(with this thought in mind) by our colleagues in Forensic Pathology at The London Hospital, they have indeed found the posterior nares blocked with mucopus in a case of cot death.

We are continuing to investigate upper airway obstruction in the infant. If this theory of causation is correct it may be that the incidence of cot deaths could be reduced by vigorous treatment of 'minor' nasal infection in those infants who are particularly at risk.

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K. W. CROSS and SHEILA R. LEWIS*

From the Department of Physiology, The London Hospital Medical College, Turner Street, London E.1

*Present address: King's College Hospital, Denmark Hill, London S.E.5.

Decreased Duodenal Monoamine Oxidase Activity in Coeliac Disease

The enzyme monoamine oxidase (MAO; EC 1.4.3.4.) has been extensively studied in recent years (Davison, 1958; Sandler, Collins, and Youdim, 1971). Its activity varies widely from tissue to tissue and from species to species. In the human (Levine and Sjoerdsma, 1962), unlike some other animals (Penttilä, 1968), the small intestinal mucosa possesses one of the highest levels of activity in the body. While the precise function of MAO remains a matter of some dispute, it seems likely that the mucosal enzyme of the normal gut forms a first line of defence against an excess of exogenous (dietary) amines such as tyramine (Sandler *et al.*, 1971). It may also be concerned in the inactivation of endogenous amines, notably 5-hydroxytryptamine. This amine is present in relatively high concentrations in the mammalian gastrointestinal tract (Erspamer, 1966).

The status of gut mucosal MAO in disease has so far received scant attention. In malabsorption syndromes there may be an overproduction of certain monamines within the gut (Haverback, Dyce, and Thomas, 1960). There are also histochemical data on record (Spiro *et al.*, 1964; Riecken *et al.*, 1966) to indicate that gastrointestinal MAO activity is reduced. Thus any toxic effect the amines may exert on the whole organism is likely to be magnified.

It, therefore, seemed important to confirm by quantitative means these histochemical impressions and to investigate further the nature of the enzyme defect.

Subjects and Methods

The 16 children selected for this study were aged between 1 and 9 years. Coeliac disease was considered a possible diagnosis as they were failing to thrive and were passing frequent offensive stools. In those children in whom coeliac disease was confirmed histologically, the faecal fat excretion exceeded 5 g/day and the clinical condition improved rapidly following a gluten-free diet.

Collection of biopsies. Patients were starved of solid food for 12 hours and then sedated with pethidine and promethazine half an hour before biopsy. A Watson intestinal biopsy capsule (port size 5 mm) was passed into the third or fourth part of the duodenum and its precise position identified radiologically. Once obtained, the tissue was rapidly divided into two pieces, one being preserved in 10% formol saline for histological examination and the other placed in a glass bottle and stored at −20 °C before quantitative assay of MAO activity.

Histological examination. Tissues were sectioned, stained with haematoxylin and eosin, and examined microscopically.

Quantitative MAO assay. Biopsy specimens were homogenized in a small amount of distilled water (approx. 1 ml) using an all-glass tissue grinder; duplicate portions (0·1 ml) of the homogenate were assayed according to the microfluorimetric method of Kraml (1965) using kynuramine as substrate.

All values of MAO activity are expressed as microgrammes of 4-hydroxyquinoline (4HOQ) formed per mg protein per 30 min incubation at 37 °C. Protein was determined by the method of Lowry *et al.* (1951) using crystalline bovine serum albumin as standard.

Platelet MAO assay. Venous blood (5 ml) was drawn using a plastic syringe and placed in a plastic tube containing 10 mg sodium edetate. An equal volume of isotonic saline containing 2% (w/v) sodium edetate was added. The mixture was subjected to centrifugation at 1200 g for 6 min; the platelet-rich supernatant was separated and recentrifuged at 2500 g for 15 min at 4 °C. The supernatant was removed by decantation and the platelet deposit resuspended in 1·0 ml distilled water. Duplicate portions (0·1 ml) were assayed for MAO activity and protein as described above.

Results

Of the 16 children investigated, 7 were shown histologically to have subtotal villous atrophy. The mean MAO activity ± SE of the duodenal mucosa of these 7 was 3·80 ± 0·66 μg 4HOQ/mg protein per 30 min. These values are significantly lower ($P<0·01$) than the mean level of 13·99 ± 2·95 μg 4HOQ/mg protein per 30 min found in the other 9 children who had normal duodenal morphology. The subjects with normal mucosa tended to be somewhat older (mean age 5 years 3 months) than the patients with coeliac disease (mean age 2 years 2 months); there did not appear to be any correlation between MAO activity and age (Fig.). In 5 of the patients with coeliac disease, mean platelet MAO activity ± SE was 1·57 ± 0·27 μg 4HOQ/mg protein per 30 min, within the normal limits for this laboratory of 0·4–4·1 μg 4HOQ/mg protein per 30 min. Three out of four platelet samples from the control subjects also possessed activity within this range; the fourth showed an unaccountably low value.

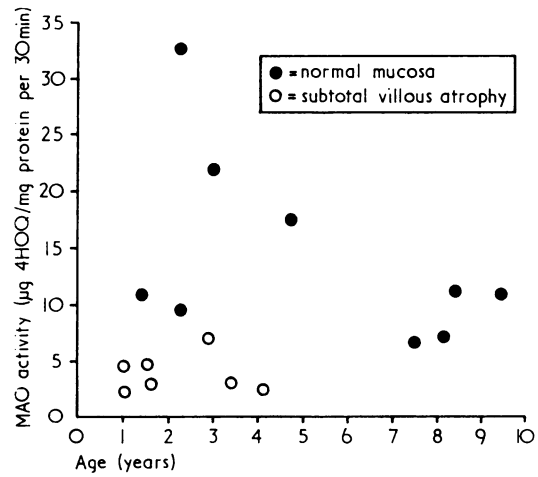

FIG.—*Correlation of platelet MAO activity with age in 2 groups of children: normal children and those with histologically proven coeliac disease.*

Discussion

As noted by other authors (Levine and Sjoerdsma, 1962) and confirmed here, there is intense MAO activity in histologically normal small intestinal mucosa. The present quantitative data, which agree with earlier histochemical impressions (Spiro *et al.*, 1964; Riecken *et al.*, 1966), show unequivocally that there is a sharp drop in activity in coeliac disease. Platelet MAO level has been used as a possible indicator of broader involvement in the pathological process (Robinson *et al.*, 1968). Normal activity was present in these children, however, so that the particular biochemical lesion under investigation is likely to be confined to the gut.

While the action of a local inhibitory agent, perhaps deriving from the action of gut flora on unabsorbed residues, cannot be ruled out, it seems that MAO is only one of a number of enzymes which show decreased activity in the malabsorption syndromes (Spiro *et al.*, 1964; Riecken *et al.*, 1966). It probably follows that the change is secondary, deriving from a pathological process causing general cellular damage rather than from a primary enzyme inhibitor. Whatever the mechanism of the enzyme deficit, an overspill of potentially toxic amines into the circulation is a likely consequence. Future cases of coeliac disease should perhaps undergo careful assessment to establish whether these amines are responsible for any of the clinical features of the illness.

In similar manner to earlier work on MAO activity in the human endometrium (Southgate *et al.*, 1968), a sensitive microassay procedure has been used to quantify an earlier histochemical impression. Such an approach offers a more precise measure of the severity of a biochemical lesion than the subjective assessment of staining intensity, and seems likely to be widely applicable to future problems.

Summary

Significantly lower levels of monoamine oxidase were present in the duodenal mucosa of 7 children with histologically proven coeliac disease compared with a control group of 9 children with histologically normal mucosae. The intestinal enzyme defect is probably a consequence of local cell damage rather than the result of a specific inhibitor. Increased amine levels, secondary to the enzyme deficit, may play a role in the clinical pattern of coeliac disease.

We would like to thank Professor Neville Butler, Dr. John Apley, and other paediatricians in the South-West region for allowing us to study their patients.

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D. N. CHALLACOMBE,* M. SANDLER, and JENNIFER SOUTHGATE

*Present address: Institute of Child Health, Francis Road, Birmingham 15.

From the Bristol Royal Hospital for Sick Children, and the Bernhard Baron Memorial Research Laboratories and Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, London W.6.

Correspondence to Dr. M. Sandler, Queen Charlotte's Maternity Hospital, Goldhawk Road, London W.6.

Femoral Arterial Thrombosis in Nephrotic Syndrome

The loss of a limb is always a tragedy, above all in a child. Primary arterial thrombosis is rare in childhood, but in this patient appears to be explicable on the grounds of the tendency to coagulation found in the nephrotic syndrome, corticosteroid therapy, and femoral vein puncture.

Case Report

A girl presented at the age of 1 year 9 months with a typical pure nephrotic syndrome, and renal biopsy revealed a 'minimal change' lesion. She was treated with prednisolone, but relapsed and remained on prednisolone for 7 months. She again relapsed following an upper respiratory tract infection and mild gastro-enteritis. The dose of prednisolone was increased to 30 mg/day and a week later she was admitted to the West Kent General Hospital with cold extremities, impalpable peripheral pulses, and a blood pressure of 80/60 mmHg (12·7 cm cuff). Bladder catheterization revealed oliguria, and with some difficulty blood was obtained by femoral puncture; both groins were needled at this time. The blood urea was 146 mg/100 ml, and the patient was transferred to Guy's in case she should require dialysis. On arrival her blood pressure had improved to 135/85 mmHg but within six hours it was clear that the arterial supply of the right leg was obstructed, with no pulse palpable below the femoral. Infusion of low molecular weight dextran produced no improvement. Arteriography revealed an obstruction at the popliteal artery which was then explored; an embolus with distal clot was found and removed. A femoral arterial catheter was left *in situ*, and through this heparin, urokinase, bretylium tosylate and tolazolazine hydrochloride were variously infused without effect. Tolazoline hydrochloride was also given orally, and the child was maintained intermittently in hyperbaric oxygen. Despite disobliteration of the posterior tibial artery as far as the ankle, the foot remained grossly ischaemic with a line of demarcation at the hind foot, and four weeks later Mr. J. Batchelor performed a through-knee amputation.

During this part of her course the nephrotic syndrome was controlled with prednisolone 30 mg/day, leading to hypertension (diastolic 120–140 mmHg) treated with methyldopa. When healing of the stump was satisfactory, cyclophosphamide therapy was begun (Moncrieff *et al.*, 1969). Assessment at this time showed a grossly Cushingoid child with a height of 86 cm (10th centile) and a blood pressure up to 160/120 mmHg.

Cyclophosphamide was continued for 16 weeks while prednisolone and methyldopa were gradually withdrawn. Seven months later she was walking well with her artificial limb and was on no drugs. Her blood pressure and appearance were normal and her urine remains protein-free in spite of occasional upper respiratory infections and routine immunizations. She had grown 7 cm and was on the 25th centile for height.

Discussion

A number of factors may have contributed to what seems certain to have been a femoral artery thrombosis, with subsequent embolism of clot into the popliteal artery.

Increased coagulability of the blood of patients with the nephrotic syndrome has been discussed by a number of authors, but the exact mechanism is not clear. An increase in a number of coagulation