The Biochemistry of Burns

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GENERAL PATHOLOGICAL CONSIDERATIONS.

The condition which develops after a severe burn is characterized by the symptomatology of shock; and when the injury is lethal death commonly occurs in the secondary shock stage. Secondary shock is a familiar phenomenon to the physician and the surgeon—it is of immense clinical importance—and therefore it would seem unnecessary here to discuss it. But a few notes concerning it may be of value in the short consideration which is to follow of its etiology in the case of burns.

The physiological changes in all forms of shock are practically the same; low arterial and venous pressures, small pulse, reduced blood volume, increased haemoglobin content, increased red blood cell volume, leucocytosis, ketosis, lowered basal metabolism, lowered body temperature. Primarily, then, shock is a vascular phenomenon.

If the burned patient survives this stage, other symptoms develop: bloody diarrhoea, vomiting, delirium, and circulatory failure, these commonly regarded as toxic in nature. And since it is known that a toxic condition will produce shock, the most obvious explanation of the physiological changes resulting from a burn is that burned tissue produces toxins which are absorbed into the circulation and thereby makes possible the systemic effects of the injury. The evidence for this view is overwhelming. Of course, there must always be left room for other factors, but the importance of this factor certainly cannot be minimized. Practically all burns involve areas of vascular tissue, making possible maximum absorption into the blood stream. Much experimental work has been done to confirm the theory of the toxicity of burns, and some of that should be noted here:

1. If from a burned animal the injured area is removed and transplanted into a normal animal, it is the second, not the first, that develops the symptoms of burn.
2. If the circulatory systems of two animals are united, and one of them is severely burned, both develop toxic symptoms.
3. If a burn is shut off from the general circulation by local thrombosis, the characteristic toxic symptoms do nto develop.

The nature of the toxic substance or substances is commonly held to be that of the products of protein autolysis. This is a sound view, for after severe burning of any part histamine is known to be increased in the body; and the symptoms of shock most certainly can be elicited by histamine and allied substances. Furthermore, there appears in the urine of burned patients a comparatively high concentration of products of proteolysis, and in their blood an increase in non-protein nitrogen and urea nitrogen. In the face of all this, Aldrich, at the Johns Hopkins Hospital, in 1937, as a result of some investigations was bold enough to state that toxemia following burns was caused solely by infection of the injured tissues with beta-haemolytic streptococci, which he claimed to have found in all those which he examined. Needless to say, there is very much to indicate otherwise, and other investigators have been unable to corroborate his findings.

At this point as a matter of interest it may be noted that successes have been reported (Bauer) from treatment of burned patients based on the idea of toxic shock, the treatment being daily drawing of blood from the patient and replacing it by transfusion, some of the toxic substances in the circulation being removed with the blood.

BLOOD CHANGES.

A presentation and discussion of the general blood picture are of particular importance not only from the purely biochemical standpoint, but from the clinical, as many of the pathological changes resulting from severe burns are in the blood and the vascular system. Toxicity, haemoconcentration, and dehydration are not only of biochemical interest, but are the main factors to be dealt with clinically. The toxicity and its etiology have been discussed elsewhere. Let us now examine the phenomena of haemoconcentration and dehydration, which bear an obvious relation to one another.

Toxic substances are undoubtedly responsible for the vascular changes which allow the escape of oedema fluid from the blood stream into the burned area. In a severe burn this inflammatory oedema leads to a large loss of blood plasma, with consequent dehydration. Keeley, Gibson, and Pijoan, who were using splenectomized animals as controls, report that concurrently there is a release of red cells from the spleen sufficient to maintain a normal blood volume despite the great plasma loss. It is generally agreed that haemoglobin rise is proportional to plasma volume decrease. At any rate, haemoconcentration does occur, and even though oxygen-carrying power may be theoretically increased the dead animals show evidence of anoxia. It is evident that haemoconcentration means slower blood flow, with consequent impairment of gaseous exchange between blood and the tissues, oxygen starvation being the result. And it may be, too, that oxygen consumption is increased. Anoxia in itself causes increased capillary permeability, and impairment of circulation initiated by fluid loss from the burned areas may be increased progessively by leakage from capillaries in other parts of the body where stagnation of the blood flow is causing an anoxia. Oxygen therapy is here indicated. The administration of fluids either by mouth or intravenously will tend to correct the disturbance in water balance. Restoration of plasma volume is of prime importance.

Before considering further the general blood picture a summary of other more important changes may be made. (Actual figures would seem of little value for present purposes, as they have been given by a considerable number of workers, and the striking of an average is difficult;

there is quite a wide variation; and it is almost beyond hope that uniform conditions can be studied either clinically or experimentally):

Decreased:

1. Serum protein.
2. Plasma prothrombin.
3. Serum sodium.
4. Serum chloride.
5. Blood cholesterol.
6. Blood glucose.

Increased:

1. Blood urea N. and other N. P. N.
2. Serum potassium (blood potassium normal).
3. Blood chloride.
4. Haemoglobin concentration.
5. Corpuscles.

An increase in capillary permeability is the important factor behind many of these changes, and the toxicity developed as a result of the injury must be considered in seeking the cause of this change in the condition of the capillary walls.

The oedema fluid is rich in protein, whereas the loss of protein from the blood is considerable. Therefore it must be assumed that the plasma proteins, to which the capillary walls are ordinarily impermeable, now are able to filter through in the exudate. This loss of blood protein is a serious matter, and must be remedied if it is pronounced, transfusions of plasma being indicated.

Greater permeability, or perhaps one should say less selective permeability seems to be exhibited by all cell membranes of the body, not only by those of the capillary endothelium. For instance, venous blood from a burned area contains less sodium than arterial blood, which indicates that sodium is lost into the injured tissue. And there is evidence that some sodium passes into the erythrocytes. At the same time potassium must be passing out of the erythrocytes into the plasma, for it becomes decreased in the cells whereas its concentration in the blood itself remains normal. The highly selective permeability of the red cell membrane by which potassium is maintained inside the cell and sodium outside has apparently been partially destroyed. Therefore the cause of many changes in blood chemistry which result from burns must be sought in changes in the permeability of cell membranes, and, as in the particular case of change in capillary wall permeability, the toxic condition of the body seems to be at the root of such phenomena.

Serum chloride decreases, whereas blood chloride increases. Chloride ion, of course, passes through the red cell membrane, and apparently here chloride becomes concentrated in the red cells. The change in chloride concentration can be understood largely when haemoconcentration is considered.

As yet no investigators have been able to state that that any blood changes, even those of such importance as sodium decrease, are primarily responsible for the circulatory failure of secondary shock.

PARENCHYMATOUS DAMAGE.

It is noteworthy that the escape of oedema fluid which follows severe burning is first into parenchymatous organs from the capillaries, then into all parts of the body. It can hardly be expected that such a process would not result in damage to those organs, and consequently to an upset in their function, although of course toxicity and anoxia must also be regarded as of perhaps greater importance. And dysfunction or impaired function of those organs playing a role in metabolism will naturally produce chemical changes in the body.

The composition of the urine is to be considered here as a partial index of the metabolic disturbances that occur, even though following sever burns, when the symptoms are most acute, the patient very frequently suffers from anuria or oliguria. However, analysis have been made of the urine of burned patients and of the urine of experimentally burned animals.

Significant is an increase in nitrogen, indicating a high basal metabolic rate with much destruction of protein. This also holds for creatinine nitrogen, and as creatinine is of endogenous origin it may be inferred that actual increased destruction of body tissues takes place. Albuminuria and peptonuria also are present, and there is increased excretion of amino-acids and lower polypeptides. The protein loss from these sources, in conjunction with the loss of plasma proteins through the exudate would certainly indicate, from a therapeutic standpoint, a high protein intake.

At least superficially a nephrosis seems to be produced, but the possibilities of actual kidney damage are not too great. True, there may be some splanchnic paralysis, as evidenced by the frequently occurring oliguria and anuria, but there is much to indicate that actual abnormal destruction of protein does occur, and that the kidneys function normally or very nearly so in excretion.

In many cases of fatal burns post-mortem examination has shown necrosis of liver cells; and in extensive burns there is a good deal of evidence that hepatic function is impaired, this being of course of very great importance in explaining many of the accompanying metabolic changes. For instance, the hyperbilirubinemia which often follows severe burning may be due to abnormal destruction of erythrocytes, but it may also be due to diminished excretory power of the liver. Other evidences of subnormal liver function are decreased hippuric acid output and a decreased plasma prothrombin. Furthermore, after burns there are hyperglycemia and a rapid loss of glycogen from liver and muscles. Impairment of liver function and consequent complete or partial failure of urea formation may also be responsible for the raised residual nitrogen of the blood. Haemorrhagic phenomena (haematuria, haemolysis), icterus, and various nervous signs, all of which sometimes occur, likewise are indications of liver damage.

Of great importance is the fact that after severe burns there is decrease of adrenalin in the tissues and organs—and this, by the way, may be in part responsible for the anuria. Adrenal cortex hormone increases the tone of capillary walls, and its absence would certainly be conducive to the vascular phenomena of shock. It is known also that the adrenal cortex hormones function in the regulation of sodium and chloride metabolism, and its administration in the form of desoxycorticosterone acetate has been of avail in restoring the sodium level of the blood (Wilson and Stewart). It also has been responsible for the correction of other blood changes, including increased cellularity, but has been of no avail in correcting the condition of advanced secondary shock. Injury to the adrenals has been observed in cases of severe burn, and all in all there is much to indicate that impairment of adrenal function is very likely responsible for many of the symptoms that have been noted.

LOCAL TREATMENT.

The local treatment of burns by tannic acid, 2½% solution, is commonly considered the best available. It is perhaps of interest to note that the treatment was introduced by Davidson at the Children's Hospital of Michigan in 1925, on the theory that the toxic products of protein breakdown which were liberated in the burned area would be precipitated by the tannic acid. But it seems unlikely that this particular reaction is of any importance. Rather the tannic acid acts very importantly in precipitating all proteins in the area, forming a tough protective coating over the injury. Advantages of the treatment that have been claimed are as follows:

1. It minimizes any toxemia resulting from absorption from the burned area.
2. It lessens loss of body fluids from the burned area.
3. The coagulum is a mechanical protection against infection.
4. Pain is lessened.
5. The coagulum acts as a scaffold for the growth of young epithelial cells.

The application of a mixture of tannic acid powder and some inert powder has been quite successful, having the advantage of being absorbent as well as tanning, and for this reason may partially satisfy those who object to the tanning treatment on the grounds that the tough coagulum dams back toxic products into the blood stream, and who would for this reason use only saline compresses or baths.

Silver nitrate and gentian violet have also been used very successfully in the local treatment of burns, often in conjunction with tannic acid. Their action on proteins is the same. In addition, gentian violet has an antiseptic action which seems to be enhanced by silver nitrate.

Experience in the treatment of burns in the present war has confirmed the effectiveness of the tanning treatment. Ross and Hulbert, writing in the British Medical Journal, November 23, 1940, report great success in treating war burns by Dennison's method—gentian violet, silver nitrate, tannic acid, applied in that order.

Many of us remember the days of "grease" therapy for burns. The author has in mind an article which appeared in Science News Letter many years ago, shortly after treatment with tannic acid was begun, in which it was contended that in cases where grease was used locally on severely burned tissue the patient, if he recovered, did so in spite of the treatment. However, on March 1st, 1919, E. F. Pratt had published in the British Medical Journal an article advocating the local use of paraffin on burns, and he claimed good results. He writes again in the Journal on December 28, 1940, to let us know that he is still going strong.

Leonard A. de Dombal, writing in the British Medical Journal, January 14, 1941, states that tannic acid-silver nitrate is the best local treatment, but considers that it should be applied only in hospital. He reports good results from first treating for shock, then applying a solution of flavine and paraffin, 1/1000 (flavine perhaps for antisepsis). Even if the case is to be hospitalized later this treatment is carried out for its immediate soothing effect.

SUMMARY.

The symptoms following severe burning are those of shock, therefore treatment for shock is at once indicated. Toxicity, haemoconcentration, and dehydration are the important factors to be dealt with. Plasma transfusions to correct haemoconcentration and to restore lost blood protein and electrolytes are valuable. Many of the blood changes have their etiology in an increased permeability of the capillary walls, which is a symptom of shock, and damage to parenchymatous organs is undoubtedly a factor behind some of these changes as well as changes manifested in metabolic disturbances. The adrenals seem to be particularly affected. Tanning is considered the best local treatment.

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'Cultivate, then, gentlemen, such a judicious measure of obtuseness as will enable you to meet the exigencies of practice with firmness and courage, without at the same time hardening "the human heart by which we live." '—*Sir William Osler* (Aequanimitas)

"Do not let yourselves be discouraged, because with many of the sick neither help, nor faith, nor art, nor benevolence, nor anything will help them;—Be gentle and merciful, and judge of your charities as to what aim, use and fruitfulness they may arrive, and trust nothing to unreason." —*Paracelsus*.

"It is better to have a future than a past."—*Cathell*.