posure to slightly cool environmental temperatures may cause diversion of calories intended for brain growth into 'fuel' for heat production.

Summary

In order to assess the effects of ambient thermal conditions on postnatal head growth in low birth-weight infants, 42 asymptomatic neonates were reared under 4 combinations of caloric intake and thermal environment after the first week of life. Exposure to a subthermoneutral temperature (abdominal skin temperature of 35°C), together with a relatively low caloric intake (120 cal/kg per day), was associated with significant retardation of head growth over a 2-week study period.

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Simultaneous occurrence of diabetes, liver cirrhosis, and 47, XX, 21+/46, XX chromosomal pattern

There is an unduly high incidence of diabetes among patients with Down's syndrome (Burch and Milunsky, 1969; Serrano-Rios *et al.*, 1973), and also of autoimmune processes (Burgio *et al.*, 1965; Harris and Koutsoulieris, 1967). There also

appears to be some connexion between liver cirrhosis and diabetes (Creutzfeldt, Wille, and Kaup, 1962), but the simultaneous occurrence of these two conditions in a patient with a 21-chromosome abnormality has not been previously reported.

Case report

The female patient had been admitted first at the age of 6 years with stunted growth, upper respiratory infections, urticaria and other allergic symptoms, and an enlarged liver. Liver function tests had been abnormal; serum IgG level was raised.

Her diabetes became manifest at the age of 8 years, since when she has been on insulin treatment. The diabetes was labile, and hyper- and hypoglycaemic episodes have occurred frequently. At that time the thymol turbidity test was 12-19 units; SGOT about 100 IU; serum bilirubin level normal. She had never been jaundiced. Tests for Australia antigen negative. Direct antiglobulin test negative. Tests for antibody formation proved normal.

Reinvestigated at 18 years, her development was infantile, height only 134 cm, weight 36 kg. The liver reached the umbilicus. The IgG level was raised (Table).

TABLE
Serum protein fractions

	Before onset of diabetes	After onset of diabetes	After prednisolone treatment
Total protein (g/100 ml)	10.8	9.7	6.4
Albumin (%)	35	24	35
Serum electrophoresis			
α_1 (%)	3	5	6
α_2 (%)	7	12	21
β (%)	10	13	18
γ (%)	45	46	20
Immune electrophoresis			
Prealbumin		--	Normal
Albumin		--	--
β_2 C complement		++	+
IgA		+	+
IgM		++	++
IgG		+++	Normal

Slightly decreased —, decreased — —, considerably decreased — — —. Slightly increased +, increased ++, much increased +++.

Lymphocyte culture showed a 47,XX,G+ pattern in 20 cells of the 208 cells examined. The same 47,XX,G+ karyotype was seen in 2 out of 30 bone marrow cells. Giemsa staining showed the extra chromosome to belong to the 21 pair. On the other hand, in a fibroblast culture all the 97 cells examined yielded 47,XX pattern. The karyotype of the parents was normal. In view of these findings, bone marrow, liver, and spleen biopsies were carried out.

Laparoscopy. The left lobe of the liver was seen to fill the upper abdomen; it was slightly yellowish pink in colour, its surface nodulous, the margin sharp.

Liver biopsy. Abnormal structure throughout, with pseudolobules of various size divided by connective tissue septa replacing the normal regular lobules. The cytoplasm was mostly loose, the nuclei differing in size and dye binding. The connective tissue between the pseudolobules was infiltrated by lymphocytes and plasma cells. The bile ducts were normal, iron and copper were not detectable. The histological diagnosis was hyperactive cirrhosis.

Spleen biopsy. Chronic congestion with some myeloid metaplasia.

Bone marrow biopsy. Anisocytosis with predominating red blood cells poor in haemoglobin. LE cells absent.

As the findings have pointed to an autoimmune process, 'immunosuppressive treatment' was started; in view of the low leucocyte count (2000–4000/mm³), only 5 mg prednisolone was given three times a day. Under its effect the liver function tests improved (thymol turbidity 1.4; SGOT 9 IU), and a repeat liver biopsy showed less activity.

At present, her diabetes is under control, but she has slight proteinuria, and ophthalmoscopic fluorescein angiography revealed multiple microaneurysms.

Discussion

In spite of her chromosomal pattern, the patient shows no clinical signs of Down's syndrome, except for subnormal growth which was present before the onset of diabetes, and a susceptibility to respiratory infections. Immunobiological disturbances are common in Down's syndrome. The liver cirrhosis had presumably developed before her diabetes was manifest. Although the association of liver cirrhosis and diabetes is well accepted, cirrhosis remains a rarity in juvenile diabetes. While the IgA level is raised in Laennec-type cirrhosis, in autoimmune processes, as a consequence of the plasma cell accumulation in the liver, IgA and IgM levels rise slightly, IgG levels markedly (Engle and Wallis, 1969). Our patient showed the latter pattern. The presumption of an autoimmune process was supported by the satis-

factory improvement of the liver function tests and liver biopsy.

The relation between Down's syndrome and diabetes has been the subject of discussion for many years. Kay and Esselborn (1963) observed Down's syndrome with hyperthyroidism in 3 patients and of these 2 were diabetics. According to Burch and Milunsky (1969), the genes, which by their mutation initiate an autoimmune process bringing about degeneration of the β -cells of the pancreas, are on the 21 chromosome.

The coexistence of growth failure, liver cirrhosis, diabetes, and 21-chromosome abnormality is unlikely to have been coincidental.

Summary

A girl with juvenile diabetes, liver cirrhosis, and 47,XX,21+/46,XX chromosomal mosaicism is described. The immunoglobulin pattern suggested an autoimmune process. After prednisolone treatment the IgG level and liver function tests became normal and the liver histology improved.

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