Discussion

The first case conforms in the main to the usual peripheral type of nervous lesion. It has, however, a feature of special interest—namely, the pain on the eighth day occurring in place of and not along with the serum rash, and preceding by a long interval the onset of paralysis accompanied by general reaction. The absence of urticaria may cast doubt upon the diagnosis, but the time of onset of the pain and the lack of any further cause appear to be conclusive, a point which has been noted in other reported cases.

With regard to the second case, the age of the patient and the changes in the cerebrospinal fluid suggested at the time an alternative diagnosis of cerebral thrombosis or some other acute meningo-vascular disturbance. The sudden onset of neurological signs, coincident with the onset of serum disease, and the rapid recovery with disappearance of the serum rash, are characteristic of such rare cases, however, and were considered to be sufficiently conclusive.

Although the pathogenesis of serum neuritis and other nervous complications of serum therapy has given rise to much conjecture its exact aetiology remains obscure. Among various theories of origin, the one now generally favoured supposes that a perineural oedema, comparable to the oedema of serum disease, causes a compression or ischaemic paralysis of nerve trunks. Other theories have suggested direct toxin action on the nervous system, affecting nerves of low chronaxie, as in lead poisoning, or a perivascular infiltration with widespread capillary haemorrhages in brain and spinal cord, such as has been found experimentally in acute anaphylaxis.

A high percentage of the recorded cases have followed the injection of tetanus antitoxin, but this may be accounted for by its frequent use as a prophylactic agent. Certain other factors—such as the age of the serum, degree of refinement (we have not been able to trace any reference to nervous complications after the use of crude horse serum), and sensitization of the patient by a previous administration of serum—may be of aetiological importance.

Though recovery may take several months the ultimate prognosis in the majority of cases appears to be good. According to Bennett (1939), however, about 20 per cent. of cases are left with a varying degree of disability. Nevertheless, in view of the great rarity of such manifestations the consensus of opinion is that the remote possibility of this occurrence should not affect the employment of one of our most valuable therapeutic measures.

Summary

Involvement of the nervous system as a complication of serum therapy is discussed.

Two cases showing symptoms referred to the nervous system following the injection of anti-scarlatinal serum are recorded.

Theories of the origin of the nervous complications are reviewed.

The prognosis in the majority of cases appears to be good.

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LOCAL TREATMENT WITH PRONTOSIL SOLUBLE

BY

JOHN ALEXANDER SMITH, M.R.C.S., L.R.C.P.

Assistant Medical Officer, Worcestershire Mental Hospital, Barnsley Hall, Bromsgrove

The value of local treatment with chemotherapeutic drugs is still unsettled, but if the method proves satisfactory it will have the obvious advantages of economy and atoxicity. The result of using prontosil soluble locally in one case was so striking that the procedure was tried in a variety of conditions. Five of these cases are reported below.

Case Reports

Case 1.—A young woman who was admitted to hospital with lobar pneumonia developed a pneumococcal empyema which drained for over four months, about 60 oz. of thick greenish pus being discharged in the twenty-four hours. Her general condition was poor, and nursing was rendered difficult because of marked oedema extending from the lower costal margin to the feet. As the condition did not respond to the usual method of treatment 5 c.cm. of 5 per cent. prontosil soluble was injected into the pleural cavity; the next day the discharge was very much thinner and contained only flakes of pus. Twenty-four hours after the second injection, given on the third day of treatment, the drainage was much less, there was no frank pus, and the fluid was sterile on culture. A third injection was given on the fifth day; the discharge from the pleural cavity rapidly diminished and the oedema began to recede. A fortnight after starting treatment the tube was removed. The patient rapidly regained her health, and four weeks later she was discharged from hospital fully recovered.

Case 2.—A middle-aged female melancholic in poor physical condition developed an abscess in the gluteal region to the left of the sacrum. Following treatment with fomentations a cavity large enough to hold a tennis ball was discovered. This appeared to be walled off by gangrenous muscle, while the discharge consisted of foul-smelling greenish-black pus containing strips of necrotic tissue. Treatment with eusol packings over a period of a week produced no improvement. The cavity was then packed with gauze soaked in prontosil soluble. Within twenty-four hours the foul odour had practically disappeared and the wound was remarkably clean. The cavity now rapidly filled with healthy granulation tissue, and epithelium started growing at the edge. Three weeks after the first treatment with prontosil soluble the wound was completely healed and was covered with healthy skin.

Case 3.—This patient, a female, suffered from a varicose ulcer four inches in diameter on the outer aspect of the right leg; it had resisted all attempts at treatment. The discharge was copious, and each dressing was filthy when removed. An ointment containing 5 c.cm. of prontosil soluble to the ounce of lanolin was prepared, and was applied to the ulcer once daily. The odour disappeared in twenty-four hours; healthy epithelium began to invade the raw surface, and in four weeks the ulcer had healed completely and was covered with healthy skin.

Case 4.—A female mental defective, this patient complained of pain in the anal region, and on examination a perineal ulcer about the size of a five-shilling piece was discovered.

The anal mucous membrane and the skin of the outer edge of the ulcer were undermined, and the odour was extremely unpleasant. The condition rapidly became worse during treatment with eusol dressings: the surrounding skin broke down to a distance of two inches from the margin of the anus, the perineum was denuded of skin, and the ulcer extended to the posterior vaginal wall. The patient became incontinent and her temperature rose to 102°. Treatment with proseptasine, one tablet (0.5 gramme) thrice daily, had to be stopped on the third day owing to vomiting. A culture from the ulcer revealed a very mixed infection in which *B. coli* predominated. On the eighth evening prontosil ointment was applied, and the next morning the temperature dropped suddenly, the ulcer was cleaner, and the odour had disappeared. After three weeks' treatment with prontosil ointment the wound was completely healed and was covered with normal skin.

Case 5.—This patient had had both her breasts destroyed when she was severely burned in September, 1937; her neck and right arm were also involved. Examination in January, 1939, disclosed a large raw surface on the chest, neck, and arms. Some degree of healing had taken place, but the wound appeared to be sluggish and unhealthy. The granulation tissue was inactive, and the skin showed no signs of growing over the area. The patient was admitted to hospital, and the original treatment—vaselin gauze—was continued for one week. As there was no improvement prontosil ointment was applied. The odour which had been present now disappeared, the wound showed rapid improvement, and epithelium began to invade the raw surface. The area is not completely covered, but remarkable progress has been made in the ensuing six weeks, and the remaining raw surface is about four square inches. The patient should soon have completely recovered.

Discussion

In view of the widespread interest in chemotherapy it is rather surprising that the local use of these drugs has excited so little attention. Thus of the innumerable publications on chemotherapy only a handful refer to local treatment, although some good results have been reported. Tiling (1936) successfully treated cases of streptococcal empyema with intrapleural injections of prontosil soluble, and numerous workers have given prontosil soluble or sulphanilamide intrathecally in meningitis, along with oral or parenteral administration. Jaeger (1936) and Merz (1937) claimed good results in the local treatment of certain skin diseases with prontosil, while Bosse and Bosse (1939) treated purulent cavities, burns, and varicose ulcers with applications and packings of prontosil dispensed in different ways. Schlenker (1938) also described rapid improvement following intrapleural injections of prontosil soluble in empyema, and Childrey (1939) used the same drug for irrigation treatment of resistant sinus infections. An interesting application of this method has been reported by Jensen, Johnsrud, and Nelson (1939), who packed the cavities of compound fractures with solid sulphanilamide.

It is difficult to explain the action of prontosil soluble applied locally, as the drug has no direct antiseptic effect and the content of active substance is very low. It may be concluded, however, from the results described above (and achieved in twenty-five other cases) and from the literature that prontosil soluble has a powerful anti-bacterial effect when in contact with infected tissues. This treatment may be of great value in war wounds and injuries, all of which are certain to be contaminated. A striking feature of this treatment is the deodorant and stimulating action of the compound, an effect which may be produced by the dye substance contained in prontosil soluble, and it should be noted that no toxic effects were observed.

Summary

Successful local treatment with prontosil soluble in empyema, ulcers, abscesses, and other conditions is described. The drug has anti-bacterial, deodorant, and stimulating action in such cases, and toxic effects do not occur.

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Clinical Memoranda

Progesterone and Vitamin E Treatment during Pregnancy

The case here reported raises the question whether any hormone or other insufficiency can be considered partly responsible for the long sterility followed by a mal-presentation and a placenta praevia. The first normal pregnancy and labour certainly followed the use of progesterin; a subsequent untreated pregnancy ended in abortion, and even after the successful fifth pregnancy lactation could not be normally established. The case suggests that the combination of progesterone and vitamin E may be worth a trial in patients with similar bad obstetric histories.

CASE HISTORY

Following ten years of marriage and sterility the patient underwent dilatation, curettage, and carbolization, and her first pregnancy began soon after. Both she and her husband had been extremely desirous of having a child.

First Pregnancy.—The patient, aged 33, was delivered of a full-term dead child. The labour was difficult, the presenting part being a breech, with extended legs; the arms also were extended. Scopolamine and morphine were used. During and after the confinement the mother was physically quite well, and at no time were the kidneys functioning abnormally.

Second Pregnancy.—The patient became pregnant about a year later. At the seventh month a placenta praevia was discovered. The child was born dead.

Third Pregnancy.—Throughout this pregnancy, which occurred in 1937, progesterin was given in 1-mg. doses at weekly intervals. The patient was made to rest for several days each month at times of the usual periods. At no time was anything physically wrong discovered in her. One month before the expected date of delivery she was examined radiologically to find the exact position and lie of the child. The report was as follows: "This reveals a normal pregnancy lying in vertex presentation and in the right occipito-anterior position. The head has not yet entered the pelvic brim, but the relative size of the head and the maternal pelvis appears satisfactory so far as one can judge from the radiograph. The development of foetal bones indicates that the pregnancy is of about thirty-four weeks' duration. The whole general appearance is very satisfactory from the point of view of the x-ray findings." A month later the mother was delivered of what appeared to be a normal child. The labour was straightforward and rapid. Pains were almost absent, and scopolamine and morphine were used. About four weeks later the child began to regurgitate its feeds and lose weight. In hospital an x-ray examination showed the presence of pyloric stenosis. Medical treatment was tried for a week without avail.