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ENERGY REQUIRMENTS AND BODY COMPOSITION IN CYSTIC FIBROSIS

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Summary

A wide range of nutritional deficits causing many deleterious effects have been described in cystic fibrosis. The heights and weights of many cystic fibrosis patients are markedly skewed towards lower centile bands, particularly with increasing patient age. Body composition studies performed in Brisbane suggest that underweight cystic fibrosis children have a deficit in body cell mass and body fat with a reduction in lean mass and muscle mass and an excess of extra-cellular water compared to control subjects. The failure of development of body cell mass can be present from the first few weeks of life as judged by studies of newborn cystic fibrosis infants diagnosed by neonatal screening. These nutritional abnormalities seem likely to be caused by a combination of inadequate absorbed intake, nutrient losses and increased requirements. There has been growing interest in the relationship of alterations in energy metabolism and utilisation in cystic fibrosis since recognition of an apparent maladaptation to under-nutrition with increased protein turnover in these patients. We have provided evidence that shows that well nourished patients with normal lung function, have markedly excessive energy expenditure as judged by the doubly labelled water method and have suggested that deficits in both body composition and energy metabolism may be established very early in life in cystic fibrosis, and if not corrected, lead to progressive nutritional growth retardation with increasing age. Studies of active nutritional therapy which provide adequate absorbed energy for needs show that these potentially serious problems can be at least in part corrected by an active nutritional programme.

I. INTRODUCTION

Cystic Fibrosis (CF), an hereditary disease of exocrine gland secretion, is characterised by recurrent pulmonary infections, pancreatic insufficiency with maldigestion, and malabsorption. Recent work has localised the gene on the long arm of chromosome seven, and biochemical studies have suggested that the defect occurs in the regulation of inorganic ion transport, resulting in abnormal exocrine function. Advances in therapy have greatly improved life expectancy of this common disorder and this ha resulted in an increasing population of patients requiring long term medical care.

The adverse effects of CF on nutrition and growth have long been recognised and with improving life span the assurance of normal nutrition and growth is becoming increasingly important. Certainly nutritional problems are common and it has been shown that potentially reversible nutritional factors may influence growth, the course of the pulmonary disease, and possibly the long term outcome of this condition. It is however important that an accurate assessment of nutritional status and growth response to nutritional therapy be available. Frequently this is not the case, especially in young children where there is a wide normal distribution for parameters such as weight, height, skinfold thickness, etc, which often result in erroneous clinical impression of nutritional status. In addition, techniques for assessing energy requirements have vastly improved in the last few years with the advent of stable isotope measurements, measuring total energy expenditure and protein turnover. Until these techniques have been fully applied to a CF population, any knowledge of energy requirements and the establishment of optimum nutritional therapy must remain largely empirical. However, a body of data is accumulating on these aspects of malnutrition in CF and these studies form the basis of this paper.

II. ENERGY BALANCE IN CYSTIC FIBROSIS

The consensus view is that negative energy balances are created where intake is insufficient in the face of anorexia, dietary restriction, and suboptimal therapy of malabsorption to meet the increased energy expenditure, which has been empirically recognised for many years in this disease. Certainly the energy depleting insults of recurrent or chronic lung infections contribute to this and in addition, at certain critical phases of life (eg infancy, adolescence), it is not difficult to see how chronic under-nutrition and nutritional growth retardation occur.

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In the last decade however vast improvements in achieving adequate dietary intakes and optimising absorptive therapy have been achieved, particularly with the demands of the energy deficient low fat diet, and the advent of acid resistant preparations of pancreatic enzyme supplements, as well as work on nutritional supplementation. However, only a limited work has been done on energy requirements in cystic fibrosis.

Energy requirements can be assessed by a number of different techniques, including empiric indirect methods of assessing intake required to achieve growth, assessing the energy needs of protein turnover. the measurement of resting energy expenditure by indirect calorimetry, and by measuring total energy expenditure. Until lately, methods for measuring total energy expenditure have been quite restrictive and impractical and subject to variance, particularly in children. However, the recent application of the doubly labelled water method for measuring total energy expenditure in free living subjects has helped to overcome this latter problem.

We have conducted a series of studies using stable isotope techniques on protein turnover during different phases of the disease (Figure 1). In normal sex and height match controls, as one would expect, protein synthesis exceeds catabolism resulting in net protein deposition. During acute exacerbations of pulmonary disease in CF, there appears to be a marked reduction in overall protein turnover, probably because of diversion of energy to handling the increased energy needs. This results in negligible protein deposition during acute pulmonary exacerbations (See Figures).

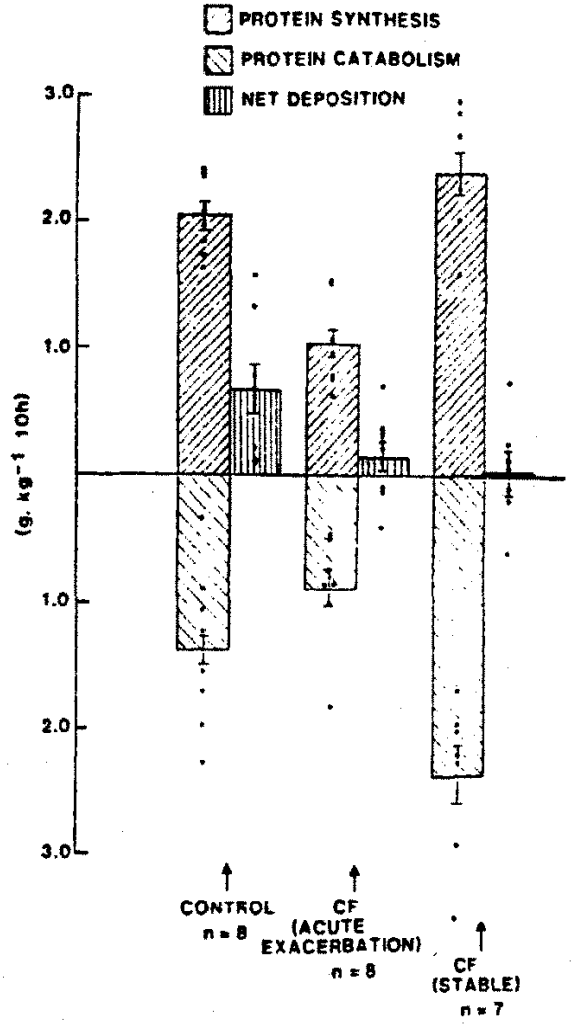

Figure 1 -Protein synthesis catabolism and net deposition in a group of healthy children and age matched CF children during an acute exacerbation and when they are clinically stable. From Holt T L, Ward L C, Francis P J, Isles A, Cooksley W G E, and Shepherd R W. Whole body protein turnover in malnourished CF patients Am J Clin Nutr 1985:41:1061-1066.

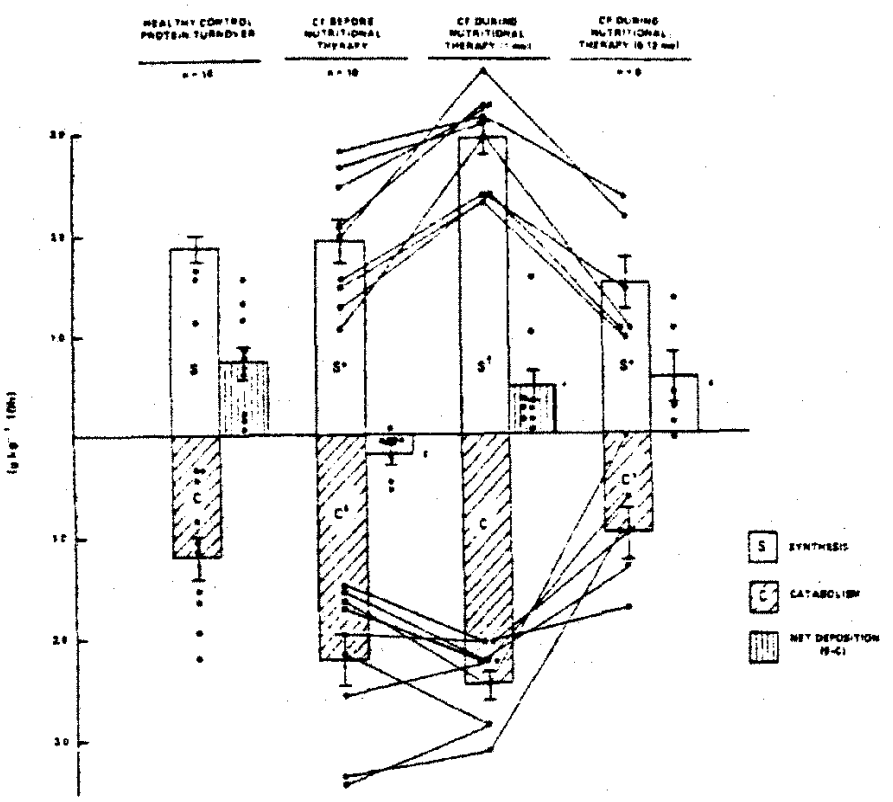

Figure 2 - Whole body protein turnover in healthy controlled children and in malnourished CF children before and during nutritional therapy from Shepherd R W, Holt T L, Thomas B J, Isles A, Francis P J and Ward L C. Nutritional rehabilitation in cystic fibrosis: Controlled studies of affects on nutritional growth retardation, body protein turnover and the course of pulmonary disease Journal of Pediatrics 1986: 109:788-794.

In stable but somewhat more undernourished patients with chronic lung disease, there is negligible net deposition which appears to be due to excessive protein catabolism. What we have found is that if we provide short term nutritional therapy to such patients, we can improve synthesis and net deposition, but have made no inroads into the apparent excess catabolism, although over a long period of time with complete normalisation of growth after a year or more of nutritional rehabilitation, this excessive catabolism slowly reverts closer to the normal range (Figure 2).

There have been two studies of resting energy expenditure in CF. Buchdahl et al from London studied a group of CF patients aged 18 months to 18 years using indirect calorimetry. They found that resting expenditure was increased to about 110% of expected values with only a weak correlation between the excess resting energy expenditure and pulmonary function. A Toronto group studied a large number of CF individuals aged 9 to 35 years using indirect calorimetry and developed predicted values for normal energy expenditure from the Harrison-Benedict equation. From this uncontrolled data, they found that resting energy expenditure was 95-153% of predicted values and they felt that this was mainly related to the degree of pulmonary dysfunction and the degree of under-nutrition.

We have measured total energy expenditure by the application of the double labelled water method in a small group of well nourished CF infants diagnosed in the neonatal screening programme, measured at home while they were clinically well. None of these infants had any evidence of any lung disease during the time of the study. Comparative normal data for healthy infants was obtained from a large sequential study of total energy expenditure using this technique in healthy infants. In this group of patients (Figure 3) total energy expenditure in calories per kilo averaged 98 calories per kilo body weight, whereas the mean for the whole of

the matched group was only 77 calories per kilo body weight. We found no correlation between the total energy expenditure degree of underweight, and as I mentioned, none of these patients had any significant lung disease. Although sub-clinical disease activity cannot be excluded as a determinant of the total energy expenditure in these infants, the possibility of an energy requiring basic defect was suggested by us as a factor in this observed increase in total energy expenditure. Some confirmation of this suggestion has come from studies of the basic defect which centres around the chloride channel. Cells from subjects with CF consume more oxygen than normal and expressed increased electron transport activity, possibly in the maintenance of a normal intracellular level of ions in the face of ion losses from the cell.(See Figure).

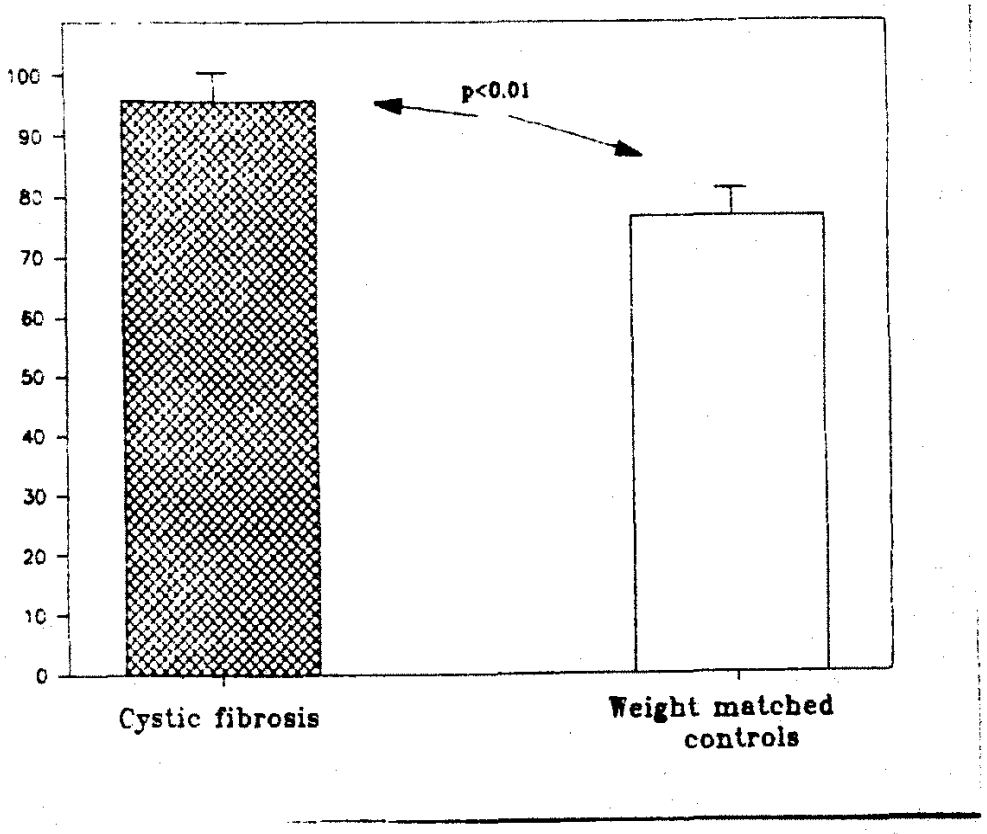

Figure 3 - Energy expenditure measured by the double labelled watrer method in calories per kilogram of body weight comparing CF infants and weight matched controls from Shepherd R W, et al. Energy expenditure in young children with cystic fibrosis, Lancet 1988 2:1300-1303.

In summary, there is accumulating evidence that the energy requirements in CF which have long been recognised as being greater than normal are contributed to by a combination of an energy requiring basic defect, as well as the catabolic affects of chronic lung disease and under certain circumstances, intermittent suppression of protein synthesis. All of these dynamic changes need to be taken into account when assessing possible energy requirements for an individual CF child.

III. BODY COMPOSITION IN CYSTIC FIBROSIS

Moore et al (1965) have shown that energy utilisation and the critical metabolic functions of the body are directly related to the body cell mass (BCM) which is the work performing energy using, and in children, the vitally growing component of the body. The BCM is potassium and nitrogen rich in contrast to body fat. Inadequate accretion of BCM during growth and/or a depletion of BCM is therefore an appropriate indicator of a serious chronic disturbance in nutritional status. For most applications, BCM is readily derived from total body

potassium (TBK) measurements by whole body counting technique. In most diseased states there are significant changes in extra-cellular water and if there is a reduction in the BCM there will also be a change in the intra-cellular water. Lean body mass, which is often mentioned in nutritional assessment, is the difference between total body mass and body fat and consists of a non-homogenous part of the body containing water, extra-cellular solids and bone as well as the BCM. As such the lean mass is not a particularly good sequential measure, mainly because of the rapid changes in body water which contribute to lean mass. Because of these considerations we have elected to study the changes in body composition in CF by measuring all body compartments, ie fat, water, BCM, extra-cellular solids, in relation to total body mass using the four compartment model as described by Bruce et al.

In CF patients, we have conducted longitudinal studies of a group of 25 infants between birth and two years of age, diagnosed by neonatal screening, and we have conducted a large cross-sectional study of 161 CF patients aged between two years and 17 years. In addition, in a group of under-nourished CF children, we have studied the affect of nutrition therapy on changes in body composition.

Between birth and two years of age, our studies have indicated that at early diagnosis, there is reduced fat stores, an expansion of extra-cellular water, but relatively normal BCM. In the first twelve to eighteen months of life following institution of therapy, there are significant improvements in the relative amounts of total body fat and BCM relative to normal, but that the defect in expanded extra-cellular water persists. This latter expansion of extra-cellular water has been a consistent abnormality at all ages of CF patients.

When body composition has been related to age in a cross-sectional study of a large number of CF children, we have found that when looking at weight and height, there is significant skewing of the population against normal percentiles but that the BCM relative to weight is normal despite the fact that these patients are not accumulating their body cell mass at the same rate as normal healthy children during growth. This reduced rate of accretion of BCM and continued expansion of extra-cellular water, which is characteristic of nutritional growth retardation, seemed to be the major characteristic of CF. This pattern of nutritional stunting of growth appears to be beginning to be established early in life and if not corrected may lead to increasing changes with increasing age.

With nutritional rehabilitation (Figure 4) malnourished patients who are deficient in body fat and muscle mass but who have expansion of extra-cellular water, show an increase in body fat and an improvement in muscle mass which is the major component of BCM. This process could be at least in part corrected with significant catch up of BCM with long term nutritional rehabilitation. (See figure)

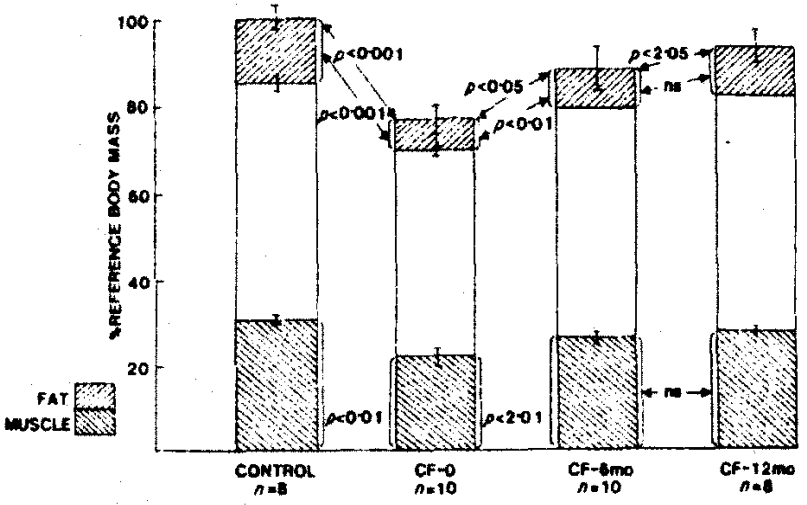

Figure 4 - Body composition in malnourished CF children compared with age matched controls before and at six months and 12 months after nutritional therapy.

IV. CONCLUSION

Our studies of nutritional growth retardation in CF show that the condition is related to an inadequate accretion of BCM and relative excess in extra-cellular water. This potentially serious disturbance of nutritional status is established early in life and is associated at this time with altered energy metabolism. The metabolic defect appears to be further compromised by later occurrence of acute and chronic lung disease. Nutritional therapy, which meets this excess metabolic demand can minimise this problem and optimise the growth of the critical metabolic functioning of the body, that is the BCM. These dynamic changes occurring in body composition, nutritional status and energy metabolism throughout the course of this disease, all require careful consideration in providing optimum nutritional therapy. Further studies, particularly of total energy expenditure during critical phases of the disease seems warranted.

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A full list of references was not supplied to the Editor but the author will make them available on request.