cutaneous layer of muscle was necrotic; the epithelium was limited in extent, it being apparently more resistant than the deeper tissues.

In rats the histological reaction was similar. When 0.75 mg. dissolved in 0.15 c.cm. was injected intramuscularly the lesion was small, but when it was injected subcutaneously considerable oedema and necrosis occurred. When 20 mg. in 0.3 c.cm. was injected very extensive oedema and necrosis occurred, whichever route was employed.

The damage caused by mepacrine was compared with that caused by quinine. The monohydrochloride was employed. This is less acid than the more soluble bihydrochloride generally used clinically, and consequently the lesions should be less extensive, being due only to the quinine radical and not to the acid part.

When 20 mg. dissolved in 0.6 c.cm. of water was injected intramuscularly into rabbits the lesions were closely similar in appearance and extent to those caused by 50 mg. of mepacrine. In rats the lesions produced by 10 mg. of quinine were less extensive than those produced by 20 mg. of mepacrine, but those caused by 4.5 mg. of quinine were greater than those caused by 0.75 mg. of mepacrine.

Discussion

Since the macroscopic evidence of injury is usually slight compared with the microscopical evidence, the present findings are easily reconcilable with those reported in the literature. They show that the intramuscular injection of mepacrine always causes a limited area of necrosis around the site of injection, presumably due in large part to the direct action of the mepacrine base. With 0.375 g. (as for man) instead of 0.05 g., the extent of the damage would be somewhat larger, but still not great enough to constitute an absolute contra-indication to the practice in selected cases. As compared with quinine, the damage caused by 50 mg. of mepacrine was similar in extent to that caused by only 20 mg. of quinine. Since the standard dose of mepacrine methanesulphonate (by intramuscular injection) is 0.375 g., while an average dose of quinine is 0.5 g. ($7\frac{1}{2}$ gr.) of the bihydrochloride (which is more acid than the monohydrochloride and possibly more injurious locally), it would seem that a therapeutic injection of mepacrine should cause less than a third of the damage done by a therapeutic injection of quinine.

The relative and absolute merits and demerits of the administration of mepacrine by intramuscular injection cannot properly be discussed here. According to Hecht (1936) most of the mepacrine is absorbed from the site in one to three hours; and this statement about the rapid absorption is in agreement with my own experience and with the reports reviewed above. Clearly, mepacrine should not be injected by any route unless it is impracticable to give it by mouth. The intravenous route avoids local damage, but entails a certain risk to life unless the injection is given very slowly; the intramuscular route is certain to cause a small amount of local injury, but the risk to life from over-rapid absorption is much less (although this is not absolutely excluded, since 4 patients died from mepacrine intoxication out of the 681 treated by intramuscular injection during the Ceylon epidemic). The choice between the two routes of injection must depend upon clinical experience and upon the discretion of the medical man responsible for the case.

Summary

A review of the literature shows that intramuscular injection of mepacrine (atebrin) is considered to be free from local reaction in most cases, to cause pain and swelling in some cases, and to cause local abscesses in rare cases.

Mepacrine methanesulphonate (atebrin musonate) was injected intramuscularly and subcutaneously into rabbits and rats. The macroscopic lesions were often inconspicuous, but microscopical examination always showed a certain amount of necrosis at the site of injection. The damage caused by a therapeutic injection of mepacrine is similar in kind to that caused by a therapeutic injection of quinine, but probably less than one-third as extensive. For patients who cannot take mepacrine by mouth this local damage does not contraindicate parenteral injection, but its occurrence should be borne in mind when choosing between the intramuscular and the intravenous routes.

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POST-VACCINIAL ENCEPHALOMYELITIS

BY

SAMUEL DUNN, M.D.

The nervous complications of vaccination have been recognized for many years. Turnbull (Turnbull and McIntosh, 1926) reported a fatal case occurring in 1912, but chief interest in the condition arose after 1923. The Report of the Committee on Vaccination was issued in 1928. The cause of the nervous complications of vaccination is still unknown. The condition very rarely follows vaccination in infancy; adults who are undergoing their primary vaccination are most susceptible. The patient whose case is described below had been successfully vaccinated in infancy: a well-marked scar could be seen close to the present pustule. According to her, considerable bleeding occurred at the time of the vaccination, and it seems likely that a "cross-hatching" method was employed. Some authorities consider that linear scratches are not so likely to be followed by nervous complications as "cross-hatching" methods.

In this patient the cerebral symptoms preceded the spinal symptoms by two days, and consisted of lethargy, mental confusion, and insomnia. The interval between vaccination and the onset of symptoms was 15 days; the average period is said to be about 12 days. The paraplegia developed very rapidly, and was complete in 12 hours. Bronchopneumonia and cystitis are the usual causes of death. In the present case cystitis gave rise to the main anxiety. Sulphanilamide certainly kept the urinary infection within bounds, but had no apparent effect on the nervous symptoms. On the whole the administration of plasma appeared to be beneficial, but it is difficult to estimate its value in a condition such as this, in which there is a strong tendency to spontaneous recovery. The plasma seemed to have a very favourable influence on the mental symptoms; these passed off after the first dose. The mortality of post-vaccinial encephalomyelitis is between 50 and 60%, but the prognosis is probably better in the spinal forms than in the severe cerebral types.

As a result of experience in treating the present case it is advised that suitable serum or plasma should be given as soon as possible. This is obtained from a person vaccinated about 21 days earlier. When mass vaccination is going on at the time there will probably be little difficulty in obtaining a suitable donor. In other circumstances it would be necessary to vaccinate a donor; the interval of waiting before the plasma can be obtained would then be a great drawback. One might seek some service or institution—e.g., a hospital—where the entrants must be vaccinated before admission, and it might be possible to find there a recently vaccinated individual who would consent to act as donor. The plasma used in the present case contained 3.8% sodium citrate solution. Originally 50 c.cm. of citrate was added to the blood as preservative; 220 c.cm. of plasma was obtained, and presumably nearly all the citrate was in the plasma.

It is interesting to note that the patient had an attack of tetany during the administration of the plasma. There had

been some vomiting before the attack. Her chief complaint was of agonizing pains in the arms, for which large doses of morphine were given.

REPORT OF CASE

The patient was a woman aged 21, a school teacher. Vaccination had been successfully performed in infancy. She was in good health when vaccinated on July 9, 1942, and a few days later travelled to Glasgow. She was first seen on July 20, when she complained of a very painful arm which kept her awake at night. There was a well-marked reaction around the pustule, with a little oedema of the arm, but no signs of sepsis were present, and the glands in the axilla and the neck were not enlarged.

On July 24 she complained of feeling easily tired; she became drowsy and took little food; on the following day she could be aroused only with difficulty, and considerable mental confusion was present. On the 26th she was very drowsy; the temperature and pulse rate were normal. The vaccination area was covered by a thick scab. She had passed no urine for 24 hours. Examination showed a flaccid paraplegia. There was complete loss of sensation over the lower limbs and over the abdominal wall below the level of the umbilicus. The abdominal muscles were flaccid and there was considerable abdominal distension, even after emptying the bladder by catheter. The knee-jerks were present at this stage but disappeared a few days later. The plantar reflexes could not be elicited. The fundi and external ocular muscles showed no abnormality. The pupils were dilated and reacted sluggishly to light. Mental confusion was pronounced. On the 27th she complained of pain in the neck. The posterior neck muscles were tender to the touch, but there was no nuchal rigidity and Kernig's sign was absent. She required regular catheterization. Constipation was marked, and repeated enemata gave no result. The temperature rose to 100° F.

On July 28 the patient could move the toes of the left foot. She began to have severe pains in the arms and had to have morphine regularly. These pains persisted for about three weeks. The urine was now heavily infected and the temperature was continuously raised. She was restless and delirious and had frequent attacks of vomiting. Sulphanilamide was given, a total of 18 g. being administered in a week. On Aug. 5, when her condition was giving rise to the most acute anxiety, she passed some urine into the bed. This incontinence persisted for another 10 days, but the urinary infection soon passed off. At this date she had no sensation in the lower limbs and the mental confusion was still present. On Aug. 6 she had slight rotatory movements at each hip-joint. During the day she was somnolent and at night restless and excited. On Aug. 20 plasma was obtained from a recently vaccinated individual, and 20 c.cm. was administered intramuscularly each day. The patient's mental condition improved after the first injection, and in two days was normal. The abdominal muscles regained their tone, and after a period of persistent vomiting the distension passed off. On Aug. 25, after 100 c.cm. of plasma had been given, she had an attack of tetany. Plasma administration was stopped for two days and then restarted, using smaller doses. A further 120 c.cm. was given. Several attacks of tetany of less duration occurred.

From this date the patient rapidly recovered the movements of the limbs—first dorsiflexion of the ankles, then flexion of the hip-joints, and then flexion of the knee-joints. On Sept. 4 the left plantar reflex was extensor. Sensation was not yet fully restored. Deep sensibility seemed to be normal, but she had difficulty in locating touch and pain and in distinguishing between the finer grades of temperature. There was slight atrophy of the muscles of the thighs. On Sept. 9 the left knee-jerk was elicited for the first time since it was lost at the beginning of the illness. She still had imperfect bladder control. By the 13th she could raise each leg from the bed, and by the 23rd could shuffle a few steps.

Thereafter she progressed rapidly. On Dec. 24 the only muscular weakness which could be made out was in the extension of the right big toe and in dorsiflexion of the right ankle. She had difficulty in distinguishing between the finer grades of temperature, and her tactile localization was still deficient over the lower limbs. Her bladder control was normal, but she still had a little frequency. She began work early in Jan., 1943.

I wish to thank Dr. George Allan and Prof. T. K. Monro of Glasgow for their advice when they saw the case in consultation with me; to the latter I am also grateful for making arrangements to obtain the special plasma from the Glasgow and West of Scotland Blood Transfusion Service.

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Medical Memoranda

Kienböck's Disease: Aetiology

Kienböck's disease of the semilunar bone is by no means rare, and is described in most textbooks. It is regarded by most authors as being of the same class as Köhler's disease of the tarsal scaphoid, Calvé's disease of the spine, and Perthes' disease of the head of the femur. But whereas these, being essentially epiphyseal in origin, are found in children, Kienböck's disease is found only in adults. The typical case shows a syndrome consisting of pain over the semilunar bone, limited movement of the wrist, possible ultimate retraction of the head of the third metacarpal, and degeneration of the semilunar seen by radiographs. Most authors agree that the condition is fundamentally an avascular necrosis (Maingot, 1939; Handfield-Jones and Porritt, 1940), but there is a divergence of opinion concerning the aetiology. It is for this reason that the following cases are published.

CASE HISTORIES

Case 1.—A leading aircraftman aged 33 reported sick on April 6, 1942, complaining of pain in the right wrist. Three years previously he had had a septic left thumb, which healed on treatment. Shortly afterwards, for no apparent reason, the right wrist became painful. He was treated for neuritis of the wrist for three years without improvement. No radiograph was taken. He denied having ever sprained or sustained any injury to the wrist. On examination the right wrist showed no obvious deformity. Palmar flexion was limited; extension was normal. Passive adduction caused pain on the radial side of the joint. Tenderness was elicited over the semilunar bone on the dorsal surface, and over the scaphoid in the "anatomical snuffbox." There was no shortening of the metacarpal heads. Radiographs showed gross disorganization of the semilunar bone, with irregular absorption of bony trabeculation. The degree of opacity indicated avascular necrosis of the bone. Arthritic changes were seen around the cuneiform and the articular surfaces of the radius. Diagnosis: Kienböck's disease.

Case 2.—A gunner aged 30 was seen on May 9, 1942. He complained of pain in the left wrist of one year's duration, and had been treated for a sprained wrist for that period of time without improvement. No radiograph was taken. Injury or trauma was emphatically denied. No septic focus could be remembered, but dental treatment had been necessary some time previously. On examination the wrist showed no obvious deformity or swelling. Palmar flexion was limited; extension was normal. Passive adduction caused pain on the radial side of the joint, and tenderness was elicited by pressure on the radial and ulnar sides: the pain was transmitted to the semilunar area. Pressure over the semilunar bone itself caused sharp pain. There was no retraction of the head of the third metacarpal. Radiographs showed gross disorganization of the semilunar bone, with arthritic changes around the articular surfaces of the radius and the scaphoid. The degree of opacity indicated avascular necrosis. Diagnosis: Kienböck's disease.

COMMENTS

It is stated (McGregor, 1939) that the nutrient artery to the semilunar bone is carried by the posterior ligament, which consists of the deep fibres of the dorsal radio-carpal ligament. The commonest fracture of the bone is a separation of a small fragment from the posterior part (Hosford, 1939). If this fracture involves the nutrient foramina and interferes with the blood supply, then avascular necrosis will follow. Watson-Jones (1941) states that there is also an anterior nutrient artery which enters via the anterior ligament, and it is only when both supplies are disorganized, as in complete dislocation of the bone with rupture of these ligaments, that avascular necrosis occurs. Rupture of the posterior ligament alone is not usually sufficient to interfere with adequate nutrition.

Many authors assert that trauma involving the blood supply is the aetiological factor in producing Kienböck's disease; others say the cause is unknown. In Case 1 there is no history of trauma, but of a septic focus. It seems, therefore, that in this instance the condition is the result of the entry of organisms of mild virulence, and a sequel of an osteitis.

Case 2 also gives no history of trauma, but the possibility of a septic focus (teeth) cannot be dismissed. It appears that when trauma can be definitely excluded haematogenous infection must be considered as an aetiological factor in producing the condition known as Kienböck's disease.

SUMMARY AND CONCLUSIONS

Two cases of Kienböck's disease are described.

The possibility of bacterial infection as an aetiological factor is suggested in cases not directly attributable to injury.

The need for x-ray examination in all cases of injury and disability of the wrist-joint is indicated, with follow-up radiography later in all cases that do not respond to treatment.

According to A. J. Mueller and others (*Johns Hopk. Hosp. Bull.*, **72**, 110) the minimum requirements of enzymic casein hydrolysate for maintenance is between 0.4 and 0.7 g. per kilo. This indicates its approximate equivalence with intact protein for maintenance, since maintenance of the latter is usually regarded as between 0.4 and 0.7 g. per kilo.