SALM. TYPHI OSTEOMYELITIS

REPORT OF A CASE, WITH A REVIEW OF THE LITERATURE

BY

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A case of osteomyelitis due to *Salmonella typhi* seen recently, demonstrating many of the characteristic features of that uncommon condition, has prompted publication of this review.

Case Report

A merchant seaman aged 22 was admitted to an isolation hospital on November 24, 1948, having had diarrhoea for four weeks. He was found to have typhoid fever. The urine and faeces yielded *Salm. typhi*, and the Widal reaction was positive. He had never had prophylactic inoculation, and the disease was severe. Chloramphenicol was not then available. By December his general condition had much improved, but aching pain had developed in the right middle finger and left upper thigh. However, these pains subsided, and he was discharged on January 20, 1949, in good general condition, the urine and faeces being negative on culture.

Painful swelling of the right middle finger recurred a few weeks later, and he was admitted to Greenock Royal Infirmary with a provisional diagnosis of typhoid osteomyelitis. X-ray examinations showed a rounded cavity in the middle phalanx without periosteal reaction (Fig. 1). At operation the cavity was curetted, and pus yielded *Salm. typhi* on culture. Primary healing followed.

FIG. 1.—A focus of *Salm. typhi* osteomyelitis in middle phalanx of finger. Positive pus was recovered.

FIG. 2.—A focus of *Salm. typhi* osteomyelitis in mid-shaft of right tibia. This lesion subsided without pus formation.

FIG. 3.—A focus of *Salm. typhi* osteomyelitis at junction of middle and lower thirds of left radius. Positive pus was recovered.

On April 25, 1949, readmission was necessary because of severe aching pain in the right tibia, both great toes, right temporomandibular joint, upper right femur, and left seventh rib (see Fig. 4). There was high fever and collapse of the lower lobe of the left lung. X-ray examination of the affected bones was negative, except that in the right tibia a small rarefied area was seen in the middle third (Fig. 2). The spleen was not palpable and blood culture was negative. The condition resolved under treatment with sulphathiazole and penicillin, and all the bone foci subsided without pus formation.

On August 24, 1949, he was readmitted with a painful swelling of the left lower radius (Fig. 3). At operation a "collar-stud" abscess was opened and curetted. The pus again yielded *Salm. typhi*, and healing was again by first intention. On October 4 the Widal reaction showed *Salm. typhi* (H) agglutinated at 1 in 60 and no agglutination with *Salm. typhi* (O); on November 21 *Salm. typhi* (H) agglutinated at 1 in 240. By this time chloramphenicol had become available and a course of it was given, using the high dosage recommended by Smadel *et al.* (1949)

designed to prevent relapses in acute typhoid fever: a total of 33.5 g. was given over a period of 19 days. The patient was seen again in December and a herniorrhaphy was carried out: he was then free of bone pains, and remained so until May, 1950, when a painful swelling developed on the right tibia but subsided in a week without pus formation.

At this stage the patient returned to sea and was not seen again until August, 1951, when he reported with a fluctuant swelling in the left temporal region of six months' duration (Fig. 4). A subperiosteal abscess was opened and curetted, the pus again yielding a pure culture of *Salm. typhi*. The organism showed a marked susceptibility, *in vitro*, to "aureomycin," and a course of that antibiotic was therefore given.

FIG. 4.—*Salm. typhi* osteomyelitis with multiple foci, showing sites and dates. The responsible organism was recovered at the sites underlined.

Review of Literature

Typhoid osteomyelitis was first described by Maisonneuve (1835). After the discovery of *Salm. typhi* by Eberth in 1881, Ebermaier isolated the organism in pure culture from two cases of osteomyelitis. Chantimusse and Widal in 1887 recovered the organism from the marrow following inoculation into rabbits. Quincke and Stuhlen in 1894 recovered the organism from the marrow at necropsy in nine typhoid fever victims. The most comprehensive review of the subject is that of Winslow (1923).

Pathology and Clinical Features

In the initial bacteraemia of typhoid fever bone-marrow cultures are often positive, and the value of marrow culture as a diagnostic measure has recently been confirmed by Hirsowitz and Cassel (1951), who obtained a positive result in 18 of 28 cases (64.3%). The marrow forms a suitable nidus for continued survival of the organisms in a dormant state, from which a recurrent bacteraemia may at any time give rise to osteomyelitis.

In view of the frequency of positive marrow cultures it is surprising that the incidence of osteomyelitis after typhoid infection is so low. Thus Murphy (1916) found an incidence of only 0.82% in 18,000 cases, and Winslow (1923) a total of only 101 proved cases. This low incidence is even more surprising when it is remembered that until recently no specific treatment was available for typhoid fever. It is possible that the true incidence may be higher than usually supposed, and that some cases escape notice because the onset is delayed for years after the enteric infection, which may have been mild, forgotten, or not diagnosed as such, or because the clinician, in the case of osteomyelitis, accepts a laboratory report of "coliform organisms" without further investigation. This last point is well brought out in the case reported by Lever and Barber (1945). On the other hand, it is possible that some cases described before the present century may, owing to inadequate bacteriological methods, have been wrongly attributed to typhoid.

The onset of osteomyelitis is, as in the present case, usually in convalescence, and of the reported cases only

about 25% occur later. The disease is, however, well known for its tendency to appear for the first time many years after the enteric infection. Striking examples of this include those of Tubby and Hicks (1913), 13 years; Brock (1935), 14 years; Wardle (1935), 10 years; Lever and Barber (1945), 33 years; and van Dyk (1933), 24 years.

There is no doubt that injury is an important localizing and precipitating factor, particularly in cases in which the onset of bone involvement is delayed for years after the initial infection. The cases of Wardle (blow by hockey-stick), van Dyk (kick by horse), and Lever and Barber (repeated head injuries from low roof) demonstrate this. A bone operation may likewise be a precipitating factor, as in the case reported by Schein (1942). Ritter and Bochner (1936) described two cases (husband and wife) infected from the same source at the same time, both of which developed bone lesions. There is, however, no real evidence to suggest that a particular strain of organism accounts for the cases with bone involvement.

The disease affects mainly the long bones. Thus of 101 cases the tibia was involved in 56, the femur in 27, the ribs and costal cartilages in 27, and the skull in 11 (Winslow, 1923). The present case shows the tendency of the disease to attack the long bones, ribs, and skull, but involvement of the phalanges has also been a noticeable feature, and this appears to be only the third recorded case of involvement of the phalanx. Multiple foci occurred in this case, but are found in only 5% of cases (Veal, 1939).

The diaphysis is affected rather than the metaphysis, and the process begins under the periosteum, which becomes thickened and raised by sero-sanguineous fluid or pus. The process may subside or spread through the cortical bone of the medulla, forming a "collar-stud" abscess, partly within and partly without the bone, as was found on two occasions in this case. Sequestration is not an obvious feature, and sequestra are always very small (Winslow, 1923). Microscopically the pus may be full of small sequestered spicules (Veal, 1939). When the skull is involved a Pott's "puffy tumour" with extradural abscess may form, as in the case of Lever and Barber (1945).

After adequate surgical treatment sinus formation is rare, but when it does occur it is noteworthy that the organism may persist in pure culture over a prolonged period (Winslow, 1923). The patient with a persistent sinus is a danger to the public health, and Bigelow (1912) reported that three people were infected from a sinus. It is also possible that, in the recurrent bacteraemia postulated in this disease, organisms may also be excreted in the urine.

The severity of the osteomyelitic process is very variable, although normally slight; it bears no relation to the original enteric infection. Fatalities are rare and have been reported mainly in Continental literature up to 1916. Winslow (1923) mentions that the periostitis may result in formation of exostoses, and that persistent bradycardia may occur. Neither of these was noticeable in the present case.

Treatment

Keen (1898) stated that surgical excision and closure without drainage, as against the drainage and packing methods then used in ordinary osteomyelitis, was the treatment of choice; and despite its antiquity that statement remains accurate. First-intention healing was obtained on three occasions in the present case, and also in the cases of Brock (1935) and Ritter and Bochner (1936) in rib and costal cartilage, and of Wardle (1935) in the tibia. Primary healing is especially desirable in view of the risk to the public health of a persistent discharge.

The typhoid spine is reported to clear up with prolonged immobilization (Veal, 1939), and the same author rightly insists on the necessity for primary closure of the infected joint.

In the past, treatment by vaccines, both stock and autogenous (Garr, 1927), and by bacteriophage, both locally and intravenously (MacNeal, 1932), have been used.

The above case is one of the few, so far published, treated by chloramphenicol. Good results from this antibiotic have been claimed in the U.S.A. by Morse and Geiser (1950), in France by Barcat *et al.* (1950), and in this country by Gilles (1951) and Morgan (1951).

The present case relapsed after seven months, while Morgan's case has remained healed for a year. Morse and Geiser followed their case for only five months before reporting it. In view of the known natural history of the disease, and the relapses in the present case, it is unlikely that any of these cases are permanently cured. Gilles and Morgan both used chloramphenicol locally, and believe that healing of the wound was assisted. In the present case primary healing was obtained by surgery. Much should not be expected of chloramphenicol in this disease, since an apparently adequate course does not always prevent relapses in acute enteric fever (Douglas, 1950), and failures are usual in chronic biliary carriers (Woodward *et al.*, 1950). It appears clear that while chloramphenicol is helpful in dealing with the individual bone focus it is not curative, and its importance will lie in the more effective treatment of the initial enteric infection.

In the present case there have been no biliary symptoms, the faeces have been repeatedly negative, and cholecystectomy has not been advised.

Summary

A case of *Salm. typhi* osteomyelitis, with multiple foci, showing many of the characteristic features of typhoid is recorded and the relevant literature reviewed.

Adequate surgical treatment of the individual focus remains the only effective treatment. Chloramphenicol failed to prevent a recurrence.

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Continued record breaking in athletics, and not least in this year's Olympic Games at Helsinki, has prompted *World Sports*, the journal of the British Olympic Association, to persuade Professor A. V. Hill, F.R.S., to answer the question "Where is the limit?" in its August issue. In what he calls speculations, Professor Hill discusses whether there are physiological and anatomical limits to faster running and higher jumping, and begins by declaring that the human race is not improving, and it is very doubtful if the present generation of middle- and long-distance runners have a better supply of oxygen to their muscles than the best of their fathers and grandfathers. The secret lies in the efficiency with which muscular energy is used. The greatest efficiency is to run at a constant speed, and unfortunately high speeds spend proportionately much more energy than low ones. Thus in running a mile in four minutes a man who could cover each quarter-mile in exactly 60 seconds would use 4% less energy than a man who lapped 57, 63, 67, and 53 seconds per quarter-mile.