NUTRITION: RESISTANCE AND REACTION TO TRAUMA

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Physical injury means essentially damage to tissue protein. Nutrition is involved because it affects the state of the response of the patient who has received the injury. The evidence relating nutrition to resistance to infection is very complex. When we look at the information from experiments on animals it is equally difficult to relate the two, because among diets which are apparently quite adequate for growth or the reproductive cycle in experimental animals some will confer greater resistance to experimental infection than will others. Moreover, if we take the positive state where nutrition is sound, and the negative where it is inadequate, it is necessary to consider these not only in relation to resistance to infection but also to the metabolic response to the injury and the healing process. Resistance to infection may be appraised under resistance to bacterial infections, to virus infections and to protozoal infections. A good state of nutrition will generally imply a good state of resistance to bacterial infections, and a state of poor nutrition will imply the reverse. But in the case of viruses, such limited experiments as have been done suggest the opposite effect for, if the nutritional state is poor, viruses which seem to have a higher requirement for nutrients appear to be inhibited. Thus an increased resistance to bacterial infection may be associated with a decreased resistance to virus infection; in the case of protozoal infection the same relationship seems to pertain as with viruses.

In the case of the metabolic response to injury the effect of nutrition is much more positive, a previously good state of nutrition being associated with a greater catabolic response; healing is also generally better with a good state of nutrition and tends to be poorer with inadequate nutrition. If there is also oligaemic shock, and some degree of this is almost inevitable in severe injury then the chances of bacterial infection through the mucosa of the alimentary tract are greater owing to desquamation of the mucosa.

Neoplastic disease may lead to protein depletion and there may therefore be the same state of negativity in respect to the response to injury as in the state of inadequate nutrition, but the whole subject is very complex and the above are simply generalizations.

The catabolic phase of the reaction to injury is interesting, and I became personally involved many years ago when I had metabolism beds in hospital and was attempting to find out why certain fractures failed to unite. I did some balance experiments and found that

whereas there was little difference in the calcium balance, there was in the first ten days after injury a marked loss of nitrogen, sulphur, and phosphorus. In a very early experiment—back in 1928—I studied the nitrogen excretion of a fractured patient of 34 years. The diet was constant with 15.6 G. daily nitrogen intake, which is quite high, and yet the nitrogen excretion in the urine rose to a maximum of some 28 G. at about the fifth to sixth day after the injury and then declined. There was also a parallel rise in the basal consumption of oxygen.

Traumatic fever is not necessarily associated with microbial infection, but is one of the responses to serious trauma in those surviving the initial damage, and is associated, as the name implies, with elevation in body temperature and pulse rate. This is all part of the catabolic phase of protein metabolism after injury. It happens after burns, lacerations, severe dislocations, and so on, and is a fairly constant phenomenon of severe injury in the normally nourished. The source of the catabolites is more general than local, because in experiments on animals the loss of tissue locally is not adequate to explain the general loss in the urine.

I then wondered how far this might be due simply to the imposed rest consequent on splinting, so I persuaded some students to go to bed encased in splints, and I measured their nitrogen and sulphur excretions. There was first of all a slight fall in excretion for a day or two, and then a slight rise in excretion which continued over the period studied. Imposed rest in an uninjured person while causing a slight loss of substance does not lead to such an extraordinarily marked rise in nitrogen excretion as follows injury. When the diet of fractured patients was increased to 3,600 Calories with a very high protein intake (the latter about three times the normal), there was still at the height of the catabolism a negative state of nitrogen balance, though it became positive shortly after. It seems that during this catabolic phase which occurs during the first ten days after certain injuries, and more particularly after fractures due to violence, even though the patient can be persuaded to eat a very large amount of food, the catabolic phase cannot generally be overcome at the height of the response to the injury. For example, in severe burns there is a negative nitrogen and potassium balance, while sodium balance may be positive and subsequently becomes negative. In rats we found that fracture of a femur produces the same kind of reaction as regards nitrogen, sulphur, phosphorus, and potassium, with practically no change in sodium or creatinine but a rise in creatine excretion.

Professor A. W. Wilkinson has carried out experiments on himself and on volunteers, as well as on cases of gastrectomy and

other conditions, to find out how far this reaction is in part simply the result of inadequate food, with consequent catabolism of body protein to provide the necessary sustenance and energy to keep things going. Patients after gastrectomy were given water but no food for periods up to four days; potassium excretion fell in these circumstances whereas usually it rises after injury, and the same was true of nitrogen. There was a fall in sodium excretion on the starvation regime.

Therefore, our advice is not to try to overfeed a patient during this phase but to feed to appetite. Later on, when the patient is in an anabolic phase, extra feeding may be employed with advantage. Other people have also found this.

We then tried various agents in an attempt to enhance the rate of healing. A potent pituitary extract produced by Professor F. G. Young—then at the Natural Institute for Medical Research—induced marked anabolic changes in body weight in rats, but when given to rats wounded by removing a circular piece of skin, it had no influence on the rate of wound healing. Thyroid hormone had a slight but statistically positive effect in accelerating the rate of healing. It seems that stimulation of metabolism by thyroid tends to enhance the rate of wound healing. Later we found in the rat that a fracture on a protein-free diet did not produce the usual catabolic effect. This was an unexpected finding and occurred even when the animal was allowed to eat as much as it liked of the protein-free diet. My colleagues in Glasgow then studied the effects of fracture in the rat at different levels of protein in the diet—no casein in the diet, ten per cent casein, and 25 per cent casein, and found that the metabolic response to fracture proved directly proportional to the level of protein in the diet. Thus one index of a good nutritional state is a marked catabolic effect of severe injury, and if the animal or the patient is depeleted of protein this effect fades. Hence this effect is not something one should try to rub out dietetically in the first few days, but accept as natural provided the patient's state is not deteriorating. Feed to appetite during the first few days after injury, but don't try to overwhelm the patient with an excess of food. To make good blood or plasma loss is even more important.

Traumatic fever with its increased oxygen consumption is another reaction to injury and this we studied further. We constructed a calorimeter capable of registering accurately and directly the heat production of an animal (we have also one for use with patients). We put rats with a fracture in the calorimeter and measured their heat production; we had another group outside, in which we measured nitrogen excretion after similar injury, and on the assumption that the heat produced was related to increased oxidation of protein we

made a calculation for comparison with the actual heat production as measured physically. The calculated heat production on the basis of catabolic utilization of the protein as represented by the nitrogen in the urine, paralleled the actual increase in heat production, so that it would appear that this increase in metabolism, noted earlier in terms of oxygen consumption, is essentially due to an enhanced catabolism of body protein. The nitrogen in the urine is mainly in the form of urea, and sulphur is mainly as inorganic sulphur. On a protein-free diet, instead of a rise in heat production following fracture, there was a fall. This tends to fall into line with the findings in the previous experiment, namely, that when an animal is in a protein-depleted state, the catabolic reaction fails to appear.

This kind of catabolic response to injury also occurs in cold-blooded animals, as well as in man and the rat. It has been found in worms and in crabs. The reaction is therefore pretty general throughout the animal kingdom.

In some of our more recent work my colleague, Mr B. F. Fell, and I found that almost immediately after death a series of desquamatory changes occur in the epithelium, particularly in the upper portion of the small intestine. We think that these changes also occur transitorily after injury and when there is a lowering of oxygen supply because of haemorrhage or any other form of oligaemic shock. This also means that most specimens by the time they are obtained post mortem have already shown this change; in part it may be an artefact due to the time lag before immersion of the intestine into fixative, and therefore not necessarily related to the condition at the time of removal. But considerable disorganization takes place in a short time after death and, as I have just stated, I think that the same thing happens after severe injury, with oligaemia, and may indeed lead to passage of organisms across this barrier into the body. There may then be toxaemia due to invasion of clostridia and other organisms from the bowel. Some of the ulcers found after trauma may arise from this kind of change: but the intestinal mucosa has a very rapid recovery rate.

To sum up, I would repeat that there is no evidence whatsoever that giving more nutrients than are necessary for normal nutrition will enhance the body's response to infection. It has been suggested that an adequate diet for recovery after injury might be one held to yield about 40 to 60 Calories per kg. body weight, and about 1.2 to 2G. of protein per kg. body weight, though some would place protein at a higher level but I think that so long as the diet is what we would normally enjoy and attention is paid to elimination of any infection, appetite should return and the patient should do as well as the amount of the damage done will permit.