METABOLIC RESPONSE TO TRAUMA*

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This paper is deliberately restricted in its scope. It is intended only to consider some of the more important systemic effects of trauma and to relate them, in principle at least, to those widespread biochemical and metabolic changes which are comprehensible and significant in practice.

WEIGHT CHANGES

Before the convalescent stage a gain in body weight generally reflects excessive water administration which should be avoided. Weight loss is more common and may become significant when oral ingestion of food is limited and there is inadequate replacement of overt and occult water loss in the urine, breath, and through the skin: even when water replacement is accurate, there is likely to be a daily weight loss of 0.5 kilogram which represents the endogenous catabolism of 0.3 kilogram of body fat and 0.2 kilogram of body protein.

By studying nitrogen changes in patients with acute oliguric renal failure it is relatively simple to determine how much of the daily weight loss is due to endogenous protein catabolism. In such cases the nitrogenous breakdown products of protein catabolism cannot be excreted and the blood urea rises in consequence. Compared with cases of uncomplicated acute oliguric renal failure in which the daily rise of blood urea is only 15–25 milligrams per cent, the daily rise of blood urea in cases which follow trauma is frequently 70–90 milligrams per cent. If therefore in an average male patient weighing 70 kilograms there is an average daily rise of blood urea of 80 milligrams per cent, bearing in mind that this urea is distributed in equal concentration in the blood, extracellular and intracellular fluid—indeed in the total body water which is approximately 60 per cent of the body weight—it follows that the average daily production of urea will be $70 \times \frac{60}{100} \times \frac{800}{1,000} = 33.6$ grammes. And since one gramme of urea is derived

from the metabolism of six grammes of protein, it follows that approximately 200 grammes of protein are metabolised each day. If the total daily weight loss is 0.5 kilogram the weight loss due to endogenous fat metabolism will therefore be 0.3 kilogram.

These catabolic changes which follow major trauma are fundamental and, so far as is known, are not deleterious provided that unwanted breakdown products of protein catabolism can be excreted in the urine—that is, provided acute oliguric renal failure does not exist. The protein catabolism in such circumstances cannot be countered by administration of anabolic steroids and only artificially and not really by intravenous administration of amino-acids. The fat loss is of no significance because there is usually an adequate body store. It is necessary only to give carbohydrate, usually dextrose, to prevent ketosis: 100 grammes each day, by mouth, or intravenously as 2 litres of 5 per cent dextrose in water, provided the water can be excreted by the kidneys, is adequate. When oliguric renal failure is present, water restriction must be practised and hypertonic sugar solutions may have to be given through a caval catheter (*vide infra*).

The body fat and carbohydrate, unlike protein, are both catabolised completely to carbon dioxide and water and therefore do not raise any significant problem regarding the excretion of their metabolic end-products: they provide calories for energy. Protein catabolism also

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contributes calories but, equally important, provides material for replacement of the inevitable protein loss which occurs, for example, as a result of epithelial desquamation in the alimentary, respiratory and urinary tracts, and provides the raw materials for the processes of wound healing and tissue repair. The plasma proteins have high biological priority and their concentrations in the blood tend to remain normal even when there is gross body wasting: hypoproteinaemia usually signifies dilution rather than deficiency.

Endogenous protein catabolism is minimised by administration of carbohydrate (100 grammes of dextrose or lactose a day) but weight loss cannot be prevented by such means. The depleted body protein stores, together with fat and carbohydrate, are eventually restored during convalescence although full restitution may take several months in the severely injured patient: wound healing is generally not impaired unless vitamin C deficiency, oedema, or infection is present.

In the presence of normal renal function the nitrogenous by-products of protein catabolism are excreted in the urine. When, however, acute oliguric renal failure complicates trauma, these substances, which include urea, uric acid, and creatinine, are retained in the body, acid products of cell metabolism such as phosphates and sulphates cannot be excreted, and intracellular cations such as potassium and magnesium are liberated into and remain in abnormally high concentrations in the extracellular fluid. The blood urea rises, metabolic acidosis—manifested by a decreased carbon dioxide combining power—develops, and hyperkalaemia ensues. Liquefaction and absorption of effused blood and damaged muscle at the site of injury adds to the basal production of nitrogenous substances, the acid products of protein catabolism, and the liberation of potassium. Post-traumatic fever, by increasing the metabolic rate, exaggerates the whole picture.

At times it becomes expedient to effect artificial removal of these by-products of protein catabolism before renal function undergoes spontaneous restitution and their natural mechanism of excretion in the urine returns. The artificial kidney fulfils this task. And a severely injured patient with acute oliguric renal failure may require such treatment on several occasions and at short intervals. Generally speaking, haemodialysis on the artificial kidney should be undertaken before the blood urea concentration becomes more than 400 milligrams per cent, the carbon dioxide combining power less than 14 milli-equivalents per litre and the potassium more than 7.0 milli-equivalents per litre.

Attention has already been drawn to the protein-sparing property of carbohydrate. An adult patient with post-traumatic acute oliguric renal failure should receive 500 millilitres of 20 per cent lactose by mouth or 500 millilitres of 40 per cent dextrose intravenously through a poly-vinyl-chloride catheter passed through a subcutaneous vein of a forearm into an innominate vein or the superior vena cava (the risk of infection should preclude the use of the inferior vena cava). This treatment should be instituted as soon as acute renal failure is recognised (when the urine volume is less than 400 millilitres in twenty-four hours with a specific gravity less than 1.012 and a urine urea concentration less than one gramme per cent) and should be maintained until spontaneous diuresis ensues. Water restriction is imperative. To the basal daily allowance of 500 millilitres, to balance insensible loss, should be added volumes equal to the volumes of any urine or extra-renal losses such as vomit. Generally speaking, there are usually 100–200 millilitres of urine each day. Complete anuria is rare and when present should suggest a mechanical cause such as post-renal obstruction: urethral catheterisation, retrograde cystography, cystoscopy and retrograde pyelography, or even aortography may be required for diagnosis.

The rise of serum potassium may be partly controlled by oral or rectal administration of ion-exchange resin (Resonium A, 45 grammes) and by rapid intravenous instillation of 100 millilitres of 40 per cent dextrose with 20 units of soluble insulin, while its cardio-toxic effect may be decreased by administration of intravenous calcium gluconate (20 millilitres of 20 per cent solution) which alters the Ca/K ratio and reduces myocardial cell irritability.

The metabolic acidosis may be temporarily helped by intravenous $1/6$ or $1/3$ molar sodium lactate, but not more than one litre should be given because the renal excretion of sodium is impaired and sodium retention will occur.

The conservative management of patients with post-traumatic acute oliguric renal failure by restriction of fluids, administration of 40 per cent dextrose, insulin, ion-exchange resins, calcium gluconate, and sodium lactate, has been responsible for the fact that nowadays the blood urea concentration, and not the hyperkalaemia or the metabolic acidosis, usually indicates the need for haemodialysis.

ANOXIA

Anoxia may be ventilatory or circulatory. Ventilatory anoxia is equivalent to suffocation and is well understood: it may follow respiratory obstruction, respiratory paralysis, or depression of the respiratory centre. It may complicate facio-maxillary or head injuries, chest injuries and high lesions of the spinal cord.

If ventilatory anoxia is allowed to persist, carbon dioxide retention, with a raised carbon dioxide combining power, will rapidly develop and may be responsible for the development of vaso-motor paresis, cardiac arrhythmias and hypotension. Indeed, the cause of otherwise unexplained circulatory abnormalities may be ventilatory. Urgent treatment may be required and tracheostomy or intubation and assisted respiration may be life saving. Oxygen administration is no substitute for ventilatory inadequacy: indeed it may depress the respiratory system.

Circulatory anoxia is perhaps not so well recognised. It is a sequel to inadequate tissue perfusion by the blood. Indeed, the blood may be regarded as an organ of respiration for, among other functions, it conveys oxygen to the body cells and carries carbon dioxide away from them. In the presence of an inadequate circulation, tissue anoxia and carbon dioxide retention develop. When severe, such anoxia can significantly affect the kidneys (with production of acute renal failure due to necrosis of the tubules or cortex), the liver, the brain and the myocardium. Circulatory anoxia provokes anaerobic carbohydrate metabolism with production of excessive amounts of lactate and pyruvate. And these substances, together with excessive amounts of sulphates, phosphates and amino-acids produced by endogenous cell catabolism, produce metabolic acidosis (manifested by a decreased carbon dioxide combining power).

Depression of liver function, itself a reflection of circulatory anoxia, and impairment of renal function with reduced urinary excretion, both exaggerate these metabolic sequelae.

The tissue anoxia which results from circulatory impairment is dependent on a reduction of blood flow rather than on the level of oxygen tension in the arterial blood. The oxygen capacity of the arterial blood is usually normal in such circumstances unless there has been intrinsic haemodilution or extrinsic replacement of blood loss by fluids which contain no red cells. The oxygen content of the venous blood, however, is markedly reduced so that the arterio-venous oxygen difference is increased.

The commonest cause of a reduction of blood flow is blood loss. It can also follow excessive plasma loss, for example in burns, exudation from open wounds, or at the sites of skeletal fractures, or water loss, for example from the sequestered water loss at the site of trauma. Blood loss, revealed in cases of open injury, or concealed in cases of closed injury, is frequently underestimated. Indeed, a fall in arterial blood pressure, the traditional index used by surgeons and anaesthetists to assess reduction of the effective circulating blood volume, is really a late manifestation. A fall of venous pressure is an earlier sign. Collapsed peripheral subcutaneous veins reflect a decreased venous return to the right side of the heart and hence a decreased output from the left ventricle.

A normal, or virtually normal, arterial blood pressure in the presence of a reduced blood volume is a reflection of an active compensatory vaso-constriction and may be looked upon

as a homeostatic response to maintain selectively an adequate circulation to the brain. An otherwise healthy young adult may maintain an unaltered blood pressure despite a loss of 10–15 per cent of the total blood volume—although the vaso-constrictor changes may be reflected by a decreased pulse pressure and by pallor of the skin. The circulatory state which follows depletion of the effective circulating blood volume is not static but dynamic and, provided peripheral circulatory failure is not allowed to develop, restitution will ensue if early replacement, preferably by blood, is instituted. But when replacement is delayed, capillary pooling, due to failure of the metarteriolar sphincters, will invalidate the potential effect of transfusion so that peripheral circulatory failure occurs despite full correction of the blood volume. The venous pressure is then raised above normal and yet the arterial pressure remains low.

When a depleted blood volume is only partly corrected some extracellular fluid migrates into the blood stream. This occurs within twenty-four hours and is a further manifestation of homeostasis. It produces a dilutional anaemia but, of course, no alteration of the urea and electrolyte composition of the plasma because the concentrations of these substances in the extracellular fluid and in the blood are the same. Intravascular migration of the extracellular fluid is encouraged by the exaggerated hydrostatic pressure gradient which occurs when arterial hypotension is present. It is, however, a self-limiting process because the resultant hypoproteinaemia decreases the capillary osmotic pressure and this, in turn, impairs further migration of fluid from the extracellular space into the blood stream.

When blood replacement is undertaken after haemodilution has occurred, hypervolaemic overloading of the circulation may occur and, in elderly patients with myocardial inadequacy, particularly when depression of renal function and oliguria exist, congestive cardiac failure may easily be produced. The neck veins should always be observed for early signs of congestion. Administration of large volumes of dextran, saline or dextrose intravenously may be dangerous. As a first-aid measure it is justifiable to infuse 1.5–2.0 litres while awaiting the result of blood cross-matching. Incidentally, it is expedient, whenever possible, to send blood for biochemical determination as well as for cross-matching. The biochemical values (urea, sodium and potassium) not only provide a basis for comparison if subsequent complications develop but may reveal otherwise unsuspected chronic renal disease.

High molecular weight dextran with a molecular size of $+135,000$ will be retained in the circulation for many hours, but it tends to cause bleeding not only by its hypoprothrombinaemic and hypofibrinogenaemic dilutional effect but also because it has a peculiar direct effect on the blood platelets. Saline or 5 per cent dextrose solutions rapidly migrate from the vascular compartment into the extracellular space. If acute oliguric renal failure subsequently develops, the excess fluid cannot be excreted and the resultant oedema may significantly worsen the overall prognosis. When large volumes of stored blood are given, hypocalcaemia may develop because the citrate content of the acid-citrate-dextrose preservative of the donor blood binds the extracellular calcium. If the serum ionised calcium is low the cardio-toxic effects of potassium excess are exaggerated. It is not uncommon to find potassium concentrations of 15–20 milliequivalents per litre in stored blood more than a week old and it is expedient to give calcium gluconate (0.5 gramme per litre of blood) when significant blood transfusions are required.

ENDOCRINE RESPONSES TO TRAUMA

Much has been written about the endocrine responses and their effects on the metabolism of trauma. Little of what has been written, however, has much practical significance. The adrenal cortex responds, by the excretion of aldosterone, to a contracted blood volume and extracellular space and effects homeostatic sodium and water reabsorption by the renal tubules: by so doing it contributes to the spontaneous intrinsic correction of oligoemia. The adrenal medulla, by secretion of adrenalin and nor-adrenalin, also plays some part in effecting

homeostatic readjustment of the circulation after blood loss: in contrast to the adrenal cortical effect, it is an early rather than a relatively late response. Both these responses, the adrenal cortical and medullary, like those of the pituitary, are probably much less important than renal function when the metabolic management of the post-traumatic patient is under practical consideration.

METABOLIC MANAGEMENT OF THE POST-TRAUMATIC PATIENT

Provided patients after trauma are able to excrete the by-products of tissue catabolism, they are unlikely to come to metabolic harm even when uninformed caloric, fluid, and electrolyte therapy has been instituted. It is, however, important to insist that the nursing staff maintains an adequate fluid balance chart and, equally important, that the urine specific gravity is measured and recorded each day: quality of urine is often as important as quantity. If the medical staff prescribes fluid and electrolytes on the basis of the previous twenty-four-hour excretion by the patient, imbalance will be rare or negligible. Calories may be safely provided by carbohydrate administration: there is usually an ample supply of body fat. Protein feeding should be avoided until it is clear that renal excretion of the nitrogenous end-products of endogenous protein metabolism is effective: this may be assumed when the urinary urea concentration is greater than 1·0 gramme per cent and there is no sustained and significant rise of blood urea. Oral ingestion of fluids, electrolytes and caloric providers is always preferable when possible. Managed in this way, the metabolic responses to trauma will cause little or no trouble to the patient and his medical attendants.