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Review of thermal burns : with especial reference to shock and toxemia

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A REVIEW ON THERMAL BURNS

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A REVIEW ON THERMAL BURNS

The tale of thermal burns is as old as fire itself, yet re-enacted with each turn of the clock. Graecian mythology teaches that of all the animals man was the last race created and in consequence thereof, was most poorly endowed with physical gifts. So Prometheus stole fire from the hearth stone of the Gods on Mount Olympus and bestowed it as a gift which would set men apart from all other animals. And so it has. But the sword with which civilization was founded is a two-edged one and since time immemorial the followers of Aesculapius have sought to bring relief to those luckless mortals who have felt its sting.(4) A review of all that has transpired through the centuries would entail a narration of infinite length. Such a text would, however, undoubtedly reveal that the treatment of burns, as the adage of history, has repeated itself. Historically there is little new in this respect. At the present time and for many years past we have employed therapeutic methods which were in vogue at one time or another in the course of the intervening centuries, and which have been recently reintroduced and exploited.

Substances--animal, mineral and vegetable--upon which the treatment of burns has importuned, are limitless. Relief from pain has been preeminent, and attained, to a variable degree by anything which protects the injured tissues from the air, hence, salves, ointments and oils have had their proponents among the profession and the laity through the ages. Hippocrates, in 430

B.C., used a combination of oil and resin in the treatment of burns. The use of limewater and oil, which was the forerunner of carron oil, was recorded in the third century, B.C. Alum and other astringents were used in the sixth century, A.D. Water bathes were used in 1858. Tait used paraffin in 1864 but it did not become popular until 1915. Lister used boric acid compresses for burns exclusively and it is possible that he had the present popular infection theory for the toxemia of burns in mind at the time. The Chinese, in 5000 B.C., used a strong infusion of tea as wet dressing which is the antecedent of one of our most modern treatments. In general, one may say that burns have passed through periods of fad and fancy without much real investigation until the last fifteen years. It is to this latter period that this review will be confined in general, and to those features which promote the greater advance in the understanding of burns and their treatment, in particular.

Much has been done to establish a greater clarity in regard to the pathology of the local lesion, but most impressive is that work which treats with the reaction of the body in general to severe burns. To understand both phases of burn pathology is essential to good treatment and it is this knowledge which has served to decrease the mortality attendant upon extensive burns.

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Burns are said to be but a type of trauma, thermal in this instance, and trauma but a noxious influence which, when severe, over-

taxes the compensatory and recuperative powers of the animal organism. (47) The term 'thermal burns' will be understood to include only injuries caused by liquid and by dry heat, or, scalds and burns, respectively. With the occurrence of such a burn the question of prognosis should arise and can be foretold to a degree when a cursory examination of the patient and the burn is conducted to ascertain the following data (77):

1. The nature of the burning.
2. The age, sex, occupation and individual tolerance of the patient.
3. The extent of the body surface affected.
4. The degree of depth of the burn involvement.
5. The particular regions of the body burned.

The knowledge thus attained when compared with information based upon previous burn pathology serves as a reliable criterion of prognostic import.

Scalds are more serious than dry heat, and are responsible for the worst sloughs.

The younger the patient the more serious are the symptoms. About 45 per cent of all deaths due to burns occur from birth through the fifth year. (76) Old age is more apt to succumb to the exhaustion attendant upon a slow and laborious healing. Occupations of salubrious nature tend to predispose physical resistance to deleterious influence varying in direct proportion. Certain authors propose an individual resistance. (91) Burn mortality

is greater for the female than the male.

According to Pack and McLeod the extent of the burn is more important than the depth. Most burns of first degree are fatal if two thirds of the body surface is involved. All burns of second degree are fatal in adults if one third of the body surface is involved (64), and in children if one seventh is involved. (16) All burns covering one third of the body surface are extremely serious, if not imminently fatal. All burns covering one tenth of the body surface should be considered serious. Berkow's work is useful in the estimation of the extent of surface lesions. He concludes that the lower extremities, including the buttocks, comprise 38 per cent of the body surface; the trunk, including the neck, 38 per cent; the upper extremities 18 per cent, and the head 6 per cent. The hand is one quarter of an upper extremity and the arm three quarters. Of the lower extremity the foot is one sixth, the leg one third and the thigh one half. The area of the head is divided equally between the face and scalp.

The depth of the burn is of less importance than the surface area in calculation of mortality. However, in the consideration of cosmetic and functional results the depth of penetration is of much interest. In this respect burns have been classified as to degrees. These, in the literature, may be found to vary in number and interpretation thereof. In America and Germany this classification includes three degrees, whereas in France and England six degrees are used to denote the various depths.

American Classification

1. Erythema.
2. Vesicle and bulla formation.
3. Eschar formation and gangrene.

French (Dupuytren's) Classification

1. Erythema of the skin.
2. Vesication.
3. Destruction of the cuticle and part of the cutis vera; the tips of the papillary downgrowths remaining intact.
4. Destruction of the entire integument and part of the subcutaneous tissue.
5. Encroachment on the muscles.
6. Disorganization and charring of the tissues.

It must be realized, however, that the morbidity and mortality attendant upon a burn is dependent upon both surface area involved and degree of penetration. Burns of the fourth and fifth degrees are attained with the severest toxemia, because of the amount of tissue destruction; further, they command consideration, because of the cicatricial contractures and deformities consequent to their healing. Assuming equivalent total areas and degrees, multiple and scattered burns have braver prognostic importance than a single continuous burn, because the former, although ultimately healing quicker, is less conducive to rest and interferes with the

ease of dressing.

Burns of the scalp are peculiarily susceptible to erysipelatous inflammation, but are not so often followed by cerebral mischief as one would think. When the burn is limited to the extremities or to the back, where the thick dorsal muscles serve as effectual protection to the subjacent viscera, the outcome is encouraging. However, burns of the abdomen, with the dangerous visceral proximity, have the highest mortality. Burns of the genitalia, the anterior thoracic region and the face (over the area of trigeminal distribution) cause symptoms and dangers far out of proportion to their area allotment. Mucous membrane involvement, especially of the pharynx and larynx, adds to the gravity of the case. Burns of the flexor surfaces are more serious than on the extensor surfaces.

Various factors of concern such as shock, toxicity, infection and complications will be considered in more detail in the ensuing pages.

PATHOLOGY

The local lesions discussed in accord with Dupuytren's classification are well described by Gunn and Hillsman (43), 1935, in the following excerpt.

FIRST DEGREE--This consists of simple erythema with vascular reactions similar to that of any simple inflammation due to the action of an irritant. It is essentially a reflex and exudative reaction. The reflex phase consists of contraction followed by dilatation of the arterioles and venules, resulting in an increased flow of blood to the affected area and a local stagnation of the current. This naturally causes the redness and increased heat invariably associated with this type of burn. The exudative reaction is explained by an increased capillary permeability and consists of an infiltration of plasma into the tissue spaces, the migration of leucocytes, and the diapedesis of red blood cells. Within a few days the outer layer of the epidermis separates and peels off.

SECOND DEGREE--This is essentially a degree of vesication. The epidermis undergoes true coagulation necrosis. By virtue of the increased capillary permeability there is an exudation of serous fluid and filtration of leucocytes from the tips of the papillae, resulting in the formation of blebs and bullae. In mild cases the exudation occurs within the epidermis and leaves the basal cell layer intact, thus forming the bleb. In the more serious cases the fluid collects in larger amounts beneath the full thickness of the epidermis, resulting in larger and more serious bullae. In the

very severe cases the fluid may even resemble plasma and in such cases organization of the fibrinous exudate is more likely to follow than absorption. It is well to remember that in this type of burn scarring may take place, particularily if infection complicates the picture.

THIRD DEGREE--In this the epidermis is entirely destroyed as is part of the corium. Its distinguishing factor is that the interpapillary processes remain intact. The papillae appear as a reticular framework containing serum, bits of persistent living epithelium, leucocytes and fibrin. The papillae show as red points on a white background. Two things should be noted about this type of burn. First, the exposed nerve ends in the interpapillary processes remain intact and as a consequence this is the burn accompanied by the most severe pain. Secondly the sebaceous glands, the hair follicles and the sweat glands are intact and will regenerate new epithelium providing infection does not destroy their epithelial cell lining.

FOURTH DEGREE--In this there is destruction of the entire thickness of integument and complete disorganization of the skin involved. If the traumatizing factor is dry heat this area will vary from brown to black in color, be insensitive and leathery to touch. If on the contrary moist heat is the agent the affected area will be white, insensitive, and finger pressure will not induce the usual color changes. Surrounding this zone will be areas of lesser degree burns, shading off from a third degree to a simple hyperemia

of the first degree. An acute inflammatory process starts very early and the eschar retracts leaving a groove between the dead and living tissues. Sloughing of the dead tissue begins and is completely normal within two weeks. At the same time proliferation occurs. Fibrinous exudation upon the surface exerts a chemotactic action upon the new tissue cells. The capillaries proliferate tufts of endothelial cells accompanied by a new growth of fibroblasts, to grow along the fibrinous framework after the manner of healing by secondary intention. The endothelial cells hollow out to form arches of new capillaries giving nourishment to the growing tissue. Scarring and contracture deformities result.

FIFTH DEGREE--This type of burn varies only from the fourth degree in that the underlying muscles are involved. The resulting scar is, as a consequence, more deforming and may cause great functional impairment. The scar has a great tendancy to break down and ulcerate.

SIXTH DEGREE--In this degree the tissues are carbonized and the heat may even fracture the underlying bone. It is usually seen in the very severe type of burn involving the digits and demands, invariably, amputation of the part.

If a burn undergoes an exhaustive suppurating process, the amyloid infiltration of the viscera, which so commonly follows chronic destructive infections is likely to ensue.

In addition to this local pathology, Pack(75), 1926, disclosed numerous pathological manifestations effected upon remote tissues

and organs by the toxemia or sepsis arising from the burn site. His observations are ennumerated as follows:

NERVOUS SYSTEM--Necropsy reveals hyperemia of the brain and meninges. The arachnoid vessels may be engorged with blood and contain occasional thrombi. Korlenko (55) states that the sympathetic nervous system is seriously involved. The cerbral cortical cells and ganglion cells are not injured except in the instances of shock, in which the nerve exhaustion is accompanied by chromatolysis or partial destruction of Nissl's granules. (Crile)

LUNGS--The lungs show congestion and may contain fibrinous plugs. Thrombi have been reported in the smaller branches of the pulmonary artery, exerting additional strain on the right ventricle.

KIDNEYS--The kidneys due to the excretion of the tissue toxin suffer an acute glomerulitis. Cloudy swelling and fatty degeneration appear later in the proximal convoluted tubules. With severe burns necrotic foci become abundant in the kidney and grow larger and more extensive as the toxemia persists. These necrotic areas incite cell multiplication, and a proliferative process results, with irreparable damage to the kidney. Hemoglobin pigment is formed in the kidneys, being most abundant in the straight uriniferous tubules, although occurring also within Bowman's capsule and the convoluted tubules. This blood pigment is responsible for the dark brownish red color of the kidneys, as described in necropsy reports, and which has erroneously been attributed to excessive hyperemia. This hemoglobin is excreted through the glomeruli and appears in the

ADRENALS--The adrenals in burned patients may increase to four or five times normal size. The glands are swollen and deep red, due to hyperemia and ecchymotic areas of hemorrhage among the parenchymal cells. These pathological changes are more or less in direct proportion to the burned area. The type of changes is similar to that occurring in diphtheria intoxication and anaphylactic and peptone shock. The epinephrine content is low or absent.

HEART--In the heart, subendocardial and subepicardial hemorrhages are often found. If toxemia has persisted for sufficient length of time the cardiac musculature exhibits areas of hyaline and fatty degeneration and necrosis of the muscle fibers.

LIVER--The liver often manifests hyperemia, focal necrosis and parenchymatous degenerative lesions.

SPLEEN--The spleen is usually softened and enlarged. Focal necroses occur in the Malpighian bodies. The lymphoblasts undergo karyorrhexis and karyolysis and are rapidly ingested by phagocytic endothelial leucocytes. The latter cells may proliferate so rapidly that they completely fill the Malpighian bodies and are bordered peripherally by a narrow rim of lymphocytes. These lesions reach their height within 72 hours after the injury. Later the lymphoid nodules appear homogeneous, due to hyaline degeneration changes. (114)

LYMPH GLANDS--The germinal center of the follicle is first edematous. Swelling and distortion of the lymph cells of this area are soon followed by necrosis and dissolution, the changes gradually extending peripherally. McCrae (69) states that there is a prolif-

ation of phagocytic endothelial cells identical with that seen in typhoid fever and other acute infections.

BONE MARROW--Necropsies on human subjects and dogs reveal focal necrosis, if the subjects live long enough to permit the start of an active leucopoesis. Burn toxin in mild amounts is positively chemotaxic for leucocytes and stimulates the bone marrow to increased activity, but, like many other irritants, an excessive quantity destroys instead of stimulates.

GASTRO-INTESTINAL TRACT--Swelling and pathological changes of the solitary and agminated lymph follicles are similar to the lesions described in the other lymph structures. There is a generalized hyperemia of the mucous membrane of the stomach and intestines, particularly in the ileum near the cecum. The peptic (Curling's) ulcer will be considered later.

SEROUS CAVITIES--The pleural, peritoneal and joint cavities are prone to contain an accumulation of serous exudate, expecially with a burn or a scald in the skin overlying the serous cavity. The exudate is occasionally hemorrhagic.

This evidence proves beyond doubt that the body as a whole is subjected to the insults of some malific substance in the circulating blood. The acknowledgment has stimulated extensive and intensive experimentation and clinical investigation hoping to apprehend the occult marauder. At this writing the finger of guilt seems to incriminate a toxin or infectious process arising in the burn site and transported in the blood, or, a change in the blood

itself, this in the form of a marked concentration, or an alteration in its biochemical constituents. These considerations will be discussed at greater length presently in their proper sequence.

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The present status of thermal burn pathology, hence, permits an axiomatic stand upon the existence of constitutional phenomena arising in consequence of, and concomitant with, the local manifestations. However, the noteable inconsonance on this subject causes no little trepidation and concern in seeking a manner of presentation which will be in accord with the bulk of evidence and at the same time afford a practical conception of the whole.

One can, I believe, derive the greater understanding of the situation by assuming the phenomena of thermal burns to be a sequence of events which exhibit definite reflex, biochemical and toxic manifestations. To this end, five phases (120) are enumerated:

1. Primary shock
2. Secondary shock
3. Acute toxemia
4. Septic toxemia
5. Healing

As will soon become evident, some of these phases may be active at the same time, but this division assumes that their manifestations will be maximal at that specified period. Before making fur-

ther concessions to this seemingly categorical classification full knowledge of the involved characters is essential, hence, a review of clinical and experimental observations is necessarily apropos. Irrespective of the clarification proposed by this evidence the uniformity of results obtained and the paradoxical divergence of etiological contention is not a little confusing. The most disquieting feature is that proof in most cases seems conclusive.

Previously the chief theories as to the origin of shock were the nervous and toxic theories. In 1930 a physical theory was introduced and recently the adrenal gland has been implicated.

It is to be remembered, as pointed out by Simonart (94), 1930, that the problem of shock in burns may be quite separate from that of shock due to other types of trauma.

Harkins (47), 1938, in an excellent article, summarizes the various theories of burn shock under the following heads, which will serve to segregate the features in the ensuing discussion:

A. Nervous and adrenalin theory.

B. Fluid loss (physical) theory.

C. Toxic theory.

D. Bacterial theory.

NERVOUS AND ADRENALIN THEORY--Underhill, Kapsinow and Fisk (107), 1930, believe that the first ill effect of a severe burn may be a reflex shock phenomenon due to pain and fright. They have noted that in animals burned under anesthesia the primary shock seen in the clinical stage did not occur. Lee (58) states that wound shock

in burns is greater than in any type of traumatic wound because the skin denudation and its consequent exposure of the myriad of sensitive nerve terminals, permits irritation and gross insult to the nervous system. Harkins (47) contends that a purely nervous theory is not generally held, varying in this respect with traumatic shock in general where many workers support a purely nervous theory. In burns the immediate effect of the painful injury may be syncope, or a primary type of shock, but usually by the time the physician sees the patient this is over.

Several separate theories have been attached to the adrenals alone. Both medulla and cortex have been indicted separately, and, several authors, arguing chiefly from necropsy evidence, have attributed death to the adrenals as a whole. Harkins (47), 1938, noted no pathologic changes in the adrenals in five necropsies. Weiskotten (113,114), 1917, 1919, on the other hand noted adrenal changes in ten necropsies following uncomplicated superficial burns. Numerous other and later authors have likewise found evidence to inculcate the adrenals. Brooks and Blalock (13), 1934, however, present evidence to show that somewhat similar changes will follow hemorrhage and trauma to muscles indicating that they are not specific to burns.

Freeman and associates (36-38), 1935-1937, have proposed a theory of shock that consists in essentially an overexcretion of adrenalin to keep the blood pressure near normal despite a lowered blood volume. If the blood volume decreases more, and this it tends

to do because of the capillary exudation with increase arteriolar resistance, the increased adrenal output can keep the blood pressure compensated only so long, and then it collapses. Thus, this theory suggests that an overproduction of adrenalin is a factor. Saito (88), 1932, believes contrariwise, that in burns a deficiency of adrenalin is the chief factor and he has prolonged the lives of experimentally burned animals by intraperitoneal injections of adrenalin.

Other writers have accused the cortex as being the site of injury with resultant hypofunction and death. The reported experiments tending to show a similarity between adrenal cortex insufficiency and traumatic shock. The injection of 'cortin' was said to control the insufficiency and combat the shock. Wilson, Rowley and Gray (121), 1936, have taken the practical application of extract in three cases of burns, two of which they believe would have died otherwise. However, they mention that no sweeping conclusions can be drawn from this small series.

FLUID LOSS (PHYSICAL) THEORY--Underhill and his associates (101-109), 1930, were the first to draw attention to the extensive local loss of fluid in burns. The hemoconcentration resulting from such fluid loss had been reported earlier by Baraduc (2), 1862; Tappeiner (98), 1881; Hock (52), 1893; and Locke (59), 1905. Underhill and his associates produced experimental burns and found that the edema at the site of the burn reached a maximum at the end of 24 hours and was reabsorbed in five to six days. Chemical an-

alysis of the edema fluid showed it to be closely similar to blood plasma. Underhill measured the amount of this edema fluid by squeezing it out of the soggy tissues and found it to be equal in some instances to 70 per cent of the total blood volume. Loss of such fluid is of much more serious consequence than loss of an equal amount of mere watery transudate. As Harkins (47) has pointed out, a person can urinate three liters a day, but can hardly part with a similar amount of blood in the same time.

Blalock (11), 1931, determined the amount of fluid lost into the tissues by burning one side of an animal and then bisecting the animal and weighing the two sides. In a series of burned dogs the edema fluid averaged 3.34 per cent of the body weight (about one half of the blood plasma volume). In plasmapheresis experiments Blalock found that 3.5 per cent of the body weight of plasma removed would kill the animals. The edema fluid in Blalock's exeriments was similar to plasma as shown by Beard and Blalock (6), 1931, and hence, in the burned animals enough plasma was lost to kill them alone without invoking the action of any toxin at all. Harkins, however, makes no such sweeping conclusion. Johnson and Blalock (54), 1931, next showed that the cardiac output was markedly decreased following burns.

Harkins (46,47), 1934-1935, performed experiments confirming Blalock's data when unilaterally burned animals were besected. Furthermore he placed the burned animals on a tipping apparatus so that as the burned side grew heavier a kymographic tracing measured

the weight shift. This furnished a graphic method of recording the local accumulation of fluid in experimental burns. The accumulation began at the time of the burn and continued in the form of decelerating curve until death. Accompanying the collection of fluid was simultaneous increase in the percentage of hemoglobin and in the hemocrit readings. After most of the fluid had accumulated, the fall in blood pressure set in and continued rapidly until death occurred in a state of secondary shock. Harkins also showed that the bleeding volume of burned animals is markedly decreased. It is interesting in this connection that histamine did not appreciably lower the bleeding volume under similar experimental conditions when it has lowered the blood pressure to shock level. Schievers (89), 1936, has shown that the blood volume is reduced by as much as 50 per cent in experimental burns. He attributed this partly to the destruction of red cells but mainly to transudation of plasma. This work fits in with that of Harkins on bleeding volume and along with those of Simonart(93), 1928, is one of the bases for Schiever's support of the physical theory.

McIver (71), 1933, presented some evidence that may be taken to support the physical theory. He showed that in human patients the blister fluid was similar to blood plasma and that the hemoglobin and hematocrit readings were markedly increased in such patients.

Gunn and Hillsman (43), 1935, have concluded that secondary shock is due to an actual reduction in blood volume. Locke (59),

1905, found a red count of over nine million in four of ten burn cases at the Massachusetts General Hospital. Weiner, Rowlette, and Elman (112), 1936, reported marked blood concentration with most red counts above six million, two being over eight million in 40 burned patients. They pointed out that the low plasma protein, due in this instance to plasma loss, is quite different from that in dehydration from diarrhea or vomiting where the plasma protein is elevated, being in some instances over 10 gms. per 100 cc. In this McClure (68), 1936, pointed out that very little of the fluid loss in burns is due to evaporation, the slight increase being due to increased surface temperature.

TOXIC THEORY--From the very start of the interest in burns, the toxic theory has been to the forefront as an explanation for the cause of shock and resultant death. Scores of poisons have been indicted, more often on an entirely empirical or theoretical basis, and the very number of suspected toxic substances is one of the chief evidences against positive proof for a toxic basis. On the other hand just because some work has been against a toxic theory for death in other kinds of shock this has no absolute bearing on the subject of burns, for they represent a separate problem.

Parascandolo (78), 1904, was one of the early experimental proponents of the toxic theory. In work on rabbits he reported that death was due to toxic poisoning caused by a circulating substance acting on the liver and kidneys as well as other organs causing fatty degeneration. He also reported the blood of burned

rabbits was toxic when injected into other animals. In an extensive monograph, Pfeiffer (79), 1905, in experiments on guinea pigs and rabbits that deaths in the first two to six hours are due to shock, while thereafter they are caused by decomposition procucts of burned protein which he reported to have isolated.

Robertson, Bruce and Boyd (84), 1923, reported very definite results in their search for a burn toxin. After producing skin, subcutaneous and muscle burns experimentally, they reported finding a burn toxin that was present in whole blood and cells, but not in the serum. Therefore it was absorbed on the cells. They reported that alcoholic extracts of burned skin would reproduce symptoms when injected intraperitoneally or intravenously in experimental animals, but that these results did not follow the injection of similar extracts of normal skin or skin burned after death. They reported that blood from burned animals injected into guinea pigs produced toxic symptoms and "autopsy findings in the fatal cases were identical with those seen in burned animals". They claimed to have separated a thermostabile neurotoxic and a thermolabile necrotoxic element in their toxin, which toxin consisted of primary and secondary proteoses. Because of the presence of this toxin they advised exsanguination transfusion and concluded: "From a purely clinical point of view, that the burned tissues are responsible for the production of some toxin which is taken up by the blood stream."

Underhill and Kapsinow (109), 1931, repeated the work of Rob-

inson and Boyd on the injection of alcoholic extracts of burned skin and reported that the control extracts were fully as lethal as the extracts of burned skin and the lethal factor in either case was merely the alcohol. They correlated the irregular action of the control extracts with a lack of a statement in Robertson and Boyd's papers on the number of controls done. Underhill and Kapsinow concluded: "Our experience with burns leads us to doubt the existence of a 'burn toxin', and to believe that the persistence of this viewpoint is an obstruction in the way of clarification of the burn problem."

Underhill, Kapsinow and Fisk (108), 1930, presented data which showed absorption of such substances as strychnine and phenosulphothalein from burned areas. Since there was fluid loss from the capillaries they found that these absorption experiments showed that the increased permeability was in one direction only, namely, from the blood into the tissues. Mason, Paxton, and Shoemaker (62), 1936, performed experiments somewhat similar to the preceding ones, only they used a substance of low molecular weight for their absorption tests--sodium iodide. This was excreted in almost identical quantites in the urine of burned and control animals after subcutaneous injection, the injection being made in the case of the burned animals into the area on the abdomen six hours after burning.

Harrison and Blalock (50), 1932, performed experiments, the results of which opposed the toxic theory. These were repetitions

of experiments that had been reported by others as favoring the toxic theory. (1) The transplantation of burned skin had no effect on the recipient animal. (2) The effects of debridement on the survival of burned dogs: The survival averaged seven and one-half hours in the debrided series and seventeen and one-half hours in the control dogs. (3) Transfusion of blood from burned to normal dogs was without effect. Blalock and his associates (6,11), 1931, reported work favoring the loss of plasma-like fluid being a potent cause of death following burns (section on physical theory), but Mason and others (62), 1936, quote him as saying in 1934: "I believe that deaths which occur from three to ten days following severe burns are due in large part to absorption of protein decomposition products". Straus (96), 1937, was unable to isolate substances in burned guinea pigs which, when injected into other animals, would act like a toxin.

Japanese investigators, on the other hand, have practically invariably supported the toxic theory. Nagamitu (72,73), 1933, 1935, found that blood serum or fulid perfused through the burned hind limbs of dogs or rabbits when tested on cats blood pressure or guinea pigs uterus or intestine showed a histamine-like depressor action. However, the action was not abolished by histaminase. Shimada (92), 1934, believed that the burn toxin is nothing other than histotoxin which can be differentiated from histamine by its action on the toads kidney. Miura (65), 1934, perfused the burned hind legs of rabbits and found a toxin. Inouye (53), 1933, has

seen autopsies on three burned patients with changes in the adrenals. He believes the changes in burns are much the same as those cause by strychnine, barium chloride and picrotoxin. He said that Pfeiffer (79), 1905, attributed these changes in the adrenals (disappearance of lipoid bodies, loss of chromaffine affinity, hemorrhage, hyperemia and focal necrosis) to the accompanying low blood pressure due to shock. He further quoted Kolisko, Nakata and Niemeyer as postulating that a toxic action caused the adrenal changes and the adrenal injury in turn killed the animal. On the other hand, Takeuchi said that the adrenal changes are only a part of the general picture and not the direct cause of death. Inouye himself adhered to Takeuchi's theory but believed also that the adrenal damage may be one of the factors in the causation of death. Murai (66), 1933, has studied the effects of injections of heated skin and gastric mucous membrane extracts, finding the former more toxic. Ravdin and Ferguson (80), 1925, and Davidson (26-30), 1925,1927, favored the toxic theory. Davidson's whole tannic acid therapy was founded on the concept of prevention of toxin production by the absorption from injured or autolyzed tissue. Harkins, Wilson and Stewart (49), 1935, presented work that was evidence against the toxic theory. They made protein-free extracts of normal and burned skins of rabbits by means of trichloracetic acid extraction. The extracts of normal skin contained an apparently identical depressor substance. Such substances showed no increased depressor activity, but sometimes a diminution, which

is probably due to dilution of the depressor content of normal skin by edema fluid. Later, Wilson, Jeffrey, Rosburgh, and Steward (119), 1937, again used rabbits as the experimental animal, but this time they did not use protein-free extracts and this time the extracts did show evidence of toxic properties and, when collected 48 hours after burning, it was frequently lethal to healthy animals of the same species. The development of toxicity was independant of the action of bacteria and seemed to be related to the autolysis of injured tissue. The toxic principles were associated mainly with the globulin fraction and their action was on the nervous and circuletory systems and in the production of degeneration of liver cells.

Bernhard (9), 1936, found that extracts of an experimentally burned skin were toxic when injected into other animals. From autopsy changes in a girl aged four years dying 17 days after a third degree scald of the left hand 9 by 5 cm. in area, with the observation of changes in the heart muscle and kidneys Brenner (12), 1936, favored the toxic theory. The size of this burn and death after the time when infection has taken place might indicate that death in Brenner's case might be due to infection rather than autolytic toxins. It is to be pointed out that one definition of a burn is "an infected wound produced by heat". Catiano (15), 1882, believed that when ammonium formate, derived from the sweat, was heated in the process of burning skin, it lost water and became HCN, the cause of the toxic action of burns.

Barsoum and Gaddum (5), 1936, reported a rise in blood histamine in burned patients reaching a peak of five times normal seven days after the burn. They stated, however: "The relation of this rise in blood histamine to shock is uncertain. There was no clear evidence of any correlation between blood histamine and the clinical condition of the patient". The rise was probably due to interference with the function of the kidneys or other histamine excreting mechanisms. The rise occurred later than the time of the secondary shock, but the writers attributed this to the fact that the patients were Egyptian!

Fender (35), 1933, gave an excellent review of much of the earlier work favoring the toxic theory, listing 17 toxins proposed by 34 different workers, and showed that many of their exponents were open to question (see Table I). Merely because there is confusion as to the name of the toxin is of course not evidence against its presence. Fender found changes in the spleen and lymph glands of burned rabbits, but he concluded: "The theory of causation of death by a toxin cannot be said to rest upon adequate experimental evidence at present". Simonart (94), 1930, also found no evidence for a toxic action. Lesser, 1880, attributed the toxic action of burns to a functional impairment of the red cells that pass through the burned area making them foreign to the organism and giving rise to anemia in the functional sense.

A session of the 1937 French Surgical Congress (39) was devoted to the subject of burns. Pierre Duval gave a report favor-

Table I

Partial List Of Toxins Postulated As The Result Of Burns

No.	Toxin	Author
1	Ammonia	Edenbuizen
2	Ammonia and urea	Billroth
3	Fibrin	Foa
4	Urea	Ponfick
5	Hydrocyanic acid	Catiano(15)
6	Ptomaine	Lutzgarten, Kitjanitzin, Parascandolo(78)
7	Pyridine base	Reiss
8	Hemolysins and hemo-agglutinins	Von Dieterrichs
9	Choline-like substance	Kolrausch
10	Methyl quanidine	Heyde
11	Diamino acids	Eden and Herimann
12	Primary and secondary proteoses	Robertson and Boyd(84)
13	Peptone	Olbrycht
14	Inorganic intracellar material	Turck
15	Unspecified protein cleavage products	Pfeiffer(79), Fraenkel and Spiegler, Brancate, Il Seung O, Nishimura
16	Unspecified toxin	Avdakoff, Boyer and Guinard, McCrae(69), Scholz, Vacarrezza, Bardeen(3), Weiskotten(113), Pack(75), Davidson(26-30), Speese and Bothe, Weidenfeld
17	Potassium salts	Schjerning
18	Toxalbumin	Dorrance and Bransfield
19	Anaphylaxis	Tuder
20	Abrin and ricin-like toxin	Stengel and Fox

Adapted from Fender(35), 1933, and Pack(75), 1926.

able to the toxic theory. He believes that autolyzing tissue at the site of the burn acts as a toxin. He reports that in animals it was found that repeated burns conferred a state of sensitization, which in turn confers a certain immunity or resistance toward burns.

The experiments of Rosenthal (86,87), 1937, are one of the most recent units in evidence of the toxic theory. If these can be confirmed they certainly represent strong reasons for adopting this idea. Rosenthal found a substance in the blood of burned shoats, adult pigs, guinea pigs, and human beings that caused contraction of a virgin guinea pig uterus. The substance was at first linked with the red blood corpuscles, but it was later found in the serum. It differed from histamine in several ways. The sera of shoats, pigs and human beings that were burned were tested on the guinea pig uterus. However, normal serum has this action to some extent. No controls using blood concentrated by some other means than by burning alone were used in these experiments.

BACTERIAL THEORY--Aldrich (1), 1933, aroused interest in this theory and to combat bacterial action gentian violet was introduced as a method of treatment. For the first twelve hours, the burn areas were found to be sterile. After this period it was found that in about 100 per cent of the severely burned patients and in a large majority of the minor burns the beta-hemolytic or gamma streptococcus could be grown from repeated cultures. The concentration of these organisms increased with the obvious signs of

sepsis and the beginning of toxicity of the patient, until after 48 to 56 hours pure cultures of the streptococcus would be obtained having outgrown all the other organisms. Coincidentally, the characteristic bad effects of the burn were shown by the patient.

Clark and Cruickshank (21), 1935, believed that infection of burns, particularly by Streptococcus hemolyticus, is common even with tannic acid and is responsible for the fever and toxemia during the first four or five days of the illness. Therefore, they added 20 per cent dettol to the tannic acid and even suggested the administration of scarlet fever antiserum. Cruickshank (25), 1935, reported detailed bacteriological studies of burns. He believed that the high incidence of infection by this organism is probably favored by the congregation of patients in wards, as he discovered hemolytic streptococci in the throats of patients more frequently during their first week in the hospital than at any other time of their admission; these bacteria were numerous in the atmosphere and dust of the wards in which the burns were treated.

Harkins (46a), 1936, reported that in a series of burns the only two fatal cases within the first three weeks resulted from sepsis. The first of these was a male, aged 44 years, with second degree burns of the left leg, face, neck, thorax, and arms; third degree burns of hands and forearms, following a gasoline explosion. Blood concentration with hemoglobin, 140 per cent, and red count, 7,200,000, was noted 24 hours later. On the seventh day pyarthrosis of the left knee due to Streptococcus hemolyticus with a fever

of 106.6°F. each of the last six days of life and at necropsy a typical Curling's ulcer was found. These cases demonstrate that not only many of the toxic manifestations present after the first few days but also some of the complications of burns may be explained on the basis of a septicemia, although this is not conclusively proved. However, these cases do not have marked infection during the first 24-48 hours, which is the time when shock with blood concentration and low blood pressure, low cardiac output, and low blood volume occur. Death from true secondary shock usually occurs in the first day after the burn, which is earlier than infection becomes active.

Blood Chemistry Changes Produced By Burns

According to the physical theory of the production of shock in burns, the minor qualitative changes in the various blood constituents are of less importance than in the quantitative reduction in the amount of blood as a whole. This is said to be caused by the loss of plasma, and the fact that albumin may be lost in slightly greater quantities than globulin and sodium chloride to a larger extent than sugar depends merely on a somewhat selective permeability of the burned capillaries for smaller molecules.

Blood chemistry changes have been noted following burns, and to many they represent the cause rather than the result of the shock factors present. Davidson (28-30), 1926, 1927, made an extensive study of the chloride and protein metabolism in burns. He found a significant lowering of whole blood and plasma chlorides. This was believed due to a lowering of the plasma chlorides below the renal threshold rather than to a primary kidney change. Davidson also found a hypoproteinemia with especial reduction in the amount of albumin. Underhill and other (105), 1930, also found a lowering of blood chloride (whole blood) while McIver (71), 1933, found normal plasma chlorides. It is to be pointed out in this connection that in such marked blood concentration and altered hematocrit and a difference in the chloride concentration of the cells and plasma a chloride study of both cells and plasma should be made in burned patients. Therefore, since the cells normally contain less chloride than plasma and since in burns the cells are increased this would

explain the finding of low whole blood chlorides on the basis of the hematocrit changes alone but would not account for the difference in the results on plasma chlorides reported by Davidson and McIver.

Cicala (16-20), 1935, working on rabbits, reported a decrease in blood chlorides, and an increase in non-protein-nitrogen. He believes that some of the increase in nitrogen is due to histamine-like substances. The creatinine and uric acid increased, the latter he believed being due to renal tubular damage secondary to traumatic shock. He found the reduced glutathione of the blood to be increased. It is to be remembered that hematocrit changes alone may explain many of these changes in non-protein-nitrogen, etc, when done on whole blood. Christophe (24), 1933, finds that the presence of albumin in the urine, increased non-protein-nitrogen, hypochloremia, and low albumin:globulin ratio become most marked ten days after experimental burns in dogs. Lambret and associates (56,57), 1936, have reported increased non-protein-nitrogen and hypochloremia, but their results are not open to the criticism that blood concentration changes alone may account for the alterations as their protein analyses were done on plasma and cells with reduction in both instances.

Mattina (63), 1935, reports an increase in the concentration of the blood magnesium of burned rabbits. The increase began 24 hours following the burn, reaching a maximum in ten days and returned to normal in 40 days. Fazedas and Bacsich (34), reported

an increase in lipoid bodies in the blood leucocytes beginning in five hours reaching a maximum in 24 to 48 hours, and returning to normal after five or six days or longer. In fatal cases these bodies increase up to 24 hours and an hour before death may suddenly drop to below normal in number. Slocum and Lightbody (95), 1931, reported that in both normal and adrenalectomized rabbits the sugar and lactic acid concentration of the blood is increased following burns. Since the adrenalectomized rabbits also showed the rise, this is interpretated as indicating that adrenal hyperfunction is not a factor. Van der Hulst (110), 1937, reported a decrease in the rapidity of the sedimentation of red cells during the first 24 hours with marked increase thereafter. These changes were not due to infection or blood concentration. Fasal (33), 1937, found a shift to the left and toxic granules in the leucocytes.

Analyses of the edema fluid that leaks out into the tissues after burns are of interest. The chloride content is a little higher than in plasma, the sugar and non-protein-nitrogen contents are about the same, and the protein content about 80 per cent of that of plasma (Beard and Blalock (6), 1931; Underhill and Fisk (103)).

Underhill and associates (102), 1923, found percentage of hemoglobin in 21 cases of severe burns between 117 and 209. Ravdin and Ferguson (80), 1925, noted a hemoglobin of over 100 per cent in all but two of their clinical cases.

CONCLUSIONS

From this merely representative transection of the mass of work edited upon this subject the lack of uniformity is egregiously apparent. In gross analysis, however, it seems to conform with the various sequential stages previously proposed.

PRIMARY SHOCK- Concomitant with the occurrence of the injury the individual may experience a condition of low blood pressure of varying degrees. This is attributed to derangement of the vasomotor mechanism by afferent impulses of pyschic or reflex origin. This period of primary shock has been specified as the two hours immediately following the accident. During this first two hours there is no noteworthy change in the blood chemistry or corpuscular sedimentation rate. The hemoglobin is also usually normal. This may then be considered as a transitory phenomena which quickly passes away or responds to treatment within a reasonably short period.

SECONDARY SHOCK--This may be described as a hypotension occurring between the second and tenth hours subsequent to the injury. The features of surgical shock always appear once the main collapse of the arterial pressure has begun. This phenomena is due to an anhydremia or increased concentration of the blood. This is detected and most accurately recorded by the rise in hemoglobin which may attain an average height of 115 per cent. This extravasation having started with the occurrence of the burn, reaches a peak in twenty-four hours, is practically stationary for twenty-four hours, and then is slowly resorbed. Underhill and his colleagues have

shown that there is no resorption for the first twelve hours which eliminates the possibility of toxic or septic etiology in this stage. There seems to be a direct relation between the extent of the skin surface involved and the rapidity and severity of the shock. Depth is likewise a factor. No constant change in blood chemistry was noted, and even the carbon dioxide combining power, a fall which is generally regarded as characteristic of traumatic secondary shock, was rarely significantly lowered. (120)

ACUTE TOXEMIA--The occurrence of toxemia is much more erratic and uncertain than that of secondary shock; it may follow lesions of small or moderate extent after which secondary shock is rarely seen. Further, it is frequently absent or mild. The first sign is usually vomiting accompanied by hyperpyrexia, which is characteristic, usually persistent and progressive, accompanied by shallow respirations and cardiac failure. The onset may vary from six to fifty hours, usually twelve to fifteen hours. There are frequently no blood changes. During a fulminating toxemia the leucocyte count may remain normal and the sedimentation rate unchanged. Analysis of the blood chemistry usually reveals a decrease in chlorides, carbon dioxide combining power and plasma albumin, and a rise in non-protein-nitrogen and urea nitrogen. These are neither constant or proportional to the severity of the systemic disturbance.

SEPTIC TOXEMIA--Although Aldrich (1) attempts to show that the toxic state may be due entirely to a septicemia, Wilson and his associates (120), 1938, state that "there is little doubt that acute

toxemia is a condition distinct from septic or bacteriogenic toxemia". Sepsis may become evident on the second or third day and continue on through the next few weeks. Relative to time of appearance and period of activity the acute toxemia and sepsis may be considered under a single head as does Harkins in a recent paper.

HEALING--This phase is beyond the scope of this paper and will be mentioned only in the consideration of therapeutic measures.

PRINCIPLES OF TREATMENT

The logical consummation of such theoretical and experimental endeavor is the establishment of fundamentals from which a superior therapy may arise. That the present management of burns surpasses any preceding, we are assured, but, nevertheless, momentarily humbled by the knowledge that our present tannic acid therapy was used by the Chinese in 5000 B.C. in the form of tea. (47) The superiority of present day therapy is attributable to the consideration given the constitutional symptoms of the patient beyond the local treatment.

With full understanding of the sequence of the various phenomena attendant upon severe burns the problem of treatment is somewhat simplified.

PRIMARY SHOCK--The treatment of initial shock is essentially that of other types of shock; sedatives to suppress the afferent stimuli, warmth to maintain body temperature and cardio-respiratory stimulants to sustain these vital mechanisms. Frequently, however, his phase will have passed or terminated fatally before the patient is seen by the physician.

SECONDARY SHOCK--This is the period of increase blood concentration. The anhydremia must be combated from two aspects: inhibiting the loss of fluid, and, replenishing the lost fluid. To this end Wilson, Macgregor and Stewart (120), 1938, advise immediate coagulation of the burned area and intravenous gum acacia solution or blood. The coagulum serves to prevent the loss of fluids and

chlorides by sealing off the capillaries. The colloidal solution is recommended because several writers have reported that large quantities of intravenous saline or Ringer's solution alone may prove harmful. Beard and Blalock (7), 1932, have shown in experimental animals, that a crystalloid solution if injected, carries more protein out of the blood stream than would have been lost were the animal left strictly alone. Blood transfusion is especially advised by Riehl (81,82), 1932, 1933. Since the blood is concentrated, the possibility of giving intravenous plasma rather than whole blood is to be considered. This procedure is not generally adopted but is used by Lambret and Driessens (56), 1937, and by Weiner, Rowlette and Elman (112), 1936. Certainly until the matter is finally settled, if blood is available, blood should be given. Furthermore, even though the recipient's blood is already concentratied, the donor's blood is relatively dilute in comparison. The use of saline and other crystalloid solutions should be undertaken with the full understanding that they not only run right through the capillary wall, but may carry valuable blood constituents with them, leaving the blood more concentrated in red cells and lower in plasma volume than before. (120) Working under other ideas, Gunn and Hillsman (43), 1935, advise giving 5000 cc. of saline solution intravenously immediately in severe burns. McCandy (70), 1938, suggests the use of suprarenal cortex. This extract, as in the case of Addison's disease, increases the efficiency of the circulatory mechanism and apparently checks some

of the salt loss through the kidneys.

ACUTE TOXEMIA--From the previous discussion one concludes that toxemia results from the toxins absorbed into the circulation from the burned tissues; also, form the work of Underhill and his associates, that there is no resorption at the burn site for the first twelve hours. This knowledge permits of various theoretical therapeutic approaches. It is self-evident that treatment, relative to the potential toxemia, within the first twelve hours subsequent to the injury permits the therapeutist to be the aggressor--the toxin being still localized within the burned tissues. Coagulation, or eschar formation, serves to fix the burned tissues and seal in the toxin, preventing its dissemination. In respect to the numerous benefits derived from a protective eschar it is only just to discuss the subject at greater length, which shall be done shortly. Another method of inhibiting the advance of the toxin is that proposed by Ravdin and Ferguson (80), 1925--removal of the offending tissue, or debridement. This method was opposed by Taylor (99), 1936, who believed that it removed skin islands which may be left, and by the experimental work of Harrison and Blalock (50), 1932, who showed that burned animals are more likely to die if debridement is performed.

Working upon the theory of withdrawing the toxins from the burned tissues some prominent workers have advocated the external application of hypertonic solutions. Wilson (116), 1927, is a proponent of this theory of exosmosis, advocating sodium chloride

and glycerin and later a saturated boric solution. Robertson and Boyd (84), 1923, and Goldblatt (42), 1927, use hypertonic soda bicarbonate solutions.

Once the toxins have gained the blood stream--after twelve to twenty-four hours--Robertson and Boyd (84), 1923, propose its rather heroic removal by exanguination, accompanied by transfusion. In a similar vein, to combat the toxin at this point, it would be most advantageous if one were able to inject a neutralizing substance. This, however, is at present impossible as has been shown by the marked divergence of opinion and lack of any definite proof regarding the identity or singularity of such a substance.

SEPTIC TOXEMIA--Aldrich (1), 1933, has shown that the heat required to produce the injury served to render the burn sterile, which state he observed to persist for twelve hours. Hence, as was the case in the treatment of acute toxemia, the physician is accorded a certain grace period between the occurrence of the injury and the earliest possible onset of sepsis. Prophylacticly, then, it is theoretically possible to seal the burned area with this period and thus obviate the possibility of subsequent infection. This was accomplished quite satisfactorily, though not ostensibly, by the tannic acid treatment introduced by Davidson in 1925. However, following his studies on the bacterial theory, Aldrich, after some experimentation with various antiseptics advocated the use of gentian violet to supercede the tannic acid treatment because of its coagulant and analgesic effects and its

specific bacteriacidal powers against the gram-positive cocci. In addition to this, it is claimed that gentian violet is less injurious to the small islands of epithelium that persist in the burned area and, hence, epithelization occurs faster than with tannic acid. Some workers who choose to see especial advantages in each use a tannic acid-gentian violet mixture and purport satisfactory results. (22)

Crile (23), 1936, in an apparently unbiased consideration states that both tannic acid and gentian violet have antiseptic properties and either, when applied to a second degree burn, will result in an eschar which will be dry and free from infection. But, neither of these agents is capable of preventing the ultimate development of pockets of pus beneath the eschar in areas of third degree burn. He further observes that he has found little choice between the two methods.

Wilson and his associates (120), 1938, report in their cases that the local signs of bacterial infection of deep burns was rarely present before the fifth day, and usually not obvious before the seventh day. Even in fatal septicemia and pyemia, hemolytic streptococci did not appear in the blood before the ninth day. With this data they suggest the use of sulfanilamide administered by mouth on the third day as a prophylactic measure, with supplementary doses intramuscularly at the first sign of infection with the hemolytic streptococci. Clark and Cruickshank (21), 1935, have suggested the administration of scarlet fever antiserum in the latter event.

Marsh (61), 1935, a radical supporter of the bacterial theory, without definite evidence to show that a staphylococcal infection existed, went on to advise empirically "that every case of severe burn should receive intravenously at the earliest possible moment an injection of staphylococcus antitoxin..."

If the observations of Crile be correct it would be folly to cover a burn of third degree with an eschar, in view of the fact that its subsequent removal would be inevitable. To obviate this contention it would seem adviseable to maintain this type of wound open for repeated inspection. This may be nicely accomplished the constant application of moist saline packs supplemented by hypertonic saline baths as advocated by Blair, Brown and Hamm (10), 1932. This treatment has great value from the standpoint of promoting rapid healing with a minimum of infection and scarring. It, however, is less efficient in that it requires more equipment and nursing care.

HEALING--It is not my intention, herein, to consider this subject beyond a cursory summation of acceptable data. We learn from clinical deduction that if there is rapid and widespread healing and return to function without much scarring or deformity, this means that the full thickness of the skin has not been lost, and that regeneration has occurred from the deep glands of the derma. This point of rapid healing is of importance in evaluating various types of treatment of burns, because, when it is claimed that a certain method will insure complete healing without scarring, it

is apparently not realized now healing occurs. If the full thickness of skin is lost over a large area, the result is a raw surface or open wound, regardless of the type of treatment employed. In this case spontaneous healing occurs by an extension of epithelium from the sides, thus covering granulations that are converted into scar. (10) The size of these defects is relative for various parts of the body: a loss of an eyelid or the back of a hand of only a few square centimeters may be as crippling as a very large loss over the flank or thighs. (14)

The thin scar epithelial heling, that is so important in saving life, is many times not of sufficient strength to give the permanent surface necessary for the area. The unstable parchment-like membrane tends to crack or tear with the slightest trauma. The thick, redundant scar, on the other hand, is definitely to be avoided because of the subsequent contracture and deformity, which is a matter of common observation. Consequently, where there is danger of loss of function or of deformity, or in an area subjected to trauma the wound should never be allowed to heal by slow epithelization but should, in the experience of most current workers, be treated by early and adequate grafting, the type of graft depending upon the area to be covered and the site. To this end, the saline pack method of preliminary treatment proposed by Blair, Brown and Hamm (10) may again be mentioned as being of outstanding value.

COMPLICATIONS

CURLING'S ULCER--This complication of burns was described by Long (60), in 1840, and by Curling (26), in 1842. Since then sporadic reports of peptic ulcer following burns have appeared in the literature including recently the reports of Willems and Kuhn (115), 1936, Glover (41), 1937, and Kapsinow (55a), 1934. The latter attributes them to blood stasis and concentration with capillary oozing and rupture, while other authors believe them to be toxic in origin. Glover (41), 1932, states that bleeding from a Curling's ulcer accounted for 4 per cent of his deaths.

Underhill, Kapsinow and Fisk (107), 1930, assumed, from experimental data, that the ulceration might arise from local circulatory disturbances due to a temporary increase in the temperature of the body cavities. Curling's ulcer has been reported, however, in cases in which the abdomen was not burned. Harkins (46a), 1936, reported such an ulcer in a burned patient who died with marked sepsis subsequent to the development of a peritonsillar abscess. In such a case bacterial emboli are to be considered.

LESIONS OF THE RESPIRATORY TRACT--Them most common respiratory lesions are bronchitis, bronchopneumonia and pulmonary edema. The mucous membrane of the mouth, nose, pharynx, larynx and trachea are frequently very little affected although extensive sloughing may at times be found. Such lesions of the respiratory tract tract are believed to be caused by direct injury to its lining membranes by inhalation of flame. hot air or hot fluid. Pulmonary edema,

however, was found to be a common lesion in cases of fatal acute toxemia and apparently was prone to develop when large quantities of fluid were administered intravenously. (120)

JAUNDICE--Most have come to regard jaundice as one of the signs of acute toxemia rather than a complication, the findings being in accord with a toxic jaundice.

SCARLATINA--This is thought to be an idication of hemolytic streptococcal infection of the burned area.

TETANUS has been frequently reported as a complication of burns. Newberger (74), 1912, reported two cases and collected 47 from the literature. Of the 49 cases 38 died, making a 77 per cent mortality. Fasal (32), 1935, reported on the extensive burn material in the skin clinic of Vienna. Of 2,327 burn cases seen from 1905 to 1930, not a single one developed tetanus, but in both 1932 and 1934 there was one case thus he believes prophylaxis is to be considered. Willems and Kuhn (115), 1936, stated that of 752 collected burn cases only 23 received antitetanic serum, but as none of the other 729 cases developed tetanus, the physicians in attendance on those particular cases evidently did not use poor clinical judgment in refraining from administering serum.

FAT EMBOLISM is a rare complication of burns but Strassmann (97), 1933, reported on 125 cases of fat embolism due to blunt force and five following burns. He quotes Carrata as saying that in 46 per cent of burn cases coming to autopsy fat emboli are found.

Globus and Bender (40), 1936, reported a case of FATAL DISSEM-

INATED TOXIC DEGENERATIVE ENCEPHALOPATHY (disseminated sclerosing demyelination) in an eight year old boy following severe burns.

MALIGNANCY--Treves and Pack (100), 1930, have reported a large series of carcinomas developing in burn scars (Marjolin's ulcer). Of 1,091 squamous cell and 1,374 basal cell carcinomas treated over the twelve year period 1917 to 1929, 21 (2 per cent) of the former and 7 (0.3 per cent) of the latter followed burns. The average age of the patients as a whole was about 59 years and was 54 years for the burn cases. However, the age of the burn was more important than the age of the patient, as one case burned at the age of three years developed carcinoma at the age of 17 years. The average age of the scar was 32.5 years. Harkins (46a), 1936, reported two cases of sarcoma following burns. It has been repeatedly shown that such malignancies are most prone to develop in slowly or poorly healed burns.

PAIN AND CONTRACTURES--When a large wound has been open over a long period, the pain usually becomes most severe, presumably from more nerve endings developing in the bed; this forms a bad cycle for any proper wound care and is one of the underlying causes of morbidity and death in old, unhealed burns, since both patient and attendant become unable to cope with the situation.

The secondary consideration of the whole area is one of contracture and deformity of the surface, tendons and joints. Displacement and fixation due to skin and surface contracture as the wound pulls in toward the center may be called primary contracture.

All wounds exhibit this type of healing, and the more lax the area is, the easier the healing with the least apparent deformity, but widespread losses will soon lead to primary contractures and disability.

Secondary contractures may be considered those that occur in the underlying tendons which, though not damaged directly, have been held contracted so long, both voluntarily and later by the overlying scar, that they are actually shortened.

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