REFERENCES

- Andrews, G. C., and Machacek, G. F. (1935). *Arch. Derm. Syph., Chicago*, 32, 837.
- Barber, H. W. (1929). *Lancet*, 2, 363, 483, 591.
- (1930). *Brit. J. Derm. Syph.*, 42, 500.
- (1935). *Deliber. Congr. Derm. Int.*, ix, 2, 655.
- (1936). *Taylor's Practice of Medicine*, p. 943. Churchill, London.
- (1938). *Proc. R. Soc. Med.*, 31, 705.
- (1946). *Practitioner*, 156, 341.
- Bauer, J., and Vogl, A. (1931). *Klin. Wschr.*, 10, 1700.
- Cecil, R. L., Nicholls, E. E., and Stainsby, W. J. (1931). *Amer. J. med. Sci.*, 181, 12.
- Cockayne, E. A. (1933). *Inherited Abnormalities of the Skin*, p. 362. Oxford University Press, London.
- Danysz, J. (1920). *Maladies Chroniques*, p. 36. Baillière et Fils, Paris.
- Desaux, A. (1948). *Traitement des Dermatoses Communes*, p. 485. Masson, Paris.
- Dodds, E. C., MacCormac, H., and Robertson, J. D. (1942). *Brit. J. Derm. Syph.*, 54, 212.
- Garrod, A., and Evans, G. (1924). *Quart. J. Med.*, 17, 171.
- Grüneberg, T. (1936). *Münch. med. Wschr.*, 83, 561.
- (1937). *Arch. Derm. Syph., Wien*, 175, 638.
- Grütz, O. (1934). *Dtsch. med. Wschr.*, 60, 1039.
- Hunt, E. (1933). *Lancet*, 2, 351.
- (1938). *Proc. R. Soc. Med.*, 31, 708.
- Incedayi, C. K., and Ottenstein, B. (1941). *Dermatologica, Basel*, 84, 330.
- Ingram, J. T. (1938). *Deliber. Congr. Derm. Int.*, ix, 2, 671.
- Kissmeyer, A. (1935). *Int. Congr. Derm.*, 1, 282.
- MacLeod, J. M. H. (1920). *Diseases of the Skin*, p. 824. Lewis, London.
- Norrlind, R. (1947). *Nord. Med.*, 35, 1862.
- Petit, A., and Loiseau, G. (1908). *C.R. Soc. Biol., Paris*, 64, 869.
- Reiss, F. (1949). *Arch. Derm. Syph., Chicago*, 59, 78.
- Selye, H. (1946). *J. clin. Endocrinol.*, 6, 117.
- Shlionsky, H., and Blake, F. G. (1936). *Ann. intern. Med.*, 10, 537.
- Wittkower, E. (1948). *In Modern Trends in Dermatology*, p. 247. Butterworth, London.

SCIATIC PARALYSIS IN NEWBORN INFANTS*

BY

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Twenty cases of unilateral sciatic paralysis, sometimes accompanied by cutaneous gangrene of the ipsilateral buttock, have been seen in newborn infants in the maternity departments of two hospitals in Liverpool. In Hospital I, the maternity department of which has about 700 deliveries each year, three cases of sciatic paralysis occurred during 1945. In Hospital II, with an average of 3,000 deliveries annually, 17 cases of sciatic paralysis were recorded during the period from April, 1945, to June, 1948. Eleven of these cases have been studied by Fahrni (1950). The purpose of this paper is to record the development of further cases and to suggest a probable theory of causation.

Clinical Picture

Two cases are here described in detail, and the salient features of all the cases are summarized.

Case 1.—A male infant weighing 8 lb. 1 oz. (3.7 kg.) was the first child of a healthy mother aged 28. Labour took place at term and lasted 32 hours. The head presented in the left occipito-anterior position and the infant was born with the cord tightly around the neck and in a state of asphyxia pallida.

*This article is based on a paper read by one of us (F. P. H.) before the Liverpool Paediatric Club on April 22, 1949.

Routine measures of resuscitation were employed and recovery was prompt. Before the infant left the labour ward the right leg was noticed to be white and the right buttock of a bluish colour. On the following day the right leg was still pale and there was complete foot-drop.

Case 2.—A male infant weighing 5 lb. 3 oz. (2.4 kg.) was the first child of a healthy mother aged 22. Labour lasted 22 hours and the head was delivered in the left occipito-anterior position after an episiotomy. The infant was in a state of asphyxia pallida, but responded well to routine measures of resuscitation. "Bruising" of the left buttock was noticed on the day of birth. Next day the discoloration extended from the iliac crest to the inferior gluteal fold, crossing the midline slightly in the perineum only. There was a flaccid paralysis of the calf muscles and peronei, but the quadriceps and hamstrings seemed normal. The discoloration changed to a hard black necrotic area, less extensive than the original bruising and having a clearly marked hyperaemic margin (see photograph). A central slough gradually peeled away, leaving a clean granulating ulcer. After six and a half weeks a healed scar remained, and there was also complete foot-drop on the same side. At the age of 6 months movement of the toes and ankle was fairly good, but the left foot was colder and $\frac{1}{2}$ in. (1.25 cm.) shorter than the right foot.

Case 2. The hard black necrotic area eight days after birth.

In the 20 cases observed the mothers of the affected infants were of various ages and parity. All had normal pelvises and were healthy during pregnancy. Delivery was by vertex presentation in all but three cases, one infant being delivered by lower-segment caesarean section and two by breech extraction. In every case but one asphyxia at birth was recorded.

The left leg was affected in 14 cases and the right in six. Paralysis was usually noticed during the first 24 hours, but in some cases it was not recorded until the second day. The most obvious and persistent feature in all the affected babies was foot-drop. Movement has improved gradually during the first six or nine months, and in a few instances recovery has been complete. In the majority of cases some degree of foot-drop has remained and growth of the foot has been retarded. The late appearance resembles that of poliomyelitis, and some of these infants will require operative orthopaedic treatment to correct shortening and equinovarus deformity. All have been kept under supervision and have received physiotherapy.

Gangrene developed in the buttock of the affected leg in six cases; its first indication was a bluish mottling of the skin, often noticed in the labour ward. In two or three days the discoloured area had a sharply defined serpiginous margin and the centre was bluish red, often with small white patches; at the periphery there was a narrow red band. The lesion was not raised, but on palpation felt hard. Gradually a black slough peeled away, leaving a deep ulcer and finally a permanent scar. In one other

case the initial discoloration appeared to be fading when the infant was taken home against advice on the tenth day.

Two infants had generalized muscular twitchings suggestive of cerebral asphyxia or trauma. The convulsions ceased in 48 hours and there was no evidence of cerebral damage after six or nine months.

Discussion

Paralysis of one or both legs in a newborn infant may follow a difficult breech delivery, due to stretching of the lumbosacral plexus or to damage to the spinal cord; but such injuries are rare. Morgan (1948) has described radial nerve paralysis in the newborn caused by the intrauterine pressure of a contraction ring. Gangrene of an upper left extremity in a newborn infant has been described by Steiner (1945). In this case gangrene began in the fingers and progressed to the forearm so that amputation was eventually required. Trauma during delivery was thought to be the cause, the arm having prolapsed and become compressed between the child's cranium and the mother's bony pelvis.

It is of interest to note that in 39 cases of gangrene affecting the extremities of newborn infants reviewed by Heller and Alviri (1941), labour was "difficult" in 11 cases, the cord encircled the neck in two instances, and asphyxia was present in eight cases. Paralysis of the affected limb preceded the onset of gangrene in the case described by Steiner and also in a case described by Heller and Alviri.

Various causes for the lesions we have described must now be considered.

1. The adoption of some unusual method of resuscitation by a particular midwife has been suggested, but can be ruled out by the frequent changes of staff in the labour wards.

2. No prominent ridge was found on the resuscitation table which might have damaged the delicate tissues of a newly born infant.

3. A misplaced injection of vitamin K which might conceivably damage the sciatic nerve and the skin of the buttock. When an oily preparation of the vitamin was used in Hospital II, an abscess sometimes occurred at the site of injection, but paralysis or cutaneous gangrene was never recorded. Since September, 1947, a watery preparation has been used exclusively, and it has not been known to cause any ill-effects. Cases of sciatic paralysis continued to occur after the use of vitamin K by injection had been entirely stopped.

4. One of us (A. G. O'M.) suggested that "cycliton," the analeptic in regular use in Hospital II, might have been injected into an umbilical artery in mistake for the vein. When we were investigating this possibility Mills (1948) reported somewhat similar cases which he attributed to the injection of nikethamide ("coramine") into an umbilical artery. He has since reported the series in detail (Mills, 1949), and we agree in general with his conclusions. Bates and Page (1949) have recorded one similar case in which nikethamide was used as an analeptic. In 19 of our 20 cases asphyxia at birth was recorded, and cycliton, 0.3 ml. to 1 ml. was injected into a cord vessel. In one case, however, there was no record of asphyxia being present or cord injection being given, and if our theory is correct it seems probable that a busy midwife had omitted to note the fact on the case sheet.

The effects of intra-arterial injections of potentially dangerous or irritative drugs have been carefully studied by Cohen (1948). He discusses 12 cases in which the accidental intra-arterial injection of thiopentone in the antecubital fossa had serious effects. The clinical results included pallor and cyanotic mottling of the skin distal to the site of injection, paralysis, and sensory changes in the forearm and hand, and often an extensive peripheral gangrene which necessitated amputation. Most striking of all, he describes in detail patches of cutaneous gangrene

which closely resemble those which we have seen. In most of the cases described by Cohen, intra-arterial thrombosis was found when arteriotomy was performed (in one case as early as 50 minutes after the injection) or on dissection of an amputated limb.

Gammel (1927) reported necrotic lesions in the skin of the buttock after injections of bismuth and differing in character from the deep-seated abscess which may follow an intramuscular injection. In one of his cases there was also peroneal nerve paralysis. He was able to find about 30 reports of similar conditions following injection of mercury or bismuth preparations. One observer had made a biopsy of the skin lesion and had found that the cutaneous arterioles were blocked with crystals of bismuth salicylate. This important finding was confirmed by animal experiment. The inference is that the drug had been injected into a deep artery, possibly the inferior gluteal, and had caused local emboli.

Clinically the lesions we have described were comparable with others in which intra-arterial thrombosis has been demonstrated. This possibility must now be examined from the anatomical, physiological, and pharmacological aspects.

In the foetus the blood supply to the lower limb is carried by the sciatic artery, the main branch of the internal iliac artery, and the external iliac artery is a purely subsidiary blood supply. After birth this function is reversed; the main blood supply is gradually taken over by the external iliac artery, and the sciatic artery becomes quite a small vessel, functioning mainly as the nutrient artery of the sciatic nerve.

In asphyxia neonatorum of severe degree the umbilical vein, like other veins, will be collapsed. It is therefore conceivable that an injection into the cord may be given into one of the two umbilical arteries. This fluid will pass down to the hypogastric artery and so to the internal iliac artery and the sciatic artery. If such a fluid caused arterial spasm, followed by thrombosis, the blood supply to the sciatic nerve and to the buttock would be jeopardized.

Nerves have a regional and longitudinal blood supply. They receive twigs from any near-by artery, and those twigs divide in the substance of the nerve to form a longitudinal anastomosis. The latter is said to give nerves a relative independence from the regional supply. In the case of the sciatic nerve, however, Adams (1942), referring to work done on the blood supply of the nerve, says, "The results are convincingly in favour of the dominance in this nerve at least of the regional over the longitudinal." He also points out that degeneration of the sciatic nerve in a rabbit has been produced by ligation of the inferior gluteal artery. One infant died from enteritis, giving the opportunity of sectioning the sciatic nerve. At the level of the slough there were recent haemorrhages into the nerve fascicles, while distal to it the circumference of the fascicles was waxy, suggesting shrinkage. Wallerian degeneration was not seen, probably because an ischaemic nerve with complete anatomical continuity between cell body and axis cylinder still persists, Wallerian degeneration being due essentially to a structural interruption in the continuity of the axis cylinder.

Cohen suggested that the ill-effects of intra-arterial thiopentone might be due to its alkalinity. It has a pH of 10.4-10.6. Cycliton, in contrast, is acid (pH 4.92) and coramine also (pH 5.77). It is unlikely that the acidity plays a significant part in causing these lesions, as no ill-effects have followed the use of lobeline (pH 4.80) as an analeptic. Lobeline, however, is an alkaloid obtained from *Lobelia inflata*, while the other two drugs are

synthetic compounds of a similar structure. Nikethamide (coramine) = pyridine- β -carboxylic acid diethylamide. Cycliton = diethylamide of 3:5-dimethyliso-oxazol-4-carboxylic acid.

No information has been obtainable about the detailed pharmacological action of cycliton. Faust (1925) has shown that nikethamide causes vasoconstriction by local action on the vessels, a property not found when Curtis and Wright (1926) investigated lobeline. Possibly the vasoconstriction produced locally by cycliton, associated with the vasoconstriction and slowing in arterial blood flow that accompanies asphyxia, precipitates the development of thrombosis. Beyond this we can only say, as Cohen does of thiopentone, that the arterial intima appears to be particularly sensitive to cycliton.

An attempt to reconstitute the lesion in animals was made by Professor R. A. Gregory (Department of Physiology). One millilitre of cycliton was injected into the internal iliac arteries of six adult cats, under light ether anaesthesia at aseptic operation, with negative results. The experiments were then repeated, but before injecting the cycliton the animals were kept in a state of asphyxia. Again the results were negative. Finally, in order to make conditions as comparable as possible to those obtaining in the newborn infant, small amounts of cycliton (0.05–0.5 ml.) were injected into the umbilical arteries of four newborn kittens; none of these animals survived longer than 24 hours.

Summary

Twenty cases of unilateral sciatic paralysis in the newborn, sometimes accompanied by cutaneous gangrene, are described. Accidental injection of cycliton into an artery instead of the vein in the umbilical cord is suggested as the possible cause of the lesions.

Experimental proof is as yet lacking, but the evidence in favour of this theory is as follows:

1. The cases occurred only in the hospitals in the city of Liverpool in which cycliton was in use.
2. The only common factors were asphyxia at birth and injection of cycliton into a cord vessel.
3. The lesions are consistent with the results of ischaemia due to disturbance of blood flow in the internal iliac artery, and are comparable to the lesions produced by intra-arterial injection of thiopentone.
4. No further lesions have occurred since cycliton has ceased to be used. (Cycliton is not now sold in England, although it is used extensively on the Continent and in other parts of the world.)

We would like to thank Professor R. A. Gregory for the considerable amount of thought and time that he has given in an attempt to establish experimental evidence, and Professor N. B. Capon and Mr. Bryan McFarland for their interest and help in the preparation of this article. We also wish to thank Professor T. N. A. Jeffcoate for permission to publish three of the cases, and Dr. S. E. Keidan (paediatric registrar) for his interest in the problem and help in recording the clinical details of many of the cases.

REFERENCES

- Adams, W. E. (1942). *J. Anat.*, **76**, 323.
 Bates, C., and Page, A. P. M. (1949). *British Medical Journal*, **2**, 756.
 Cohen, S. M. (1948). *Lancet*, **2**, 361, 409.
 Curtis, F. R., and Wright, S. (1926). *Ibid.*, **2**, 1255.
 Fahrni, W. H. (1950). *J. Bone Jt Surg.* In the press.
 Faust, E. S. (1925). *Lancet*, **1**, 1336.
 Gammel, J. A. (1927). *J. Amer. med. Ass.*, **88**, 998.
 Heller, G., and Alvari, G. (1941). *Amer. J. Dis. Child.*, **62**, 133.
 Mills, W. G. (1948). *British Medical Journal*, **2**, 956.
 — (1949). *Ibid.*, **2**, 464.
 Morgan, L. (1948). *Arch. Dis. Childh.*, **23**, 137.
 Steiner, M. D. (1945). *Amer. J. Obstet. Gynec.*, **49**, 686.

ANAPHYLACTOID PURPURA IN PULMONARY TUBERCULOSIS

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The occurrence of purpura in association with pulmonary tuberculosis is generally considered to be a rarity. Instances of it in sanatoria reports are not common, and references to it in the literature do not seem to be numerous, most of them appearing in publications from other countries. In view of this we feel it justifiable to report five cases which all attended a general medical clinic within the space of twelve months.

The association of purpura with pulmonary tuberculosis was described as early as 1801 by Willan in his treatise on cutaneous disease. He had noted the occurrence of purple spots in the skin in the last stages of pulmonary consumption, and considered it to be a forerunner of death. In contradistinction to this, in 1890 Rendu described a purpuric eruption especially prone to occur on the dorsum of the hands and wrists, which he considered was a premonitory sign of tuberculosis. Sixteen years later Bensaude, Carnot, and Harvier reported a case of purpura as a pre-tuberculous manifestation. In that year also, Bensaude and Rivet (1906) produced their monograph on this subject. They have classified four main groups: (1) Purpura haemorrhagica occurring in the course of miliary tuberculosis—and this was more common if the miliary state was superimposed on chronic disease. (2) Purpura haemorrhagica occurring in the course of chronic pulmonary tuberculosis, usually in terminal and cachectic states. (3) Purpura haemorrhagica occurring in the course of latent tuberculosis. (4) Purpura haemorrhagica occurring in the course of extrapulmonary tuberculosis.

They also considered that purpura may occur as a pre-tuberculous manifestation, though they did not classify it as such, and they stress the importance of searching for a tuberculous focus in the presence of chronic or recurring purpuric eruptions. Single cases found in the literature—such as that of Gossner, who reported the occurrence of purpura in a man with a tuberculous testis, the eruption disappearing with the removal of the organ—can be fitted into the classification.

The gravity of purpura as a symptom in pulmonary tuberculosis was stressed by Cruice (1912), who considered that it marked either a terminal stage or an exacerbation from which the patient might die, or if recovery occurred the state of the lesion would be found to be more advanced.

The purpura may be due to a symptomatic thrombocytopenia, be a simple symptomatic purpura, or be of the Henoch-Schoenlein group. The last-mentioned form is suggested by Bauch (1916). Wits (1946) considers that in all cases the endothelial lining of the vessels is damaged, and states that the platelet count varies from case to case. Greengard (1931), in his review of two cases, also considered capillary damage to be the most important factor in its development.

Case 1

A man aged 44 was admitted to hospital from the out-patient department. He gave a history of heaviness in the abdomen associated with nausea and loss of appetite of nine days' duration. Two days before admission he had noticed a generalized