

Investigation of Blood.—During the period the child was under investigation the haemoglobin varied from 72% (10.7 g.) to 82% (12.1 g.) and the erythrocytes from 5.1 to 5.3 millions. Reticulocytes remained at 0.5%. The white cells varied from 8,000 to 13,000, with a normal differential count. The blood Wassermann reaction and Kahn test were repeatedly negative. The Donath-Landsteiner test was positive, serum haemolysins of the "cold" type being present to a titre of 1 in 4. An auto-agglutinin was present in the serum to a titre of 1 in 256 at 2–5° C. No agglutination occurred at 37° C. or at 20° C. (room temperature). When the tubes containing the "compatible" red cells which had been agglutinated by the patient's serum at 2–5° C. were warmed, complete and even dispersal of the cells occurred. No "incomplete" antibodies were detected, a direct Coombs test on the patient's red cells being negative. The acid haemolysis test (Ham, 1939) was negative. Oxyhaemoglobin and methaemalbumin (Schumm's test) were present in the serum during and shortly after an attack. The osmotic fragility of the red cells was normal.

Rosenbach Test.—While in hospital the child was encouraged to go outside lightly clad in the hope that a paroxysm might be induced; none occurred, probably owing to an improvement in the weather conditions. It was therefore decided to induce an attack artificially by a modified Rosenbach test in order to confirm the diagnosis.

Blood was taken from an arm; haemoglobin was not present in the serum, and urine passed at the same time contained no abnormal constituents. The same arm was immersed in water at about 5–10° C. for 10 minutes, no movement being allowed. Venous return was not obstructed. At the end of this period the arm was lifted from the bath. It was noted that the skin had become a mottled blue-and-white. Blood was immediately taken from the arm and a sample of urine obtained. The serum of this blood contained 380 mg. of haemoglobin per 100 ml.; methaemalbumin was present. The urine was of normal colour and contained haemosiderin, but no haemoglobin could be detected. The benzidine test was negative. Two hours later the blood serum still contained 250 mg. of haemoglobin per 100 ml. A specimen of urine obtained at this time was the colour of burgundy and contained haemoglobin and haemosiderin, the benzidine test being positive. No red blood cells were seen on microscopical examination.

Progress of Patient.—The child has been encouraged to lead a normal life and to go out in all weathers suitably clad—that is, wearing extra clothing, thick stockings, and gloves on exceptionally cold days. Eight months later no further attacks of haemoglobinuria had occurred, although occasional duskiness and puffiness of the hands in cold weather had been noticed. The child himself has not complained of any symptoms.

Discussion

In this country the only types of haemoglobinuria which need to be considered are (1) haemoglobinuria due to drugs, (2) march haemoglobinuria, (3) syphilitic haemoglobinuria, (4) paroxysmal nocturnal haemoglobinuria (the Marchiafava-Micheli syndrome), and (5) the idiopathic type.

The lack of any history of drug-taking or any preceding vigorous exercise clearly ruled out the question of drug or march haemoglobinuria. There was no past or present clinical or serological evidence of syphilis. The lack of persistent haemoglobinaemia and haemosiderinuria, the negative haemolysis test of Ham, together with the fact that the attacks occurred by day only, served to differentiate the condition from the Marchiafava-Micheli syndrome.

The diagnosis of haemoglobinuria due to cold agglutinins was finally confirmed by a provocative modified Rosenbach test and by the demonstration of autohaemagglutination at low temperatures and in high titre with complete reversal of the reaction upon increasing the temperature.

The child's paroxysms of haemoglobinuria, although dramatic and alarming events to the parents, appeared to cause little systemic upset. The degree of blood destruction

did not call for transfusion or even iron therapy. The adoption of common-sense precautions, such as the wearing of extra clothing on cold days, seems to have controlled the paroxysms without the necessity for curtailing the child's activities.

Summary

A case of idiopathic paroxysmal cold haemoglobinuria of the non-syphilitic type in a child aged 3½ is described. This is the youngest case yet reported.

The differential diagnosis of the types of haemoglobinuria met with in this country is discussed.

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INTRA-ARTICULAR STREPTOMYCIN IN TUBERCULOSIS OF THE KNEE

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Until recently the accepted treatment of synovial-joint tuberculosis was prolonged immobilization of the joint, general sanatorium treatment, and ultimately, in many cases, some form of arthrodesis. This leaves much to be desired, as the treatment lasts for years, a disability is nearly always permanent, and in children there is serious disturbance of growth.

With the advent of streptomycin many have attempted to modify the above regime, but with only a limited success. Most of the papers published (Bickel *et al.*, 1948; Smith and I-Sen Yu, 1950) have been of cases treated by systemic streptomycin in late and well-established infections. The tubercle bacillus is only moderately sensitive to streptomycin, so to obtain the best effect it is essential to procure the maximum concentration of the drug at the site of the lesion. This should be done early before extensive fibrosis and cartilage damage obliterates the joint space, damages the joint, and reduces the blood supply to the affected areas.

Early Diagnosis

To obtain these optimum conditions we have attempted to diagnose cases early by gland and/or synovial biopsy, and we have given streptomycin by the intra-articular route (Streeten, 1949).

By performing gland or synovial biopsies early in suspected cases a definite diagnosis can often be made (Arden and Scott, 1947). In the case of knee-, ankle-, wrist-, and elbow-joints a gland and/or synovial biopsy will give a positive result in 70–80% of cases. In the case of the hip- or shoulder-joint a synovial biopsy is hardly justified, but a gland biopsy can be readily carried out. We believe that all cases showing a chronic inflammatory process in a single large joint should be submitted to biopsy. Only by this method will it be possible to make an early diagnosis of a tuberculous infection of a joint.

It has been found necessary to give streptomycin intrathecally to cure cases of tuberculous meningitis. Streptomycin given locally into tuberculous sinuses has also been found to be most effective (Ahern, 1950). Jones (1948) has demonstrated that intra-articular penicillin can remain in a joint up to 48 hours after intra-articular injection, and that this was the best method of preventing joint infections in war wounds.

The Investigation

This report is an analysis of 10 cases of synovial tuberculous infection of the knee which have been treated by intra-articular streptomycin. Most of the cases had been treated previously, for varying periods, by rest and in a sanatorium, without much improvement. Only three cases were diagnosed early (within four months of the onset of symptoms).

The follow-up is fairly short (20.4 months) and the number of cases is small, but in a few the results have been promising enough to encourage further trial.

Since it is possible to cure 50% of cases of tuberculous meningitis, equal or better results should be possible in the case of joint infections.

In some cases difficulty was experienced in entering the joint cavity owing to fibrosis and partial obliteration of the joint space. During the period of treatment all joints were treated either by traction and immobilization or by immobilization in a plaster backslab. Later the joint was left free when the clinical appearance and sedimentation rate were normal.

In four cases streptomycin blood levels were estimated at six and twelve hours after the intra-articular injections (see Table). The level at six hours was about 100 μg . per ml.,

Blood Levels of Streptomycin after Intra-articular Injection

| Case No. | Intra-articular Dosage of Streptomycin | Blood Level ($\mu\text{g}/\text{ml}$) | |
|----------|--|---|-------------------------|
| | | 6 Hrs. After Injection | 12 Hrs. After Injection |
| 1 | 1 g. | 93 | 5.0 |
| 4 | 1 g. | 106 | 8.0 |
| 5 | 1 g. | 93 | 4.8 |
| 6 | 1 g. | 106 | 3.5 |

but by twelve hours it had fallen to less than 10 μg . It would appear to be unnecessary to give systemic streptomycin as well. Efforts to estimate the joint streptomycin level failed owing to there being insufficient joint fluid.

Case Reports

Case 1.—Boy aged 12. Pain and swelling of right knee first appeared in February, 1945. Had received prolonged conservative treatment, but condition reactivated on several occasions. Tuberculous focus in right upper zone of chest in 1947. Moderate synovial thickening of knee; 90° movement at start of treatment. No osseous focus and joint space normal on x-ray examination. Synovial membrane biopsy (May 25, 1949) positive for tuberculosis. *Treatment*: 21 bi-weekly intra-articular injections of 1 g. of streptomycin (August to November, 1949). Immobilization for three months in a Thomas splint. *Result* (21 months after treatment): Knee cool, no swelling; x-ray film as before; normal activities. *Comment*: Undoubtedly benefited from local streptomycin therapy.

Case 2.—Boy aged 6. Focus right hilum in 1947, and right talo-navicular joint in 1948. Recurrent effusions into right knee during 1948. Marked synovial thickening; warm; 10° movement at start of treatment. X-ray examination showed no osseous focus and normal joint space. Synovial membrane biopsy (April 13, 1950) positive for tuberculosis. *Treatment*: Four bi-weekly injections of 0.5 g. Child very uncooperative. Treatment stopped August, 1949. Traction for nine months in a Thomas splint. *Result* (24 months after treatment): Knee cool, no swelling; 10° movement;

1½ in. (3.8 cm.) lengthening; wearing calliper. X-ray appearances unaltered. *Comment*: Diagnosis proved eight months after a very short course of streptomycin. Re-activated 10 months after streptomycin therapy, with backward subluxation of tibia. Settled after further five months' conservative treatment.

Case 3.—Woman aged 28. Bilateral hilar foci and two spinal foci in 1947. Synovial swelling in right knee, with effusion, since May, 1949. At start of treatment movement not noted. X-ray examination showed no osseous focus and moderately reduced joint spaces. *Treatment*: Ten bi-weekly injections of 1 g. of streptomycin (August to September, 1949). Three months in plaster shell. *Result* (23 months after treatment): Knee cool, no swelling; movement 140°; normal activities. Final x-ray film showed no osseous focus and very much reduced joint space. *Comment*: Presumptive evidence of tuberculous infection very strong. Benefited from local streptomycin.

Case 4.—Girl aged 13. Pain and slight synovial swelling in right knee, July, 1949; one month in plaster cylinder. 5° movement at start of treatment. X-ray films showed no osseous focus and normal joint space. Bilateral healed hilar foci, August, 1949. *Treatment*: 10 bi-weekly injections of 1 g. of streptomycin (August to September, 1949). Nine months' traction in Thomas splint; nine months in walking calliper. *Result* (23 months after treatment): Knee cool, no swelling; movement 80°; calliper discarded after 11 months. X-ray film as before. *Comment*: Marked improvement following local streptomycin.

Case 5.—Man aged 29. Pain and swelling of right knee first appeared in April, 1949. Five weeks in plaster before admission in July, 1949. On admission knee cool; no swelling; movement 5°. X-ray film showed no osseous focus and normal joint space. *Treatment*: 22 bi-weekly injections of streptomycin 1 g. (August to November, 1949). Three months' traction in Thomas splint; six months in walking calliper. *Result* (21 months after treatment): Knee cool; no swelling; 25° movement. X-ray films showed a patchy decalcification of lower end of femur and upper end of tibia and normal joint space. *Comment*: An unusual patchy decalcification noted six weeks after start of streptomycin therapy—probably a streptomycin effect. Very slow to clear.

Case 6.—Man aged 21. Left-sided pleurisy in 1948. Pain, synovial swelling, and effusion in left knee first appeared in March, 1949. Tubercle bacilli not present in fluid on admission in July, 1949. Knee cool; slight swelling; 20° movement. X-ray films showed no osseous focus and normal joint space. *Treatment*: 22 bi-weekly injections of 1 g. streptomycin (August to November, 1949). Three months' traction in Thomas splint; seven weeks in walking calliper. *Result* (21 months after treatment): Recurrence of slight pain (May, 1951); slight swelling at inner side left knee. Final x-ray appearance: small localized osseous focus in upper inner border of tibia; good joint space. *Comment*: Had regained 90° movement by June, 1950. Slight synovial swelling had persisted since treatment. Mild reactivation with small osseous focus in May, 1951. Thirty degrees movement retained.

Case 7.—Woman aged 40. Tuberculous right hip in 1939; and tuberculous right kidney in 1949. Pain and swelling of right knee following a fall in October, 1948, about a year before admission. On admission slight synovial swelling; 30° movement. X-rays showed reduced joint space; very slight erosion of joint surfaces. *Treatment*: 12 thrice-weekly injections of 0.5 g. of streptomycin (February to March, 1950). Eleven months' traction in Thomas splint. *Result* (17 months after treatment): Knee cool, no swelling; 60° movement; 10° flexion contracture. Plaster cylinder applied on discharge in June, 1951. X-ray film showed no appreciable alteration. *Comment*: Quiescence not attained with local streptomycin. Synovial swelling and tenderness persisted. Settled subsequently after a further 15 months' conservative treatment and a course of systemic streptomycin.

Case 8.—Girl aged 3. Pain, synovial swelling, and effusion in left knee in July, 1949. Warm, tender, moderate swelling and effusion, and almost full movement, at start of treatment. X-rays showed no osseous focus and normal joint space. Biopsy showed inguinal glands, superficial and deep, to be positive for tuberculosis on December 9, 1949. Focus right hilum in July, 1949. *Treatment*: 12 thrice-weekly injections of 0.25 g. of streptomycin (December, 1949, to January, 1950). Two months' traction in Thomas splint. *Result* (19 months after treatment): Knee cool, no swelling; Full movement. X-ray film as before. *Comment*: An early case; proved infection overcome with local streptomycin therapy.

Case 9.—Boy aged 16. Pain and swelling of right knee in December, 1947; then treated conservatively for two years. At time of admission moderate synovial swelling; movement 20°. X-ray films showed coarse trabeculation, slightly reduced joint space, and irregularity of posterior part of femoral condyles. Biopsy showed inguinal gland (January 18, 1948) to be positive for tuberculosis. *Treatment*: 12 thrice-weekly injections of 1 g. of streptomycin (December, 1949, to January, 1950). Two months' immobilization in Thomas splint. *Result* (19 months after treatment): Moderate swelling persisted; 40° movement. January, 1951: Charnley's arthrodesis. X-ray film showed bony fusion. *Comment*: Local streptomycin failed, but moderately advanced erosion of joint surfaces was present at start of treatment.

Case 10.—Male, aged 44. Pain and synovial swelling right knee since March, 1949, x-ray film showing rarefaction. Pulmonary tuberculosis, March, 1949; positive sputum. *Treatment*: 12 thrice-weekly injections of 1 g. of streptomycin (April to May, 1950) plus 2 g. of P.A.S. intra-articularly thrice-weekly for same period. Eight months in walking calliper. *Result* (15 months after treatment): Pain and synovial swelling persisted. Charnley's arthrodesis, February, 1951. Synovial membrane at time of operation positive for tuberculosis. February 12, 1951, x-ray film showed bony fusion. *Comment*: Local streptomycin failed.

Discussion

The affected knee is indistinguishable from normal in Cases 1 and 8. Cases 3 and 4 are progressing well, have 140 and 80 degrees of movement and no pain, wear no support, and are back at work. Quiescence was attained in Case 5, but only 25 degrees of movement was regained. Quiescence was attained temporarily in Case 6, with 90 degrees of movement. Reactivation occurred 21 months later. Quiescence was not attained with local streptomycin in Cases 2, 7, 9, and 10. It is perhaps not without significance that treatment was discontinued after four injections in Case 2.

Reactions were few. One case developed a rash which did not interfere with treatment. A positive sputum in this case became negative on completion of treatment. A slight local reaction with increased temperature and tenderness not lasting more than 24 hours was occasionally noted, but this occurred only when difficulty was encountered in entering the joint and some of the streptomycin was injected into the soft tissues.

It will be at least two years before enough cases have been treated and followed for any final opinion on this method of treatment to be given. We feel justified in publishing this interim report in the hope that other surgeons seeing these cases early will try to establish a diagnosis and begin treatment before cartilaginous damage takes place.

The average case admitted to an orthopaedic hospital has had symptoms for a year or more.

Summary

The results obtained with intra-articular streptomycin in synovial tuberculosis of the knee are encouraging.

Early diagnosis by gland and/or synovial biopsy is essential.

Four of our ten cases have progressed well, and in two normal function has been re-established.

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ANGIOMA VENOSUM RACEMOSUM WITH ANGIOMATOUS LESIONS OF SKIN AND OMENTUM

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Vascular malformations and tumours of the central nervous system are sometimes associated with similar lesions of the skin and viscera. Such associations are known by the names of Sturge-Kalischer-Weber, von Hippel, and Lindau when the nervous tissue involved is either the cerebrum or cerebellum.

Wyburn-Mason (1943) quotes numerous instances of skin naevi coexisting with a variety of vascular lesions of the cord. However, he notes only seven instances in which angioma venosum racemosum is associated with a skin naevus, and quotes the cases of Cobb, Alexander, Rand, Sterling, and Jackinowicz, adding three cases of his own. In only one of these (his Case 12) was the skin lesion non-segmental. All cases described had the cord lesion in either the lower dorsal or the lumbar areas.

Subsequently, Cross (1947) published the first case of extensive subarachnoid blood vessels involving the whole of the cervical region associated with an angioma of the left side of the neck and prominent vascular markings of the upper part of the chest and over the seventh cervical vertebra. The present case appears to be the second one on record. Of additional interest is the occurrence of numerous small angiomas of the omentum and a further large skin naevus of the flank.

Description of the Case

The patient was a well-built boy aged 15. Three years before admission he jumped off a 5-ft. (1.5-m.) wall and landed on his feet. He sustained no obvious injury, but 30 seconds later, while walking, he developed occipital headache. He was laid up for two weeks at home, complaining of pain at the back of his head, across both shoulders, and radiating down the left arm as far as the elbow. He stated that for several weeks his left leg tended to drag, but that ultimately recovery was complete. He was well until 10 days before admission, when he made a racing dive, swam two lengths of the swimming-bath, and then suddenly developed pain across the forehead and at the back of the neck. He got out of the water and almost lost consciousness on account of the severity of the pain. He was taken home, where his headaches continued for two days, accompanied by vomiting.

Five days before admission, while lying in bed, the pain in the nape of his neck suddenly became worse and again