STUDIES OF AMINO ACID HANDLING IN KWASHIORKOR WITH A POSSIBLE EXPLANATION FOR THE INCREASED AMINO-ACIDURIA*

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Approximately 2 years ago we reported at Research Forum our observations on the increased amino-aciduria of 8 infants with kwashiorkor (protein malnutrition), who received both natural and synthetic meals. Since that time we have accumulated evidence† from an additional 8 cases confirming: (1) That the amino-aciduria reflects an increased excretion of 2-10 times the figure in our controls; (2) that it is the result of increases in at least 7 amino acids, and (3) that the increased excretion is temporary, returning to control levels after approximately 3 weeks of treatment. We are at present more particularly concerned with the possible mechanisms which may be responsible for this phenomenon.

Studies of renal function were designed in which 5 infants with kwashiorkor were fasted for 6 hours and were then given a test meal of skimmed milk providing approximately 1 g. of protein per kg. of body weight. Blood was taken every half hour and

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urine collected every 15 minutes by catheter for a 3-hour period following the test meal. Total amino acids were estimated in the urine and plasma by the Van Slyke gasometric technique. Urinary creatinine was also estimated.

It would appear that, in 4 of these cases, there was a tendency for the plasma amino acids to rise higher or remain at their maximal concentration for a longer time after the test meal; in fact, these increases are significantly greater ($p < 0{\cdot}02$) than those of the control series. This tendency is most pronounced in the severely ill cases and is reduced with treatment.

The same tendency also appears in the data on urinary amino acid, viz. the most severely ill infants show the greatest urinary excretion of amino acids, and this excretion is reduced on treatment.

More important for the purpose of this investigation, however, is the observation that in these cases of kwashiorkor, there appears to be a relationship between the concentration of plasma amino acid and the degree of amino-aciduria: wherever the plasma concentrations were highest, the urinary excretion of amino acids was greatest. It would appear, therefore, that renal function, in so far as amino-aciduria is concerned, is probably normal in kwashiorkor, but that the utilization of amino acids is altered, thereby causing the renal threshold to be exceeded. There is also some suggestion of a relationship between the urinary excretion of amino acids and creatinine—presumably a common, renal mechanism. The explanation that this is an artifact resulting from errors inherent in the 15-minute urine collection interval, appears justified by further investigations.

In an additional investigation 24-hour urine collections were made throughout the treatment of 4 cases of kwashiorkor and compared with collections made over a period of 2 weeks from a normal, active child of a similar age living in a home environment and eating a mixed diet.

It was observed that the urinary excretion of amino acids increases to a maximum within the first week of adequate treatment and is not related to fluctuations in creatinine excretion. These urinary amino acids were partitioned during 3 phases in treatment: on the first 2 days, on 2 days at maximal excretion, and on the final 2 days, at cure. These partitions confirm our earlier observations that the increased amino-aciduria of infants with kwashiorkor results from increases in the excretion of at least 7 amino acids.

SUMMARY

Renal function and other studies suggest that the increased amino-aciduria of kwashiorkor is due to altered utilization of absorbed amino acids causing the renal threshold to be exceeded. As yet, we have no evidence of a defect in renal tubular function.