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IDIOPATHIC HYPOGLYCEMOSIS IN CHILDREN AND CENTRAL NERVOUS SYSTEM DAMAGE

McQuarrie and co-workers,[1, 2] in their reports of 1949 and 1953, called attention to a syndrome noted in children consisting of hypoglycemic episodes and convulsions. While they reported on thirty-eight cases with episodes of spontaneous hypoglycemia from various causes, the most fascinating of the group were twenty-five children with the condition that these authors referred to as "idiopathic hypoglycemosis." Investigation of this group of children revealed no specific organ, system or hormonal etiology, but the children were found to have increased sensitivity to injected insulin or impairment of the normal response to hypoglycemia. Some children had undergone partial or subtotal pancreatectomy without relief of symptoms. Nor did the histologic examination of the pancreas provide a clue to the disorder. An alpha cell abnormality, once suspected to be the etiologic factor, has as yet to be proved.

Eleven of the twenty-five patients included as idiopathic hypoglycemics showed a familial or hereditary factor in the etiology. Twenty-one of the twenty-five patients had the onset of clinical hypoglycemia under two years of age. There were eighteen boys and seven girls in the group. McQuarrie and co-workers stated that they saw only children who had the severest conditions, and undoubtedly a far greater number of children who have the less severe type are never diagnosed properly, recover spontaneously, or automatically adjust their own diets by voluntary food selection.

The presenting complaint in nineteen cases was convulsions, coma with convulsions in three, and staring, pallor, strabismus, tremulousness, and so forth in three. Fasting blood sugar levels as low as 10 to 15 mg. per 100 ml. of blood (macro) were noted. On corticotropin, 10 mg. every six hours, the fasting blood sugar levels could be maintained in the range of 50 to 90 mg. per 100 ml. and convulsions could be prevented. The nondiabetic type of curve was noted on the epinephrine and glucose tolerance tests.

While mental retardation and obvious brain damage were present in many of McQuarrie's patients, there were a few who were normal and later normoglycemic without treatment. In some instances the severely damaged infants were known to have developed normally before the onset of the convulsions.

Gall and Burke[3] reported two additional cases of hypoglycemosis, one in which the patient was a four and a half-month-old boy in whom a severe degree of cortical atrophy was demonstrated, and a second in which the patient was a severely damaged eight-month-old child in whom convulsions had been noted from the second day of life.

The beneficial effects of corticotropin therapy did not appear to be temporary in some of McQuarrie's cases. Of the cases reported by Gall and Burke, one child succumbed following progressive deterioration and convulsions at four and a half years of age, while the other child was severely damaged mentally though continually receiving corticotropin therapy.

All of the authors cited above call attention to the importance of obtaining fasting blood sugars in infants having convulsions, because salvation from severe damage of the central nervous system could be effected by corticotropin therapy. It is apropos to mention dangers to the brain of hypoglycemic episodes from overdosage of insulin inasmuch as resultant damage to the brain would be the same.

Though no protocols have been published in any of these above-cited cases many authors have demonstrated changes in the brain consequent to insulin shock therapy or hypoglycemic episodes.

Baker[4] in 1939 subjected rabbits to repeated insulin shock insults and killed the animals at various time intervals during the study. He noted that nerve cell damage did occur, but was by no means as striking as cerebral hemorrhage, areas of demyelinization, encephalomalacia and glial reaction. The changes were thought likely to be only temporary in the brains of animals subjected to one or several hypoglycemic episodes. Baker suggested that cerebral damage in hypo-

glycemia might be due to qualitative circulatory disturbance, inasmuch as blood reaching the brain is deficient in the proper nutritive materials.

Heberden and Friedlander[5] in 1955 reported pathologic changes in the brain of a two-year-old diabetic child who had suffered from prolonged overdosage with insulin and who finally succumbed to convulsions many months later. In this same child ventricular dilatation and cortical atrophy were suspected following neurologic, electro-encephalographic and pneumo-encephalographic studies.

Numerous authors were cited by Heberden and Friedlander in a discussion of the histopathologic changes in the brain associated with recurrent and prolonged hypoglycemic episodes. Gross vascular lesions, complete necrosis of nerve cells, and encephalomalacia of the cortex, thalamus, and caudate and lenticular nuclei occurred. Lesions of the basal ganglia similar to effects of severe anoxia, carbon monoxide poisoning, cardiac arrest and status epilepticus have also been described as neuropathologic changes in hypoglycemic deaths.

Heberden and Friedlander concluded that coma up to three hours can be associated with a lack of demonstrable brain damage and that the level of blood sugar seems to bear little relationship to the duration of coma. A progressive rise of the blood sugar is not necessarily accompanied by a return to consciousness.

In diabetics, use of the long-acting insulins has, in a sense, added a further threat of hypoglycemic coma because of the insidious approach of the coma and the sustained action of the agent.

Experimentally, hypothermia and barbiturates have been noted to protect animal brains from hypoglycemic damage. Cortisone and corticotropin have been recommended to alleviate the prolonged hypoglycemia.

It is generally accepted that nerve cells require glucose for oxidative processes and that the cells themselves have meager glucose reserves. Hence, the cells depend on blood glucose to a large extent.

Those of us treating children, therefore, must be particularly alert to the hazards of hypoglycemic episodes, whether from administration of insulin or from other causes, because the immature central nervous system is more susceptible to convulsions and perhaps to permanent brain damage than the mature central nervous system.

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Max Rubner
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Few people have made contributions to the field of metabolism comparable to those of Max Rubner. His development of the Isodynamic Law and the Law of Surface Area, and the determination of the calorie equivalents of foodstuffs along with other fundamental work, gave impetus to studies of energy metabolism.

Max Rubner was born in Munich on June 2, 1854. He received his early training under Carl Voit in Munich. During this time he was associated also with Pettenkofer. Voit and Pettenkofer had recently developed a method of estimating carbon dioxide, and this procedure enabled Rubner to carry out his studies. He also spent a year with Carl Ludwig at Leipzig.

When Rubner was twenty-four he embarked on experi-