



THE LIMITS OF ADAPTATION OF FUNCTIONAL PROTEIN SYNTHESIS TO SEVERE UNDERNUTRITION

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1. OBJECTIVES

This project was designed to investigate the limits of adaptation of protein metabolism in the state of severe childhood malnutrition, representing as it does chronic dietary insufficiency of macronutrients and superimposed infection.

2. TASKS

The tasks included measurement of concentrations and rates of synthesis of nutrient transport proteins and hepatic acute phase proteins in severely malnourished children during their acute illness and a recovery.

Measurements of these same things in normal controls.

3. PROGRESS

Rates of synthesis of both types of proteins were measured simultaneously using two tracers, U-¹³C glucose and H³-leucine in pilot experiments. Both tracers gave similar results and because the cost of the U-¹³-glucose was substantially greater than the leucine, the latter was used as the sole tracer in all subsequent experiments.

In these experiments, we measured fractional synthesis rates of nutrient transport and hepatic acute phase proteins in 3 children, one in the acute phase and two in the recovered phases. Each subject received 2H³-leucine as a primed (22.5 μ mole/kg) constant (30 μ mole/kg/h) intragastric infusion. Feed was offered at 100 cal/kg/d and protein, 1.2 g/kg/d. Four blood samples of 1 ml each were taken at baseline and after 3.4 and 8 hours of infusion.

The isotopic enrichments of triplicate samples of the 7 proteins extracted from blood showed good reproducibility of isotopic enrichment determinations.

The infusion protocol labelled the slowest turning over protein, albumin to an isotopic enrichment which allowed precise measurement of its synthesis rate.

Fractional synthesis rates of nutrient transport proteins were found to be depressed in the acute stage by 15-58% while those for the hepatic acute phase proteins were elevated by 28-125%. These relationships were reversed in the recovered stage.

Since these pilot examinations have been completed, 5 additional patients have been recruited and 3 of these have had all studies done. Mass spect analyses have not yet been performed and these are not scheduled until February 1995 when Dr. Terrence Forrester will transport specimens to CNRC.

| FRACTIONAL SYNTHESIS RATES OF NUTRIENT TRANSPORT AND HEPATIC ACUTE PHASE PROTEINS IN 3-12 MONTH OLD INFANTS | | |
|---|--------------------|---------------------|
| PROTEINS | RECOVERING (FSR%H) | KWASHIORKOR (FSR%H) |
| NUT PROTEIN | | |
| Albumin | 0.61 | 0.52 |
| RBP | 4.42 | 1.85 |
| Transthyretin | 1.82 | 1.00 |
| VLDL APO B-100 | 21.0 | 14.5 |
| HDL APO A-1 | 1.75 | 2.0 |
| ACUTE PHASE | | |
| Transferrin | 0.86 | 1.07 |
| Fibrinogen | 1.56 | 2.0 |
| Haptoglobin | 1.98 | 4.46 |
| A-1 acid glyco | 1.25 | 2.04 |

4. CONSTRAINTS

Dr. John Morlese, the fellow assigned to the project, was appointed in 1994. Since then there has been a reduction in admissions to the TMRU ward of babies with severe childhood malnutrition. This reflects a fall in the recorded prevalence in the society. To compensate for this, Dr. Morlese travels to peripheral hospitals to recruit subjects.

5. PROJECTIONS

At the current rate of admissions this project will run for another year.

6. REQUEST

A request is hereby made for an extension of the current grant at the same rate to cover the 1994-95 period.