no inquiry had been made about the administration of mercury compounds at the first interview with the parents, so that the possibility that mercury was the cause of the nephrosis would not have come to light had our suspicions not been previously aroused. Our experience with Case 3 shows that a considerable amount of mercury may remain in the body for long periods and that more than one course of dimercaprol may be necessary to eliminate it adequately. If the treatment with dimercaprol is instituted promptly complete recovery of renal function is possible. Cast 4 shows that in some cases spontaneous recovery may occur when the intake of mercury is stopped, though its excretion may continue for relatively long periods. On the other hand, Case 5, in which no dimercaprol was given, proved fatal.

In view of these findings we urge that mercury compounds should be eliminated from all teething powders and that other mercury compounds, such as grey pills, be used with care, and prolonged administration be avoided in young children. Teething powders not containing mercury are free of the risks we have described.

Summary

Five cases of mercury nephrosis are described. Complete recovery in a short period in three cases treated with dimercaprol is reported. Of two cases not treated with dimercaprol one patient recovered and one died.

We are indebted to the resident medical and nursing staffs who have cared for these children while in hospital, to Miss J. Summerscales for assistance with the mercury estimations, and to Miss P. M. Gorse for routine biochemistry in some of the cases.

REFERENCES

Fanconi, G., Botsztejn, A., and Schenker, P. (1947). *Helv. Paediat. Acta*, Suppl. 4, 2, 3.
Leschke, E. (1934). *Clinical Toxicology*, pp. 32-57. Churchill, London.
Milton, R. F., and Hoskins, J. L. (1947). *Analyst*, 72, 6.

FATAL HYPOKALAEMIC ALKALOSIS WITH TETANY DURING LIQUORICE AND P.A.S. THERAPY

BY

N. J. ROUSSAK, M.B., B.Sc., M.R.C.P.
Medical Registrar, Manchester Royal Infirmary

This is a report on a patient who, while receiving treatment for tuberculous meningitis, developed unexplained electrolyte abnormalities, from which she died. Papers published subsequently have thrown light on the mechanism of her death.

Case Report

A girl aged 15 received a full course of streptomycin for miliary tuberculosis with tuberculous meningitis, and was discharged from hospital on February 24, 1950, having made a satisfactory recovery. She was seen at intervals as an outpatient, and gained weight and strength. On May 27 she was readmitted with a recurrence of the meningitis, and was treated with intramuscular and intrathecal streptomycin and sodium *para*-aminosalicylate (P.A.S.). The P.A.S. was given in a mixture containing 2 g. of sodium *para*-aminosalicylate and 12 min. (0.72 ml.) of ext. glycyrrh. liq. *B.P.*, and the dose was increased gradually to 20 g. daily. About 595 ml. of ext. glycyrrh. liq. was taken over the whole period. The meningitic symptoms showed signs of improvement, but on August 3 she complained of stiffness of her arms and legs, and there was twitching of the face. Later in the day she was reported to have had two epileptic attacks.

There were no further attacks during the next two weeks, during which phenobarbitone was prescribed, but stiffness was still a complaint. About August 24 muscular cramps occurred, and it was plain that she was having severe tetany, with carpopedal and facial spasm, and slight respiratory difficulty. There was no evident hyperpnoea. The serum calcium was found to be low (7.5 mg. per 100 ml.), and plasma alkali reserve 82 vols. CO_2 per 100 ml. The urinary calcium was normal as judged by Sulkowitch's reagent. Repeated administration of calcium gluconate intravenously had only a transient effect on the attacks of tetany, which increased in duration, and Trousseau's sign was constantly positive. On August 27 the electrocardiogram showed ST depression as occurs in hypokalaemia. On three occasions generalized convulsions with opisthotonos occurred during severe attacks of tetany. She gradually became weaker, with rapid shallow respirations, and died on September 2. The biochemical findings on the last two days of life were those of a hypochloraemic hypokalaemic alkalosis, and are shown in the Table.

Date	Plasma CO_2 Vols./100 ml.	Serum K mg./100 ml.	Plasma Cl mg./100 ml.	Serum Ca mg./100 ml.	Serum Na mg./100 ml.	Serum Inorganic Phosphorus mg./100 ml.
Aug. 25	82		374	7·5		
,, 26	82		410			
,, 28	82	13	386	8·5	345	3·7
,, 30			386	8·5		
,, 31	92	13	421		345	

On August 28 the serum alkaline phosphatase was 5 K.-A. units. On August 31 the serum albumin was 2·1 g.% and globulin 3 g.%.

At the post-mortem examination there was evidence of active tuberculous meningitis.

Discussion

One month after this patient had died, Borst *et al.* (1950) showed that liquorice had a deoxycortone-like action, and Strong (1951) has reported that two patients with tuberculosis who received P.A.S. flavoured with liquorice developed tetany with similar electrolyte findings to those of my patient. Also, Strong was informed by Cayley, who had recorded the development of hypokalaemia in three patients having P.A.S. (Cayley, 1950), that liquorice had also been given in his cases.

There seems to be good circumstantial evidence that liquorice was responsible for the electrolyte changes shown by these patients and the fatal case here recorded. The tetany seems to have been less severe in the cases reported by Strong than in the present case. His patients, although having cramps and positive Trousseau's sign, had a negative Chvostek's sign, but my patient had facial, carpopedal, and laryngeal spasm, with convulsions. The low serum calcium was due to the hypoalbuminaemia (2.1 g. of albumin per 100 ml.). The presence of a normal urinary calcium, as estimated by Sulkowitch's reagent, suggests that the diffusible calcium was normal in amount in the serum. Thus the tetany was unrelated to the low serum calcium.

Hypochloraemic hypokalaemic alkalosis is found in Cushing's syndrome and can be produced in man by cortisone, but the only evidence I can find of its production by D.C.A. is recent work by Seldin *et al.* (1951). These workers suggest, as a result of experiments, that D.C.A. has no direct effect on the renal excretion of potassium, but that a potassium diuresis may follow D.C.A. administration as a passive consequence of sodium retention. They were able to produce a hypochloraemic hypokalaemic alkalosis by D.C.A. if sodium was given freely, and in fact my patient was receiving the sodium salt of P.A.S., and was later given intravenous sodium chloride because of the hypochloraemia. Tetany is not mentioned by these workers, nor in reports of cortisone toxicity, and in fact the low serum potassium would make the occurrence of tetany unlikely. Tetany in

other forms of metabolic alkalosis is, of course, well recognized. The P.A.S. could hardly have produced the observed electrolyte changes, because salicylate causes a respiratory alkalosis, with low alkali reserve, but the addition of a mild respiratory alkalosis to the metabolic alkalosis caused by the liquorice would favour the occurrence of tetany.

It is understood that difficulty has been found in producing electrolyte abnormalities experimentally with some preparations of liquorice, and it is possible that there may be a variation in the D.C.A.-like activity of different batches of liquorice extract.

It is interesting that the urinary chloride concentration, estimated by the Fantus test, remained very high (4–8 g. per litre) throughout the last week, contrary to what one might expect from the combined effects of hypochloraemia, alkalosis, and D.C.A.-like liquorice. In fact, this is often found in hypokalaemia, as Fourman (1951) points out.

Summary

A patient receiving sodium *para*-aminosalicylate for tuberculous meningitis developed a metabolic alkalosis, from which she died.

Liquorice, used as a flavouring agent with the P.A.S., appears to have been responsible.

I am grateful to Dr. N. Kletts for permission to record this case. My thanks are also due to Mr. Varley for the biochemical determinations, and Dr. D. A. K. Black for helpful advice.

REFERENCES

Borst, J. G. G., Gerbrandy, J., Jong, J. C. de, Lenstra, J. B., Molhuysen, J. A., Turner, K. P., and Vries, L. A. de (1950). *Lancet*, 2, 381.
Cayley, F. E. de W. (1950). Ibid., 1, 447.
Fourman, P. (1951). *British Medical Journal*, 2, 1284.
Seldin, D. W., Welt, L. G., and Cort, J. (1951). Paper read to American Society for Clinical Investigation. Abstracted in *J. clin. Invest.*, 1951, 30, 673.
Strong, J. A. (1951). *British Medical Journal*, 2, 998.

CASE ILLUSTRATING HAZARDS OF MANIPULATIVE TREATMENT IN LUMBO-SACRAL DISK PROTRUSIONS

BY

ROBERT HAFNER, F.R.C.S.

Orthopaedic Registrar, St. Peter's Hospital, Chertsey

A recent experience having a bearing on the practice of manipulation of the spine for lumbo-sacral disk lesions seems worth recording.

Case Report

A man aged 36 who was engaged in heavy work had a sudden onset of low-back pain spreading down the back of his right leg to the foot. There was a past history of two previous similar attacks. A radiograph of the lumbo-sacral spine showed the L.5/S.1 joint space to be diminished posteriorly; otherwise there was no abnormality.

The patient was suffering from a protrusion of an intervertebral disk of the lumbo-sacral spine. The physical signs did not alter during five weeks' rest in bed, although the symptoms were definitely diminished. He was encouraged to move his back under intravenous procaine analgesia (5 ml. of a 1% solution of procaine). Although only 30 degrees of flexion was allowed he suddenly experienced very severe pain down the back of his right leg, which caused him to cry out. Morphine was necessary. Flexion of the spine and raising of the straight leg were not possible. The pain continued for 48 hours, until laminectomy was performed.

At operation the cauda equina was displaced backwards by a large disk protrusion, over which the first sacral root was tightly stretched. Furthermore, deep to this, in the intervertebral space, was a considerable quantity of "sequestrated" nuclear material, lying free and comprising the remainder of the nucleus pulposus. This could have been forced into the spinal canal by pressure resulting from increased movement of the spine. The operative findings are illustrated in Fig. 1; the disk material after removal is shown in Fig. 2.

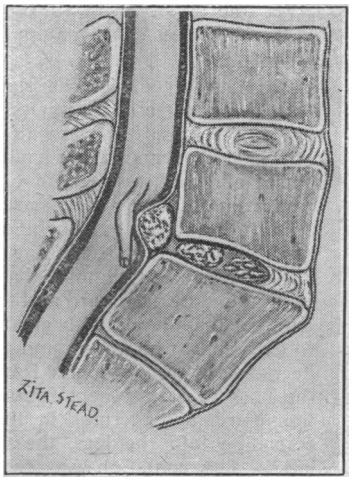

FIG. 1.—Diagrammatic representation of the operative findings.

Follow-up Report.—On the day after operation, February 12, 1951, the patient was free from pain but had some numbness of the right foot. He remained free from symptoms and was allowed up 17 days after operation. He was discharged to his own home on March 5, and returned on April 2 to the same heavy work that he had been doing pre-operatively. He has since been at this work, and when last seen (September 16) he was symptom-free.

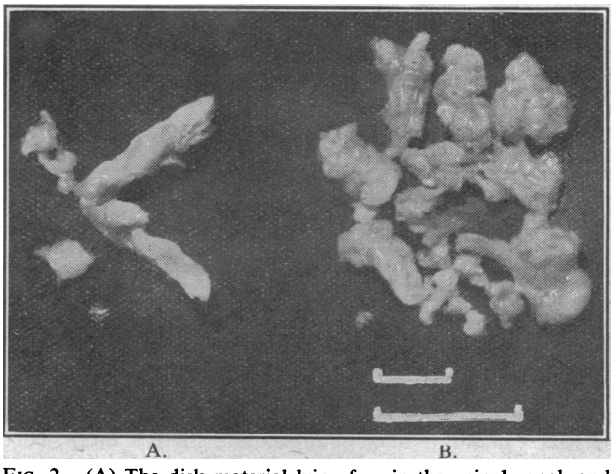

FIG. 2.—(A) The disk material lying free in the spinal canal, and (B) the disk material in the intervertebral space. Marked distances equal 1 cm. and 2 cm.

Commentary

The increased flexion of the spine forced more disk material into the spinal canal, exaggerating the symptoms and signs of lumbo-sacral root pressure. The operative findings of more "free" nuclear material lying ready to enter the spinal canal demonstrates that had more flexion been obtained, as in a forceful manipulation for instance, the size of the "tumour" in the spinal canal might well have produced a cauda-equina lesion.

Although it is not our practice to use manipulation in the treatment of lumbo-sacral disk lesions, we considered the possibility that we were dealing with an uncommon type in which the extruded disk material was nipped by the posterior margin of adjacent vertebral bodies and so prevented from returning. We wondered if the muscular relaxation and increased movement of the spine, made possible by analgesia, would result in sufficient widening of the intervertebral space to allow the prolapse to reduce spontaneously.