

presence of oxygen does not indicate that there are other reactions between oxaloacetic and acetoacetic acids besides (1) and (2) in sheep heart muscle. Under the conditions of our experiments oxaloacetic acid had no effect on the *oxidative* breakdown of acetoacetic acid. The intermediate stages of this process must still be regarded as obscure.

Experimental details are to be published in the *Biochemical Journal*.

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Substitution of Whole Stomach Extract for Vitamins in the Treatment of Malignant Infantile Pellagra

DURING the last three years, close on three hundred children suffering from acute malnutrition have been admitted to the non-European Hospital, Johannesburg. More than 60 per cent of these infants manifested the clinical signs of infantile pellagra. The dominating features of this disease were oedema affecting upper and lower extremities, and in severe cases the face, eyelids and genitalia; this oedema was associated with pellagrous skin lesions on the legs, buttocks, back, arms and face, grey hair or alopecia, as well as patchy or diffuse dermal depigmentation. The stools were, as a rule, bulky, pale and foul-smelling, and contained much unsplit fat. The serum proteins, both albumen and globulin, were extremely low, a mild microcytic anaemia was common, and the liver, on biopsy and at post-mortem, was diffusely fatty. This severe form of malnutrition is apparently identical with that described by other investigators^{1,2,3,4}.

Trowell⁵, an outstanding worker in this field, has repeatedly recorded the unresponsiveness of this disease to vitamin therapy, including nicotinic acid, and recorded a 90 per cent death-rate. For this reason he decided to discard the name 'infantile pellagra', and to call it 'malignant malnutrition'.

In our experience, not only has vitamin therapy failed to save the lives of more than 50 per cent of these children, but also in many instances we strongly suspected that vitamin therapy aggravated the disease and even hastened death. This opinion is substantiated by the sudden increase in oedema, as well as of fatty change in the liver, when vitamins were administered. Blood and serum transfusions also proved valueless. In these circumstances it was essential to seek some other method of saving the lives of these children.

We established, by an improved liver biopsy procedure, that the microscopic appearance of the liver is a most valuable method of assessing the severity of the condition and is certainly more reliable than the clinical picture or any of the laboratory findings. We therefore adopted the liver biopsy method as a routine procedure in gauging the condition of the child on admission and the effectiveness of our therapy. Twenty children were studied by this method. Of these, seven were treated with thiamin,

nicotinic acid or brewers' yeast administered either orally or parenterally; seven were given 5 c.c. of Abbott's crude liver extract intramuscularly twice daily for seven days, and the final group of six cases were treated with 10 gm. of ventriculin (Parke Davis) plus 10 c.c. of N/10 hydrochloric acid daily, in one dose, for five days.

All these cases had extremely fatty livers which, from our previous observations, indicated a very poor prognosis. Progress was assessed by the clinical condition, the weight curves (as an index of the gain or loss of oedema fluid) and weekly liver biopsies.

Only one child of the seven treated with vitamins survived. The oedema increased progressively, the fat in the liver became more extensive, the children became more apathetic and died within two weeks. Five of the seven children treated with liver extract lived. The recovery was slow, the oedema subsiding gradually. Even after four weeks the liver still contained appreciable amounts of fat.

The response to ventriculin therapy was most dramatic, since all the children survived, despite the fact that clinically and by liver biopsy they were as bad as the cases in the other two groups. A loss of oedema fluid shown by the decrease of 1-1½ lb. in weight was usually observed within twenty-four hours. Moreover, the clinical condition improved in a remarkable fashion, and the liver was almost free of fat within two weeks.

Whole extracts of hog's stomach has occasionally been used for the treatment of pellagra in adults with good results^{6,7,8}. In seven cases of severe pellagra in adults we have found that, except for the mental symptoms, which respond slowly, ventriculin is a much more rapid and effective treatment than nicotinic acid or other vitamins.

Owing to restriction of facilities, it has not been possible to conduct a more extensive investigation of the value of ventriculin in treating severe malnutrition in children. However, even with this limited material we feel justified in concluding that: (1) Stomach extract is a life-saving drug in severe infantile pellagra and should be given universal trial. (2) Stomach extract can be regarded as a lipotrope in view of the rapidity with which it depletes the fat from the liver in infantile and adult pellagra. (3) Biopsies reveal extensive liver damage in adult and infantile pellagra. (4) In view of the fact that both adult and infantile pellagra respond to a single form of therapy, there is no justification for regarding them as different diseases.

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