Ciba Laboratories, for supplies of Synacthen. We are particularly grateful to Dr. V. H. T. James, of St. Mary's Hospital, for all his help and advice. One of us (C. L.) was supported by a grant from the Guy's Hospital Endowment Fund and we are grateful for this assistance.

REFERENCES

Bayliss, R. I. S. (1955). *Brit. med. J.*, **1**, 495.
Bethge, H., Brauns M. Th., Solbach, H. G., Winkelmann, W., and Zimmermann, H. (1966). *Klin. Wschr.*, **44**, 870.
Brooks, R. V., Dupré, J., Gogate, A. N., Mills, I. H., and Prunty, F. T. G. (1963). *J. clin. Endocr.*, **23**, 725.
Bush, I. E., and Sandberg, A. A. (1953). *J. biol. Chem.*, **205**, 783.
Cope, C. L., and Black, E. G. (1959). *Brit. med. J.*, **2**, 1117.
Dyrenfurth, I., Blair, A. J., Beck, J. C., and Venning, E. H. (1960). *J. clin. Endocr.*, **20**, 735.
Eik-Nes, K., Sandberg, A. A., Migeon, C. J., Tyler, F. H., and Samuels, L. T. (1955). Ibid., **15**, 13.
James, V. H. T., Landon, J., and Wynn, V. (1965). *J. Endocr.*, **33**, 515.
Liddle, G. W. (1960). *J. clin. Endocr.*, **20**, 1539.
Mattingly, D. (1962). *J. clin. Path.*, **15**, 374.
Nichols, T., Nugent, C. A., and Tyler, F. H. (1965). *J. clin. Endocr.*, **25**, 343.
Norymberski, J. K., Stubbs, R. D., and West, H. F. (1953). *Lancet*, **1**, 1276.
Nugent, C. A., MacDiarmid, W. D., Nelson, A. R., and Tyler, F. H. (1963). *J. clin. Endocr.*, **23**, 684.
—— Nichols, T., and Tyler, F. H. (1965). *Arch. intern. Med.*, **116**, 172.
Poisnick, J., and DiRaimondo, V. (1956). *J. clin. Endocr.*, **16**, 957.
Ross, E. J., Marshall-Jones, P., and Friedman, M. (1966). *Quart. J. Med.*, **35**, 149.

Medical Memoranda

Intracranial Hypertension in a Child during Treatment with Nalidixic Acid

Brit. med. J., 1967, **2**, 744–745

A case of bulging fontanelle, papilloedema, widening of skull sutures, and vomiting in a 6-month-old boy after nalidixic acid therapy is described. The symptoms occurred on two different occasions when he was treated with the drug for a urinary tract infection, and subsided rapidly when the medication was discontinued. The suspicion of a connexion between the nalidixic acid and the increased intracranial pressure was confirmed when, on a third occasion, the same symptoms could be provoked after administration of the drug under carefully controlled conditions.

CASE HISTORY

Episode 1 (Fig. 1).—A previously healthy 6-month-old boy weighing 6,480 g. was treated at another hospital with nalidixic acid (100 mg. orally four times daily) for a urinary tract infection. On the third day of treatment he vomited, and on the fourth day was found to have a bulging anterior fontanelle. There was a slight papilloedema on the right side. No explanation for this increase in intracranial pressure was found and he was admitted to this hospital, where *x*-ray examination of the skull showed sutures wider than normal. Electroencephalography, echoencephalography, pneumoencephalography, and blood pressure were normal and he was afebrile. High pressure in the subarachnoidal space was found on bilateral exploration (operation 1). The fontanelle was normal after the operation.

Episode 2 (Fig. 1).—Two weeks after the first symptoms the patient was discharged to the other hospital, where treatment of the urinary infection was resumed with nalidixic acid in the same dose as before. On the evening of the first day bulging over the trephine hole on the left side was noted. On the second day a bulging fontanelle appeared and he was readmitted to this hospital. There was a slight papilloedema on the right side. The general condition of the boy was quite good. A puncture was made through the trephine hole (operation 2), but the bulging reappeared rapidly. The cerebrospinal fluid was sterile. Nalidixic acid was now suspected to be the cause of the symptoms and was discontinued. Next day the bulging over the trephine hole and over the fontanelle had disappeared. Two weeks later the eye-grounds were normal. Urological examination showed a hydronephrosis and a stenosis of the ureter on the left side. Non-protein nitrogen and creatinine clearance were normal. Urological surgery was postponed until the cerebral symptoms could be explained.

Episode 3 (Fig. 2).—Three weeks after the end of episode 2 the boy was again admitted to this hospital. He was then 8 months old, weighed 8,195 g., and was in excellent condition. The fontanelle, eye-grounds, and physical and neurological examinations were all normal and no bacteria were present in the urine. Nalidixic acid was again given and the plasma levels of total free extractable drug were determined by spectrophotofluorometric assay according to McChesney *et al.* (1964). The analyses were kindly run by Mr. A. Robertson, of Winthrop Laboratories, Newcastle upon Tyne. The fontanelle was checked at short intervals. Signs of increased intracranial pressure occurred soon after the onset of medication. The patient vomited twice within the first 24 hours. A tense fontanelle was noted after about 36 hours and was definitely bulging and pulsating after 48 hours. A slight papilloedema on the right side developed at about the same rate. The medication was immediately discontinued. One day later the fontanelle was normal.

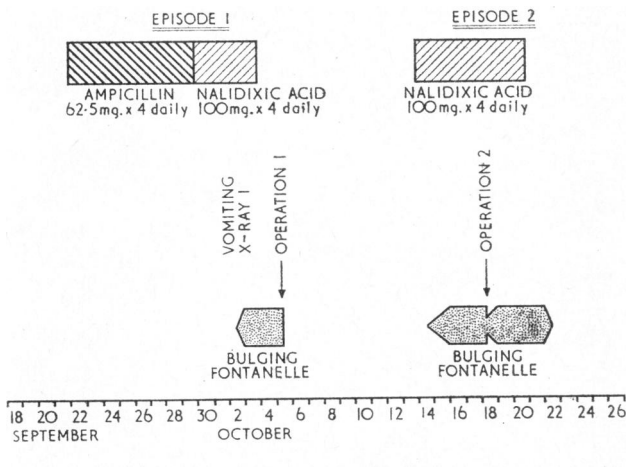

FIG. 1

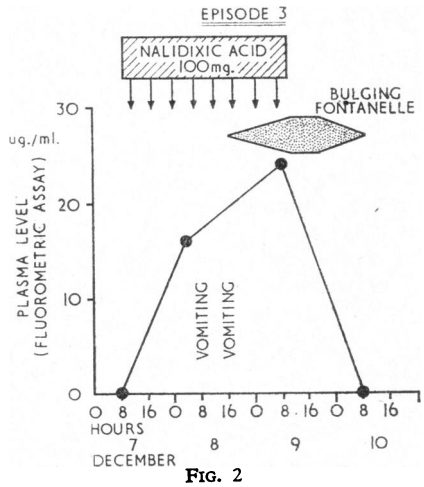

FIG. 2

FIG. 1.—Episodes 1 and 2. Intracranial hypertension during treatment of a urinary infection with nalidixic acid.
FIG. 2.—Episode 3. The same symptoms as in episodes 1 and 2 could be provoked with nalidixic acid under controlled conditions and in absence of urinary tract infection.

Three weeks after discontinuation the eye-grounds were normal and x-ray examination of the skull showed normal sutures. There were no sequelae and the boy was doing very well.

Discussion

The first two episodes of increased intracranial pressure occurred in close connexion with nalidixic acid medication. No other drugs were involved. It was necessary to obtain final proof of a cause-and-effect relation in this case because it was important to explain the reaction before surgery for the ureter stenosis was undertaken. Thus an attempt was made (episode 3) to provoke the symptom by a third administration of the drug with the patient under close surveillance.

The earlier symptoms of intracranial hypertension now promptly reappeared, and, as before, they were rapidly reversible. The plasma levels of nalidixic acid paralleled these clinical observations very closely. There was a sharp rise in concentration and a rapid decrease after discontinuation. As the drug had to be withdrawn on the second day of medication, data about its possible cumulation could not be obtained. However, according to data available in the literature (McChesney *et al.*, 1964 ; Walker *et al.*, 1966) the levels in this patient do not seem to be particularly high. The rate of disappearance of the drug from the blood also seems to be in the same order as that described by the authors mentioned above.

Benign intracranial hypertension has been reported after treatment with tetracycline (Millichap, 1959 ; Fields, 1961 ; Opfer, 1963 ; O'Doherty, 1965), with corticosteroids (Dees and McKay, 1959 ; Valentine, 1959 ; Laurence *et al.*, 1960 ; Greer, 1963 ; Walker and Adamkiewicz, 1964), and with toxic doses of vitamin A (Josephs, 1944 ; Oliver, 1958 ; Marie *et al.*, 1963 ; Persson *et al.*, 1965). A bulging fontanelle as a side-effect of nalidixic acid, however, has not previously been described in the literature, though Walker *et al.* (1966) reported that one of their patients, a 9-year-old girl admitted to hospital after a car injury, developed a slight papilloedema while receiving nalidixic acid for a urinary tract infection. Details were not given, but this suggests a drug effect, since the papilloedema disappeared when the drug was discontinued. Furthermore, the manufacturer (Winthrop Company) have informed us that in their files they have four recent reports on intracranial hypertension during nalidixic acid therapy in children. However, in none of these cases was a connexion with the medication proved and none of them has been published.

The real incidence of intracranial hypertension after nalidixic acid is not yet known. It is recommended that the possibility of this side-effect be kept in mind during treatment with the drug.

L. O. Boréus, M.D.,
Division of Clinical Pharmacology.
B. Sundström, M.D.,
Division of Medicine.
Department of Paediatrics,
Karolinska Sjukhuset,
Stockholm 60, Sweden.

References

Dees, S. C., and McKay, H. W. (1959). *Pediatrics*, **23**, 1143.
Fields, J. P. (1961). *J. Pediat.*, **58**, 74.
Greer, M. (1963). *Neurology (Minneap.)*, **13**, 439.
Josephs, H. W. (1944). *Amer. J. Dis. Child.*, **67**, 33.
Laurance, B. M., Matthews, W. B., and Shephard, R. H. (1960). *Lancet*, **1**, 701.
McChesney, E. W., Froelich, E. J., Lesher, G. Y., Crain, A. V. R., and Rosi, D. (1964). *Toxicol. Appl. Pharmacol.*, **6**, 292.
Marie, J., Sée, G., and Pignol, J.-G. (1963). *Presse méd.*, **71**, 2534.
Millichap, J. G. (1959). *Pediatrics*, **23**, 257.
O'Doherty, N. J. (1965). *Develop. Med. Child Neurol.*, **7**, 677.
Oliver, T. K. (1958). *Amer. J. Dis. Child.*, **95**, 57.
Opfer, K. (1963). *Lancet*, **1**, 116.
Persson, B., Tunell, R., and Ekengren, K. (1965). *Acta paediat. scand.*, **54**, 49.
Valentine, G. H. (1959). *Lancet*, **1**, 892.
Walker, A. E., and Adamkiewicz, J. J. (1964). *J. Amer. med. Ass.*, **188**, 779.
Walker, S. H., Salanio, I., and Standiford, W. E. (1966). *Clin. Pediat. (Philad.)*, **5**, 718.

Mendelson's Syndrome: Its Treatment by Tracheostomy and Hydrocortisone

Brit. med. J., 1967, 2, 745–746

Hall (1940) described the cases of 15 patients who had inhaled vomitus during or after anaesthesia for childbirth. He described two types of case: (1) those patients in whom the inhaled vomitus consisted of solid material ; this caused mechanical obstruction of the airway ; and (2) those in whom the inhaled vomitus was entirely liquid ; these latter patients developed marked cyanosis, tachycardia, and tachypnoea several hours later.

Mendelson (1946) also noted the two types of reaction, depending on the quality of the vomitus, which had been noted by Hall. When the vomitus contained solid material there was an acute airway obstruction with massive collapse of the lung. When the vomitus was liquid there developed, after a latent period of one to two hours, a syndrome of dyspnoea, cyanosis, tachycardia, and in Mendelson's cases generalized bronchospasm. Mendelson was able to cause a similar syndrome in rabbits by instilling either N/10 hydrochloric acid or acid gastric juice into the tracheobronchial tree. When distilled water, neutralized gastric juice, or 0.9% sodium chloride solution was used the syndrome did not develop (Mendelson, 1946).

Others have confirmed that pulmonary oedema may develop after the inhalation of acid gastric contents (Hartzell and Mininger, 1946 ; Parker, 1954 ; Hausmann and Lunt, 1955).

The presence of oedema at the blood/gas interface in the lungs may upset gaseous exchange with the atmosphere, and if extensive it may be fatal. It is now recognized that tracheostomy by reducing the respiratory dead space will improve the efficiency of alveolar ventilation (Shackleton, 1959). Though this operation has been employed in the management of patients who have inhaled vomitus, it has been for the relief of acute airway obstruction due to the impaction of solid undigested food in the larynx and upper trachea (Merrill and Hingson, 1951). There is a dearth of case reports in which a tracheostomy has been employed to reduce the respiratory dead space in patients with Mendelson's syndrome. One such case is reported.

Case Report

A 31-year-old primigravida was admitted in labour at 42 weeks. Owing to incoordinate uterine action labour was prolonged, and after 32 hours she was delivered by caesarean section under endotracheal general anaesthesia. Operation and anaesthetic were uneventful.

About 30 minutes after returning to the ward she had a bout of vomiting with transient cyanosis. The mouth and pharynx were sucked clear of vomit, the colour improved, and her condition appeared satisfactory. Two and a half hours later she became very cyanosed with stertorous breathing. The blood pressure was 130/80, but the pulse rate had risen to 160. There were crepitations over both lung fields. The patient was unconscious. The pupils were equal and widely dilated.

A further bout of faecal vomiting occurred at this stage. The airway was sucked clear above the glottic opening and oxygen given under pressure from an anaesthetic machine, but without any material improvement in the patient's colour. She was transferred to the theatre, where oxygen was given, the trachea was intubated, and tracheal suction was performed, some vomitus being obtained from the trachea. A further bout of faecal vomiting occurred as these procedures were being carried out.