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SYMPOSIUM ON 'SURGERY AND NUTRITION'

Historical approach

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It was within this hospital some 53 years ago that I found in cases of accidental fracture of major long bones, and in certain non-bony injuries and operations, what seemed to me a most unusual disturbance of protein metabolism shortly after injury. To explore this further I was successful in obtaining a small nursing unit which provided two small side rooms accommodating five to six patients. There was also a small kitchen where we compounded the diets from relatively constant sources of supply and which we analysed from time to time. Latterly there was a sister in charge. This was one of the earliest metabolic units in the country.

Although before and during the First World War there were occasional references to rises in urinary nitrogen following haemorrhage and operation, no-one had really explored the condition. So there was here a relatively wide open but unknown field to chart. Having found that disuse atrophy might only be a small and contributory cause, I reported in a series of papers from 1930 onwards the characteristics of an increase in general catabolism over anabolism describing the parallel increments in urinary N, P, S, K, also the extent of the creatinuria without marked change in preformed creatinine. I also found that there was a tendency for a parallel increment in the resting consumption of oxygen taken under almost basal conditions. This hypermetabolism with slight febrile rise generally occurred, but not always if the patient was already undernourished at the time. In general, the more well built the subject prior to the incident the greater the effect and the more severe the accidental injury the greater this hypercatabolism which generally reached a peak between the 4th to 8th d after injury. The total loss of N in one case during the first 10 d was 137 g N, a reduction on the body's content of 7·7%. Accidental injuries gave greater effects than elective operations (Cuthbertson, 1929, 1930, 1931, 1932). We also showed that there was often an appreciable rise in fibrinogen in the plasma and a slight fall in albumin and marked rise in 'globulin' (Cuthbertson & Tompsett, 1935).

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The question naturally arose in these early days as to whether increased intake of foodstuffs, protein in particular, could stem the loss of body substance due to trauma. It was found that if diets very rich in first-class protein and of high energy value were consumed by patients who had suffered fractures of one or more long bones of the leg, the considerable loss of body N was reduced: however, at the height of the catabolism such diets frequently failed to prevent loss of N.

The rat proved a very suitable experimental animal for such studies and the information obtained confirmed and amplified our work in man (Cuthbertson *et al.* 1939). The loss of body substance could not be fully accounted for by the loss of muscle substance from the site of injury (femoral fracture) or indeed from the whole injured limb. These observations on the rat supported the view the author had earlier put forward (Cuthbertson, 1930) namely that injury in the wild state leads to a reduction in the capacity to gain food and so to provide fuel for maintenance and for recuperation, the primitive reflex of the organism is to catabolize its reserve protein and fat to meet these needs. Subsequent work on the rat by Al-Shamma *et al.* (1979), if investigated further, indicates that the greatest proportionate bodily change during the first 10 d following severe burning is loss of protein, thereafter loss of body fat increases until it provides 80% or more of the energy loss of the body.

I introduced the term 'ebb' to characterize the period of depressed metabolism associated with the initial phase of the reaction to moderate to severe trauma recognized as the period of shock in the classical literature on trauma. This is a period of general inhibition of protein synthesis though certain acute phase reactant proteins increase in the blood. I used the term 'flow' for the phase of increase in metabolic rate in those that recover from the 'ebb' phase. This is also sometimes referred to as the period of traumatic inflammation and is characterized by increased oxygen consumption and heat production and increased urinary losses of nitrogenous, sulphur- and phosphorus-containing metabolites (Cuthbertson, 1942, 1979).

H. N. Munro, who was working with me in Glasgow in the late 1930s and early 1940s, suggested we should test out the effect of injury on rats on a protein-free diet, given before and continuing after the injury. No increment in the low level of urinary N output occurred (Munro & Cuthbertson, 1943) and later Munro with the help of Dr Margaret Chalmers showed that the level of extra urinary N eliminated was directly related to the level of protein in the diet (Munro & Chalmers, 1945). In 1957, at the Rowett Institute we were able to show in the rat that on a protein-free diet fracture of a femur produced no increment in heat production and that on a normal diet the urinary N output was closely related to the increase in heat production (Cairnie *et al.* 1957).

Effect of environmental temperature on the response to injury

Observations on the rate of wound healing and on the metabolic response to fracture in rabbits and rats by Erici (1956) in Sweden, Caldwell (1962) in the USA and in Scotland by Campbell & Cuthbertson (1966, 1967) and Cuthbertson &

Tilstone (1967) indicated that in the zone of thermo-neutrality, 30–32° for the rat, there was an improved rate of healing of superficial wounds and the extent of protein catabolism was reduced. On the basis of favourable reports from Sweden on the course of illness of the severely burned patient (Barr *et al.* 1968) I visited Dr Liljedahl's unit in Stockholm and saw the good clinical condition and appetite of the patients maintained in a relatively dry, warm climate (32°) with sterile, warm, dry air blown over the burn sites. Their cases also exhibited a reduced resting O_2 consumption at the higher ambient temperature. In our turn we showed in man that the protein metabolism response to moderate to severe fractures, involving frequently more than one major long bone of the leg or other multiple injuries, was also reduced by placing the patient soon after injury in an environmental temperature of 28–30° and a relative humidity of 35–45% (Cuthbertson *et al.* 1972). In general, we have found that such patients tolerate these warmer, drier conditions, particularly if around 28–29°. There was also less disturbance in the acute phase reactant proteins. The advantage of the higher environmental temperature over the provision of extra bed covering for patients with burns is obvious but this is an advantage also to those with fractures. The surface of the extremities of injured limbs may be at a slightly higher temperature under these conditions but the dorsum of the large toe may be as much as 12° higher (Cuthbertson & Rahimi, 1973).

Parenteral and enteral nutrition

I have always been glad that I made most of my observations on male fracture and osteotomy cases for these have generally had no previous impairment of food intake and have within a few hours been able to resume an adequate intake for a normal person at rest. Nor did I detect in them any impairment of digestive and absorptive function. My contacts here some 35 years ago with the Burns Unit revealed how bad the nutritional state of such patients can become through their general misery, sepsis and lack of appetite, similarly in certain other forms of illness where this is associated with grave sepsis or reduction of the digestive or absorbing surface of the alimentary tract. Supplementation by vein other than blood and plasma was not then available.

Recently at the 1st Meeting of the European Society for Parenteral and Enteral Nutrition in Stockholm I described the history of the development of this subject and pointed out that it was in 1656 that Sir Christopher Wren reported his success in injecting wine and ale into the blood of the live dog by vein in good quantities. Wren used slender syringes or bird quills fastened to bladders containing the matter to be injected. It was suggested by Wren that food material following digestion in the stomach might be withdrawn and then injected and probably found to be effective. Courten (1710) reported the first parenteral administration of fat in animals. Hodder of Toronto (1873) infused fresh milk into the vein of a man apparently dying of cholera. The man recovered.

Henriques & Anderson of Denmark (1921) demonstrated that N equilibrium could be maintained in the goat with intravenously injected amino acids, the product of an enzymic hydrolysis, as the sole source of N.

During the 1930s and 1940s isotonic solutions of glucose had come to replace saline more and more. Elman (1937), who had worked with Professor W. C. Rose at Illinois reported the application of a protein hydrolysate of casein fortified with tryptophan (which is destroyed during acid digestion and should be supplemented with additional methionine and cystine). Since then, modern developments have been spectacular and cases are reported of severely-ill patients surviving for many years on complete and total intravenous supply. Professor Wretlind of Stockholm has been in the forefront in Europe with his complete and total intravenous nutrition system, that is, containing all known nutrients and these in adequate amounts without adverse reactions. His solution of a safe means of providing fat was largely responsible for this success (Wretlind, 1976).

In the USA until quite recently no such means of providing a safe intravenous infusion of fat had been discovered. Now it is being introduced. To overcome this earlier drawback Dudrick *et al.* (1968) developed in Philadelphia their system of hyperalimentation given through an indwelling catheter into deep veins. Their definitive paper was published in 1968 and was a great step forward. A 30% solution of glucose was thus able to be used and a daily allowance of 10·1 and 10·9 MJ (2400 and 2600 kcal) could be given.

Use of glucose, insulin and potassium, was an incomplete intravenous system reported by Hinton *et al.* (1971) as being effective in reducing the excessive protein breakdown of patients with burns. It is useful as a 'cyclic' support system for short periods of treatment.

In conclusion, the evidence indicates that once the period of shock is over and the blood and plasma losses have been made good, the first consideration is the need for an increased energy supply with conservation of heat loss and with adequate amino acids being available as intact protein by mouth or by other entry to the upper digestive tract, and, where neither route is feasible as providing a sufficiency of nutrients to meet the hypermetabolism of trauma that then exists, recourse should be made to parenteral nutrition. We all owe our foetal life till parturition to the passage of nutrients from our maternal blood vessels into our own blood vessels as they traverse the chorionic villi.

This brief sketch of the emergence of our knowledge of how the injury done produces both the disposition and the means of cure has been largely biographical for obvious reasons. Since World War I the tempo of contributions has mounted first slowly but now since the early 1960s there is a tremendous upsurge for the problem of how to treat the critically ill following injury is a great human concern.

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