Comment

The technique of human basophil degranulation has not been used for diagnostic purposes because these cells are few in number. Nevertheless we[4,5] and others[3] have shown their usefulness when obtained in large amounts through partial enrichment. Our results in hydatidosis show that HBDT is a very sensitive test, since the degranulation was highly significant for at least one antigen dilution in all patients. Moreoever, HBDT proved to be specific—we never had a false-positive result, even in controls suffering from another helminthiasis. Finally, the results were reproducible, as proved in two patients retested after an interval of a few days.

We conclude that HBDT is a useful diagnostic test for hydatidosis, and its simple technology could be made available for endemic areas. We are studying its value in diagnosing schistosomiasis.

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Service de Médecine et Service de Chirurgie Générale, Hôpital Rothschild, 33 Boulevard de Picpus, 75012 Paris
F LEYNADIER, MD, chef de clinique-assistant
H LUCE, MD, attaché
A ABREGO, MD, attaché
M HUGUIER, MD, professeur agrégé
J DRY MD, professeur

Service de Chirurgie Digestive, Hôpital Saint-Antoine, 184 Faubourg Saint-Antoine, 75012 Paris
C L HUGUET, MD, professeur

Malaria with disseminated intravascular coagulation and peripheral tissue necrosis successfully treated with streptokinase

Disseminated intravascular coagulation sometimes complicates malaria[1,2] but there is no report of peripheral ischaemia resulting from it. We describe two white children (brothers) infected at the same time and developing disseminated intravascular coagulation with tissue ischaemia, one of whom was treated with streptokinase.

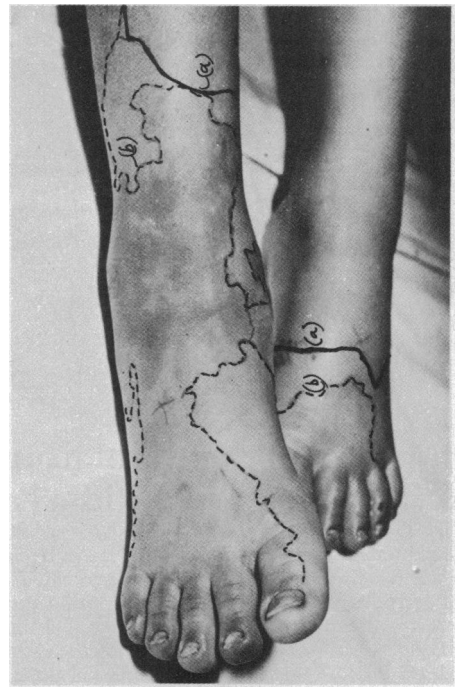
Case reports

Both brothers gave a three-day history of vomiting, rigor, and faintness. Both had stopped malarial prophylaxis in error and both showed many ring forms of *Plasmodium falciparum*, which persisted for three days after they started treatment.

Case 1 The 11-year-old brother was relatively well on admission, though vomiting and dehydrated. He was rehydrated with normal saline and treated with chloroquine, equivalent to 150 mg base twice daily. Two days later he had become somewhat drowsy and he had a spreading area of necrosis on the dorsum of the right hand starting at a venepuncture site and extending into the ring and small fingers. Results of investigations were: plasma urea 10·46 mmol/l (63 mg/100 ml); sodium 131 mmol (mEq)/l; potassium 5 mmol (mEq)/l; fibrinogen 1·4 g/l; thrombin time 8 seconds; fibrinogen degradation products (FDP) 4·0 g/l; haemoglobin 11·6 g/dl;platelets 21 × 10^9/l (21 000/mm^3); schistocytes present. Disseminated intravascular coagulation with impending tissue necrosis was diagnosed, and treatment was started with heparin 2500 units four-hourly, with a single dose of quinine 300 mg in saline infused over two hours. Two days later the patient was afebrile but his haemoglobin was 10·4 g/dl, platelets were 36 × 10^9/l (36 000/mm^3), and fibrinogen was 0·5 g/l. The platelet and fibrinogen values did not return to normal until four days later.

Case 2 The 9-year-old brother of the first patient was in a considerably worse condition on admission. He was very drowsy and feverish. Cerebral malaria was provisionally diagnosed and he was given dexamethasone 2·5 mg eight-hourly, a single dose of quinine 300 mg in saline over two hours, and chloroquine. His condition worsened over 24 hours. He became very confused and his right foot grossly ischaemic with a demarcation line above the ankle (fig). Results of investigations were: haemoglobin 12·9 g/dl; platelets 10 × 10^9/l (10 000/mm^3); fibrinogen 1·8 g/l; thrombin time 9 seconds; FDP 4·0 g/l. Heparin 2500 units four-hourly brought no improvement. Indeed, 36 hours later the patient could barely be roused, the toes of his left foot became dusky blue, and the right foot was worse. Pulses were palpable in both feet. In view of the gross ischaemia and failure to respond, heparin was discontinued and replaced with streptokinase, 200 000 units initially and then 50 000 units hourly, preceded by two units of fresh whole blood and three units of platelet concentrate. Six hours later there was a noticeable improvement in the perfusion of his feet. The haemoglobin was 14·2 g/dl; platelets 21 × 10^9/l (21 000/mm^3); FDP 1·0 g/l; fibrinogen 0·3 g/l; thrombin time—clot formed at 60 seconds and lysed at 140 seconds. Because of the very low fibrinogen cryoprecipitate 4 units was given. In a further 24 hours the foot was clearly viable and had begun to blister and the patient was conscious. The haemoglobin was 12·8 g/dl; platelets 78 × 10^9/l (71 000/mm^3); FDP 1·0 g/l; thrombin time—clot formed in 7 seconds and lysed in 10 seconds. The streptokinase was discontinued and heparin restarted. In a further 24 hours platelets and fibrinogen were normal.

Both children completely recovered.



Feet of 9-year-old boy with disseminated intravascular coagulation and peripheral ischaemia associated with malaria. Solid lines (*a*) show the demarcation between normal and cyanotic tissue; broken lines (*b*) show areas of skin returned to normal colour six hours after start of streptokinase treatment.

Comment

Extensive tissue necrosis resembling purpura fulminans has not previously been described as a complication of malaria. Its occurrence at the same time in two brothers raises the question of whether disseminated intravascular coagulation can be an inherited reaction pattern. Alternatively, a particularly virulent form of malaria may be implicated since the two boys were presumably infected by bites from the same mosquito. The disseminated intravascular coagulation in both cases was prolonged well after adequate treatment for malaria had begun. The use of streptokinase has been previously described in purpura fulminans,[3] and in view of the failure of heparin and the rapid improvement of the ischaemia with streptokinase it seems to have been of value in the present case. Its use, however, when bleeding is a complication is clearly not without con-

siderable hazard.[4 5] It must be carefully monitored and clotting factors and platelet concentrates given as soon as they are indicated.

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Department of Medicine, University of Rhodesia, Avondale, Salisbury, Zimbabwe

I R EDWARDS, MB, MRCP, professor and head of department (present appointment: consultant physician and senior lecturer in clinical pharmacology, University of Leicester, Medical Sciences Building, University Road, Leicester)

Community study of hypothyroidism in Down's syndrome

Down's syndrome is associated with autoimmune diseases affecting the thyroid, pancreas, gastric mucosa, and adrenal glands. Mongols have an increased tendency to produce thyroid antibodies.[1] Sare *et al*[2] found thyroid abnormality in 20 of 121 patients between the ages of 13 and 48 years—19 had thyroid deficiency and one hyperthyroidism. Moreover, diabetes mellitus is associated, with Down's syndrome and hypothyroidism.[3]

Patients, methods, and results

This report summarises the findings of our thyroid investigation on all children aged over 5 years and adults with Down's syndrome living in the southern district of Bedfordshire Area Health Authority. Their names were obtained from the handicap register and from the education and social services departments of the Bedfordshire County Council. Some lived at home or in hostels, others were at a MacIntyre Trust school. There is no hospital for residential care of the mentally subnormal in the district. The only bias in selection was the exclusion of children aged under 5 years. The authorities and the parents gave permission for a general examination, blood and urine tests, and recording of heights, weights, and dates of birth. The blood samples were examined by radioimmunoassay. Thyroxine (normal range 60-180 nmol/l (4·7-14·2 mg/100 ml)), thyrotrophin (normal range <1-8 mU/l), and thyroid antibodies (thyroglobulin and thyroid microsomal antibodies) were measured with the Thymune-T and Thymune-M haemagglutination kits.

The total number of patients studied was 101 (64 male, 37 female). There were 45 in the age group 5-14 years, 38 in the age group 15-21 years, and 18 in the age group 22-47 years. Thirty of the 101 gave positive results in thyroid antibody tests—14 (31%) out of the 45 in the age group 5-14 years, 8 (21%) out of the 38 in the 15-21-year group, and 8 (44%) of the 18 in the 22-47-year group. The microsomal antibody tests gave positive results most often in 30 patients, and the thyroglobulin test was positive in only 5. Seven patients had biochemical evidence of gross hypothyroidism (table) and were treated. Antibodies were present in all. Nine patients had evidence of borderline hypothyroidism and were not treated. Three of these patients had antibodies and six did not.

Comment

Few teenage and adult patients with Down's syndrome are seen regularly. The difficulty in recognising hypothyroidism is the overlap of signs in a non-complaining patient. The patient with Down's syndrome is usually shorter than average; slower and less active; less alert; quieter, with a hoarser voice; and mentally subnormal. All these symptoms are also found in hypothyroidism. Early clinical diagnosis is therefore difficult. Measurement of blood concentrations of thyroxine, thyrotrophin, and thyroid antibodies is essential.

A significant number of our patients (7 out of 101) with Down's syndrome had gross hypothyroidism, due mainly to autoimmune thyroiditis, and the likelihood of abnormal thyroid function increased with age.[4] The antibody results (29% positive) in our patients compared with the 40% positive in residents of a big mental institution in Italy[5] are interesting. Our treatment of the grossly hypothyroid group was most gratifying to parents and supervisors in the adult training workshops. To quote a parent: "Instead of a vegetable you have got a person." The dwarfed teenage girls grew in height and lost their obese, coarse appearance. All became more active and alert, and the whole quality of their lives improved.

We thank Dr Jean Brown and her laboratory staff for the radioimmunoassays and Professor RS Illingworth for his advice.

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Luton and Dunstable Hospital, Luton, Bedfordshire LU1 3UF

E DE H LOBO, FRCPED, DCH, consultant paediatrician

Bedfordshire Area Health Authority, Luton, Bedfordshire

M KHAN, MB, DCH, senior clinical medical officer

J TEW, MB, DCH, senior clinical medical officer

Clinical findings before and after treatment in seven patients with gross hypothyroidism and Down's syndrome

Case No	Age	Sex	Before treatment								After treatment	
			Urine glucose	Height (cm)	Weight (kg)	T4 (nmol/l)	TSH (mU/l)	Antibodies: TGA (dilution)	Antibodies: AMS (dilution)	Thyroxine dosage (μg)	Height (cm)	Weight (kg)
											1 year later	
1	15	F	+	115	28·2	3	>50	+, 1/6400	+, 1/6400	200	126	28·6
2	16	F	–	110	30·9	24	>50	+, 1/100	–	200	119·5	25·4
3	11	M	–	125	27·0	16	>50	+, 1/400	–	100	132·5	29·5
											3 months later	
4	37	F	–	132·5	48·1	56	23	+, 1/400	–	100	No change	46·2
5	38	F	–	145	76·3	10	>50	+, 1/400	–	150	No change	69·8
6	29	M	–	152·5	61·3	48	35	+, 1/25 600	–	100	No change	60·7
											4 months later	
7	25	M	–	147·5	117·7	48	33	+, 1/1600	–	200	No change	108·8

T4 = Thyroxine. TSH = Thyrotrophin. TGA = Thyroglobulin antibodies. AMS = Automicrosomal antibodies.
Conversion: SI to traditional units—T4: 1 nmol/l ≈ 0·08 mg/100 ml.