NITROGEN BALANCE STUDIES IN ADVANCED CHRONIC RENAL DISEASE

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In chronic renal disease one of the major problems is equating the patients' protein requirements with their ability to excrete the end products of their protein metabolism. Advanced chronic renal disease is defined here as an irreversible renal lesion with a creatinine clearance of less than 15 ml./min.

METHOD

All patients in this study were ambulant in a metabolic ward. The protein diet was selected from the data of McCance and Widdowson\(^1\) to contain the chosen quantity of protein and calories for each patient. During the balance periods the nitrogen content was measured by estimations of duplicate meals using a modified Kjeldahl procedure. The nitrogen content was then multiplied by 6.25 x 4.1 to obtain the calorie intake from nitrogen whilst the calories provided by the fat and carbohydrate in the diet were calculated from the data of McCance and Widdowson\(^1\).

The nitrogen excretion in urine was assayed using the Technicon Automated Kjeldahl apparatus. Fæcal nitrogen excretion was assayed as for food.

The balance periods lasted 4-7 days and were preceded by an equilibration period of 5-6 days. Losses in faecal collections were corrected for by using chromium sesquioxide given orally\(^2\). The chromium content of the fæces was estimated by Dr. Rose using flame photometry. This was necessary as the faecal nitrogen represents such a large percentage of total nitrogen excretion when the dietary nitrogen intake is low.

The plasma urea nitrogen (P.U.N.) was estimated using the Technicon Autoanalyser. Changes in the body load of urea nitrogen (assuming urea to be distributed equally in the total body water) during the balance periods were added to the nitrogen balance data.

Loss of nitrogen from desquamation or sweating was not measured.

RESULTS

Case 1 Male. Polycystic disease of the kidneys, creatinine clearance of 5 ml./min (Figure 1).

The nitrogen intake was kept constant at 4.4 g./day in each balance period. Increasing the calorie intake, as carbohydrate, from 1500 to 2500/day decreased the extent of the negative nitrogen balance. The P.U.N., though falling in the first period, fell still further in the second.

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The patient experienced a subjective sense of well-being, his appetite improved and his pruritus disappeared.

Case 2  Male. Congenital urethral valves, bilateral hydronephrosis and hydroureters, creatinine clearance of 10 ml./min. (Figure 2).

The nitrogen intake was kept almost constant at 3.7 g./day in each balance period. During the second balance the calories from carbohydrate were reduced from about 2500 to 1500/day with an increase in the negative nitrogen balance.

Case 3  Male. Solitary polycystic kidney, creatinine clearance of 11 ml./min. (Figure 3).

Again there was an improvement in nitrogen balance during the second diet when the calories from carbohydrate were increased although there was an increment in the nitrogen intake. During the third balance period the nitrogen intake was the same as the second but the calorie intake from fat was doubled, the carbohydrate intake being reduced by an isocaloric amount. There was no significant change in nitrogen balance.

Case 4  Male. Polycystic disease of the kidneys, creatinine clearance of 8 ml./min. (Figure 4).

Initially during the first two balance periods the nitrogen intake was almost constant at 3.45 g./day. There was some improvement in nitrogen balance when the calorie intake, as carbohydrate, was increased. As the P.U.N. fell markedly the nitrogen intake was increased to 5.5 g./day during the third balance period. The total calorie intake being kept constant. The nitrogen balance became positive with no deterioration in the biochemical state.

In the next three patients the quantities of animal and vegetable protein in the diets were varied although the total calorie intake was unchanged.

Case 5  Male. Chronic glomerulonephritis, creatinine clearance of 12 ml./min. (Figure 5).

The calorie intake in the two balance periods was 3000/day. During the first the nitrogen intake was 6.2 g./day entirely of vegetable protein. In the second the nitrogen intake was increased by 10.9 g./day but 50% was of animal origin. The change resulted in a positive nitrogen balance and no serious deterioration in his biochemical state.

Case 6  Male. Chronic pyelonephritis, creatinine clearance of 12 ml./min. (Figure 6).

The nitrogen and calorie intakes were constant in both balances. The nitrogen in the first balance period was all of vegetable origin and in the second 50% was replaced by animal protein. There was little change noted in the nitrogen balance.

Case 7  Female. Polycystic disease of the kidneys, creatinine clearance of 4 ml./min. (Figure 7).

Her appetite was poor though she had been working for one year on a 3.5 g. nitrogen 2000 calorie diet. During the first balance period she was given a 6 g. nitrogen and 2000 calorie intake/day. Forty-four per cent. of this protein was of animal origin. She was in positive nitrogen balance, the
P.U.N. remaining constant. During the second balance period the nitrogen intake was increased to 10.4 g./day, 50% being of animal protein. The improvement in nitrogen balance was only obtained at the expense of a significant increase in the P.U.N.

DISCUSSION

We conclude that the total non-protein calorie intake of patients with advanced chronic renal disease should be greater than 2500/day. If this is not tolerated, as in one of our cases, then the highest possible calorific intake has to be accepted. In such cases, a partially synthetic nitrogen intake, as advocated by Giovanetti(3) may be of value. As our studies were on patients confined to a metabolic ward, we found that some increase in their total calorific intake was occasionally necessary when they left hospital. Our findings indicate that a larger proportion of the non-protein calorific intake can be supplied as fat with no adverse effect on the nitrogen balance. Some workers, as reviewed by Munro(4), have found a deterioration in the nitrogen balance on substituting increased quantities of fat for carbohydrate in the diet. The greatest changes were usually seen from 2-5 days after the changes in the diets. As this would have occurred during the equilibration period of our diet, then any temporary disturbance would have remained undetected. Also, as the possibility of an abnormal fat metabolism in uraemic subjects has been suggested(5), no final conclusions are possible at this stage.

The nitrogen intake should be related to the degree of renal failure. Some patients were fed 10 g./day without adversely affecting their P.U.N. level. But, in others with more severe renal impairment, 3.5-4.5 g./day may be the maximum tolerated. Our results concerning the relative merits of animal and vegetable proteins are incomplete and more observations are required before firm conclusions can be drawn.

In co-operation with Dr. Rose we have also studied the calcium balance in some of these patients. We emphasise that the calcium content of low protein diets is usually deficient (2.7-7.2 mg./kg. body weight), this being below that recommended even for normal persons (5.3-9.3 mg./kg. body weight)(6, 7, 8) and supplementation would seem desirable.

In all the patients we studied, adjusting their diets to contain an optimal total caloric and nitrogen intake, resulted in a marked subjective improvement.

REFERENCES

Figure 1. (Case 1) Nitrogen intake plotted upwards from zero line. Nitrogen output in urine and faeces plotted downwards from top of intake. Positive nitrogen balance above zero line, negative below. Illustrates nitrogen retentive action of increasing calories from carbohydrate.

Figure 2. (Case 2) Decreased nitrogen retention on reducing calories from carbohydrate.
Figure 4. (Case 4) Slight decrease in extent of nitrogen balance on increasing carbohydrate. Slight positive balance achieved on increasing nitrogen intake.

Figure 5. (Case 5) Illustrates beneficial effect of increasing nitrogen intake in presence of adequate total calorie intake.

Figure 6. (Case 6) No real difference shown between animal and vegetable nitrogen intake at this level of calorific intake.

Figure 7. (Case 7) Shows positive nitrogen balance can be achieved with low nitrogen and relatively low total calorific intake. Marked increase in positive nitrogen balance in second period achieved at expense of considerable increase in P.U.N.