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Burn shock : etiology, objective findings and therapeutic implications

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BURN SHOCK:

THE ETIOLOGY, OBJECTIVE FINDINGS

AND THERAPEUTIC IMPLICATIONS

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INTRODUCTION

The choice of a topic for a thesis to be written in the senior year of medical school seemed to be particularly difficult. A piece of work which constitutes approximately one-third of the work of the senior year should be of much more than passing interest. It also should do much more than merely acquaint the writer with the QUARTERLY CUMULATIVE INDEX and the names of some of the authors on a certain subject. At the same time the subject should be broad enough to be applicable to any branch of medicine which the writer may later choose. In addition the subject should have some basis in both experimental and clinical medicine. And lastly the thesis should be written upon some subject which is of contemporary interest and in which there is or has recently been some variation of opinion and evidence. Burn shock seemed to fulfill most of these requirements.

The scope of this paper is limited. The general history of burns, burn treatment and burn shock and the etiology of burn shock is given as part of the background. As further basis for the etiological considerations of burn shock some information on the local and general pathology is included. Laboratory findings on studies of the blood, urine, and edema fluid are included as a foundation for the more modern theories of the etiology of burn shock.

Burn shock is considered under the headings of 1)primary shock, and 2) secondary shock. Secondary shock is further considered under pathology, pathological physiology, symptology, etiology, and treatment.

Without attempting to be entirely complete a short discussion of treatment according to physiological principles is included. The fundamental trends of treatment today are clearly indicated by etiological considerations of burn shock. Local treatment is emerging from its state of flux of the past five years and is becoming more standardized.

The importance of burn shock is evidenced by its peace-time incidence and mortality. Six thousand persons died of burns each year in the United States before the onset of this present war (Harkins, 1942). Before the advent of the tannic acid treatment of burns the mortality in a large series of cases was 38.5%, but was reduced to 10.5% by this method of treatment. Sixty to eighty per cent of the deaths from burns are due to secondary shock (Wilson, 1928; Atkins, 1940; Harkins, 1942). In the present war heat burns constitute one of the greatest problems of management (Siler, 1944). The importance of correct therapy is shown by Elman's (1943) analysis of 78 fatal cases in which "...failure to use plasma transfusions at all or in inadequate amounts..." was probably the chief factor in early death.

The inter-relationship of the various clinical kinds of secondary shock is best stated in the words of Harkins (1940):

> "The shock that results from injury, whether that injury be caused by mechanical, thermal, chemical or operative trauma, is quite similar in all cases. The chief theories as to the causation of such shock are the toxic, the nervous and the physical theories....Some authors believe that two or all of these factors are of importance."

Beard and Blalock (1931--VIII) found that severe trauma caused whole blood loss, that mild trauma caused a smaller proportion of blood cells in the edema fluid, and that burns caused loss of almost pure blood plasma into the traumatized tissue. Later findings of Blalock and Duncan (1942) led these men to state that "It will be very surprising indeed if a constant early diagnostic alteration which is common to all types (of secondary shock) is found." They advocate use of descriptive terms:burn shock, traumatic shock, operative shock, hemorrhagic shock, to abolish inaccurate use of the term, "shock." Harkins' view is probably best substantiated by clinical and experimental findings; all types of secondary shock are related in etiology.

DEFINITIONS

Burns, burn shock and shock in general have been defined in several ways. The great French surgeon, Dupuytren (1835) defined a burn: "The organic lesion, called the burn, ustion, combustion, and so forth, is the effect of the concentrated caloric upon living tissues." Harkins (1938) states that "Burns are but a type of trauma, thermal in this instance, and trauma is but a noxious influence which, when severe, overtaxes the compensatory and recuperative powers of the animal organism." Siler (1944) takes the same view more simply: "A burn represents a thermal injury to the skin and underlying tissues." Loss of protective function of the skin and injury to the vascular endothelium of dermis and muscle are thus included.

Cope, writing in the symposium upon the Cocoanut Grove disaster in Boston (1943) decided that burn shock was a "...low blood pressure shock, with hemoconcentration and diminished blood volume due to loss of plasma into the burned area." He, like many experimental and clinical contemporaries, found that in the burned area the capillaries were permeable to plasma protein so that a plasma-like fluid entered the extracellular spaces from the injured vessels; normally only water and electrolytes of the blood pass into the extracellular spaces (Harkins, 1942; Bayliss, 1920; Star-

ling, 1896).

Moon (1938) states that "Shock is a circulatory deficiency, neither cardiac nor vasomotor in origin, characterized by decreased blood volume, decreased cardiac output and increased concentration of the blood." This definition fits the usual picture found in burn shock and the shock following slow hemorrhage, but it does not apply to the picture found in acute, massive hemorrhage. In the latter condition hemodilution rather than hemoconcentration occurs (Davis, lecture, 1944). Some authors concern their definition chiefly with the disparity between the blood volume and the capacity of the vascular system. "Shock is a condition of peripheral circulatory failure brought on by a discrepancy between volume of circulating blood and size of the vascular system and leads to deficiency in blood supply to the tissues of the body. This discrepancy may be due to decreased blood volume or increased capacity of the vascular system or to both." (Blalock, 1942.)

Militarily a sufficient definition is that shock is "...the train of symptoms resulting from decreased circulating blood volume." This statement points the way to prevention and correction of the condition of shock, of whatever source. (Bowers, 1941)

A definition of hemoconcentration is in order since, though it is getting somewhat ahead of the story, hemoconcentration has been shown to be fundamental in the development of burn shock. Moon (1939) defines hemoconcentration as a rapid increase in the

erythrocyte count of the blood. This he demonstrates by hematocrit readings, specific gravity determinations and red blood cell counts. Six million red blood cells per cubic millimeter of blood is indicative of mild hemoconcentration, and nine million represents a severe condition.

In summary, then a burn may be defined as a local lesion caused by an excess of thermal energy on skin and underlying tissues. Shock may be defined as

> "...an oligemia initiated by traumatic fluid loss, either plasma or whole blood or both and accompanied by decreased cardiac output, diminished volume flow, lowered venous pressure, decreased oxygen consumption, arteriolar vasoconstriction, acapnia, and secondary blood pressure fall; and perpetuated by a summation of these factors and possibly hyperpotassemia, increased generalized capillary permeability, anoxia, action of tissue metabolites and deficiency of adrenal cortical hormone."

Or more shortly: "Shock is a progressive vasoconstrictive oligemic anoxia." (Harkins, 1942.) Burn shock is then defined as merely the foregoing condition initiated by thermal trauma.

HISTORY

No exact division of the history into burns, burn shock, shock in general, and the treatment of burn and burn shock can be made. However, an attempt will be made to consider these subjects as entities while demonstrating their inter-relationships.

Shock in General

The term "shock" was first used in 1795 by James Latta of Edinburgh to describe the state of collapse and the syndrome with which the term is usually associated today (Harkins, 1941). The useage did not become common until considerably later. In 1870 Fischer used the word shock descriptively in the sense in which it it used today in medicine and surgery.

O'Shaughnessy noted the shock-like condition of collapse and dehydration in cholera patients in India; Thomsen analyzed the blood of cholera patients. These findings and history are discussed by Scudder (1940). O'Shaughnessy and Thomsen did their work approximately seventy years ago.

Harkins (1942) divides the historical treatment of shock writings into three phases:

1. Speculative and experimental--1870-1898
2. Experimental physiology--1899-1923
3. Experimental clinical--1923-1944.

In the first period the German workers dominated the field: Wertheim, Weiskotten, Tappeiner, Wilms, V. Lesser and many others

are quoted by Locke (1902), Bardeen (1898) and Harkins (1941). In general these men leaned toward a nervous-vasomotor exhaustion etiology of shock with stagnation of the blood in the splanchnic areas. This theory was shown to be false in 1919 by Wallace, Fraser and Drummond (Harkins, 1941).

Sherrington and Copeman (1893) and Turck (1897) demonstrated dilution in hemorrhage and concentration of the blood in other types of shock (Harkins, 1941). Bardeen is one of the best sources of historical information. His article in 1898 reviewed the experimental work before his time and found it scanty. He reviewed and discussed the pathological findings and theories of shock presented by men who preceded him.

The period 1899 to 1923 contains the work of the surgeons and physiologists of World War I. The Allied Shock Committee, The Medical Research Committee Reports of Britain (1919) and Cannon's monograph (1923) were the chief products of this period. In 1902 Locke presented a survey similar to that written by Bardeen four years earlier. The Medical Research Committee Reports stressed the principles of care for wounded in the first war; these principles are largely applicable in World War II. C. S. Wallace in the introduction states the deleterious effect of a limited water supply upon the reserve of the wounded soldier. He stresses early care in the Casualty Clearing Stations to prevent shock. Primary shock, Wallace states, is probably nervous in origin; for secondary shock he stresses that warmth, rest,

and fluids by mouth, rectum and by clysis are of value.

In the experimental-clinical period since 1930 the leaders have been Blalock, Harkins, Underhill, Davidson, Moon, Scudder, Bayliss and Wilson. In a series of nine articles (1930-1931) Blalock with various collaborators did much experimental work on various types and phases of shock. He came to the conclusion that fluid loss was the primary etiological factor in shock. His work continues to be published in outstanding journals, and his position as surgeon-in-chief at Johns Hopkins Hospital is evidence of his preeminence in his field.

Tracing the development of Harkins' ideas and experiments on shock and the therapy indicated by his investigations would be a thesis in itself. From the University of Chicago (1934) Harkins published articles corroborating Blalock's unilateral burning experiments and showed that there was sufficient increase in weight of the burned side (2.1% of the body weight) to account for many of the symptoms of shock in the animal. At Ford Hospital he continued his experiments and writings, investigated all types of trauma, and came to the conclusion that thermal, chemical, bacterial, mild continuous mechanical, and capillary injury due to inadequate circulation all caused shock by essentially the same mechanism (Harkins, 1937). At present he is doing work at Johns Hopkins Hospital. His book on THE TREATMENT OF BURNS is considered the best in its field (Blalock, personal communication).

Underhill (1919, 1923, 1930) was stimulated by his work on

war gases while in the chemical warfare service. But the New Haven theater fire gave him the opportunity and impetus to investigate thermal burns in humans. He came to the same conclusions as Blalock. He thought fluid loss from the surface and into the injured tissues sufficient to cause hemoconcentration and shock.

Davidson (1925, 1927) investigated the plasma proteins in six cases of burns and suggested that the rational manner of treatment lay in some form of local treatment, which would prevent absorption of autolytic products of protein decomposition. As a result of his investigations he suggested tannic acid in water and glycerine to precipitate proteins and prevent toxicity (1925). This began the modern treatment of burns so far as local therapy is concerned, though today the tannic acid is being discarded in favor of less toxic substances and compresses. More beneficial methods of treatment have been found, and his theory of toxic product absorption is questioned by later writers.

Moon's books SHOCK AND RELATED CAPILLARY PHENOMENA (1938) and SHOCK: ITS DYNAMICS, OCCURENCE AND MANAGEMENT (1942) suggest the logical approach to the etiology of shock through investigation of the pathology of the condition. Walter B. Cannon states in the foreword that Moon's book suggests the applicablility of pathological findings in explaining other conditions besides "traumatic shock -- for example, cholera, certain metallic and bacterial poisonings, heat stroke and severe burns." The inter-

relationship between the shock syndrome and the physiology of the capillaries and other portions of the vascular system became apparent to Moon; and he, as a result, became interested in such phenomena as "urticaria, edema, inflammation, the localization of infection, anaphylaxis, or adrenal cortical function." His book then is the attempt to fit together these jig-saw-like bits of information and lines of research into a satisfying whole. He states his shortcomings but rightfully states that his work may stimulate others to complete the picture into a logical map of the whole.

Scudder has already been mentioned as the author of a book on BLOOD STUDIES AS A GUIDE TO THERAPY (Lippincott, 1940). He traces the history of shock back to 1773 and Stephen Hale, the English minister who noticed the venous constriction and increase in venous pressure as animals bled to death. Scudder also mentions the Frenchman LeDran and credits him through an English translation of first using the word "shock". He points out further that John Hunter used the term "shock" in a publication in 1840, and that James Latta used it to describe a condition following the treatment of epilepsy with electricity as done by Benjamin Franklin. In a seven-page review of the historical conceptions of the theory of the etiology of shock, Scudder lists Hale and LeDran as at least indicating that vasoconstriction and capillary congestion with increased venous pressure were part of

the syndrome. Cannon and Bayliss are listed as exponents of the toxemic theory of the etiology of shock. These men were opposed by Phemister, Blalock and Johnson, who favor fluid loss as etiology. Sherrington is given as authority that loss of cirsulating fluid is cause of shock. Pare and others advocated the neurogenic theory of the etiology, among these others being Dupuytren, (1835) who said "...pain is the cause of death." Brown-Sequard and the early writings list the importance of the adrenal exhaustion in formation of shock. Scudder himself is an important contributor to the information concerning the blood cnemistry in shock and allied conditions.

Bayliss (1920) was interested in the function of the plasma proteins in maintenance of osmotic pressure of the blood and the prevention of tissue edema; but he was also concerned with the etiology of shock as a capillary phenomenon. He theorized that:

> "The toxic product responsible for the results of tissue injury are removed in some way, with a fair degree of rapidity, if the circulation is normal. They may perhaps be converted into non-toxic substances by the liver or perhaps oxidized. Probably they are to some extent excreted in the urine. The importance of raising the blood pressure high enough to reestablish the action of the kidney is recognized in cholera. The effect of massage -- shows that the effect of a suddenly increased passage into the circulation is temporary."

He states that vasoconstrictors are incorrect therapy for shock because the tissued are already anoxic and the mere increase in blood pressure without increased blood is valueless. Bayliss ruminates on the possibilities of using gum acacia in the therapy

of burn shock as well as in other types of shock. Saline, he states, was shown to be valueless in the first World War.

Wilson (1928, 1937, 1938) is an English Writer who, in the face of much contemporary evidence that fluid loss is largely responsible for the syndrome of shock, still clings to the idea that absorption of toxic products from protein breakdown, absorbed into the general circulation from the burned or traumatized area, are largely responsible for the stage of "toxemia" which he states follows the period of shock. The toxemia is considered part of shock by many of the modern investigators. Wilson is able to extract toxins from burned material and to demonstrate toxicity of the edema fluid from burned areas. Wilson refers to the success of the tannic acid treatment in reducing mortality and attributes it to prevention of "...absorption of toxic products from the burned area."

This history of shock demonstrates that the history is a long one. Secondly it shows that men of all countries and many professions have been intrigued by shock. The surgeon was interested because of the mortality in patients operated upon in shock. The physiologist was interested because of the vascular phenomena. The pathologist wished to know the terminal findings in etiologically unrelated types of shock. Therapists wished to treat and to prevent shock. As a result there was until recently a confusion regarding the supposed dissimilarity between various kinds of shock. The different groups looked at shock like the blind men

describing the elephant. Their therapies were similarly varied. With the beginning of experimentation on shock the observations of World War I became organized into more coherent grouping of observation, experimentation and treatment. Similarities between various types of shock became evident; therapy of the general condition became more standardized, though in many cases the treatment of the local concommitant conditions were still treated in varying ways.

Wiggers (1941) however, appears to have decided that animal experimentation confused rather than clarified the problem. He States that the criteria of shock in humans--skin pallor and generalized sweating--are absent in animals; that the facies, apathy and muscle weakness are obscured by anesthesia in experimental animals. He states that the barbiturates which are commonly used for shock experiment anesthesia do not allow the true picture to be revealed. Wiggers also states that many modern workers are investigating pre-shock rather than true clinical shock.

Still, Wiggers' attitude seems to set back the knowledge instead of advancing it; for pre-shock is easier to treat than shock. The cardiovascular signs he decries as being used as criteria of shock--lowered blood pressure, increased pulse rate, thready pulse and pale mucous membranes--are also present in humans. And reversal of the trends these signs indicate prevents the inception of the true, but often irreversible, shock of Wiggers.

Burns in General

Burns have both a local and a general pathology. Dupuytren

(1835) was probably the first to divide the cutaneous burns into degrees such as we use today. He described six degrees of burns from erythema to and through total carbonization of the part. Berkow (1924) devised a method of estimating the area of burn by dividing the surface area of the body into regions and assigning to them their proper percentage of the total body area. Carrying on almost to the degree of absurdity, Dingwell (1943) describes a method of using flourescine intravenously to determine the degree of burning. The method still leaves clinical judgment as the method of differentiating between second and third degree burns.

"Curling's ulcer" is often described as one of the systemic pathological quirks following extensive burns. Though Curling is given the credit for discovering this oddment, Bardeen quotes Long (1840), several years before Curling, as the discoverer of duodenal ulcer following burns. Locke (1902) notes that Wertheim and Schultze in 1863 studied the pathology of the kidneys in corpses with extensive burns. Both found extensive thromboses and deposition of hemoglobin crystals in the large collecting tubules. They also noted a leukocytosis and variability in the proportion of red blood cells. Bardeen (1898) did autopsies on five patients who died following extensive burns. Weiskotten (1919) made special notation of the swelling and redness of the suprarenal glands following burns. He was impressed with the appearance of the suprarenal and the lymphoid tissues of the whole body. Following this observation much of the burn symptomatology was ascribed to adrenal damage.

V. Lesser (1881) is quoted by Locke as finding that there was free hemoglobin in the blood serum after burns. Lesser's conclusion, substantiated by experiments on burned rabbits and dogs was that this constituted a loss of "function" of the red blood cells. Locke found that Lesser had written in 1881 that dyspnea in burned patients was due to an extreme anemia, due chiefly to functional loss in the red cells. Schultze (1865) is also listed by Locke as having found that heat caused fragmentation and loss of coloring material of the erythrocytes.

Cope (1944) demonstrated hemoglobinuria in many of the patients treated at the Massachusetts General Hospital following the Cocoanut Grove fire. Locke (1902) had similarly found that though some hemolysis took place following burns, destruction was not sufficient to cause the symptoms of burn shock.

Hoppe-Seyler(1881) stated flatly that transudation of fluids into the burned areas was not the cause of the pre-death symptoms after patients were burned. Harkins, Blalock and others have refuted this many times over. Tappeiner (1881) is said by Locke to be the first to specifically note the extreme hemoconcentration in burn patients. Tappeiner noted one blood count of 9 million red cells per cubic millimeter after a severe burn. Elman (1942) quotes Tappeiner as saying "The concentration of the blood in burns occurs not through simple water loss but by loss of a fluid whose composition of solids is close to that of blood." Tappeiner concluded "I consider as the cause of death in severe

burns the concentration of the blood in the burned skin and recommend therapeutic transfusion of serous fluid." This is indeed modern therapy, the foundation of the treatment of burn shock and prevention of this greatest cause of death from burns.

Salvioli (1891) quoted by Bardeen (1898) thought that thrombus formation was part of the etiology of death in burn patients. He also found contracted arterioles and change in the red blood cells to which he ascribed part of the picture at death. Hemeconcentration probably explains this picture better today than any other theory or fact.

Moon (1942)(1938) reviews the history of blood findings: Baraduc in 1862 and 1863 first found the blood dark and thick; he noted failure of the blood to coagulate. Tappeiner in 1881 found red cell counts between eight and nine million between six and seventeen hours after the burn, in four fatal cases. Wilms noted hemoconcentration in 1901. Locke (1902) on investigating ten patients found that the highest red count in non-fatal cases was 7,266,000, while in five of six fatal cases it was above 9,000,000. In 1923 Underhill and others found 114-226% hemoglobin with decreased venous return and decreased circulating volume of the blood. These workers said that the cause was from decreased heart output, along with anoxia, decreased tissue metabolism and decreased arterial blood pressure. Wilson et al (1936, 1938) described the symptoms of "toxemia" after trauma and burns and said that the symptoms resembled poisoning

in the toxemic stage of the injury. Harkins in many articles between 1935 and 1944 ascribed all or nearly all of the symptoms in the primary stages to hemoconcentration, to localloss of blood plasma and resultant decreased cardiac output. Bardeen (1898) and Moon (1938, 1942) interpret pathological findings as showing that local transudation is not the cause of the hemoconcentration.

Of historical interest only is the finding very early in the experimental work on burns that there was a loss in heat regulating function of the skin. This was thought to cause rise in body temperature in the first 36 to 48 hours, followed by a terminal fall (Markusfeld and Steinhaus, 1895; quoted by Bardeen, 1898).

Harkins (1942) divides the clinical stages through which the patient must be carried by correct therapy into:

1. Stage of primary shock and conflagration
2. Stage of secondary shock (burn shock)
3. Stage of toxemia and liver necrosis
4. Stage of sepsis and complications.

The first stage lasts, primary shock or fainting, lasts only for a few minutes to an hour. Burn shock may last for the first sixty hours, reaching its peak at between 24 and 48 hours. The toxemia begins at about 24 hours and may last for 120 hours. Sepsis does not begin until the third day but may continue through death or be replaced by healing.

An interesting new finding is that of Lucido (1940) of Washington University who found considerably increased non-protein

nitrogen excretion in burn cases. Accompanying this was a high blood level of non-protein nitrogen products, in some cases giving a "pseudo-uremia" despite a high urinary output. He infers from this that there is a "toxic" destruction of protein in burns. This may lend support to Wilson's hypothesis already stated. Other workers refute the claim of toxic destruction of tissue.

Etiology of Burn Shock

As can be seen, there is a great deal of intermingling of experiments, clinical information, and history of the various clinical types of shock. Etiology mingles with treatment; history is often discussed along with experimental findings; and conclusions are to be found along with charts and graphs.

The history of the etiological discussions of burn shock is perhaps best divided into a set of five theories which embody sub-theories.

1. A miscellaneous group of theories
2. Nervous theories
3. Toxic theories
4. Blood-vascular pathology theories
5. The physical (plasma loss) theory.

In part these theories have already been discussed elsewhere. Bardeen (1898) grouped the theories into the following:

1. Interference with respiration, excretion and heat regulation in the skin
2. Vasomotor exhaustion

3. Injury to red blood cells causing thrombosis

4. Toxemia.

Bardeen himself held to the toxic theory, demonstrating the swelling of the lymphatic tissues and focal degeneration of parenchymal organs as evidence in point. Clinically he said the burned patient was much like one suffering from acute poisoning: "...apathy, sleeplessness, more rarely delerium, cramps, feeble pulse, irregular heart, cyanosis, albuminuria, diarrhea and nausea, are not infrequently noted."

The noted Canadian, Meakins (1943), classified the theories of the etiology of shock into the following groups, giving the men most closely associated with the theories:

1. Nervous
   a. Vasomotor collapse--Fischer, 1870
   b. Exhaustion--Crile, 1897-1920
   c. Inhibition--Meltzer, 1908

2. Fat embolus--Bissel, 1917; Porter, 1917

3. Arterial vasoconstriction and capillary congestion--Mapother 1879; Malcom, 1893-1909; Starling, 1918

4. Acapnia--Henderson, 1908

5. Acidosis--Cannon, 1919

6. Hyperactive adrenal medulla--Bainbridge and Trevan, 1917; Freeman, 1933

7. Exhaustion of the adrenal medulla--Sweet, 1918

8. Adrenal cortical insufficiency--Swingle, Pfeiffner, et al, 1933

9. Traumatic toxemia--Cannon, Bayliss and Brit. Med. Res. Committee, 1918

10. Traumatic metabolites causing capillary atony and

tissue anoxia--Moon, 1932-1938

11. Local fluid loss--Phemister, 1927-1930; Blalock, 1930

12. Progressive oligemic anoxia--Harkins, 1940

Meakins then states that the etiology is still not proved, though a rational therapy may cure or mitigate the incipient or actual burn shock.

Harkins (1942) considers that there are three chief theories of the etiology of all kinds of traumatic shock, including burn shock.

1. Nervous theory
   a. Metzer, 1908
   b. Crile, 1923
   c. O'Shaughnessy and Slome, 1935
   d. Lorber, Kabat and Welte, 1940, and others

2. Toxemia theory
   a. Cannon, 1923
   b. Moon, 1938, and others

3. Fluid loss theory
   a. Short, 1913
   b. Phemister, 1928
   c. Blalock, 1930
   d. Harkins and Harmon, 1937, and others

4. Additional factors
   a. Overactive adrenal medulla--Freeman, 1933-1939
   b. Anoxia--Cannon, 1923; McClure and Hartman et al, 1935-1939
   c. Adrenal cortical insufficiency--Swingle et al, 1933-1937.

These theories and the evidence presented in their support will be discussed at length in a later chapter.

Klebs (1877) was among those who emphasized the alteration in the circulation; he believed that the change in the blood elements was unimportant. He found stasis and concentration of the

blood, but believed that cardiac weakness was of primary importance. Boyer and Guinard (1895) believed that the heart was paralyzed by poisonous substances in the blood. Hoch (1893, 1895) studied 16 fatal burn cases and found increase in the specific gravity of the blood in the first 24 to 48 hours, but he ascribed the fluid loss in the blood to injury to the red blood cells. Bardeen quotes Hoch: "In any case the thickening of the blood does not seem to be a lesion of great importance."

Locke (1902) studied four cases in which nine million or more red cells per cubic millimeter of blood were found. He thought that the loss of the plasma portion of the blood was caused by venous stasis resulting from dilatation of the peripheral vessels and heart weakness.

The nervous theory has had its adherents both recently and in the early literature. Sonnenberg (1878, 1879) experimented with cutaneous burns in rabbits. He found that transection of the cord prevented the severe constitutional symptoms caused by superficial burns. He reasoned that the nerve reflex exhaustion and decreased vascular tone caused death. He also thought about the possibility of overheated blood damaging the heart. Bardeen criticized the previous author's findings.

Among the recent adherents of the nervous theory are Mahaffey(1939), Lorber and Kabat and Welte (1940) and Kabat and Hedin (1942). Kabat and Hedin burned spinal preparations of animals and control animals with a Bunsen burner. They found that "Thus,

elimination of the nervous factor decreases the rate and maximum extent of hemoconcentration following burns."

Several writers on the other hand oppose the nervous theory. In 1895 Markusfeld and Steinhaus discarded the nervous theory because they found that interruption of the nerve to the burned ear did not prevent shock. But they found that tying off the blood vessels did prevent the symptoms of shock from ensuing (Davidson, 1925).

Dupuytren thought that pain was the cause of death in burned patients. But his contemporary, Baraduc (1863), disagreed, saying that "...death from burns was not due to pain but to physical and chemical changes in the blood resulting from loss of the serum and subsequent hemoconcentration (which) initiate the chemical approach to the toxemia...." (Scudder and Elliott, 1942.) This is a statement consistent with the views of the fluid loss group of workers of today. Bardeen quotes Baraduc (1862) as holding the same view. In the same year Baraduc also noted the similarity between the dehydration of cholera and that of burns. Locke says that Baraduc was the first to emphasize the change in the blood; other authors have found earlier references to hemoconcentration and plasma loss; Buhl (1855) is said by Elman (1941) to be the first to find that plasma protein loss from burns caused shock similar to that found in cholera.

Of the more recent writers Blalock was one of the first to attack the problem of fluid loss by exudation and edema experimentally. In 1930 Blalock stated that he favored the fluid loss theory

in the etiology of general traumatic shock (including burn shock). Through the years and with various investigators as collaborators Blalock experimented and expounded on various kinds of shock to become one of the foremost contemporary authorities. Beard and Blalock (1931) were the first to use the comparative weights of burned and unburned limbs of anesthetized dogs to determine the presence or absence of increase in weight of the burned limb. This has become the basic type of experimentation in burn shock. Blalock (1931, VII) determined that approximately 3.34% of the body weight of the burned dog was the difference between the burned and unburned sides. This represented 57% of the body plasma of the dog. With these findings Blalock and his co-workers were content to name plasma loss into the burned area as the etiology of burn shock. They refuted the arguments for toxic absorption. The background of Blalock's theory was laid by Starling (1896). Starling showed that the hydrostatic pressure of capillaries was almost exactly balanced by the osmotic force of the plasma proteins, since these substances were of colloidal size and did not normally filter into the extracellular spaces through the capillary endothelium.

Though Blalock and Harkins will probably receive most of the credit for experimenting and persevering upon the physical or fluid loss theory of burn shock, Underhill (1919) was responsible for a still earlier concise statement of the theory that hemoconcentration was produced by extensive superficial fluid loss from skin

and muscle capillaries.

To Harkins (1934, 1935, 1937, 1938, 1942, and 1944) goes the credit for clearly showing the essential similarity of the various kinds of shock. To Phemister and his co-workers (1928, 1933) and their plasmaphoresis experiments we are indebted for the determinations showing the least amount of plasma protein which could be removed to cause death in most respects identical to that found in burn patients.

Final proof of the importance of increased permeability of capillary endothelium in and about burned tissues is presented by Glen, Muus and Drinker (1943) with their capillary measurements of increased lymph flow away from a scalded area on a dog's foot, thus indirectly demonstrating increase of capillary permeability. Cope and Moore (1943) use a refinement of this technique to further prove the importance of local loss of plasma loss into the burned area.

The toxic theory of the etiology of burn shock still has adherents. In 1920 Bayliss said, "Another state in which toxic products are most probably concerned is that after extensive burns." He appears to have been clear on the importance of the loss of plasma proteins, but he thought that a circulating toxin caused generalized increased vascular endothelial permeability.

> "The toxic product responsible for the results of tissue injury are removed in some way, with a fair degree of rapidity if the circulation is normal. They may perhaps be converted into non-toxic substances by the liver or perhaps oxidized. Probably they are to some extent excreted in the urine. The importance of raising the

> blood pressure high enough to reestablish the action of the kidney is recognized in cholera. The effecto of massage --- shows that the effectof a suddenly increased passage into the circulation is temporary."

Saline and vasoconstriction he found valueless, a finding whose importance is sometimes forgotten today in treatment of shock.

Cannon (1923) also was an adherent to the toxic theory of the etiology of shock. He was a product of the experimental period just during and after World War I, and his book is mostly concerned with the wound shock resulting from war traumata.

More recently, Bielschowsky and Green (1943) in Britain have been able to discover a shock-producing substance in fresh voluntary muscle, which is rapidly destroyed after death. This substance causes all of the chief symptoms of clinical shock. They thought adenosine triphosphate was the toxic substance.

Robertson, Bruce and Boyd (1923) were leading exponents of the toxemia theory. Burned tissues, they found, liberated toxins which were taken up by the blood, one a neurotoxin and the other a thermostable necrotoxic element extracted with the primary and secondary proteoses. They used alcoholic extracts, but Underhill and Capsinow, checking later, found that alcohol itself was toxic and that normal tissues were as toxic as the burned. Lewis (1927) in his book discussed the H-substance or histamine-like substance which caused systemic circulatory disturbances when present in large amounts.

Harrison and Blalock (1932) in studying burns could find no

evidence of a burn toxin. They found that transfusion of whole blood from burned dogs practically without effect on normal dogs. To somewhat anticipate another topic, these investigators also found that survival time was decreased if the burned areas were debrided; this is in line with the findings of the Massachusetts General Hospital treatment of the Cocoanut Grove firevictims in 1942.

Treatment of Burn Shock

Much has already been said about the "ancient" history of the treatment of burns, burn shock and sequelae. But a few statements on the more recent developments in burn treatment are not amiss. The treatment of burns and resultant shock along physiological lines may best be divided into the treatment of 1) the local causes of burn shock (as they are understood), 2) the treatment of the systemic causes of burn shock and 3) the treatment of both in a single regime.

The treatment of the burn with a degree of success goes back only about twenty years, to Davidson (1923) at the Henry Ford Hospital. At that time Davidson originated the tannic acid method of treating burns. Davidson decided upon some method of coagulation of the superficial tissues in the burned area because of the then prevalent theory that autolytic products of protein decomposition were responsible for the systemic effects of burns--shock and death.

Aldrich (1939) was the logical successor in the line of coagu-

lation treatment. He suggested treatment by use of gentian violet in the hope that it would decrease the infections found so often with the tannic acid treatment. This treatment was in line with Aldrich's theory that hemolytic streptococcus infection was the cause of the toxemia of the late stages of the acute phase of burns. Later (1937) Aldrich suggested a tripple dye to overcome some of the defects of the single dye treatment. A mixture of tannic acid and dye treatment followed, as did mixtures of tannic acid and silver nitrate, and silver nitrate and the dyes. A quick-drying eschar with pliability and antibacterial qualities was the desired result. None of these methods met the need.

By 1940 several groups were objecting to the use of tannic acid and other tanning methods. Colebrook, Wakely and Wilson in a British symposium (1940) found fault with the use of tannic acid in battleship, tank, plane and other burn casualties. They found that tanning decreased pain; however, exudation was not entirely stopped, and bacterial growth was not stopped. Col. Colebrook suggested the use of sulfanilamide powder to decrease sepsis and prevent delayed healing.

Bunyan (1940) recommended the use of oiled silk envelopes with sodium hypochlorite irrigation, especially for burned extremities. Transparency and decrease of contamination were the chief advantages, according to articles in the same year and in 1941.

Pickrell (1941) tried sulfadiazine in triethanolamine as a spray to form a film without coagulation tissue. It decreased

the incidence of infection according to his statistics.

Siler (1942) proposed to accept the principles of local treatment of burns as outlined by Koch (1935). They treated burns like any other superficial wound. They recommended the use of pressure dressings of the burned area and surrounding tissues. In view of the advantages of this treatment in caring for large numbers of persons, Cope (1943) and Harkins (1944) found it the fastest, cheapest and most applicable method (with some minor modifications). In 1944 Koch reiterates his stand for the use of the simple surgical and rest treatment of burns. Lee and Rhoads (1944), writing in the same issue of J. A. M. A. with Koch (1944), state the case for tannic acid, pointing out the great reduction in mortality from burns with the use of the tanning method of treatment. Lee and Rhoads state that tannic acid treatment in a very large series of cases resulted in a mortality of 10.5%; Siler (1942) cites statistics on 134 patients treated by the compression method and gives a mortality of 3.7%. Neither set of figures can be shown to be wholly the result of the local treatment alone.

The case for super-specialized ointments as the cure-alls for the local burn lesion may be summed up in the use of bio-dyne ointment. Hirshfeld, Pilling and Maun of Detroit Receiving Hospital (1943) found that plain petrolatum was better because it did not adhere to the tissues, lessening pain on change of bandages.

At the 1944 American Medical Association meeting in Chicago McClure and Lam showed that tannic acid and other tanning treat-

ments caused severe and often fatal liver necrosis. These methods also further damaged remaining viable tissue left after the burn. Dyes did not decrease infection, but they did delay wound healing. Sulfonamides locally did not decrease the incidence of infection but did occasionally lead to a dermatitis. Advertized preparations, mostly emollients supposedly to stimulate healing and hasten slough in third degree burns, were found not to have substantiated their claims. Clean wounds and early healing were found to result from vaseline gauze and pressure treatment. Cannon and Cope (1943) substantiate these findings in a very nice clinical demonstration of the effects of the various methods of local treatment upon donor areas of uniform depth.

Systemic treatment of burns is practically synonymous with the use of intravenous plasma, serum, albumin or whole blood. Robertson (1921) used transfusions for the first time to treat severely burned infants and young children. He was influenced by the toxic theory of burn shock and thought that bleeding prior to the transfusions eliminated the toxic products absorbed into the circulation. By his radical treatment, near-exsanguination followed by transfusion, seven severely burned children were treated and five survived. This is a low mortality for the period by other treatments.

Elkinton (1939) subscribed to the use of plasma to treat burn shock, but thought that adrenal cortex extracts were of value to decrease what he thought was a generalized increased permeability

of the vascular system. His formula for the administration of plasma according to weight, hematocrit, plasma protein levels and hemoglobin has been found by most hospitals to be far too cumbersome. Lam (1941) used plasma to treat burn shock, explaining that burn shock was a type of secondary shock caused by plasma loss.

Rhoads, Wolff, and Lee review 190 cases at the Pennsylvania and Graduate Hospitals in Philadelphia in 1941 and found that 5-10 cc. of adrenal cortical hormone administered every six hours (for adults) was of some value in treatment of the fluid shift, decreasing the permeability of the capillaries to plasma proteins. They also found that when plasma transfusions were administered the circulating volume of the blood was restored more quickly when the extract was used. However, in 1943 Rhoads, Wolff, Saltonstall and Lee reversed Rhoads' previous stand and found no value in giving cortical extract to burn patients.

Elman (1943) states the case for plasma transfusions thus in an analysis of 78 cases of fatal burns: "...failure to use plasma transfusions at all or in inadequate amounts was one of the chief factors contributing to early mortality." This statement emphasizes that the systemic treatment of burn shock is a therapeutic emergency.

Coordination of the local and general treatments are essential to the treatment of the patient as a person, instead of treating one part of the patient as he dies of other causes. Following Davidson's statement of his results with tannic acid the stress

fell chiefly on the local burn therapy, done with disregard, often, for the general treatment. The tendency today is to treat the systemic conditions caused by burns at the expense of the treatment of the burn site (Harkins, 1942). It is foolish to dress the local lesion perfectly while the patient sinks into irrecoverable shock; therefore, coordination of local and general treatment is essential.

The Cocoanut Grove disaster of 1942 gave several Boston hospitals a timely opportunity to care for large numbers of burned patients in a short period of time. The state of preparedness of the Massachusetts General Hospital was in contrast with that of other institutions. Clowes, Lund and Levenson (1943) of Boston City Hospital discuss the integrated treatment of 109 patients from the 1942 disaster and append the information gathered on another group of 103 patients burned elsewhere. Intravenous plasmawas their sheet anchor of systemic treatment. Three standard methods of local treatment were used. The Symposium by members of the staff of t e Massachusetts General Hospital (1943), Cope (1943) and Cope and Moore (1944) point out the necessity for preparation for the handling of large numbers of injured persons. Of the local treatments these authors agree that the best can be rapidly applied, are simple, follow sterile techniques, protect the burn wound, reduce the local plasma loss and give the greatest comfort and ease to the patients.

No historical survey of recent material would be complete

without mention of the seven recent articles in the J. A. M. A. of June 24 and July 1, 1944. Harkins (1944, June 24) states the problems concerned in burn patients. In the same issue Cope discusses the present attitudes in the chemical aspects of burn treatment. Lam in the same issue discusses the general care of the burned patient. The July 1, 1944, issue contains the remaining four articles : Lee and Rhoads on the present views on the tannic acid treatment (already cited), Koch on the general surgical principles involved in burn treatment, Gurd and Gerrie discussing the early plastic care of deep burns, and finally John S. Davis' paper on the late plastic care of burn scars and deformities.

PATHOLOGY

Just as pathology and physiology are the fundamental studies necessary to the thorough understanding of the clinical portion of all medical studies, so these subjects are important in understanding the etiology of burn shock.

The pathology of burns may best be divided into three portions:

1. Local pathology in the burned area
2. General pathology of the various organs and systems
3. Pathological physiology.

In his collected and translated lectures from the Hotel Dieu Dupuytren (1835) defines six degrees of burns. These degrees of burns are:

1. First--erythema or redness of the epithelium
2. Second--inflammation with desquamation of the superficial epithelium
3. Third--destruction of part of the rete mucosum, or germinal epithelium
4. Fourth--total destruction of the cells of the epithelium, including sweat glands and hair follicles
5. Fifth--slough of the superficial muscle tissue
6. Sixth--total carbonization of the part.

Common usage today as given by Bancroft in Christopher's TEXT-BOOK OF SURGERY (1942) includes the last three of Dupuytren's degrees of burning in the third degree. Bancroft himself prefers to use a fourth degree to designate destruction of connective tissue below the epithelium.

Berkow (1924) originated a method of estimating the extent of superficial burns. By his calculations the regional areas were:

Head		6%
Upper extremity		
Both arms and forearms	13.5%	
Both hands	4.5%	18%
Trunk		
Anterior surface	20%	
Posterior surface	18%	38%
Lower extremity		
Both thighs	19%	
Both legs	13.7%	
Both feet	6.3%	38%
Total		100%

According to Berkow children have a proportionately greater area on feet and hands, but the difference is relatively insignificant. Some of the formulas for calculating plasma dosage are based on Berkow's formula for surface area. Prognosis is similarly so gauged.

Clinically the degree of burn may be very difficult to determine. Clowes, Lund and Levenson (1943) said that a second degree burn destroys only part of the epithelium; whereas third degree burns destroy the whole of the epithelium and result in growth of granulation tissue in the recovery stages. The second degree burns usually have weeping surfaces or blebs and appear pink beneath. In contrast the third degree burns have a brown, leathery and dead appearance, sometimes being charred.

As a matter of fact the local treatment used may obscure the

degree of burn and cause death of viable epithelium. Cannon and Cope have already been cited on the healing of donor areas cut to uniform depth with a Padgett dermatome and treated by various methods. The common escharotics, especially tannic acid, caused loss of viable epithelium and delayed healing. Infection likewise may delay epithliazation and destroy regenerative power of the basilar layers of the skin.

The systemic, general pathological findings of burned patients who have succumbed to the results of burning have interested pathologists for almost one hundred years. Locke (1902) and Bardeen (1898) are the authorities substantiating most of the findings prior to their time. Bardeen says that Cumin (1823) made "...good anatomical observations..." on burned patients, finding much evidence of"internal inflammation." Heyfelder (1828), Long (1840), and Curling (1842) are also reviewed by Bardeen. Long first made the observation of duodenal ulceration in burned patients, though Curling is usually given credit for this observation. Heyfelder's autopsies impressed him with the loss of skin; he thought that this caused loss of respiratory functions of the skin.

According to Locke both Wertheim and Schultze studied the parenchymal changes in the internal organs, "...expecially the kidneys, where they found extensive thromboses with deposition of crystals of hemoglobin in the large tubules." Ponfick (1876) followed Wertheim and worked out the pathology in the kidney more carefully.

Bardeen himself (1898) wrote for the Johns Hopkins Journal and was a pathologist. He reviewed the literature of the pathology of burned patients up to his time, noting that there were few accurate post mortems and little animal experimentation of value. He summarized the chief lesions of five children who were very severely burned and autopsied soon after their deaths. They had been hospitalized a few hours after being burned. He noted that children were more susceptible to the noxious effects of superficial burns than adults. The chief lesions Bardeen noted were hyperemia of the thoracic organs, the abdominal viscera and central nervous system. Intestinal pathology varied. A bloody or serous exudate was sometimes found in the body cavities. Where the patients survived the burns for some time, gastrointestinal organs, lungs, plurae, kidneys and meninges were inflamed. The The lymphatic tissues appeared to Bardeen to be affected as by a circulating toxin. He found lymphatic tissues were swollen and showed focal degeneration. Bardeen also noted a slight increase in the specific gravity of the blood, indicative of hemoconcentration, in the light of today's findings. He saw some injury to erythrocytes and some increase in platelets, along with a polymorphynuclear leukocytosis. He found lysis and thrombosis of blood and attributed it to circulating toxins in the blood plasma. He postulated some decrease in resistance of the blood to bacterial invasion to account for the tendency of all burns to become infected. He also noted an increase in the fibrin content

of the blood. Clinically, Bardeen thought the symptoms much like that of an acute poisoning, thereby deducing a toxic etiology of burn deaths.

Weiskotten (1919) was again impressed by the inflammatory condition of the tissues of the ten fatal cases on which he performed necropsies. The swelling and redness of the suprarenal glands especially intrigued him. He noted that:

> "The results of the experimental work have been rather contradictory and inconclusive. Some of the experimental work points to the existence of a toxin acting in the body after extensive burning of the skin, some to loss of function of the erythrocytes and the production of thrombi as the essential factor in causation of symptoms and death, while the work of others points to severe affection of the nervous system as the main factor."

Toxins, if present, he states, are complex and unproved. Weiskotten refers to Bardeen's five autopsies and the latter's conclusion that a toxin caused inflammation of lymphatic structures. Weikotten set down in detail his findings:

1. External -- variable areas and degrees with nothing characteristic

2. Suprarenals -- The "most prominent and characteristic of necropsy findings were the changes in the suprarenals". They were swollen, red, and surrounded by edematous fat which displayed hemorrhage in some degree on gross examination. Microscopically the vessels were congested, red blood cells were hemolyzed; the glands were pale and swollen. Polymorphonuclear leukocytes and histiocytes were demonstrable. All this was comparable to $CHCl_3$ poisoning in the guinea pig.

3. Spleen -- grossly normal. Microscopically edematous in the germinal follicles.

4. Lymph nodes -- germinal centers involved uniformly, suggesting a circulating poison.

5. Heart --Two specimens grossly showed subendocardial hemorrhage. Microscopically there was hyaline degeneration, infiltration of polymorphonuclear leukocytes and endothelial leukocytes.

6. Kidney -- grossly inconstant findings. Microscopically there was fibrin the glomerular tufts and thrombosis of some vessels.

7. Gastrointestinal -- punctate hemorrhage submucosally and in lymphoid tissues.

8. Liver -- macroscopically inconstant findings. Microscopically there were foci of necrosis in two of the specimens.

9. Pericardial cavity -- hemorrhage under the pericardium in one specimen.

10. Lungs -- moderate congestion in two and moderate edema in two specimens.

11. Peritoneal cavity -- congestion in the abdominal vessels of three, all of whom had died in three days.

12. Other tissues -- brain, pleura, thymus, pancreas and other organs unchanged to any notable degree.

Erb, Morgan, and Farmer (1943) noticed the uniformity of liver pathology in cases treated by tannic acid. They found definite evidence of liver necrosis in 25, or 61%, of a total of 41 cases treated by tannic acid coagulation therapy. But 20 cases not receiving this treatment did not show liver necrosis at autopsy. Baker and Handler (1943) found that the pH of the tannic acid used made no difference; hepatic necrosis still ensued in experimental animals, being more prominent where solutions of 10% or more were used. Hartman and Romence (1943) found that tannic acid gave

patients clinically evident liver damage, as shown by jaundice. They found that silver nitrate caused local necrosis and edema with some liver degeneration without clinical jaundice. Often, using ferric chloride, was found to cause necrosis, edema and jaundice upon injection into experimental animals.

Pathological physiology

The pathological physiology of burns is in reality the stepping-off point into the investigation of the cause of burn shock. At the expense of later repeating some items the chief findings will be examined here. Klebs (1877) emphasized the alteration, believing it more important than the change of blood elements. He noticed the "crowding together" of the red cells. However, he thought thromboses in the brain caused death in burn victims. Boyer and Guinard (1895) thought that the heart became paralyzed and caused the altered circulation.

Starling stated the fundamentals of the integrity of the vascular endothelium in 1896. Bayliss (1927) discussed the relationship of the hydrostatic pressure within the vessels and the osmotic pressure of the colloids and crystalloids of the blood and tissues. He emphasized the importance of the osmotic pressure of the proteins and the fact that they are normally filtered into the perivascular spaces. Thus the colloids acted to withdraw fluid back into the vessels on the venous side of the capillaries.

Bayliss (1920) knew that histamine gave a generalized increase in the permeability of the vascular endothelium when administered

intravenously. He understood the importance of maintenance of circulating volume to excrete toxic products or carry them to the liver to be detoxified. He noticed a fact that some physicians even today disregard, that vasoconstrictor drugs were an incorrect form of therapy, causing further constriction of peripheral vessels and increasing the tissue anoxia.

Davidson and Matthew (1927) further boosted the fund of information in pathological physiology of burns and burn shock. They studied six cases of severe burns and found that whereas the total albumin in the blood was decreased, the total globulin was relatively increased along with increase in red cells per unit volume of blood. They concluded that plasma protein was the substance lost in burn shock, since if water or water and electrolyte were lost the plasma protein would be increased instead of decreased in total amount.

Underhill, Carrington, Capsinow and Pack (1923) agreed that albumin decreased for the first three days following burns and slowly reformed, whereas globulin was stimulated to reform earlier. This was in agreement with Davidson and Matthew.

Meakins (1943) lists as clinical observations of altered vascular physiology the following:

1. Capillary stagnation /
   / cyanosis and slowed capil-
2. Tissue anoxia / lary filling
3. Autonomic imbalance--sweating and cold skin
4. Decreased venous return

5. Local and pulmonary edema

6. Embarrassed circulation--tachycardia and decreased pressure

7. Cerebral anemia--restlessness, drowsiness and unconsciousness

8. Renal failure--oliguria

9. Hepatic failure--jaundice.

As to the cause of the altered vascular physiology noted by Meakins above, Harkins (1942) may be quoted. He says that 50% of the total shift of plasma into the burned tissue occurs in the first hour after burning. Glenn, Muus, and Drinker (1943) and Cope and Moore (1944) have used refined methods to show the increase in the permeability of the vessels near the burned area. The former group found that immersion of a dog's foot in hot water caused increased filtration of plasma fluid and proteins into the interstitial spaces, and thence to the lymphatic vessels. The latter group at Massachusetts General Hospital used dyes to tag proteins, then investigated the rate of appearance of these plasma proteins in the lymph to measure directly the capillary permeability caused by pathological degrees of heat. A radioactive bromide ion also was tagged on plasma proteins to trace their rate of disappearance from the blood after burning.

Normally there is 2 to 2.5% protein in the lymph fluid; after burning the protein content rose to 4.5 to 5.0% , usually reaching this maximum within one-half hour after burning. Adrenal cortical extract did not alter the systemic permeability of the vascular

endothelium. Normal dogs which were allowed to live for 17 to 27 hours under the conditions of the experiment without burning showed increased permeability in only one case. This occurred in the cervical trunk 20 to 24 hours after cannulation and was brought about by an upper respiratory infection. A generalized permeability was never found to be due to burns.

LABORATORY FINDINGS

The clinician is primarily interested in the state of the blood-vascular system. Laboratory tests to determine the condition of the blood are the most important to properly treat and diagnose burn shock. However, urinary findings and examination of the edema fluid are also important as bases for understanding burn shock and the etiology of the condition.

Historical references have already been given to show the general trends of findings of blood chemistry, urinalysis and analysis of the edema fluid about the burned area. To a large degree these will not be repeated. Bardeen noticed the increase in blood specific gravity, polymorphonuclear leukocysosis and increase in fibrin content of the blood.

In 1923 Underhill, Carrington, Kapsinow, and Pack wrote a paper entitled "Blood Concentration Changes in External Superficial Burns and Their Significance for Systemic Treatment." They were writing on the findings found in studying 21 victims of a theater fire. They stated that hemoconcentration was present in the patients and theorized that this had some relation to the resultant burn shock and circulatory failure. In 1930 Underhill, Kapsinow and Fish studied the mechanism of water exchange in the animal organism in burns and investigated the composition of the edema fluid and blood components. In experimental burns on rabbits they found that local subcutaneous edema developed rapidly. Hemoconcentration rapidly ensued, reaching its peak in 24 hours, to be slowly

reabsorbed in five to six days. Though the internal body temperature was increased the general body temperature was not greatly raised until about 24 hours after the burn, then being due to infection in the burned area. Underhill and his assistants originated a technique of using dyes to illustrate permeability in the burned area. Approximately 70% of the blood volume was lost in some experiments. Their analysis of the edema fluid caused them to state that the "...edema fluid so closely resembled the serum of the blood of the burned animal that it must be regarded as blood plasma." Wilms, Tappeiner, Harkins and Blalock have already been cited as having shown the hemoconcentration which must result from such a loss of blood plasma without the loss of blood cells.

Blalock has collaborated with several scientists investigating the etiology of all kinds of shock. Beard and Blalock (1931) in the eighth of a series of articles on shock give the following findings on the chemistry of normal blood plasma and the blood plasma following burns on experimental animals:

	Sugar, mg.%	NaCl, gm.%	N.P.N., mg.%	Prot., gm.%
Normal	104	676	54	9.0
After burning	134	686	62	7.6.

These are the average figures from a number of dogs in which deep anesthesia was administered and then the animal was burned until the blood pressure dropped to the desired level. The femoral vein was then tapped and tests made upon the plasma from this source. To check upon the makeup of the fluid in the burned area a block

of tissue was excised and the fluid extracted centrifugally for analysis. These investigators thought that the increase in non-protein nitrogen was from either increased destruction of protein or decrease in urinary secretion. "In the experiments the protein content of the (edema) fluid that was obtained from the damaged area was nearly identical with that of normal blood...." They stress the pathological physiology of loss of oncotic pressure through loss of plasma proteins into the burned area. These investigators indicate the fundamental importance of local escape of plasma proteins and fluid with resultant hemoconcentration, followed by the well known train of events of burn shock.

Meakins (1943) generalized his laboratory findings as follows: There is a decrease in blood volume, increase in red cells per unit volume of blood, increase in hemoglobin, decrease in plasma protein, decrease in blood chlorides, increase in blood potassium, hyperglycemia, decrease in muscular tone, and the appearance of a cortin-like substance in the urine following burns. Meakins remains unconvinced by the arrays of evidence for one or the other of the theories of the etiology of burn shock.

Many articles contain laboratory determinations found by analyzing the body fluids. Scudder and Elliott (1942) and Harkins, Lam and Romence (1942) may be compared and contrasted in this respect. The first two men consider the case of a man with 58% of his body area burned to second or third degree. He had the greatest hemoconcentration ever seen in a surviving patient at the

New York Presbyterian Hospital. The patient of the last three named men had a total burn of 47% of his body area. The patient of Scudder and Elliott was clinically jaundiced, demonstrating that the liver had been injured. Incidentally he had been treated locally with 5% tannic acid and 5% silver nitrate coagulation solutions; this treatment may have been the cause of his liver damage. Harkins does not mention jaundice in his patient, but he too was treated with tannic acid. Both patients received adequate plasma therapy and general supportive treatment indicated by the best burn therapists in the United States.

Scudder's patient showed rapid rise in both hematocrit and hemoglobin, normal values of each being respectively 47% and 14.5 gms., to values of 73% and 23.2 gms. within 24 hours. These values slowly dropped and were finally subnormal seven days after the burn. Plasma proteins continued to drop for six days, never regaining normal for the total of 22 days recorded. A low of less than five grams of total protein is seen on the second to the sixth day. Plasma sodium was variable, usually being about 10 milliequivalents/liter less than the normal value of 142. Plasma chlorides showed a slight rise from the normal of 103 milliequivalents/liter to as much as 115 on the eighth day. Plasma CO_2 combining power was never as high as the normal of 27 milliequivalents per liter. Potassium of the plasma, whole blood and the cells was variable.

Harkins et al give figures which corroborate those of Elliott

and Scudder. In addition they found that the white blood count was considerably elevated by the fifth day, to 17,600. The hippuric acid test of liver function showed slightly decreased function.

The urine has been mentioned as showing increased nitrogen content following burns. Lucido (1940) verifies this statement and says that there is "toxic" destruction of protein as the cause. Some investigators found hemoglobin in the urine of burned patients (Cope, 1943). Others found albumin, still others noted an oliguria.

Etiology of Burn Shock

Before discussing the various theories of the etiology of burn shock it may be said that at least one investigator, Wiggers (1942), does not approve of the method of most investigators and theorists of consolidating information and findings in support of their conclusions and theories.

But when we go beyond the known facts and develop hypotheses we must use the facts as bridges to take us from known items of symptomatology, pathology, and pathological physiology to more theoretical positions. Cannon holds a view opposite from that of Wiggers. Cannon says:

> "A theory of shock not only has the values which a theory of any other obscure state may have, in concisely systematizing and rationalizing our comprehension of a complex group of phenomena, and in making clear where knowledge is lacking and thus suggesting lines of further work; it is also likely to have a direct application to practice."

Thus the toxic theory suggested that prevention of absorption of the toxic products would prevent the inception of burn shock. The fluid loss theory infers that replacement of the lost plasma will prevent or reverse the trend toward shock. Thus theories are likely to "...have a highly practical consequence and therefore should be examined with care." (Cannon, TRAUMATIC SHOCK, 1923.)

Harkins has variously enumerated the acceptable theories of burn shock. In 1935 he said that two theories were acceptable; they were 1) the physical theory, and 2) the toxic. Of the physical theory he said that there were three factors at work.

1. Local leakage of fluid into the burned tissue
2. A resultant change in circulation, including diminished blood volume, diminished cardiac output, and

resultant collapse of blood pressure, and

3. Resultant concentration of the blood with increased percentage of hemoglobin.

At this time Harkins' comments were that though the blood pressure might remain near normal until just prior to death, the hematocrit and hemoglobin rose until just immediately prior to death. Barbital anesthetized control animals without burns showed no such fluid shift. He eliminated the psychogenic (peripheral nerve impulse effect from pain) element for lack of proof, but said that it could not be positively excluded.

In 1938 Harkins restates the theories of the etiology of burn shock. He lists them as follows:

1. Nervous and adrenaline
   a. Syncope may follow burns, later blending into secondary shock.
   b. Adrenal malfunction--Bardeen and Weiskotten

2. Toxic--circulating toxin absorbed from burned area
   a. Robertson, 1923
   b. Underhill and Kapsinow, 1931

3. Bacterial infection
   a. Aldrich, 1933, showed that after 12 hours 100% of burned areas showed streptococcus infection on culture.

4. Physical theory (local fluid loss)
   a. Underhill, 1923-1930
   b. Blalock, 1931
   c. Harkins, 1934-1935

By 1942 Harkins had redivided the theories of the cause of shock. He then divided them into three primary etiologies and a subsidiary group. He then listed them as 1) nervous, 2) toxemic, 3) fluid loss, and 4) additional factors operating. Of group four Harkins

says that the adrenal malfunction, anoxia and other effects are probably secondary rather than primary factors in the etiology of shock. He also stated that primary shock is an uncomplicated decrease in blood pressure causing an ischemia of the brain temporarily. True shock or secondary shock, on the other hand, is a true oligemia with the initiation and continuation of the cycle of decreased cardiac output, vasoconstriction, tissue anoxia and increased permeability of vascular endothelium. (Harkins, 1941)

In the same article in 1941 Harkins had given still another classification of theories. To enumerate these headings would only be redundancy.

In 1923 Cannon thought there were several theories worthy of thorough discussion in his book on TRAUMATIC SHOCK. These were:

1. The theory of inhibition--introduced by Meltzer in 1908 to explain gastro-intestinal inhibition after peripheral trauma.

2. The theory of vasomotor paralysis--introduced by German investigators in 1864 based on peripheral stagnation of the blood.

3. The theory of exhaustion--most recently promoted by Crile and his associates, who by burning and other means of traumatizing caused the central nervous system to become "fatigued."

4. Fat embolism--promoted chiefly by German investigators who reported that long bone trauma was particularly likely to cause shock and fat emboli in the blood stream.

5. Adrenal factor theory--promoted by various physiologists, some of whom thought over-activity was the cause and others of whom thought that exhaustion was the cause.

6. The theory of "Acidosis"--this followed the finding that carbon dioxide combining power was greatly reduced in shock.

7. Acapnia--as part of the sequence of hyperpnea, acapnia, failure of venopressor mechanism, and finally venous anoxemia, tissue asphyxia and acidosis, followed by acute oligemia.

8. Theories of vasoconstriction and capillary congestion--following upon notation of arteriolar constriction and "paralysis of vasodilator nerves."

9. Traumatic toxemic thory of shock--More will be given later on this theory.

Blalock (1942) suggests two types of classifications for the pathogenesis of shock. According to the first the causes in reverse order of importance would be:

1. Hypotheses of toxemia

2. Theory of disturbed nervous system

3. Theory of local loss of blood and/or fluid.

The second classification of pathogenesis Blalock gives as follows:

1. Hematogenic or "secondary shock"--loss of pooling of body fluids including blood, resulting in hemoconcentration

2. Neurogenic type--primary shock or syncope; like the hematogenic type there is decrease in blood pressure but to a lesser degree and little or no decrease in blood volume. This type is rapid in onset, for example, following spinal anestheia or carotid sinus syncope.

3. Vasogenic--due to vasodilation acting directly on vessels and not mediated by nerve impulses, for example, that from histamine, anaphylaxis, Addison's disease, and following perforation of a peptic ulcer.

Enough has been said by the various authors quoted and paraphrased to show that the same authors may vary in their statement

of the relative merits of the theories of the pathogenesis of burn shock and other types of shock. Current levels of information and fads of research also affect the trend of thought. Yesterday's theories are outmoded by today's research. Still we may be sure that yesterday's theories are the basis for the research of today and tomorrow.

The writer chooses to take the view that there are three theories which have foundation in fact and are acceptable to logical interpretation of the pathological physiology of burn shock. These theories are (Harkins, 1942):

1. The nervous theory
2. The toxemic theory
3. The fluid loss theory of physical theory.

There may be additional factors which sustain or enhance the primary factors: overaction of the adrenal medulla, anoxia, and adrenal cortical insufficiency.

Nervous

Toxic Theory

Sonnenberg (1878, 1879) was one of the first investigators to experimentally search for foundation for the nervous theory of the etiology of burn shock. He burned dogs and rabbits and noted the severe constitutional symptoms which resulted. However, he found that after transection of the cord, no such bad effects ensued after burning of the animals. It appeared then that nerve reflex exhaustion led to decrease in vascular tone, terminating in death. Bardeen (1898) criticized Sonnenberg's conclusions, emphasizing the difference between the rabbits' and dogs' re-

sponses to burns. (These animals do not form blebs as do humans after being burned.)

Kuess is quoted by Boyer and Guinard (1895). Kuess' addition to the nervous theory of burn shock etiology was in his suggestion that nerve stimulation to respiratory reflexes was destroyed. Bardeen thought that there was little to recommend this theory. Remy (1835) suggested that responses carried by sympathetic pathways from the burned area to internal organs was responsible for burn shock. Bardeen was also critical of this idea.

From this more or less unscientific and conjectural period we may turn to the experimental period after Meltzer (1908). Meltzer supported the nervous theory of the etiology of shock, based on both clinical and experimental evidence. Symptomatically the profound apathy, decreased sensibility, extreme motor weakness, grave pallor, and signs of respiratory and circulatory collapse and subnormal temperature were given as evidence of central nervous system failure. Yet Meltzer was not entirely convinced of the acceptability of the nervous cause of shock and said "...the experimental era has not yet solved the mystery of shock...."

Crile (1923) was the chief of his contemporaries in many lines of physiological investigation; he was also leader of the group which thought that the nervous system was the seat of primary malfunction in shock. Crile found that trauma of all kinds inhibited splanchnic processes and "stimulated the brain." He also found that fear, faith and other emotional conditions seemed to inhibit

or decrease the effect of injury. On the other hand chronic fear or chronic anger could cause lowered resistance to shocking conditions. He felt that exhaustion from fear and painful stimuli should be eliminated by the use of morphine.

More recently Mahaffey (1939), Lorber, Kabat and Welte (1942), Freedman and Kabat (1940) and Kabat and Hedin (1942) have brought forward evidence and essays in support of the nervous theory of shock etiology. Mahaffey felt that the clinical response of surgical patients to neo-synephrine, ephedrine and epinephrine when blood pressure dropped during surgery was valid evidence of the importance of the sympathetic nervous system exhaustion as at least part of the etiology of shock. Mahaffey's evidence seems somewhat bare of good experimental foundation.

Freedman and Kabat investigated the pressor response to adrenaline in the course of traumatic shock. These University of Minnesota workers found that in the incipient stages and in full-blown shock there was an increased pressor response to adrenaline; while in the terminal stages there was failure of response to this drug. By means of hind limb trauma in which fluid loss to the damaged tissues was prevented by close taping to decrease fluid loss, they were able to produce fatal shock in experimental animals within two and one-half hours. However, preliminary transection of the upper lumbar spinal cord prevented the death of the animal.

Lorber, Kabat and Welte (1942) found that transfusion alone was insufficient, though given in adequate amounts, to prevent death

from shock in experimental animals. Spinal anesthesia gave more lasting benefit from the use of plasma transfusions used to decrease shock. Separation of the traumatized hind limb except for the nerves to the part did not prevent shock. Ether analgesia seemed to these men to prevent or inhibit the inception of shock. Significantly these workers say that their work will "...shed no light whatever upon the relative importance of this as compared with other causative factors."

Kabat and Hedin in two articles in 1942 used more precise methods of determining the importance of the nervous element in shock. They used cats whose cords had been transected and control cats without transection. Each group of cats was burned with a Bunsen burner for 10 to 15 minutes. In the control animals there was an abrupt blood pressure increase to 100 to 160 mm. Hg. which was held for 10 hours. The spinal cats, however, showed an initial decrease to 60 to 90 mm. Hg. which returned to 80 to 100 mm. in one and one-half hours. (Spinal animals without burns showed a blood pressure of 90 mm. for long periods of time.) Consequently these investigators concluded that there was a reflex blood pressure rise in normal animals when burned, which masked a fall due to non-nervous factors. Further, studies by Kabat and Hedin show demonstrable differences in the blood chemistry of spinal animals and control animals similarly burned. These differences are shown on the chart on the following page.

	Spinal	Control
Blood Concentration(Hb.)		
Increase in 30 min.	14.5%	34.5%
Maximum	32.0%, 7 hrs.	44.0%, 8 hrs.
Blood Specific Gravity (by falling drop method)		
Increase in 20 min.	0.0027	0.0106
Maximum increase	0.0066	0.0127
Local fluid loss, percentage of body weight	1.5%	2.5%

These authors then conclude: "Thus eliminating of the nervous factor decreased the rate and maximum extent of hemoconcentration following burns." Their local fluid loss determinations were made by the method of Blalock and Harkins by comparing the burned and unburned hind-quarters of the experimental animals. The authors state that the "...decrease in hemoconcentration resulting from removal of the nervous factor may perhaps be accounted for on the basis of elimination of the reflex rise in arterial pressure, contraction of the spleen and vasoconstriction. Filtration of fluid into the burned skin is apparently decreased by functional deafferentation." This is probably the clearest and best supported evidence in favor of the nervous theory of the cause of burn shock. More work is needed for checking this information. It is clear that nervous influences are only adjuncts to the loss of plasma and resultant hemoconcentration.

There are no recent direct experimental findings completely eliminating the nervous element as the cause, or at least part of the cause, of burn shock. But in 1895 Markusfeld and Steinhaus

experimentally showed that rabbits whose ears had been burned developed shock despite interruption of the nerves to the burned area. However, interruption of the blood vessels to the part did prevent shock. Modern work and new methods are needed to investigate this experimental approach to burn shock.

Toxic Theory

The idea that some toxic product of burned tissues was responsible for the manifold symptoms of burn shock, in many respects like an acute poisoning, has had followers for many years. Bardeen has already been shown to have supported this theory because of his pathological findings. The more modern investigators include the following whose theories and findings inclined them toward the toxic theory:

1. Weiskotten, 1919
2. Robertson, Bruce and Boyd, 1923
3. Cannon, 1925
4. Lewis, 1927
5. Davidson and Matthew, 1927
6. Wilson, 1928
7. Wilson, Jeffry, Roxburgh and Stewart, 1937
8. Wilson, Macgregor and Stewart, 1938
9. Lucido, 1940
10. Moon, 1938, 1939, 1942.

Weiskotten's pathological findings have already been given under the heading of "Pathological Findings." Because of these findings

he decided that the "...characteristic lesions in suprarenals, lymphatic tissues and heart muscle indicate the presence in this class of cases of more or less specific poison in the circulating blood." This forthright statement of theory is somewhat typical of the men who favor a toxin as the etiology of burn shock and resultant death.

Robertson, Bruce and Boyd (1923) found two types of toxins in burned tissues which were taken up by the blood. They used alcoholic extracts of burned tissues to demonstrate a neurotoxin and a thermostable necrotoxic substance. Underhill and Kapsinow repeated these experiments using alcohol alone and normal tissue extracts (non-alcoholic) and found that both alcohol and normal tissues were toxic. The normal tissues were as toxic as the burned tissue used by Robertson, Bruce and Boyd.

Cannon (1923) begins his discussion of the theory of "traumatic toxemia" by stating that

> "None of the theories thus far discussed has offered a satisfactory account of the initiation of secondary shock. The problem still requires the demonstration of some factor, naturally related to the onset of shock, which may so operate in the body that, when hemorrhage and infection are ruled out, the persistent low blood pressure characteristic of the shock state will become gradually established."

Cannon was chiefly interested in shock due to war wounds, but it has already been shown that all types of shock have physiological bases in common. Cannon observed the cases in the Laboratory of Surgical Research at Dijon, France, after the World War and experimented on lower animals by the multiple trauma method.

He observed the pulse, respiration, alkali reserve and corpuscular volume, and all findings were typical of secondary shock.

Cannon was also interested in the nervous element in shock. His transection of the cord of experimental animals did not prohibit shock. "It is clear that there is no essential relation between the production of shock and the excessive stimulation of the central nervous system." This statement bears review in the light of the group of investigators at the University of Minnesota, headed by Kabat, Hedin and Lorber.

In the critical experiment (to Cannon) the blood vessels to the leg were tied prior to trauma and left in place for 33 minutes after trauma. There followed no sign of shock. However, when blood flow was restored, "...the pressure promptly fell to a low level. This phenomenon can be explained on the supposition that a pressure-lowering substance passes from the traumatized region to the rest of the body by way of the circulation when blood is again allowed to flow." A check upon his theory was possible by traumatizing the thigh muscles and allowing the blood pressure to fall before ligating the iliac vessels. The drop in blood pressure was slowly reversed and returned to normal. Cross-circulation experiments were also in support of Cannon's theory. In the light of more recent experiments by adherents of the fluid loss theory these findings have been as logically explained by the latter group.

The "H-substance" demonstrated by Lewis (1927) gave impetus to search for a toxic substance which might cause shock, when

administered intravenously in fairly large amounts. Subsequent authors used this to support the toxic theory. In the same year Davidson and Matthew investigated six cases of severe burns. They found severe hypo-proteinemia following burns and noted the hemo-concentration. However, they still spoke of a "toxemic" period in which there was an alteration of the capillary permeability and presumed it to be due to toxins absorbed from the burned area.

W. C. Wilson and his co-workers between 1928 and 1938 supported the theory of a toxic etiology of burn shock. In 1928 Wilson stated that Davidson's coagulation method of treating burn wounds decreased the absorption of toxins from the burned area and prevented burn shock, thus reducing mortality to 8 to 12%. In 1937, Wilson, Jeffry, Roxburgh and Stewart stated that burn shock was clinically like a toxic condition. In support of their thesis they tested the toxicity of edema fluid about the burned area and found that there was a gradually increasing toxicity up to 48 hours after the burn, often then being lethal. This toxicity was found to be independent of bacterial contamination and growth, but to be indicative of autolysis. Several components of the toxic material were found, mostly in the globin fraction.

In 1938 Wilson, Macgregor and Stewart were more interested in the clinical aspects of burn shock, finding it "...so closely resembling that following trauma that there seems to be no reason to doubt that aetiologically the conditions are essentially similar." In the discussion of the toxemia they found three mechanisms

of production:

1. Toxins in the burned area absorbed to the circulation
2. Anhydremia and hemoconcentration
3. Bacterial infection with hemolytic streptococcus.

Lucido (1940) found increased destruction of protein in burn patients causing raised non-protein nitrogen levels in the blood and urine. He thought this finding indicative of toxic destruction of protein.

As Professor of Pathology at Jefferson Medical College, Moon's views deserve attention. His two books, appearing in 1938 and 1942, are very intent on correlating the many pathological evidences of infection, poisoning with heavy metals, hypersensitivity, trauma, healing, etc., as being closely related phenomena. To a degree he succeeds, and lends his support to the toxic theory of burn shock. Moon is quite frank in listing evidence contrary to his own views on shock, just as he is insistent that there is good evidence in favor of a toxic factor. He states the findings of Underhill and his associates who showed that substances injected into the burned area were but slowly absorbed. Moon also restates experiments by Harrison and Blalock which failed to show intoxicating effects from transplantation of burned skin from one animal to one not burned, of bad effects from transfusion from burned to non-burned animals. Blalock also showed that debridement, instead of lessening "toxic" conditions following burns rather increased or speeded the inception of shock. Moon recognizes that local fluid loss is an important factor: "None will question that such loss is an im-

portant factor--important in proportion to the volume of fluid lost. But," he continues, "local loss of fluid alone does not disturb systemic fluid balance." This last statement will be countered by plasmaphoresis experiments by Phemister and bleeding experiments by Blalock and Harkins. Moon cites ascites, pleural effusions and anasarca as being local accumulations of fluid which do not lead to shock. This however, does not seem an appropriate comparison, for these losses are slow in formation and do not lead to a hemoconcentration; whereas, the local edema in burned tissues is sudden in onset, giving no opportunity for the body to adequately compensate by gastro-intestinal or other absorption. Further, the fluid lost from the blood is largely of the same composition as blood plasma, thereby causing the loss by the blood of oncotic pressure necessary for reabsorption of fluids from tissue spaces.

Moon describes an experimental series by Christophe who in 1939 grafted a leg of a normal dog onto the neck of another normal animal, anastomosing the femoral artery to the carotid of the second dog. Burning of the grafted leg then was followed by all of the signs and symptoms of burn shock in the living dog. Nervous impulses were thus eliminated as the cause of burn shock; however it will at once be seen that fluid loss into local tissues so burned could not be eliminated as the cause of the shock. In fact, this is probably better evidence in favor of the next theory to be presented, the physical of fluid loss theory of burn shock,

than for the toxic theory.

Moon's book of 1942 goes to considerable length to explain the mechanism of shock and compensatory means to reverse or obviate the condition. In summary Moon found that there was a generalized increase in the permeability of the capillary endothelium, greater than in the normal semi-permeable state, which allowed the escape of blood plasma. This reduced the circulating volume, and, if allowed to go too far, became irreversible and resulted in death. After discussing the pathological findings of Bardeen, Moon, Lewis, Locke and many others moon states with finality: "Such findings indicate that the hemoconcentration is not due entirely to local transudation in and about the injured areas." He then presumed that a circulating toxin was absorbed from the burned area and must account for the pathology and pathological physiology of burn shock.

Weil and Meakins (1942) of McGill University and the Royal Victoria Hospital infer that the pathological findings cited by Moon can all be explained upon the basis of the hemoconcentration of burn shock. That is, it is conceivable that late complications of burns--liver damage, kidney damage, gastro-intestinal ulceration and so forth may originate in the initial marked hemoconcentration and may become manifest days later. Accordinely Weil and Meakins state that a toxemia need not be postulated. This attitude is the concensus of the men who favor the physical theory as the best single explanation of the primary causes of burn shock.

Physical, or Fluid Loss, Theory

Several men, most of them early German investigators, have been given credit for being the originators of the fluid loss theory of the etiology of burn shock. Elman (1941) says that Buhl (1855) was the first to realize the importance of plasma protein loss as a cause of burn shock. Tappeiner (1881) has been cited by Locke, Elman, Harkins and Harmon and others for advanced thinking on burn shock. Tappeiner thought that the loss of blood plasma by transudation was the chief cause of death in severely burned patients. He noticed that 2 to 3% of the blood plasma was often lost. He was very conscious of the increase in the number of red blood corpuscles per cubic millimeter of blood, noting counts between 7,810,000 and 8,960,000 in four cases which he studied.

Baraduc (1863) has been advanced by Locke and Bardeen as the first man to stress the part played by the blood and the loss of plasma in skin burns. Bardeen says that Baraduc "...thought that the blisters resulting from the burn extracted large amounts of serum from the blood; that the blood is thus thickened and the rapidity of flow lessened, the thick blood then giving rise to thrombosis." Except for the mention of thrombosis, which occurs late, this statement could have come from Harkins or Blalock.

Underhill and his various co-workers should not be lightly dismissed merely because they did their work twenty to twenty-five years ago. In 1919 Underhill was in the Chemical Warfare Service. He then advanced the "new" theory that the mechanism produc-

ing the systemic effect in extensive superficial burns was acting by way of hemoconcentration from fluid loss on the surface injured. Underhill stated that a concept of treatment based on this theory should give good results. In 1923 Underhill, Carrington, Kapsinow and Pack were still using the terminology of "toxemia" and "capillary permeability" together, indicating that they were thinking in terms of the World War physiologists and surgeons. But Underhill et al clearly state that the fluid poured out "...on the surface is plasma or at least modified plasma." They thought that hemoconcentration was the cause of the ill effects of burning. At this time the early experiments of Blalock had already been published. Blalock had concluded that local fluid loss was sufficient to cause death in experimental animals and that the fluid lost was of approximately the same constitution as plasma.

Blalock wrote five articles in this early series. Without attempting to be complete, rather trying to give the important findings and conclusions, we may discuss these articles by number, I to V.

I. Rabbits were burned by a standard method. Subcutaneous edema in the burned area rapidly formed. Hemoconcentration rapidly ensued, reaching its peak in 24 hours. This edema fluid was very slowly reabsorbed, taking five to six days. Systemic pathology was regarded as being due to hemocondentration rather than to a circulating toxin. The slow absorption of material from the burned area supports this view.

II. By using dyes to test capillary permeability and reabsorption it was found that burns cause a local increase in capillary permeability. Reabsorption was slowed, after a short latent period.

III. Significant fluid loss was found in six hours after

burning, leading to subcutaneous edema. The maximum was reached in 24 to 36 hours and slowly reabsorbed. Approximately 70% of the blood volume may be lost.

IV. The "...edema fluid so closely resembles the serum of the blood of the burned animal that it must be regarded as blood plasma." However, the percentage of globulin was relatively less than in blood plasma.

V. Whole blood chloride is decreased because of the hemoconcentration.

Thus Underhill and his co-workers were creating and following the trend toward chemical and physiological investigation of burn shock.

Phemister (1928) is said by Harkins to be the first to record the definite statement of the importance of local fluid loss into the tissues in the production of all types of secondary shock. Phemister recorded the increased volume of the traumatized limb of experimental animals and thought it sufficient to account for the hemoconcentration and resultant decrease in blood pressure. "In fact, the volume of blood that it was necessary to withdraw intermittently in the course of an hour in order to kill an animal was always less than the increase in volume of the traumatized limb of the other animal, which was due very largely to hemorrhage in the tissues." Phemister could not support the view that a histamine-like substance was the cause of traumatic shock. He collaborated with Room and Keith (1933) and executed skillful plasmaphoresis experiments on animals, finding that 4.4% of the body weight lost as blood plasma caused certain death. Harkins checked this experiment and found that this was a conservative statement. The later work of Blalock et al. supported Phemister. In article VII

he found that 3.34% of the body weight lost as plasma into the burned limb of an experimental animal (57% of the body plasma) would cause death. He found that the fluid loss was solely or primarily into the burned area, not through a generalized loss from the vascular system of the body.

In article VIII Beard and Blalock investigated the composition of the fluid after mild trauma, severe trauma, and after burns, with a view to comparing their composition (of the fluids). These results have already been discussed. However, in summary, we may state that severe trauma causes loss of whole blood; mild trauma causes a smaller proportion of blood cells to be lost into the area injured; burns cause the loss of plasma only. Hemorrhage causes a sudden decrease in blood pressure and decrease in hydrostatic pressure of the blood as the result of hemodilution. Burns cause an increased local capillary permeability and resultant hemoconcentration with local plasma loss. They concluded that loss of plasma protein was the chief factor in production of low blood pressure and shock.

Blalock and Johnson (article IX) proposed to determine by plasmaphoresis how much blood plasma loss would lead to shock and death. They found that 2.6% of the body weight of blood plasma lost would cause death under their experimental conditions. This is less than the amount found necessary for death by Phemister. They compared the effect of loss of whole blood and of red cells alone and found that loss of whole blood was better tolerated than

either plasma alone or red blood cells alone. They concluded then that "It does not seem necessary to assume the action of a poison which exerts a general bodily effect" in order to account for the multiple symptoms, signs and pathological findings of burn shock.

Harrison and Blalock (1932) did further studies on the cause of death following burns. Upon investigating the possibility of a toxin as the cause of death within 48 hours after the burn they found that 1) burned skin which was transplanted from the burned animal gave no toxic effects, merely sloughed, 2) debridement of burned areas of dogs decreased survival time following burns by increasing the amount of weeping in the burned area, and 3) whole blood transfused from burned dogs had no toxic effects on normal dogs. They then concluded that there was no evidence of a burn toxin which might account for the evidences of burn shock. Rather, they reiterated a statement made earlier by Beard and Blalock (1931) that "...they believed the loss of blood plasma into the burned area to be the principle if not the sole cause for the shock that developed within 48 hours following burns."

Scudder's book on blood studies and therapy in shock has already been quoted and discussed at some length. In his study of six patients burned in the Hindenburgh disaster in 1937 he found that there was an increase in specific gravity of the blood of 13% from a normal of 1.0556 to an average of 1.0630 in the burned patients. There was an average increase in hemotocrit of 34%, one being increased by 80%. From the normal plasma proteins of 70 grams per

liter these patients had an average of 56 grams per liter, a drop of 20% (in patients I and V). Scudder was very interested in the potassium changes in whole blood, cells and plasma. He found that an increase in plasma potassium was the one common denominator in all types of shock; this amounted to 22 to 25% above normal in these patients despite adequate fluids, salt, cortical extract repeatedly--this being found 18 to 84 hours after the burns.

Harkins has been one of the leaders in shock, especially shock experimentation and therapy, since 1935. In 1934 Harkins found that if 2.2% of the body weight of plasma proteins was lost by exudation in burned animals, death would invariably ensue. This compares with the findings of other men as follows:

1. Harkins (1934)--2.2%
2. Blalock and Johnson --2.6%
3. Harkins and Harmon (1937)--4.0%
4. Phemister et al--4.4%.

In 1934 Harkins had found that there was decreased cardiac output and a decrease in bleeding volume following experimental burning. At a level of 80 mm. of Hg. (normal being 100 to 115 mm.) the animals were bled to death. Bleeding volume was found markedly decreased by this method: but 20.3% of the calculated blood volume was obtained, using one-thirteenth of the body weight as the normal bleeding volume. To recheck this finding Harkins and Harmon (1937) bled dogs after burning them; it was found that after burning the bleeding volume was 1.6% of the body weight.

Normal bleeding volume is 4.17% of the body weight. In a later article in 1937 these same men found that many conditions caused the same hemoconcentration, giving levels on bleeding volume determinations which approached that found before by burning and plasmaphoresis experiments to be fatal. These conditions were: burns, freezing, bile peritonitis, tissue autolysis in vivo, acute pancreatitis, pneumonia and pulmonary edema, intestinal manipulation, portal and mesenteric obstruction, external strangulation of a colostomy, and release of constriction on an anoxic extremity. These types of trauma may be roughly divided into:

1. Thermal
2. Chemical and bacterial
3. Mild continuous mechanical
4. Capillary injury from inadequate circulation.

The importance of this article lies in establishing a common basis for all types of shock; a common line of systemic therapy is thereby inferred.

By 1940 Harkins had become more certain of the common basis of various types of shock, yet he was still not sure enough to be dogmatic. He said:

> "The shock that results from injury, whether that injury be caused by mechanical, thermal, chemical or operative trauma, is quite similar in all cases. The three chief theories as to the causation of such shock are the toxic, the nervous and the physical theories....Some authors believe that two or all of these factors are of importance."

He considered hemorrhage essentially the same as shock except for

the "time element." But loss of plasma is less well tolerated than loss of whole blood.

The work of Glenn, Muus, and Drinker (1944) and of Cope and Moore (1944) have already been given as the most recent and exact types of investigations into capillary permeability and plasma loss in burned areas.

TREATMENT

The subject of the treatment of burns logically follows the discussion and determination of the cause of burn shock, shock being the chief problem and the main source of mortality from burns. The problem of treating burns will be stated; the general or systemic treatment will then be taken up; the local treatment will conclude the discussion of the treatment of burns.

Burn shock accounts for 60 to 80% of the deathscaused by burns. (Blalock and Duncan, 1942; Harkins, 1942; Atkins, 1940; Hook, 1942--the latter man in a panel discussion of Harkins 1942 article). The present war has many casualties from burns: "It has often been stated that this is a 'burn-war' and it is rather generally agreed that at the present time there is no one type of injury that is more important or more frequent." (Blalock and Duncan, 1942).

Harkins (1943) has stated that the problems of burns are four in number:

1. General treatment of the burned patient
2. Local care of the burn wound
3. Early plastic care of granulating surfaces (in third degree burns)
4. Late plastic care of deformities.

Harkins ideas will for the most part be followed for the first two phases of the care of burned patient. The last two phases do not logically come under the consideration of this thesis.

General Treatment

The general treatment of the burned patient does not resolve itself into the administration of adequate doses of blood plasma, but if adequate amounts are given the remainder of the general care of the patient becomes mere good nursing. Elman has shown that a majority of 78 patients who died at his clinic died because no plasma or insufficient was given. The administration of plasma and the rest of the general care should be continued through the time when local treatment is given; the two should be carried on conjointly and concurrently without intervening delays.

Harkins (1944) divides the general care into three divisions:

1. Early general care in the shock phase--At least 60% of thedeaths occur here.
   a. Plasma, human albumin, or plasma substitutes given intravenously--the basis of treatment
      1) Doseage:
         a) 50 cc. per per cent hemoglobin over 100%
         b) 100 cc. per point hematocrit over 45
   b. Crystalloid solutions--saline, glucose, etc.
   c. Sodium lactate--orally or intravenously for acidosis
   d. Whole blood--limited quantities where plasma short
   e. Oxygen
   f. Conserve patient's body heat--don't add hot water bottles.

2. General care of the middle phase of toxemia and sepsis--third to tenth day, with liver damage, sepsis, etc.
   a. Sulfonamides and penicillin
   b. Prevent hypostatic pneumonia and bed sores by changing position.
   c. Control anuria by adequate fluids.
   d. Prevent liver damage by adequate protein and glucids
   e. Prevent acidosis by sodium lactate.
   f. If hemoconcentration persists, continue plasma, otherwise shift to whole blood transfusions.

3. Late general care in the healing phase--anemia, hypoproteinemia, avitaminosis, and sepsis are problems. Lasts from second week to time of last healing; deaths are due to debilitation or sepsis.
   a. Blood transfusions to control anemia.
   b. Adequate protein by mouth, or by vein as plasma or amino acids.
   c. Correlation with local treatment so that skin grafting may be accomplished as soon as possible.
   d. Sulfonamides and penicillin
   e. Adequate sulfur for epitheliazation (eggs, etc.)
   f. Iron to control anemia
   g. Adequate vitamins to prevent avitaminosis, especially B_1, B_2 and C.

In order to determine the response of the patient to early therapy repeated plasma protein determinations may be made; the same end is accomplished more rapidly by determining hemoglobin levels and hematocrit. More complex determinations are not applicable where there are a large number of patients to be cared for. The formulae of Harkins are to be used to determine plasma dosage.

Good practical demonstrations of the early problems posed by large numbers of burned patients are the Cocoanut Grove disaster of 1942, war burn cases and the very recent Hartford, Connecticut, circus fire.

Local Treatment

Local treatment should be coordinated carefully with the systemic treatment in order not to be penny wise and pound foolish, dress the burn beautifully and let the patient die in irrecoverable shock. Harkins (1942) named and described over 100 varieties of local treatment for the burn wound. If one includes the treatment

of complications and sequelae the list is even longer.

At present the method described by Koch (1935, 1944) and Siler (1942) has ridden to favor. And the tanning methods have lost many adherents because of their tendency to allow infections, to allow continued plasma loss and to cause liver damage. (McClure and Lam, 1944; Baker and Handler, 1943; Hartman and Romence, 1943; and Erb and Morgan and Farmer, 1943).

The surgical dressing method of treating the burn wound must now be considered the method of choice. The method can be used on all areas of the body; large numbers of patients can be treated with ease; the materials are relatively cheap and easy to get and plasma leakage and infection are reduced to a minimum.

Briefly Koch's method consists of the use of bland ointment on wide mesh gauze to apply over the burned area. Siler and Koch advise that the area be debrided first; Cope says that this is contraindicated because of added trauma and further plasma loss by weeping. Furthermore, debridement is an operating room procedure and requires time, equipment and an anesthesia which may further damage the liver. All groups are in agreement that large quantities of sterile mechanics waste should then be applied over the wide mesh gauze. Pressure is maintained by application of elastic bandage or tape over the waste. The comparable mortality of this method of treatment is very low--3.7% in a series of cases over a two year period, treated by Siler (1942).

The last two phases of local treatment are not strictly related to shock from burns and so will not be discussed at length.

Gurd and Gerrie (1944) stress the timing of the early plastic care of deep burns, advising skin grafting 10 to 14 days after burning, to prevent inanition and other late complications. This treatment raises the patient's morale and prevents contracture of the burned area by scars.

Davis (1944) discusses the types of flap operations for late plastic care of burn patients to release contractures. He tells how and when to excise scar tissue and do late grafting. Regional variations and change in technique for the region are stressed.

SUMMARY

Burns are merely a special type of trauma, little different in effect from many other types of trauma. Burn trauma causes a local plasma loss and localized tissue edema, sufficient in amount to cause hemoconcentration. The resultant hemoconcentration causes the serious train of events known as burn shock. Decreased venous return, decreased cardiac output, tissue anoxia and resultant focal degeneration ensue.

Burn shock can best be understood as differing from other types of shock--surgical, wound, overwhelming infection, massive hemorrhage--only in its being preponderantly the result of hemoconcentration. Hemorrhage, to cite the other extreme, results in loss of whole blood and is followed by hemodilution as the tissue fluid is taken into the circulation.

The theories of the causation of burn shock acceptable today can be listed under three headings: 1) toxic, 2) nervous and 3) physical or fluid loss. The evidence for the toxic theory lies in the clinical appearance of the patient and contestable experiments on toxicity of the edema fluid, blood and burned tissues of the burned animal. The nervous theory is supported by evidence that shock is lessened when pain is decreased. Adrenaline hypersensitivity in the early stage of burn shock, followed by hyposensitivity in the pre-death condition is considered further support for the nervous theory. The experimental laboratory worker

finds it difficult to explain all of the effects of burn shock on the basis of nervous system dysfunction.

The local fluid loss theory of the etiology of burn shock is the best single theory on the etiology of burn shock. By means of acceptable experiments the proponents of this theory have shown that most if not all of the series of events leading to burn shock and death can be explained by this theory. It is the best single explanation of the cause of death following burns. The other theories can best be considered as aiding in explaining some of the minor findings in burn shock.

CONCLUSIONS

1. The importance in war and peace of burn shock and its treatment has been shown by morbidity and mortality statistics.

2. There has been a gradual filling of the blanks of knowledge between various kinds of shock so that now a common bond of etiology has been found, namely loss of blood elements.

3. Though nervous and toxic factors have not been eliminated as a part of the causation of burn shock the local plasma loss has been proved capable of producing burn shock and its sequelae by its action alone.

4. The pathological, pathological-physiological, symptomatic and typical laboratory findings were shown capable of being produced by experimental burn shock and hemoconcentration.

5. Bacterial infection has been shown to be a late factor in burn shock, rather than an initiating influence.

6. For practical purposes local plasma loss is the greatest single provable cause of burn shock.

7. A logical and applicable system of treatment is suggested when one considers local plasma loss into the burned area the chief inciting cause of burn shock.

8. This treatment--intravenous plasma, and pressure dressings locally--decreases fluid loss, decreases infection and promotes early epithelial regeneration.

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