

PROPOSALS FOR PEDIATRIC RESEARCH PROJECTS
IN ROCKEFELLER UNIVERSITY HOSPITAL

I. Role of Sulfur Amino Acid Metabolism in Coronary Artery Disease.

It is envisaged that this project would be done in collaboration with Dr. Ahrens and would consist of direct enzymatic as well as in vivo metabolic studies of methionine, cyst(e)ine and taurine. Abnormalities of lipid and carbohydrate metabolism are more well known as risk factors for coronary artery disease. Recent work suggests that altered sulfur amino acid metabolism may constitute an additional risk factor in genetically susceptible individuals by contributing to the production of endothelial damage. It is proposed to study patients who have a paucity of known risk factors. The general approach would include direct enzymatic analysis of the enzymes of sulfur metabolism in skin culture and long-term lymphoid cell lines as well as in vivo loading tests with sulfur-containing amino acids. My laboratory has considerable background and experience in both of these approaches, although they have never been applied to this group of disorders.

II. Inborn Errors of Amino Acid and Organic Acid Metabolism.

This study would be a continuation of ongoing clinical, enzymatic and metabolic studies in patients with this group of inherited disorders.

III. The Role of Taurine in Control of Bile Salt and Cholesterol Metabolism in Man.

It is anticipated that this study also would be done in collaboration with Dr. Ahrens' group. Our group has shown that there is a nutritional requirement for taurine in man. The only known biochemical reaction which taurine undergoes is the conjugation of bile acids. There is some evidence that the conjugation of bile salts by taurine may be involved in the control of cholesterol pool sizes and cholesterol synthesis. Taurine and cholesterol are both present in large concentrations in human milk, but not in bovine milk or the manufactured formulas derived from bovine milk. Study of these interrelationships in infants, children and adults may be of considerable general nutritional interest.

IV. Transfer of Nutrients and Toxins in Human Milk.

This project would involve the use of nursing mothers and direct measurement of transfer to the infants of nutrients and possible toxins in their milk. The prototypic compound used in the first instance would be C^{13} -taurine and N^{15} -labelled polyamines. This project would involve gas chromatography-mass spectrometry with the mass spectrometer being utilized as a qualitative analytical as well as quantitative tool (mass fragmentography).

V. Amino Acid and Protein Metabolism in Nutrition in Infants and Children.

This project would also involve mass spectrometry and the use of stable isotopes in determination of rates of synthesis, turnover rates and body pools. In children the use of radioisotopes is ethically unacceptable and stable isotope techniques must be worked out to gain a more dynamic view of protein requirements in amino acid metabolism during development.

VI. Metabolic and Nutritional Studies of Anorexia Nervosa.

This fascinating disorder is a voluntary restriction of food intake which is seen mainly in adolescent young women although it is also seen in adolescent boys. There is no real anorexia but rather a voluntary restriction of food intake which is generally assumed to be of psychogenic origin. Unlike involuntary undernutrition, signs and symptoms of anemia, vitamin, and protein deficiency are often lacking. There is a paucity of hard information about changes in body composition and the reasons why the metabolic changes found in this disorder differ from those found in involuntary food restriction. It represents an interesting theoretical model as well as an important pediatric problem. It is envisaged that this problem might be approached in collaboration with Dr. Jules Hirsch.