscularly, the patient was taken to the Haifa Government Hospital, arriving there 45 minutes later. His haemoglobin was found to be 3 g. per 100 ml. (Sahli). He was transfused immediately with 500 ml. of bank blood, and the next morning his haemoglobin had risen to 5 g. per 100 ml. A further 750 ml. of blood was given, and the haemoglobin rose to 7 g. per 100 ml. and the erythrocyte count to 2,360,000 per c.mm. The results of other investigations were:—Urine: acid, albumin +++, haemoglobin +++, and crystals of haemin +++ in the deposit. W.B.C., 22,000 per c.mm. (polymorphs 80%); serum bilirubin, 10 mg. per 100 ml.; thymol turbidity and Takata-Ara, negative; Weltmann, 8 units; plasma proteins, 7.6 g. per 100 ml. (albumin/globulin ratio 1.81:1); blood urea, 100 mg. per 100 ml.; glob cholesterol, 125 mg. per 100 ml. Mantoux, negative at 1:1,000.

Recovery was uneventful and the patient was sent home after eight days, on continued treatment with ferrum redactum 3 g. daily and a full diet.

CASE 2

This boy, also aged 12, became ill 10 hours after Case 1. If anything, his condition was even worse. His haemoglobin level was 3.5 g. per 100 ml. when he left for the hospital, but by the time he reached Haifa (within one hour) it had fallen to 2 g. per 100 ml. Ultimately he also recovered after two blood transfusions, and was discharged home after two weeks. Likewise in his history there was nothing relevant, except that he also had been eating broad-beans.

COMMENT

No other case of favism occurred in the village during the year (1952). Once the condition had been recognized the villagers were warned neither to eat broad-beans nor to bring them into their homes, and particularly to keep their children away from them. One does not know how far this affected the incidence of the disease, as up to then they all had been eating the bean, cooked as well as uncooked. But the fact remains that none of the other 150 children developed the disease.

Favism has been confounded with divers conditions such as food-poisoning, acute haemorrhagic nephritis with uraemia, blackwater fever, drug haemolysis, and pneumonia. Toxic haemoglobinuria due to drugs such as quinine, the sulphonamides, potassium chlorate, nitrites, pyridine, the aniline drugs, etc., also enters into the differential diagnosis. Particularly in Israel, especially in the malarious districts of upper and eastern Galilee, one must rule out the possibility of blackwater fever. Acute infections such as typhus,