Early pathophysiology of cutaneous burns: in relation to resuscitation of the burned patient

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THE EARLY PATHOPHYSIOLOGY OF
CUTANEOUS BURNS: IN RELATION TO
RESUSCITATION OF THE BURNED PATIENT

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Introduction

There has always been controversy about the optimum early treatment of the burned patient. Even though the controversy has been resolved slowly, resuscitation has been improved. The mortality statistics comparing today and years past attest to this improvement. Forty years ago a person sustaining a fifty per cent body surface area burn had only a ten per cent chance of survival and would most likely die during the first few days postburn. Today this same person would be five times more likely to survive, and death would not come in the first few days but would occur more likely several weeks later as a result of infection. The advances in resuscitation which have prolonged life and salvaged some victims during this forty year interval have evolved from a greater understanding of the physiology of the body and the effect of burns locally and systemically. The purpose of this paper will be to present current thoughts on the early treatment of the burned patient from the standpoint of the known pathophysiology of burns in the first forty-eight hours. Based on an understanding of the cellular and systemic changes induced by a burn and an analysis of various therapeutic approaches now advocated, a rational program
for treatment can then be described.

**History.** Historically, the local therapy of the burned patient can be divided into the pre- and post-Lister eras. Before the discovery of bacteria and the demonstration by Lister in 1867 that environment could influence the course of healing, physicians were concerned with cleaning up the suppuration that accompanied burns without knowing the cause. Until the end of the eighteenth century, oily substances were generally used; at this time there was favored the use of the direct application of a form of alcohol, wine being the most highly recommended. During the first part of the nineteenth century there were introduced medications such as mercuric chloride and lime water (1835), silver nitrate (1831), lead carbonate in linseed oil (1845), tannic acid (1853), and turpentine (1868). Attempts were later made to use medicants which would be poisonous to bacterial although they usually proved more injurious to the patients. Dry cotton and wool pressure dressings were steeped in such solutions as phenol (1867), iodoform (1837), picric acid (1901), and tannic acid again in 1925. The use of the continuous bath had been introduced in 1845; whereas, the open air method was suggested in 1887.

Harkins in 1942 mentions the early application
of many different substances without stating a preference, apparently because there had been no outstanding results with any particular one. The use of tannic acid is dealt with extensively, as is the use of antiseptics such as gentian violet, silver nitrate, and mercuriochrome. Other methods held with more or less regard were continuous saline baths, open-air therapy, early mechanical debridement, and the use of astringents such as picric acid.

It was later during the same year of this publication that many of the virtues of tannic acid were discounted when it was realized, that although it decreased mortality in the first forty-eight hours, overall survival was not affected. Tanning was harmful by converting partial to full-thickness burns, by creating eschars that sealed off infection, and by injuring the liver. Sulfonamides and penicillin had just been introduced.

Systemic therapy in 1942 included the use of cold water baths, analgesics, oxygen, and intravenous fluids to combat shock and restore circulatory volume. Those substances injected intravenously were 0.9% sodium chloride (1901), gum acacia saline (1933), glucose and water (1924), blood (1925), and blood plasma (1936). In order of availability plasma was
recommended to be used first, then blood, saline, gum saline, and finally glucose and water. The amount of fluid given early postburn varied up to as high as 8000 cc the first day depending on the type of fluid, the body weight, and the patient's blood hematocrit values. Formulas had not been introduced as of yet, the quantity of fluid and rate of administration being based on the patient's clinical course.

This briefly was the picture of the development of burn therapy up to the early 1940's. World War II and the advent of atomic warfare spurred more research as a part of national defense. Furthermore, the frequency of thermal injury in civilians had increased. This was ascribed to the increase in accidents associated with high speed travel, the broadened application of hydrocarbon fuels, and the widespread use of electricity.

Pathology of burns

Thermal tolerances of skin. Modern therapy of burns calls for precise knowledge concerning the thermal tolerances of living tissues, particularly the skin. Henriches and Moritz\textsuperscript{23} investigated the various physical factors which effect the transfer of heat to and through the skin and developed a general theory of heat flow by which time-temperature relationships within the skin could be estimated during exposure to
heat. The inward flow of heat depends upon (1) the ability of the skin to absorb heat, and (2) its ability to conduct it. Using needle thermocouples they were able to measure the interface temperature at the junction of the dermis and fat revealing the rapid development of edema of the corium at surface temperatures ranging between 50° and 70° C. When skin surface temperatures were greater than 80° C, edema developed more slowly and at a deeper level. The application of constant heat up to 70° C permitted the heat to be absorbed by the accumulated fluid thereby protecting the deeper tissues. They also showed that there was at least a thousand times greater ability to injure the epidermis when the surface temperature was immediately brought to and maintained at the source temperature than when the heat source was used to raise a skin temperature by means of irradiation. Moritz and Henriques substantiated the fact that the duration of exposure as well as the intensity of heat were prime factors in the amount of epidermis destroyed. A skin temperature of 44° C for six hours produced the same amount of irreversible damage that temperatures of 70° C and higher would give in less than one second. Price, et al., using a heat source of 70° C for a ten second
duration, measured temperatures at various levels in the integument. At a depth of one millimeter dry heat brought about a temperature of 50°C; steam heat, 60°C; and flash heat, 45°C. Steam resulted in the most rapid rise in temperature, but still only reached 46°C at four to five millimeters. The type of heat used was a determining factor in the amount absorbed and conducted, and even very little heat penetration gave ultimate damage to a depth of one centimeter.

**Depths of burns.** Although different classifications have been used to differentiate depths of burns, it has been common practice to divide them into the categories of first degree, second degree, and third degree. Even though the depths of burns are often clinically indistinct, this division is of particular value to the physician in outlining the prescribed therapy.

First degree burns involve the outer portion of the epidermis and are manifest by erythema after a variable latent period. There is minimal tissue destruction and, therefore, minimal systemic effect. The epidermis peels off in three to six days leaving no scars.

A second degree burn involves all the integument down to and including the dermis but leaving many
islets of epidermis which proliferate to cover the area in about fourteen days. Vesicular formation occurs due to separation of epidermal layers or epidermis from dermis with edema fluid. When the full dermis is involved, the injury is called a deep dermal burn. Here regeneration takes place in twenty-five to thirty-five days principally from the epithelial lining of sweat gland ducts and hair follicles. Systemic derangements are more severe, and some scarring may take place.

Third degree burns are full thickness burns destroying all the regenerative components of the integument and extending down into the subcutaneous fat. Deeper or charring burns extend far into the subcutaneous tissue, muscle, or bone. Physiologic derangements are most severe; complications are frequent; and epithelization occurs only from the edge of the wound at a very slow rate. Second and third degree burns of any extent merge and are often clinically indistinct at early examination.

Morphology. Cytological and histological manifestations of thermal injury in the epidermis include a redistribution of chromatin within the nuclei of the cells, swelling and disintegration of the cytoplasm, and finally disintegration of the nuclei themselves.
Because of these changes in the basal layer and the intracellular cement substance that binds them to the dermis, an irreversible impairment of the attachment between the epidermis and dermis occurs.

Changes in the dermis are similar to those of the epidermis corresponding to the temperature and duration of exposure. There is seen in sequence immediate constriction of arterioles, vasodilatation, increased permeability of the capillary membrane, and then edema formation which is the source of the vesiculation promoting separation of the epidermis from the dermis. At 50°C the oxygen uptake and metabolism of skin abruptly decrease, ending completely at 60°C with both layers undergoing coagulation, dessication, and finally carbonization.

Physiologic consequences of burns

Capillary permeability and fluid shifts. The formation and nature of edema fluid has been extensively studied. King, et al, used Evans blue dye bound to albumin which was injected into burned animals at varying intervals to visualize the progression of transudation into the burn area. They concluded that the amount of edema was roughly proportional to the severity of the burn and to the increased capillary
permeability. Edema did not occur at the area of the full thickness thermal trauma, but it did appear in adjacent areas where the actual increase in temperature was less and presumably the damage was more moderate. The more severely burned areas which showed no dye infiltration proved to be precisely those areas which eventually became necrotic. Direct observations by Sevitt\textsuperscript{55} with a microscope, of the small vessels in the burned area revealed that the flow through these vessels becomes stagnant, the red cells adhering in clumps and finally forming tightly packed masses that blocked the capillaries and veins. Stagnant anoxia then occurs, and death of the overlying skin ensues. Two types of full thickness burns were recognized (1) those resulting from direct heat necrosis, and (2) those secondary to small vessel thrombosis. In a later study Sevitt\textsuperscript{56} investigated the local transudation of plasma and found that edema appeared shortly following the burn or was delayed in onset. He observed that in minor burns edema was not visible for as long as thirty minutes to one hour and concluded that either the transudation was delayed or it was removed as soon as it was formed. More severe burns showed an early permeability effect within a minute or two confined to the site of the
trauma; in addition and after some delay fluid appeared immediately surrounding and deep to the burn, the depth at which it evolved in the tissues increasing as the severity of the burn increased. Sevitt concluded that the early onset of abnormal capillary permeability must be a direct heat effect of heat while the delayed onset was possibly a chemical or neurochemical response. Histamine probably plays a minor role because antihistaminics have no effect.

Knisely\textsuperscript{35} attributes the increased capillary permeability following burns to the small vessel thrombosis and vessel wall hypoxia described by Sevitt and observed by himself repeatedly in burned animals and humans. Immediately following burns, he has visualized sludging of blood in the bulbar conjunctival vessels of humans which he believes is typical of blood flow throughout the body. This reduction in flow caused by the changed physical consistency of the blood leads to hypoxia of the vessel walls, loss of fluids into the tissues, progressive hemoconcentration of the passing blood, and finally stuffing and impaction of small vessels with sludge.

As fluid escapes through the capillary walls in the burned areas, extra-cellular fluid in other parts
of the body migrates through the vascular compartment to compensate for the hemoconcentration and then into the burned area. The volume and rate of these extracellular shifts are tremendous, and the losses evident at the skin surface are a small fraction of the total amount functionally lost. A thirty per cent burn untreated results in the loss of at least fifty per cent of the original plasma volume in the first two and one-half hours and seventy per cent after five and one-half hours. King, et al., have shown that the rate of edema formation is extremely rapid immediately following the burn. They reported that seventy-five per cent of the edema forms within the first fifteen minutes and eighty-five to ninety-five per cent within the first hour. Very little transudation occurs after six hours even though the capillaries remain permeable from two to four days. Maximal edema formation is present by forty-eight hours and then subsides as capillary permeability declines and reabsorption begins.

Protein and electrolyte alterations. Information concerning the content of the fluid losses has been derived by measuring the composition of blister fluid and lymph draining from burned areas. On the average, human blister fluid contains four grams of protein per 100 cc. being sixty to eighty per cent of plasma. The albumin/
globulin ratio is always greater in this transudate than in plasma, because the larger globulin molecules have more difficulty migrating across the injured capillary membrane. Therefore, the closer the A/G ratio is to being normal and the greater the protein content, the more severe would be the damage to the vessel walls.

In plasma, the loss of greater amounts of albumin and lesser amounts of globulin results in a lowering of the A/G ratio. The resulting hypoproteinemia is further increased by the influx of protein-poor fluid into the blood stream trying to compensate for the hemococoncentration that has developed.

Water and electrolytes freely permeate capillary wall membranes, plasma being a part of the whole extracellular compartment. Fox\textsuperscript{22} found that in the burned area there was an influx of sodium in excess of water and a decrease in potassium corresponding to this rise in sodium. Furthermore, in the uninjured tissues, there was a slight but significant decrease in the sodium content and an increase in potassium. These changes correspond to alterations found in plasma electrolytes following burns. Sodium and chloride concentrations begin to fall several hours after burning in the untreated patient. The degree of fall is only modified by the state of hydration of the patient and
the therapy given. With the absorption of edema in several days these levels begin to return to normal. Plasma potassium is usually found to be unchanged or only slightly raised. The amount of potassium released from damaged cells is apparently small and is freely excreted by the kidney. A temporary fall in blood bicarbonate is usually present and can be attributed in part to the sudden and temporary increase in the lactic acid content of the blood.

Postburn anemia. The amount of destruction of red blood cells can be quite variable depending on the extent and severity of the burn sustained. Second degree burns cause minimal loss. Some fall in the hemoglobin level should be expected with greater than five per cent full thickness burns; in general fifteen per cent burns or less are unlikely to show a clinically important erythrocyte loss during the first two days.

Muir has divided the red cell loss in the first six hours into an early apparent deficit and an early true deficit. The apparent deficit is due to the transudation of plasma and the pooling of stagnant blood in the vascular bed. The hematocrit during this shock period gives a falsely low idea of the available plasma and total blood volume. Most of these cells will return to the circulation with proper fluid therapy although
many may be permanently lost through sludging and thrombosis. Moritz\(^4\) has estimated that the permanent loss in this manner may be as high as thirty per cent of the erythocyte volume in animals receiving fifty per cent body burns. However, most of the early true deficit is probably a result of heat destruction of red blood cells at the time of the burn. The direct heat causes immediate hemolysis of erythrocytes trapped in the burned area. Other red blood cells are also damaged by heat and possibly by toxins released into the circulation from the burn sites. These damaged cells are seen as microspherocytes and as fragmented and crenated forms. The spherocytosis coincides with an increase in osmotic and mechanical fragility which is maximum at about twenty-four hours but which may continue for as long as eight to ten days.

The number of erythrocytes lost in the first six hours is roughly proportional to the extent and severity of a burn and usually does not exceed ten per cent of the rbc volume even in deep burns covering forty-five per cent or more of the body. Finding less than two per cent microcytes on a blood smear during the first few hours indicates that no clinically important erythrocyte loss need be expected in the next forty-eight hours; whereas, finding greater than ten per cent increases the probability of having a ten to thirty per
cent loss. During the period after the first six hours, the amount of destruction is not proportional to the area and severity of thermal injury.

Massive red cell destruction can also be assumed by noting the presence and persistence of hemoglobinuria. This phenomenon is usually seen with burns involving more than a thirty per cent area but may be present when far less is involved. Hemoglobinuria within the first few hours is from direct heat destruction of rbc's and is common; but hemoglobinuria between twenty-four and forty-eight hours indicates a loss in excess of thirty per cent of the red cell volume.

Hematocrit values during the shock period are unreliable indications of rbc loss because of the oligemia present. Later, however, after fluids have restored the plasma volume and the previously pooled blood is circulating again, hematocrit readings will fairly well reflect the degree of anemia.

Burn shock. All of the local pathologic changes previously described contribute to what has been called burn shock. These physiological alterations are sometimes divided into primary or neurogenic shock and shock secondary to the loss of circulating blood volume.

The neurogenic shock is rare in man usually producing fainting because of fright or pain from the
burns. The syncope is transient and is accompanied by hypotension, pallor, and bradycardia as a result of vagal stimulation.

The hypotension secondary to blood volume loss is usually the only type present and can come about within a few hours or sooner depending on the rapidity that oligemia develops. While there is general agreement that rapid loss of blood volume is the initiating factor in shock, there is some controversy as to the pathogenesis of this decreased blood volume.

One school of thought suggests that sodium is the prime mover in the deviation of extracellular fluid. Since the sodium content of the extracellular fluid is lowered by the excessive shift of sodium into the burn, the interstitial osmotic pressure is lowered. Water must then move from the interstitial space into uninjured cells dehydrating the extracellular space of which the plasma is a part. At present there is little evidence to support this theory.

Capillary wall injury and resulting increased permeability, as previously described, is by far the most popular concept of the mechanism of plasma transudation. Whether the capillary wall injury is the result of a direct heat, hypoxic, or some unknown effect is now not entirely clear although the hemodynamic con-
sequences seem to be well understood.

Michie, Goldsmith and Moncrief have illustrated the immediate postburn hemodynamics under rigidly controlled conditions observing burned dogs in the first six hours. They discovered the following information: the mean arterial blood pressure remained relatively stable; the pulse rate rose slightly above that of controls; the cardiac output consistently fell sixty per cent or more at one hour reaching the lowest level at six hours; the mean circulatory time increased more than sixty per cent by four minutes and remained elevated at this level throughout the six hour period; and the central blood volume fell thirty-five per cent at one hour almost reaching sixty per cent in a continual drop during this time. The fall in cardiac output and the rise in mean circulatory time coincide with the loss in blood volume. It was felt that the maintenance of a relatively stable mean arterial blood pressure coupled with a progressively decreasing cardiac output supported the concept of markedly elevated peripheral resistance whether due to vascular and/or viscosity changes. The data did not indicate whether the increased peripheral resistance is responsible for, or a compensatory response to, the fall in cardiac output. The authors believe, however, that the fall in cardiac output does follow arteriolar and/or venous
constriction rather than precede it.

This concept of vascular constriction preceding a fall in cardiac output is in agreement with the findings of Abell and Page. They studied, microscopically, the mesenteric vessels of burned cats and dogs finding that the larger and smaller arteries and larger veins constricted within an hour or two of burning, deviating blood into the capillary bed where stasis occurred. This pooling took place before there was a notable fall in blood pressure. If these visceral changes were typical of those in other vessels in the body, they felt that a marked reduction in actual circulating blood volume may take place by this mechanism alone.

Brooks has noted this sludging of blood in animals, and Anisely has visualized it in the vessels of humans. Only when a great many small vessels become occluded with sludge do the animals die.

From these findings the following sequence of events leading to burn shock has been elucidated. After a severe, large area burn there immediately ensues vascular constriction, decreased capillary flow, pooling and sludging of blood, vessel wall hypoxia, increased permeability, edema formation, hemoconcentration, further sludging and thrombosis, decreased effective circulatory fluid volume, decreased venous...
return to the right atrium, and decreased cardiac output.

Other investigators hold that the oligemia producing decreased cardiac output is a true picture of burn shock, but that the vasoconstriction does not occur as the primary initiating factor and that the sludging of blood has little to do with edema formation. They hold that only after a decreased cardiac output does vasoconstriction occur, a response to the diminished flow of blood through the body and the reduction in the uptake in oxygen. Actually, this vasoconstriction may occur at both places in the chain of hemodynamic responses.

The end result of the vasoconstriction and increased peripheral resistance is maintenance of sufficient blood pressure to continue circulation to the coronary vessels and to the brain in preference to other less vital areas such as the skin, muscle, kidneys, the gastro-intestinal tract, and liver. If untreated, and compensation is not sufficient, the heart and brain, along with the rest of the body, become hypoxic; and irreversible damage or death occur.

Pathology of internal organs. Extensive burns often bring about certain pathologic changes in specific internal organs. Lung injury is perhaps the most im-
portant in that it is presently accounting for the majority of deaths in the early postburn period. Primary lung parenchymal damage from the direct effect of heat is fairly uncommon. Dry heat of extremely high temperatures is dissipated so rapidly and cooled in the upper respiratory passages that there is little or no change in temperature in the lungs themselves. On the other hand, moist heat of a similar amount can release enough energy to cause severe burning of the respiratory passages. Although the lung parenchyma is not usually effected, either dry or moist heat may produce a fatal obstructive edema of the glottis or destroy the tracheal mucosa producing a tracheitis, and predisposing to a pneumonia. In addition, many fatalities, thought to be from respiratory burns, are more frequently the result of asphyxia and pulmonary edema secondary to the inhalation of irritating smoke or noxious fumes. Also it has been shown that following a sufficient period of hypotension varying amounts of pulmonary edema may occur which can easily be aggravated by overly ambitious fluid therapy.

Although heat has no direct effect on the kidney, prolonged shock with renal ischemia can lead to acute tubular necrosis in the first forty-eight hours. In addition, gross hemoglobinemia and hemoglobinuria may

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contribute to the renal insufficiency and oliguria by filling the tubules with pigmented casts and further limiting the outflow of urine.

Acute ulcerations may be found anywhere in the gastrointestinal tract, but are reported to be most frequent in the stomach and duodenum. The ulcers may vary from mucosal petechiae to large penetrating or perforating, punched-out lesions. The most popular theory for the etiology of these ulcers is hemoconcentration leading to stagnant anoxia of the mucosa. Furthermore, emotional stress and increases in circulating adrenaline and/or corticosteroids may lead to increases in acid production which then acts on the susceptible mucosa.

The adrenal glands show marked and specific changes. There is a three to four-fold increase in weight with the individual cells of the adrenal cortex accounting for this change by undergoing hypertrophy. These are normal morphological alterations found in all stress situations and accompanied by the increased output of adrenal hormones.

The liver may show alterations of cellular swelling, inflammation, and necrosis which are thought to be mainly secondary to shock and which are accompanied by some functional impairment.

The most common pathologic finding affecting the
central nervous system is moderate to severe edema of the brain. It is not known if this is primary to the effects of heat or secondary to therapy.

Fozzard\(^{23}\) believes that the decreased cardiac output is not only the result of fluid loss but of myocardial injury as well. He bases this belief on findings (1) that cardiac output decreases before there is a fall in blood volume, (2) that pulmonary edema is easily produced in severely burned patients, (3) that occasional myocardial lesions may be seen, and (4) that failing cardiac output responds to digitalis administration.

**Toxins.** A number of burned patients die inexplicably. Because of this, many investigators have searched for toxins or unknown substances released from the burned area that might explain these deaths.

Earlier it was stated that the potassium level in plasma is usually normal or slightly elevated. Roos, Weisiger, and Moritz\(^{52}\) studied the problem of instantaneous hyperkalemia. The high level directly affects the heart giving a cardiac standstill and death. This hyperkalemic state has been demonstrated in animals, but never in humans.

Various enzymes and protein decomposition products have been isolated as released from burned areas,
but no individual one has shown a toxic effect. Indirect proof of toxins has been demonstrated by producing toxic reactions by injecting scalded skin and serum from burned animals into perfectly well animals. Furthermore, serum from previously scalded rats have exerted a marked protective influence on other rats. Rosenthal\textsuperscript{53} claims to have duplicated this feat in humans although others have not. At present there is little conclusive proof that a toxic substance does exist in burned patients although the search seems warranted and should continue.

Systemic Therapy

\textbf{Airway obstruction.} With an understanding of the pathophysiological changes incurred by burns, one can now best determine the therapy to undertake. Attention is first directed at correcting the ill effects of respiratory tract damage, that is, airway obstruction from laryngeal, tracheal, or pulmonary edema. Damage should always be suspected and respiratory difficulty anticipated if burns are sustained about the face, if they are obtained indoors where inhalation of smoke and noxious gases is more likely, or if the source of heat, such as steam, is of a very high temperature. Establishment and maintenance of an adequate airway is most efficiently obtained through a tracheotomy. This measure
should not be delayed until the patient develops obvious signs of obstruction, but should be done immediately as a prophylactic measure whenever there is any clinical evidence of facial or upper respiratory burns. An emergency procedure through an edematous neck twelve hours after burning is much more difficult than if performed earlier. Signs of respiratory difficulty which call for emergency tracheotomy would include hoarseness, coughing, rapid respirations, cyanosis, pharyngeal inflammation, or rales in the chest. The combination of vomiting and edema often leads to pulmonary aspiration when the patient is unable to expel the vomitus. Tracheotomy helps prevent this. Because of the increased amount and high viscosity of secretions in the tracheobronchial tube, suctioning should be frequent and forceful enough to initiate coughing, but gentle and of short duration so as not to prolong coughing and create hypoxia. One hundred per cent humidification of the air breathed prevents loss of water vapor and helps decrease epithelial irritation. Tracheotomy also offers many advantages in the administration of anesthesia when skin grafting is performed later.

Thermal injury and prolonged hypotension are associated with pulmonary congestion and decreased
elasticity of the lungs. Fluid therapy may accentuate this pulmonary insufficiency and necessitate oxygen or positive pressure breathing when difficulty develops. Tracheotomy, if not done previously, may then be necessary.

**Fluids.** Severely burned patients require volume replacement to mitigate the circulatory derangements produced. The intravenous route of fluid therapy is preferable when a third degree burn covers more than a three per cent area or when a second degree burn is larger than fifteen per cent. An intravenous catheter should be inserted immediately on hospitalization through which fluids and medications can be administered. Frequently, patients cannot tolerate oral fluids, and this route of therapy is then lifesaving. Superficial veins in burned persons are often difficult to locate, and a cut-down must be performed. Injection of small amounts (one cc. of one per cent) of aqueous heparin every four to six hours appears to have a beneficial effect in preventing thrombosis at the tip of the catheter if I.V. therapy is prolonged. If no suitable cut-down site can be found, a femoral cannula should be used.

A urinary catheter must be inserted into the bladder so that accurate measurement of output can be
obtained, a provision essential for the determination of the fluid therapy.

Because of the rapidity of fluid shifts and physiologic compensatory mechanisms, prompt replacement is mandatory. To do this, a rather careful estimate of the percentage of body surface burned should be made and a tentative plan outlined for the amount and type of fluids to be used. Other factors to be considered besides extent of burn include depth of burn and general health of the patient.

The per cent of body surface burns is most easily approximated in adults by using the "rule of nines". A percentage value of nine is given to the head and neck and to each arm, a value of eighteen to the anterior trunk, posterior trunk and buttocks, and to each leg and thigh, and a value of one to the perineum and genitalia. An estimation of the depth of burn may be very difficult on initial examination. Differentiation between partial and full thickness burns relies on the fact that hypalgesia remains in the former while there is analgesia in the latter. In a full thickness burn one can lift a hair easily out of its follicle with no tissue resistance or pain associated. There is also no sensitivity to pin prick with a sterile needle. Ignoring first degree burns, the sites and
particular depths of the burns may be shaded in on
a drawn figure of the patient. In this way the total
area and total degree of thermal injury can then be
fairly accurately calculated with the "rule of nines".

Estimating the amount and type of fluids required
for resuscitation can be done using several formulae.
No plan can be a rigid guide however, for fluids must
be given and regulated according to the patient's
individual requirements and his clinical course. All
workers agree that since sodium and chloride move with
water into the burn, sodium therapy is necessary. During
the last twenty years, two schools of thought have de-
veloped as to what should be the fluid of choice to
deliver this sodium. In particular, the controversy
has been over whether colloid therapy is actually
necessary or not. At the present time the majority of
workers favor including either blood, plasma, or plasma
expanders in their early treatment.

One of the first generally accepted formulae
using colloids was introduced by Evans in 1952. He
based his formula on the finding that six hours after
a dog receives a standard twenty per cent burn,
there occurs a decrease in plasma volume of approxi-
mately one cc. for each per cent of body surface
burned per kilogram of weight. By assuming that the
plasma losses are proportional both to body weight and extent of burn, Evans concluded that a burn should receive one cc. of colloid per kilogram for each percent area of burn. This amount of colloid is arbitrarily paralleled by a similar amount of physiologic saline plus two thousand cc.'s of five per cent glucose in water to cover insensible fluid loss and insure a urine output of thirty to fifty cc.'s per hour. One half this amount is given during the second twenty-four hour period.

A modification of the Evan's formula has been worked out at the Brooke Army Medical Center whereby twenty-five per cent colloids and seventy-five per cent electrolytes, Ringer's lactate being the solution of choice, are given along with the additional 2000 cc.'s of glucose and water. One half the total amount is administered the first eight hours and one fourth in each succeeding four hour period. Again one half this amount is given during the second twenty-four period. Both of these formulae are fairly representative of the combined colloid-electrolyte therapy now used by the majority of workers.

Advocates of colloid therapy today point out several reasonable advantages in using blood, plasma, or plasma expanders. They feel that one should replace
all those elements lost during the shock-inducing period ruling out as quickly as possible any secondary changes that occur because of this loss. It is natural to replace water, salt, proteins, and erythrocytes which are lost with a similar blood-isotonic electrolyte solution. The colloids, particularly blood, have a long-lasting volume expanding and diuretic effect which are not as readily sustained with electrolytes and water. Grozinger has confirmed this statement by comparing the effects of low molecular dextran and saline therapy and finding a much greater expansion of blood volume using the dextran. Finally, Allgower, in polling numerous burn centers as to the type of fluid therapy they used and the results obtained, found the majority of survivors were at centers where large quantities of blood were used with severe burns.

On the other hand, several reasons have cast some doubt on the beneficial effect of colloids in the early treatment of burns.

(1) Because of their osmotic and plasma expanding effect, many authors believe that colloid infusions increase the likelihood of overloading the circulation and causing pulmonary edema.

(2) Increased viscosity and sludging is now believed
to be an additional factor in the promotion of shock. Colloids may not initially reduce the increased viscosity of blood as rapidly as electrolytes alone and may even potentiate intravascular thrombosis.

(3) Both the Evans and the Brooke formulae have been standardized using a twenty per cent surface burn on dogs. In more extensive burns estimates of fluid loss are calculated as proportionately larger. Fox\textsuperscript{21} has shown that fluid loss does not necessarily parallel the increase in burned area but may show a relative decrease depending upon the type of heat used and the particular area of body involved. If this is true, incorrect estimates of fluid requirements could easily be made.

(4) Perhaps the most significant facts in favor of using large quantities of electrolyte containing fluids rather than colloids comes from a number of studies comparing both types of therapy. Marxely and his associates\textsuperscript{36, 37, 38} have led the field in these studies. They found that saline solutions administered primarily by mouth to burned adults have indeed been efficacious in preventing death due to shock. Laboratory studies in the saline-treated patients have shown restoration of plasma volume, maintenance of an adequate renal circulation with an increased glomerular filtra-
tion over the plasma-treated group, and development of a favorable fluid and electrolyte balance. Significantly decreased total plasma proteins in the saline-treated patients resulted in no increase in mortality during the shock period. The overall mortality in adults was twelve percent greater in the group receiving plasma (0.4 ml/kg/per cent burn) supplemented with glucose and water than in those receiving the saline solution alone. The patients in the plasma group had a significant hyponatremia and hypochloremia as compared to relatively normal values in the saline group. Addition of plasma to saline solution did not significantly influence either shock or late mortality; however, addition of saline solution to the plasma therapy, in place of glucose and water, decreased mortality by fifty percent during the shock period. These results actually do not say anything against colloids; but moreover, they point out that electrolyte replacement is the single most important consideration in the treatment of shock. Of significance in these studies was the fact that the combination of plasma and saline solution gave a lower overall mortality in children than was found in the saline group. This difference was attributed to favorable effects of gamma globulin in the plasma. The saline solution
used in these studies contained 140 mEq of Na⁺, 93 mEq of Cl⁻, and 47 mEq of HCO₃⁻ per liter and was given orally as tolerated with burns of less than fifty percent area. The average quantity given was equivalent to ten percent of body weight the first day and half this amount the second.

Clark⁹ also compared plasma-saline and saline therapy. The types and quantity of fluid in the plasma-saline group was determined using the Brooke formula. In the group using a saline solution alone, the formula for intravenous administration was the following: per cent area burn times weight in kg. times two equals amount Ringer's lactate, plus 2000 cc. 5% D/W. Moyer's solution (3 gm. (1 teaspoon) NaCl plus 1.5 gm. (1 teaspoon) NaHCO₃ / liter water) was given orally and subtracted from that taken intravenously. In this study the saline group showed a lower mortality and a longer duration of survival than the group treated with both plasma and a saline solution.

Feller and Deweese⁰ have made a reappraisal of fluid therapy by analyzing the data compiled by various groups using several different regimens. They concluded that there is a wide margin of safety in the quantity of fluid that may be administered successfully to most patients and particularly to those having less than forty to
fifty per cent area burns. They found that with less than fifty per cent area burns, 500 to 1000 cc. of whole blood was sufficient. In addition, giving more than 1500 cc. was unnecessary and possibly harmful unless the burn was larger than fifty per cent. In most groups the volume and types of fluids actually given varied from the theoretical requirements of any particular formula and rather were determined more by the clinical course of the patient. The highest survival rates were found where fluids were individualized and given on an hour by hour basis while maintaining 30 - 50 ml. per hour urinary output and not according to a strict rate of administration.

In view of the above studies and known postburn physiologic alterations, a number of conclusions can be reached regarding fluid replacement. Blood is appropriate in the first forty-eight hours usually only where second and third degree burns cover more than twenty per cent of the body surface causing an early significant erythrocyte loss. The blood may have to be given in spite of a rising hematocrit although it can usually be delayed until other electrolyte replacement is underway and the hematocrit has stabilized or is decreasing. One must balance the possibility of hemoconcentration and thrombosis against decreased
oxygen carrying capacity. The quantity of blood that will be needed in the first twenty-four hours should rarely exceed 1000 cc. with burns of less than fifty per cent area. Giving 0.3 cc./kg./per cent area burned appears to be the proper formula to sufficiently replenish early loss of red blood cell mass and still avoid overloading the cardiovascular system. Indications that a greater volume of blood might be needed than that predetermined by formula are the presence of extensive third degree burns which result in higher erythocyte losses than found with second degree burns and a hematocrit which either never rises substantially or which even falls before fluids are given. The administration of more blood after the first day can be anticipated if a blood smear shows more than ten per cent microcytes during the first few hours, if hemoglobinuria is severe or persists beyond the first day, and if the hematocrit continues to remain decreased after the circulating volume has been restored to near normal.

With burns covering less than twenty per cent and without extensive third degree burns, colloid therapy does not seem essential if electrolyte replacement is sufficient. Despite the hypoproteinemia that develops when plasma or dextran is omitted, there appears to be no rise in mortalities in the shock period. After the
first few days as the sequestered extracellular fluid and protein is reabsorbed, plasma, and blood, if needed, can be administered to improve the nutritional status of the patient.

Electrolyte solutions now appear to be the mainstay of fluid replacement in the shock period. The fluids used should contain large quantities of sodium being as nearly physiologic as possible. An electrolyte cocktail such as Moyer's solution for oral administration and Ringer's lactate for intravenous administration seem to meet these criteria fairly well, are readily available, and have proven to be of value therapeutically. As much fluid as possible should be given orally, discontinuing this route and supplementing with intravenous fluids if intake is not sufficient to maintain an adequate urinary output or if vomiting develops.

The total volume of fluid replacement, both blood and electrolyte solution, can be estimated as equaling 2 cc./kg./ per cent area burned. If blood is given, 0.3 cc. would be subtracted from the 2 cc. and 1.7 cc. of electrolyte solution would then be determined as the required replacement over the first twenty-four hours. Two thousand cc. of five per cent dextrose and water are also included to help replace the large
insensible water loss and to assure sufficient urinary excretion. In using these formulae one should consider any burn above fifty per cent as fifty per cent when calculating fluid therapy in that there appears to be some question that the fluid requirements are proportional to the extent of burn when extremely large areas are involved.

The amount of fluid for the first twenty-four hours postburn is given at a rate to keep the urine output at thirty to fifty cc. per hour. By giving one half this amount the first eight hours and one fourth in each succeeding eight hour period, replacement will usually parallel extracellular fluid sequestration and maintain the desired output. Because edema formation diminishes progressively during the next twenty-four hours, the amount of fluid administration should also be less. One-half of the total fluid is given although the same amount of dextrose and water is maintained as the insensible water loss will continue.

Alterations in this planned regimen are desirable if based upon the clinical course of the patient. The formula is only a guide, the quantity of fluids and rate of administration being governed more by hourly reappraisals of the patient. Clinical parameters
helping to evaluate the success or inadequacy of treatment include the following: (1) Hourly urinary output should be maintained between thirty and fifty cc.

(2) Hourly hematocrit values above sixty per cent indicates oligemia. (3) Venous pressures should not exceed thirteen cm. of water. (4) Plasma solium levels should be kept above 135 mEq. as an indication of adequate hydration and electrolyte replacement. (5) If it can be practically measured, an increase in body weight exceeding ten per cent indicates overloading.

(6) Pulse rate and blood pressure should be kept stable.

(7) Thirst is one of the first symptoms of dehydration.

(8) Restlessness or disorientation may indicate cerebral hypoxia and the need for more fluids as well as oxygen. (9) Vomiting may be a sign of circulatory collapse, acute gastric dilatation, paralytic ileus, or a nonspecific effect of injury. (10) Finally, signs of pulmonary edema indicate overhydration.

**Heparin, anti-toxins, and steroids.** Experimental evidence has indicated that heparin may be useful in the future as an aid in limiting the intravascular thrombosis accompanying burn shock. In a similar experimental stage is the use of convalescent serum from severely burned patients. As of yet no conclusive evidence has been presented to establish if this
is truly beneficial though.

The use of steroids in burns could be of value according to Feller. He found that in patients with over forty per cent area burns the blood levels of circulating hormones were initially very high, dropping to normal when the patients became clinically worse, indicating a relative adrenal cortical insufficiency. Giving hydrocortisone to those showing this drop in steroid levels brought about a greater survival rate than found in a control group. He notes that his study is only preliminary and that the clinical application of steroids is yet to be established.

Pain. Another immediate concern in the treatment of the burned person is the alleviation of pain. Morphine sulfate or meperidine hydrochloride (Demerol) intravenously promptly and adequately gives analgesia and affords better cooperation on the part of the patient. The medication should not be given by any other route as it might easily be poorly and erratically absorbed because of circulatory derangements. Analgesia, not sedation, is the objective of these drugs; for signs of central nervous dysfunction are valuable guides to the adequacy of fluid administration and to the detection of airway obstruction or other ventilatory problems. Because of their depres-
sant effect and also the undue agitation they may produce, barbiturates should not be used. The dosage of morphine or demerol should be regulated according to the patient's subjective response. Often much less is needed than the regular dosage because the drug is given intravenously, because the patient is in shock and extremely sensitive to the effects of analgesics and depressants, and because the patient many times experiences less pain than is anticipated when full thickness burns are present and nerve endings are destroyed. Commonly, much of the excitement the patient shows is due to cerebral anoxia from shock rather than from pain. Not more than 3 to 10 mg. morphine or 100 mg. demerol every four hours is needed. When circulatory insufficiency has been corrected after twenty-four to forty-eight hours, the patient usually has little pain and is no longer restless. Opiates can then be withdrawn.

Infection. The role of infection in burns is a problem from the beginning. One series of bacteriologic surveys made of surface tissue in second and third degree burns immediately or shortly after injury at the time of the first dressing, showed that all were contaminated with bacteria. From two to eight different species were cultured from each wound, the majority
being of a low order of virulence although many varieties were potentially pathogenic. There was a rather high incidence of hemolytic staphylococcal (76%) and hemolytic streptococcal (51%) contamination. Also, one out of every five burns was infected with coagulase positive hemolytic *Staphylococcus aureus*, and one out of every eight by the beta-hemolytic streptococcus. The high incidence of these particular organisms agrees with the findings of initial cultures taken by other investigators. *Clostridium welchii* and *clostridium tetani* were also common contaminants on initial cultures; whereas, the incidence of the coliform organisms and of *Pseudomonas aeruginosa* was very low.

The prophylactic use of antibiotics has been shown to be of definite value in limiting bacterial invasion even though this use has brought to light additional complications. Antibiotics have decreased the incidence of local infection and later septicemia by the original invading pathogens, the sensitive staphylococci and streptococci, only to make way for more resistant organisms such as *Pseudomonas*, coagulase positive hemolytic *Staphylococcus aureus*, and the coliforms.

Penicillin therapy during the first three to five
days nearly eliminates the beta hemolytic streptococci at the end of this period and brings about a seventy-five per cent decrease in the incidence of coagulase positive *Staphylococcus aureus* at the end of one week. Broad spectrum antibiotics have an even more pronounced effect on the *Staphylococcus aureus* bacteria during the first week; however, they later give rise to a greater number of septicemias and by organisms which are extremely resistant. The lower incidence of septicemia seen with penicillin therapy is not attributed to its specific action against any of the micro-organisms involved, but rather to its lower rate in altering the existing bacterial flora of the skin, intestine, and pharynx. Because prophylactic use of the broad spectrum antibiotics never prevent septicemias or infection of burned areas, they should be reserved for use until sensitivities of the particular micro-organisms have been determined. Therefore, because of its reasonable effectiveness and fewer complications, penicillin remains the recommended drug of choice for prophylactic use during the first five days. Recommended dosages vary from 300,000 to two million units daily by the intravenous route.

Anaerobic organisms, particularly *Clostridium welchii* and *tetani*, frequently colonize the surface
of a deep burn. Clinical tetanus has been reported so that routine prophylaxis must be given. To those individuals previously immunized, 0.5 cc. of toxoid acts as an adequate booster dose. If the period since the last injection of toxoid is greater than four years, 3,000 units of prophylactic antitoxin should be administered subcutaneously after testing for sensitivity in addition to the toxoid.

Kefalides, et al,\textsuperscript{32} have shown that the use of gamma globulin therapy has a definite place in combating infection. They found an inverse relationship existed between immunologic defense and susceptibility to systemic infections following burns. The success of gamma globulin prophylaxis was especially significant in younger children and in those children with burns of less than twenty per cent area reducing the number of deaths from septicemia to almost half. Because of early shock and fluid derangements, levels of gamma globulin did not reach their peak until one week after injection. It was therefore recommended that a larger dosage (two cc./kg.) be given on admission. Although there was a reduction in deaths from septicemia in adults receiving gamma globulin, the decrease was difficult to evaluate since there was a greater preponderance of more severe burns in the
control group of adults.

Local Therapy

Surface cooling. Many investigators are now convinced that the immediate postburn use of ice water compresses can be a major factor in prolonging the length of survival time and limiting ultimate mortality. As stated before, much of the tissue damage following acute thermal injury occurs subsequent to the primary insult and is caused by factors other than temperature alterations. By applying cold directly to the burn there is a depression of cellular metabolism, a lowering of oxygen requirements, and a diminution in cellular membrane damage and permeability. Subsequently, shifts in protein, fluid, and electrolytes from vascular spaces and uninjured tissues are lessened resulting in a smaller degree of shock than might otherwise be expected. Cold also inhibits hemolysis of red blood cells passing through the burned area by means of a direct effect on the erythrocytes and by causing vasoconstriction in vessels in and around the site of injury. This vasoconstriction not only prevents many rbc's from entering the burned area but also limits the amount of toxic products from protein decomposition that may enter the general circulation and questionably have an adverse effect elsewhere in the body.
Locally, because there is less edema and fewer damaged cells, the depth of the burn is minimized.

The ideal temperature of water and the proper duration of application does not seem to have been fully determined. King and Price used water at a temperature of 15°C for thirty minutes; whereas, Vernon advocated ice water at no specific temperature for as long as twenty-four hours. Continual cold water soaks for the longer time would seem more reasonable in that it is known that sequestration of fluid continues for as long as twenty-four to forty-eight hours. Low temperatures for this length of time may also inhibit early proliferation of bacteria. No matter what temperature or length of time the cold compresses are used, the most important point to be remembered is that this procedure must be started immediately realizing that the greatest amount of damage and edema formation occurs within the first few hours.

Clinically, surface cooling affords the patient definite pain relief while easing apprehension. Lesser amounts of analgesic are thus required. In addition, a smaller amount of fluid replacement is needed than would be ordinarily anticipated. Partial thickness burns are also benefited. Cold water suppresses the redness and edema of first degree burns within a few
minutes. When pressure dressings are used after the water treatment, second degree burns can be limited to erythema without blister formation.

Wolfe has published a report dealing with the use of hydrostatic pressure in limiting the burn injury. Using dye techniques, they emersed the burned ears of rabbits in ten to twenty inches of water and found that capillary circulation remained intact in these ears in contrast to untreated ears. Also, the emersed ears weighed forty per cent less than the untreated ears indicating far less edema formation. By using water which is cooled, the advantages of local hypothermia and hydrostatic pressure might be combined. Saline pressure, especially with sterile agitation, would also serve as a good defense against infection, might provide for microscopic debridement, and may significantly decrease the water vapor loss if large areas are involved. The practicality of this method with large surface burns would be limited without proper facilities, but its use seems readily applicable to burns of the extremities. In the future, hydrostatic pressure in humans will have to be evaluated and the ideal hydrostatic pressure determined.

Local care other than cold water compresses cannot be considered an emergency procedure as it does not
affect the initial response of the patient. Many topical agents have been advocated for direct application to the burn. Most authorities prefer either the use of vaseline gauze and the closed method, or cleansing with a detergent and water and using the opening method. Sokolić et al., found that both vaseline gauze and pHisohex showed a statistically significant acceleration of healing when compared with their own controls and other topical agents. This study would indicate that either method could be used. Over a long period of time though the open method would be more convenient and probably more sterile.

Much work is now being done in primary excision and grafting of the deep burn during the first twenty-four to forty-eight hours. Autografts are preferred, but homografts can also be used if the burns are extensive. The main advantage seems to be in decreasing postburn morbidity. Local infection is reduced; skin coverage is completed in two thirds the conventional time; and the patients seem to suffer less nutritionally and become rehabilitated more rapidly. Although this procedure has generally been limited in the past to burns covering less than ten per cent of the body, more extensive grafting has not proven to have any detrimental effect on the patient or to
have increased the incidence of deaths in the immediate postburn period.

Summary and Conclusions

Burns bring about local and concurrent systemic manifestations. Depending on the temperature, duration, and type of heat source, various depths of burns occur. Full thickness burns are the result of direct heat necrosis and are also secondary to small vessel thrombosis. Similarly, increased capillary permeability with subsequent edema formation is thought to be a direct effect of heat and/or of hypoxia of the vessel walls from stasis of blood flow. The transudation of plasma and the pooling of blood throughout the body bring about a rapid sequence of physiological alterations and a compensatory shift in extracellular fluid. With these fluid shifts, the sodium and plasma protein levels are significantly lowered. Varying degrees of postburn anemia may develop depending on the depth and extent of the burn. Injury to the skin is often paralleled by damage to internal organs elsewhere in the body, notably the lungs, kidneys, and gastrointestinal tract.

Maintenance of an airway is the foremost consideration in resuscitation of the burned patient. Fluid replacement should be estimated using a specific
formula and then regulated according to the clinical course of the patient. The type of electrolyte solutions used should be as nearly physiologic as possible containing large amounts of sodium. In that electrolytes appear to be the mainstay of replacement, blood is necessary only when red blood cell loss is significant. Pain can be satisfactorily handled with narcotics. Penicillin and perhaps gamma globulin therapy appear to be the most effective early measures in preventing and combating infection. Presently, undetermined benefit may be the future use of anticoagulants, "antitoxins", and steroids. Locally, immediate cooling of the burn site limits the depth of injury and possibly subsequent systemic pathophysiology. Other local treatments considered were the cleansing of burns and the value of early excision and grafting of burned areas.
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