The importance of this factor became more apparent as the series progressed, as lower doses were ineffective. Experience showed that after 20 minutes of administration a bradycardia, possibly a vagal reflex, commonly supervened.

Furthermore, tachyphylaxis, a widespread phenomenon among sympathomimetic agents (Goodman and Gilman, 1965), may well have manifested itself. This was difficult to prove in our cases because of the lack of a steady state. Tachyphylaxis may account for the success of intravenously administered isoxsuprine as compared with other routes of administration; the former route would tend to be used for a much shorter period. Orciprenaline is, however, a far more effective drug.

Fetal tachycardia occurred with higher infusion rates. The overall effect of orciprenaline may well be to improve the fetal condition, either by increasing the fetal cardiac output (Rudolph, 1969) or by decreasing the stress of contractions (Caldeyro Barcia *et al.*, 1969). Other workers have noticed no alteration of the fetal heart rates with β-adrenergic agents (Wansbrough *et al.*, 1968). Caesarean section became necessary in one case for an increasingly severe accidental haemorrhage at 31 weeks of gestation. No difficulty was encountered with either anaesthesia or haemostasis. The infant was delivered in good condition and has thrived.

With one exception the treatment failed because of either increasing accidental haemorrhage or premature rupture of membranes. Labour is unlikely to be arrested under these circumstances. This has been noted in the case of alcohol (Fuchs *et al.*, 1967).

Caution is necessary in interpreting the results of this preliminary series. The evidence suggests that orciprenaline can stop uterine contractions and may arrest the progress of premature labour. A controlled trial is indicated, but the ethics of depriving the "controls" of what appears to be an effective form of therapy will have to be carefully considered. The major difficulty of such a trial would be the definition of the onset of labour.

Our thanks are due to Professor J. A. Stallworthy for his continuous encouragement and valuable advice and criticism. We also wish to thank the nursing staff of the Churchill Hospital and Radcliffe Infirmary for their forbearance and kind co-operation. We are also grateful to Dr. Patrick Knowlson, of Boehringer Ingelheim Limited, for his advice and help.

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Medical Memoranda

Metabolic Findings in a Patient with Hyperosmolar Non-ketoacidotic Diabetic Stupor

British Medical Journal, 1970, 4, 155–156

Diabetic hyperosmolar non-ketotic coma has been recognized with increasing frequency since it was first described over a decade ago (de Graeff and Lips, 1957; Sament and Schwartz, 1957). In the case described below we had the opportunity of measuring a wide range of biochemical and hormonal values during the acute stage before treatment. We feel that our findings may warrant a reconsideration of currently held views on the development of this disorder.

CASE REPORT

The patient, a 50-year-old man, was admitted to hospital with symptoms of dyspnoea, lethargy, and weakness. He confessed to a heavy consumption of alcohol for several years before presentation but gave no previous or family history of diabetes. On examination he was in mild congestive cardiac failure with atrial fibrillation; blood pressure was 150/100. He had Dupuytren's contracture of both hands and the liver was palpable 8 cm. below the costal margin. Glycosuria was not detected at this stage. He was given digoxin, frusemide, and potassium supplements, with good initial clinical response.

Two weeks later, during a morning ward round, he had become drowsy and confused, and frequent twitching of the extremities was seen. The tongue was dry but the skin texture was normal, as was his respiration. A random blood sugar test was reported to show greater than 1,000 mg./100 ml., and the urine contained sugar 2 g./100 ml. but no ketones. Therapy with intravenous hypotonic saline and insulin was now started.

Laboratory findings on the blood samples were as follows: haemoglobin 17·6 g./100 ml.; haematocrit 57%; white cell count 6,900/mm.^{3}; blood sugar 1,075 mg./100 ml.; urea 100 mg./100 ml.; serum sodium 135 mEq/l.; potassium 5·8 mEq/l.; chloride 97 mEq/l.; CO_2 content 20 mEq/l.; osmolarity 373 m-osmole/l.; amylase 1·9 i.u. Plasma ketones absent, plasma immunoreactive insulin 0 μ-u./ml. (mean value in this laboratory for fasting immunoreactive plasma insulin is 9 μ-u./ml. in normal adults). Plasma growth hormone (radioimmunoassay) 4·4 ng./ml., cortisol 37·5 μg./100 ml., plasma free fatty acid (Duncombe method) 610 μEq/l.

During the first 18 hours he received 2 litres of hypotonic saline intravenously and about 2 litres of water by mouth; also 140 units of insulin intravenously. The blood sugar fell to 170 mg./100 ml. and the serum osmolarity to 320 m-osmole. This was accompanied by noticeable improvement in his general condition. Insulin requirements declined gradually over the next few weeks and he was finally discharged on an oral hypoglycaemic agent. This has resulted in satisfactory control to date. Before his

discharge liver biopsy showed changes of well-marked portal cirrhosis.

COMMENT

One view concerning the pathogenesis of hyperosmolar non-ketotic diabetic stupor is that there is persistence of enough endogenous insulin to prevent ketoacidosis but insufficient to facilitate glucose utilization (Johnson *et al.*, 1969; Oakes *et al.*, 1969). Our finding of undetectable plasma immunoreactive insulin militates against this suggestion. Another suggestion (Henry and Bressler, 1968) is that long-standing unrecognized hyperglycaemic stress of the pancreatic β-cells exhausts insulin reserve; massive hyperglycaemia permits sufficient glucose utilization and inhibits release of free fatty acid, thus preventing ketosis. This seems unlikely, since hyperglycaemia per se in diabetic ketoacidosis is insufficient to prevent release of free fatty acid and ketone body synthesis (Laurell, 1956; Carlson, 1969). Seftel *et al.* (1967) postulated that there may be a block in the hepatic uptake or degradation of free fatty acid to ketones. The modestly raised plasma free fatty acid in the present case suggests that the fault is not hepatic but rather adipose tissue in origin. It seems to us that the patient's adipose tissue might have been resistant to fat-mobilizing influences, hence the failure to develop ketoacidosis. The liver disease could have been an additional factor in impairing ketone body production.

We thank Dr. S. Grieve, under whose care the patient was admitted, and the medical superintendent of Coronation Hospital, Johannesburg, for permission to report this case. Mr. G. Winternitz, of Hoechst Pharmaceuticals, kindly assisted with the transport of deep-frozen plasma samples to Natal.

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Optic Atrophy Eight Years after Tuberculous Meningitis

British Medical Journal, 1970, 4, 156–157

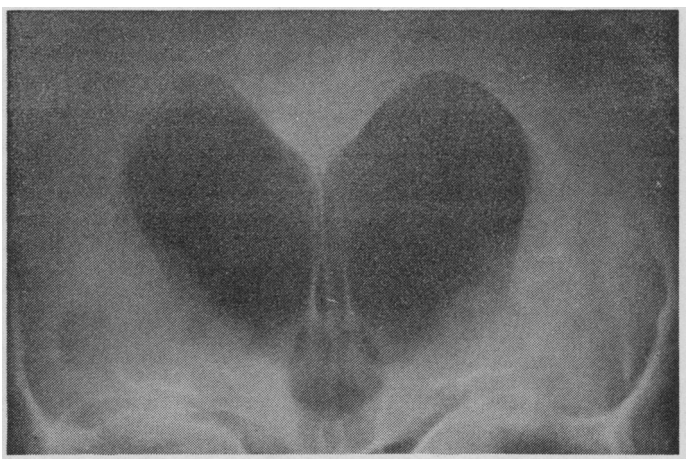
Pressure on the optic nerves or optic chiasma is a common cause of secondary optic atrophy (Brain, 1962). One patient presented eight years after the initial treatment for tuberculous meningitis. Despite this long time interval, remarkable recovery of vision occurred after decompression of the optic nerves by the Pudenz valve therapy of hydrocephalus.

CASE HISTORY

The patient, a girl aged 7 years 2 months, was referred for a routine eye examination in October 1965. With a little encouragement vision of 6/9 in each eye could be obtained without a lens. Slight temporal pallor of both discs, more on the left than on the right, was noticed. At the time no previous notes were available to indicate any underlying disease.

She was seen again in October 1967, when she had reached grade 3 at school but was having increasing difficulty with her vision. This was now recorded as 6/120 in the right eye and counting fingers at 1 metre in the left. The optic nerve pallor was increased, and was more noticeable again in the left eye. At this point it was found that she had developed tuberculous meningitis at the age of 13 months and had been treated with chemotherapy for 15 months as an inpatient, and as an outpatient for a further two years. Since then her psychomotor development had been within normal limits. At the time of referral she was regularly placed in the upper half of her class at her village school. The visual defect was her only handicap. Examination showed a normal 9-year-old girl. Occipitofrontal circumference 54·6 cm. (average for her age 55·3 cm.). Apart from the findings on ophthalmoscopy, examination of the cranial nerves was negative. Motor and sensory nervous systems were normal.

Investigations.—Purified protein derivative (intermediate strength) negative. Blood and urine analyses normal. C.S.F.: clear; O cells/cu. mm.; protein 27 mg. and sugar 61 mg./100 ml., routine cultures were negative, as were those for acid-fast bacilli. Chest *x*-ray film: healed Ghon focus in right upper lung field, otherwise normal. Skull *x*-ray picture normal. Lumbar puncture, with the patient completely relaxed, showed a mean pressure of 250 mm. of C.S.F. (range 180-300 mm.). A lumbar air encephalogram taken with 100 ml. of air showed "gross dilatation of the third and both lateral ventricles. No midline shift. Aqueduct and fourth ventricle normal. Some air seen in the basal cisterns, including the interpeduncular cistern and the cisterna magna. No air evident in the sulci over the cerebral hemispheres. Conclusion: gross obstructive hydrocephalus, the obstruction being most likely due to adhesions around the brain stem. No evidence of a mass lesion." (Fig.)



Surgical treatment of the hydrocephalus was accepted by the parents. Accordingly a ventriculoatrial shunt of the Pudenz type was inserted on 29 March, 1968. There were no complications from this procedure and the shunt has functioned normally to date.

In December 1968 the vision in each eye was approximately 6/20, but with a small myopic correction the vision could be brought up again to 6/9 in each eye. Confrontation fields appeared to be full. More careful study was attempted with perimeter and Bjerrum's screen, but these were not very accurate owing to the fact that she did not appear to fixate adequately and tried to "help" the technician, a not uncommon finding in children of her age. She has been able to continue with the school programme and was last seen in October 1969, when the corrected vision in each eye was 6/12, with partly 6/9 binocularly.

COMMENT

In this case there is no evidence to suggest a chronic tuberculous arachnoiditis. Thus it would appear that the visual deterioration was due entirely to the increased intracranial pressure. While this is most likely to have been caused by