have been excluded. Testosterone is necessary for the full development of pigmentation after ultra-violet irradiation (Edwards *et al.*, 1941). Of other steroid hormones, deoxycortone inhibits the development of melanophores in explanted chick embryo skin (Hamilton, 1940), but does not usually decrease the hyperpigmentation in Addison's disease. Cortisone inhibits pigmentation in black-hooded rats (Whitaker and Baker, 1948), but apparently not in human subjects (Järvinen, 1951). To this list may be added the effect of progesterone described here.

My thanks are due to the medical students who acted as subjects, and to Messrs. British Drug Houses Ltd., who supplied the progesterone solutions.

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Medical Memoranda

Milk Allergy

The following case is worthy of record because of the interesting way in which it presented itself.

CASE REPORT

The patient, a boy aged 4, developed slight eczema of the hands at the age of 2 months. He was breast-fed from birth, and at 7 months weaning was attempted. He showed an immediate distaste for cow's milk, and whenever given it a perioral urticarial rash developed, and his eczema became worse. Many different forms of milk were given, but to all he showed a reaction. Thus he continued being breast-fed until 15 months old, also taking solids and orange juice. He was not given cow's milk or any substitute. He was then seen by a dermatologist, who thought his eczema was due to proteins in the diet, so he was put on a relatively protein-free diet of vegetables, fruit, cereals, orange juice, and a little milk, which always caused a perioral urticarial rash. He was given a little meat, but, although it did not seem to cause a reaction, he did not like it very much. The mother discontinued her visits to the dermatologist after some months, but still kept the child on this diet.

The child was referred to us at the age of 4 years because a medical officer thought he looked undernourished, and found on questioning the mother that during the past few months he had been irritable and easily tired, played games very little, and had to have afternoon naps. Sometimes, though not often, his stools were pale and offensive.

On inquiry from his parents it was found that he was sensitive to the following food, and in addition showed various idiosyncrasies:—(1) Fish: extremely sensitive—even the smell of fish is said to cause a reaction. (2) Milk (goat's and cow's): perioral urticarial rash; eczema worse. (3) Eggs: appear to have a delayed action. (4) Meat: no reaction, but does not like it. (5) Cereals: does not like porridge; likes bread—no reaction. (6) Cheese: does not like it.

His family history showed allergies on the maternal side. His grandmother suffered from asthma, an aunt from eczema, and a cousin from urticaria. His mother herself has eczema and is highly nervous.

On physical examination the boy was very pale, with normal height and weight for his age. His lower eyelids were puffy, and small glands were palpable in his neck. He showed marked eczema of the hands, but no lesions of the skin elsewhere except cracks at the corners of the mouth. No enlargement of liver or spleen was noted.

Blood count: Hb, 75% (10.5 g.) Sahli; R.B.C., 2,800,000 per c.mm. (P.C.V. 27%, M.C.V. 96.4 μ^3, M.C.H.C. 38.8%); W.B.C., 4,800 per c.mm. (polymorphs 61%, lymphocytes 35%, monocytes 4%); reticulocytes, 0.5%; total plasma protein, 5.25 g.%. Stained blood film showed many well-haemoglobinized macrocytes.

Response to Milk.—Under surveillance the boy was given some fresh cow's milk to drink. Within five minutes he developed a well-marked perioral urticarial rash. Later he was given boiled milk, and only a very slight rash appeared. A skin-sensitivity test was carried out, using pieces of lint dipped in boiled and fresh milk. No reaction was observed with the boiled milk.

He was put on boiled milk instead of fresh milk, and was given proteolysed liver extract, folic acid, and "marmite," because of a suspicion that he might have an incipient B-avitaminosis. On this treatment he rapidly improved, and his last blood count, taken 10 weeks later, was as follows: Hb, 94% (12.8 g.) Sahli; R.B.C., 5,150,000 per c.mm. (P.C.V. 42%, M.C.V. 80 μ^3, M.C.H.C. 30.5%); W.B.C., 9,500 per c.mm (polymorphs 50%, lymphocytes 35%, monocytes 6%, eosinophils 8%, basophils 1%); total plasma proteins, 6.5 g.%. His parents stated that he was more active than they had ever known him.

COMMENT

This boy presented as a case of macrocytic anaemia associated with protein deficiency, having lived for about 2 years 7 months on a diet poor in proteins, especially in first-class proteins.

The most important factor was his allergy to milk, which normally provides the chief source of protein in a child's diet. Milk itself is one of the three commonest food allergens, being second in frequency to wheat, and equal in incidence to egg. For example, in a series of 175 cases of food allergy, Rowe (1931) found 57% due to wheat, 31% to milk, and 35% to egg, the overlapping figures being due to multiple sensitization in some of the patients. Alvarez (1937), in a group of 500 cases of abdominal distress due to food allergies, found 26% due to milk, cream, and ice-cream, and another 5% due to cheese.

In many cases of infants reacting to milk there is a history of milk incapacity in the parents, and, though this was not found in this case, there was a strong family history of eczema. The diagnosis of milk allergy in infants and children rests on the history and the therapeutic test of withdrawal of milk from the diet. Scratch skin tests have been used, but they are of small value as an aid to diagnosis.

In one series of 65 cases of milk eczema in which scratch skin tests were carried out, only 5 were positive to cow's milk (Kerley, 1936). Kerley has classified persons subject to milk reactions into (1) those who suffer from shock through ingestion; (2) those with gastro-intestinal symptoms; and (3) those with skin reactions—eczema and urticaria. At least two deaths have been reported in the shock-reaction group (Finkelstein—see Kerley, 1936). My case obviously falls into the third group.

Studies on milk allergy by Ratner (1935) have shown that the heat-labile elements in the milk (lactalbumin and lactoglobulin) are responsible for practically all cases, so that some form of heat-treated or chemically denatured milk can be safely used. Skimmed fresh cow's milk, cooked for several hours, is said to supply the best desensitized milk product for use in eczema of infants (Kerley, 1936). The skimming removes the fat, which either interferes with the desensitizing process or adds an element that bears on the production of the eczema. It is sometimes found, though it was not true in this case, that goat's milk does not give a reaction.

SUMMARY

A case of macrocytic protein deficiency anaemia in a boy suffering from milk allergy (eczema and urticaria) is described. He was able to take boiled cow's milk. The literature is briefly reviewed.

My thanks are due to the Director-General, R.A.F. Medical Services, for permission to publish this case; to Air Vice-Marshal T. St. C. Morton and Wing Commander W. P. Stamm, of the Institute of Pathology and Tropical Medicine, R.A.F., Halton, for interest and guidance; and also to Flight Lieutenant Watson, who sent this boy to the laboratory for examination.

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Two Cases of Acute Idiopathic Porphyria

A number of cases of acute idiopathic porphyria have been reported in the literature in recent years, but we think the disease interesting and rare enough to merit the recording of two further cases.

CASE 1

The patient, a single woman aged 20—height 5 ft. 8 in. (173 cm.), weight 6 st. 6 lb. (41 kg.)—was first admitted on June 18, 1948, as an acute abdominal emergency. She gave a history of five days' colicky upper abdominal pain—the onset coinciding with a period—nausea, and obstinate constipation. She had vomited on three occasions. Her past history was negative. Her parents and two siblings were alive and well.

On examination she looked ill. Her temperature was 99.6° F. (37.6° C.), pulse 80, and respirations 20. Her tongue was furred; there was no scleral or cutaneous pigmentation. The abdomen was soft, not distended, and without guarding or local tenderness. Peristaltic sounds were normal. Rectal examination was negative. Heart : apex beat forcible ; no enlargement ; no murmurs ; rhythm normal ; rate 80. The blood pressure was 170/120. Chest and C.N.S.: N.A.D. A few hours later she vomited ; her temperature was 99° F. (37.2° C.) and pulse 72. The pain continued unabated, and laparotomy was performed. No abnormality was found.

After operation the pain persisted. The urine contained a trace of albumin and "excess urobilin," the blood N.P.N. being 70 mg. per 100 ml. During the ensuing week the pain continued, and on the fifth post-operative day she had an epileptiform convulsion. The blood pressure now was 160/100. The white blood cells numbered 31,000 (polymorphs 95%, lymphocytes 4%, monocytes 1%). The urine still showed a trace of albumin with an occasional granular cast. The blood N.P.N. remained at 70 mm. per 100 ml. The chest *x*-ray picture and cerebrospinal fluid were normal, and the blood Wassermann reaction was negative. She remained slightly febrile, and 14 days after operation complained of weakness of the legs. Examination revealed weakness, with muscle tenderness of the proximal muscle groups of both arms and legs. The cranial nerves were normal, and there was no sensory loss. A repeat lumbar tap revealed normal fluid. She now began to improve, the blood pressure falling to 130/80, and she was discharged on September 22. No definite diagnosis was made.

She was next admitted on June 13, 1949, with identical symptoms. The combination of severe abdominal pain and marked hypertension, together with the history of a negative laparotomy, suggested porphyria, and examination of the urine led to quick confirmation. Up to the present she has had five attacks. Each began and evolved in the same manner, and neurological complications occurred in all but one. The last acute episode occurred in January, 1951. She has remained well since, although the urine is often coloured red.

CASE 2

A single man aged 41 was admitted on March 12, 1951. The history was of attacks of lower abdominal pain for four months, becoming more severe in the last three days, and violent eight hours before admission. He was nauseated and constipated.

On examination he was obviously in severe pain. His temperature was 98.2° F. (36.8° C.), pulse 56, and blood pressure 140/90. Some guarding and tenderness in the epigastrium were the only abnormalities noted. After some hours' observation it was decided to explore the abdomen with the possibility of a posterior perforation in mind. Nothing abnormal was found at operation.

Soon after operation he passed port-wine-coloured urine, and spectroscopic examination revealed the presence of porphyrins. On re-examination at this time he had become uncooperative and resentful; the blood pressure was 185/115, and there was obvious recent wasting of the leg muscles, especially the quadriceps. During the next few days the pain persisted, the blood pressure rose to 205/120, and the patient became deluded and irrational at times. The symptoms gradually abated, and by the 10th day after operation he was symptom-free and co-operative, the blood pressure was 130/80, and the urine was normal in colour.

He was discharged from hospital on April 14, and by that time the wasting of the legs was rapidly disappearing. He has been seen as an out-patient since, and has had no further attacks of pain or staining of the urine.

COMMENTS

Both cases were admitted as acute abdominal catastrophes. The association of severe unremitting colicky abdominal pain with vomiting and obstinate constipation suggests serious abdominal mischief, and in some cases may not unreasonably lead to laparotomy. The abdominal symptoms may be clamant, but are seldom supported by definite physical signs of local or general abdominal disease.

In neither case was a firm pre-operative diagnosis made, and laparotomy was undertaken mainly in the spirit of "it is better to be safe than sorry." The disease, although admittedly rare, is probably commoner than has hitherto been realized, and may well account for many "negative" laparotomies. It is, of course, very pertinent in the differential diagnosis of polyneuritis, Landy's paralysis, and even of some psychoses. As Petrie remarks, "The symptoms of acute porphyria tend to be remarkably stereotyped." This is well exemplified in these cases, particularly in Case 1, in which the story is almost monotonous. Yet the diagnosis on the first three occasions of her admission varied from intestinal obstruction to acute obstructive appendicitis. There is, however, the discrepancy between the symptoms and paucity of signs, which may suggest something unusual. If hypertension and neurological signs are present as well the diagnosis should be easy, but hypertension may not be present, at any rate in the initial stages, and the neuropathy tends to develop a little later. If the disease is not borne in mind the diagnosis will be missed, and this may well lead to an unnecessary laparotomy in a seriously ill patient, liable to serious and possibly fatal neurological complications at any time.

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