

A NOTE ON PURPURA IN MENINGOCOCCAL INFECTIONS

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With Plate 35

MOST of the reports that have been published since the beginning of the War on military cases of cerebro-spinal fever lay but little stress on the appearance of a rash. Bourke, Abrahams, and Rowland (1) describe the features of 161 cases that were observed at one isolation hospital in France, but they do not refer to the rash among the points discussed in their paper.

H. R. Brown (2), however, noted that a petechial rash was present in 30 per cent. of the twenty-seven cases that he had seen at another hospital in the same area; and McNee (3) states that a rash could be observed in at least 20 per cent. of those which he had seen at the beginning of the third day of illness. Flack's (4) report on sixty-one cases from the London district gives the rash as a minor feature that was present in about 13 per cent.

Brown analysed the character of the rashes that he had observed. The common form was a petechial rash, resembling flea-bites, which faded in four days, and the presence of which bore no special relationship to the severity of the case. He observed one example of large purpuric spots distributed all over the trunk and thighs, which also faded on the fourth day after their appearance. He distinguished this true rash from the purpuric mottling of the extremities which may develop when death is imminent, and is common to fatal cases of sepsis from various causes.

Several medical officers have met with fulminating and rapidly fatal cases of fever associated with a purpuric rash, which were proved to be caused by a meningococcal septicaemia; and this experience is so well known that the suspicion of a meningococcal infection is always raised now in the minds of clinicians when they have to deal with a case of fever that exhibits a petechial or purpuric rash, even though no symptoms of meningeal inflammation can at first be detected. We are not aware of any evidence which shows clearly whether these spots on the skin are to be regarded as a toxic rash or as a focal eruption caused by the local development of colonies of meningococci that had been distributed in a septicaemia. Blood cultures have not been systematically made by workers from cases of cerebro-spinal meningitis with a rash.

The first case that we describe is a most clearly cut example of this fulminating type.

Case I. Meningococcal septicaemia: death in twenty-four hours after onset.

Pte. A. E. W. marched 11 miles with his battalion on April 4, 1916, and did not feel ill enough to report sick till midday on April 5. When seen at a Casualty Clearing Station a few hours later he was extremely ill. Temperature 101.6°; pulse 144, being small and irregular; respirations 44 per minute. The tongue was brown and furred.

On examining his legs, in which he complained of great pain, a most unusual and striking appearance was seen. Bluish-black blotches, of irregular shape and of various sizes, but many of them as large as a penny, were found scattered all over the lower limbs and buttocks, while a few were evident on the arms. The ankles and feet were exceedingly tender: knee-jerks were brisk and equal: plantar reflexes were flexor in type: Kernig's sign was not obtained, nor was there any stiffness or pain in the neck muscles. He complained of slight headache, but apart from this no symptoms or sign of meningeal irritation could be elicited. The heart was normal in size and position, and the only abnormal physical signs in the lungs were those suggesting early pneumonia or a thin layer of fluid with some collapse of the left lower lobe.

His condition showed no material change during the remaining few hours of his life, and he died at 12.15 a.m. on April 5, *well within twenty-four hours of the time at which he first felt ill enough to report sick.*

An autopsy on the day of death showed as follows:

'The lower limbs and buttocks present numerous pale blue-black blotches, which are of irregular shape and vary in size from a pin's head to 3 cm. in diameter. They are present on both surfaces of the lower limbs, being more numerous and larger towards the lower part and especially upon the feet. A few are scattered on the arms and forearms, where they are for the most part smaller; there are none upon the hands, trunk, face, or neck. On section they are seen to consist of haemorrhages into the deeper layers of the skin, and not to be raised above the general surface. No bacteriological or microscopic examination of these patches were made.

'*Brain and cord.* The cortical veins are distended with dark fluid blood. This congestion is especially evident all over the vertex and gradually diminishes over the lateral aspects of the cerebrum till it disappears at the margin of the cisterna magna. There is no flattening of the cerebral convolutions. No excess of fluid in the ventricles; no haemorrhages; no fibrinous deposit or "stickiness" to be found anywhere. The cord appears perfectly normal, both externally and upon section at various levels. In short, with the exception of the above vascular condition, the brain and cord are quite devoid of any abnormal appearances to the naked eye.

'The left pleural cavity contains 10 to 15 oz. of brownish-yellow clear fluid, and the same quantity of blood-stained fluid is found in the right pleural cavity. The parietal pleurae are universally injected, and the visceral pleurae show a few tiny scattered haemorrhages. Both lungs are firm to the touch, and the cut surface exudes much frothy fluid on squeezing; sections float in water.

'The spleen is large, soft, and friable. The kidneys are unusually large, pale, and firm: on section, their substance bulges and curls up over the cut edge of the capsule, and that of the cortex is covered with glistening, slightly raised points and streaks. The urine was not examined. Similar congestion and enlargement was observed in the liver. No abnormal condition was noticed in any of the other organs.'

Captain A. W. M. Ellis, C.A.M.S. (Mobile Laboratory), had taken samples of the blood and cerebro-spinal fluid at 10 p.m. on April 5, that is four hours

before death, and he reported as follows: 'The blood was inoculated into plain broth, which showed a fairly profuse growth of a Gram-negative diplococcus in eighteen hours. Prolonged search of film preparations from the blood failed to show any micro-organism. A blood count was not made, but the appearance of the films suggested the existence of a leucocytosis, and a differential count of 500 cells showed a considerable increase of large mononuclear cells.

'The cerebro-spinal fluid from lumbar puncture was absolutely clear and limpid, giving neither sediment on centrifugalization nor clot on standing. Cell count 12 per c.mm., of which 11 were polymorphonuclear leucocytes. The fluid was centrifuged and then poured off, after which the tube was inverted and allowed to drain. The small amount of fluid remaining adherent to the walls of the tube was then picked up with a fine capillary pipette and smeared on a glass slide. This smear when stained showed a few cells, chiefly polymorphonuclear leucocytes, and large numbers of diplococci, which were morphologically meningococci. They were practically all extra-cellular, and were so numerous that fifty to ninety pairs were frequently seen in one microscopic field.

'Culture and inoculation showed the organisms isolated from the blood and from the cerebro-spinal fluid to be identical, and to be a true "Type 1" meningococcus (5).'

The case just described accords with the general experience that extensive and early purpura in a case of meningococcal infection (cp. McNee (3)) usually indicates a fatal prognosis.

The second case that we quote is anomalous, because the development of the purpura in it seems to have been influenced by the complication of trench feet, which resulted from exposure to severe cold in the trenches during the period of prostration at the onset of the illness.

Case II. Trench feet associated with necrotic purpura from cerebro-spinal meningitis.

Pte. H. —, — Regiment, aged 23. Eight months' service at front in France, during which time he had never gone sick, and had never suffered trouble with his feet while in the trenches during the winter.

About January 31, 1917, he suddenly fell ill with headache and shivering, but no vomiting, and with severe pain in both legs. The weather was severe, an intense frost having commenced on January 23. The patient had been in the trenches for six days, wearing rubber thigh waders which reached up to the gluteal folds; but his legs had been dry and warm throughout and there was nothing the matter with them immediately before the illness, although he had been wading through icy water. He had not been suffering from any cold in the head.

The patient lay down with his waders on in a reserve trench and did not at once report sick. About thirty hours later he was seen by the medical officer. The waders were then removed and his feet were noticed to be cold, but presumably no striking changes were visible because the patient was subsequently passed through a field ambulance with the diagnosis of 'Pyrexia of unknown origin'.

February 2-3. The night was passed in a Central Clearing Station, where he talked continually in semi-delirious sleep and was ignorant of the state of

his legs. T. subnormal; P. 120; R. 20. Purpura and frost-bite were now obvious on this the third day of the illness, and the case was sent down with a special note calling attention to its unusual features.

February 3. Transferred to Base Hospital, where he came under the care of Captain H. Wilks, R.A.M.C., who recognized the probability of meningococcal infection and drew our attention to the case.

February 4. Patient was perfectly conscious but complaining of headache, and he had passed water in the bed during the night. Slight stiffness of neck: abdominal reflexes lost: the thighs were too tender and painful for Kernig's sign to be tested.

The legs showed the extraordinary appearance which is depicted in the drawing made on the same day by Sergt. A. K. Maxwell, R.A.M.C. (Plate 35). From the ankles downwards the feet were grey, cold, anaesthetic, and powerless; the circulation in them had ceased. Upon the legs and thighs above this dead area was a purpuric rash of irregular distribution with red edges and central areas of greyish purple tint which looked as though they would soon become necrotic.

There was no rash elsewhere on the body except for three tiny purpuric spots on the left wrist. The finger-tips were cold and numb. There was a small patch of herpes on the upper lip.

It was evident that the patient was suffering from trench feet with serious circulatory failure in them, but the feet were neither blistered nor septic, so that it did not appear likely that from them had been derived the toxic substances which had led to the purpura higher up the limbs.

February 5. Captain H. Henry reported that blood culture was negative, but that lumbar puncture had yielded a cloudy fluid containing intracellular diplococci in the film and giving definite meningococci on culture. The patient was at once transferred to an isolation hospital, before blisters could be applied to the edge of the purpuric patch as a test for the presence of meningococci in these foci.

February 6. Neck not stiff: abdominal reflexes still absent. Lumbar puncture yielded 50 c.c. of cloudy fluid containing cells with 90 per cent. of polymorphs but no organisms.

February 8. The finger-tips were now cold and discoloured. The necrotic areas on the thighs and legs had become almost coal black at their periphery.

February 25. The patient had recovered completely from his meningeal symptoms and looked very well, despite the severe sepsis in his lower limbs. Captain Walmisley, under whose care he had been since February 6, regarded the clinical features of cerebro-spinal meningitis as having been of the mildest character throughout. No special serum had been used intraspinally, and anti-tetanic serum had never been injected for the trench feet.

The pulp of the finger-tips in both hands was now shrivelled and blue, resembling the late results of a mild attack of Raynaud's gangrene. Both the feet were dead and gangrenous up to a line of demarcation about a couple of inches above the malleoli.

The legs and thighs showed enormous areas of ulceration from which the necrosed skin had sloughed away and laid bare the subcutaneous tissues. These areas were now covered with healthy granulations, and the skin at their edges was growing vigorously.

March 5. The gangrenous feet were both removed by amputation. The patient recovered well from the operation, and continued to improve, though the ulcerated areas on the thighs were slow in healing (March 10).

Necrotic purpura of the character and distribution seen in Case II has never been observed to our knowledge in ordinary frost-bite of the legs, so that its presence here must be ascribed to the complicating factor of meningococcal

infection. But purpura in cerebro-spinal meningitis is not restricted in its distribution to the lower extremities; and it is most rare for it to be followed by necrosis, partly perhaps for the reason that, when severe, it is usually associated with so overwhelming an infection that death ensues before the local necrotic changes can make themselves manifest.

The possibility of necrosis following upon purpura in a very severe form of infection is illustrated by a case quoted by Dr. Robb of Belfast (6), February 6, 1915, in which there was a plentiful petechial eruption together with large patches of haemorrhagic purpura on feet, knees, hands, ears, and also with sub-conjunctival haemorrhages. At this time the patient was unconscious and he seemed most dangerously ill, though he slowly recovered under serum treatment. During the recovery several patches of purpuric skin became necrosed and sloughed away.

In Dr. Robb's case the rash was widely distributed and the illness of the most alarming gravity. But Case II did not conform to this type, for the rash was practically confined to the legs and the meningococcal infection was otherwise so trifling in its features that the diagnosis might easily have been missed. The probable explanation is that the infection normally would not have been accompanied by any rash at all, but that the defenceless exposure to cold during general prostration at its onset led not only to the development of trench feet, but also to an outbreak of purpura which was localized in the chilled areas of skin under the waders. Since the fronts of the thighs as well as the nates were affected, it is obvious that the localization was not of that of pressure surfaces. It should be noted that the hands were slightly frost-bitten; and that there was a little purpura on the wrist.

How cold acted in determining this outcrop of purpura remains a matter for conjecture, because there are not enough facts known to give a true analysis of the pathological process. Blood infection was not proved to exist, and Captain Henry was unable to blister the purpuric areas in search for meningococci. But inasmuch as the meningococcus is an organism of the most delicate sensitiveness to cold, it seems unlikely that the great purpuric patches should have been the index of local colonies that had found their chance to establish themselves under the skin because these areas were chilled. The history from the Central Clearing Station tells that the purpura appeared simultaneously with the trench feet, and very soon after the waders had been removed; so that we can hardly take the explanation that the legs were first chilled and devitalized, and that at a later period, when the circulation improved, meningococci commenced to grow in the subcutaneous tissues which were now warmed but had lost their original powers of resistance. It therefore appears legitimate to assume that the purpuric rash was not focal but toxic.

The influence of cold or imperfect circulation in determining the distribution of rashes has often attracted the thought of clinicians, but generalizations have not been made on this subject, because each infection seems to have its own laws of reaction in this respect. For example, the toxic prodromal rash of

small-pox seeks the warm protected surfaces of the body, whereas the pustular eruption, which is usually regarded as a focal rash of the infecting organisms themselves, breaks out on the exposed and cooler skin surfaces. The purpura of meningococcal infections appears to belong to the group which is favoured in its development by cold. A comparison with paroxysmal haemoglobinuria at once occurs to the mind in considering this question. But the analysis of this latter condition that has been made by Eason and other workers shows that there is no real analogy between it and the purpura now under discussion. In the haemoglobinuric patient, cold enables a specific haemolytic amboceptor in the plasma to attach itself to the red corpuscles, which are subsequently haemolysed when they are carried away by the circulation to warmer parts. In Case II the meningococcal purpura may or may not have required a sequence of warmth following upon cold for its full development. But the whole action of the toxin was local; and not upon the blood corpuscles, but presumably upon the capillary endothelium by some lytic body which caused their local destruction and so allowed the escape of the blood. Tissue necrosis followed from obstruction of all the capillary circulation, and this may have been due to a thrombosis caused either by the toxins or by the cold.

REFERENCES.

1. Bourke, Abrahams, and Rowland, *Journ. Royal Army Med. Corps*, Lond., 1915, xxv. 633.
2. Brown, H. R., *ibid.*, 1916, xxvii. 747.
3. McNee, J. W., *ibid.*, 751.
4. Flack, M., *ibid.*, 1917, xxviii. 117.
5. Ellis, A. W. M., *ibid.*, 1916, xxvi. 64.
6. Robb, *Proc. Roy. Soc. of Med.*, Lond., 1915 (Ther. and Pharm. Sect.), ix. 5.

DESCRIPTION OF FIGURE.

PLATE 35. Drawing made on fourth day after onset of cerebro-spinal meningitis. The greyish-yellow colour of trench feet from subsequent exposure contrasts with the purpura higher up the leg. Over the thighs are widely distributed patches of meningococcal purpura which had been aggravated by the cold and are commencing to necrose, as is shown by the semi-opaque sheen over their surface where the skin is dying.

