THE INTERNAL LESIONS IN BURNS WITH SPECIAL REFERENCE TO THE LIVER AND TO SPLENIC NODULES

An Analysis of 96 Autopsies *

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The assertion by some [1, 2] that hepatic necrosis is usual in fatal burns has been countered by others [3] with the suggestion that the hepatic necrosis is due to tannic acid which had been applied in treatment. A desire to settle this issue caused me to examine a series of autopsies which had been performed on patients who had died following cutaneous burns. This led to observations on the state of the splenic nodules in burns and to an examination of the adrenals and some of the other viscera of special interest. The splenic nodules have attracted attention ever since Bardeen [4, 5] described well marked focal areas of degeneration in them which he interpreted as being indicative of a toxemia of burns. Weiskotten [6] described changes in the adrenal glands.

The problem of the internal lesions of fatal burns has been complicated in recent years by the use of local applications of tannic acid and other escharotics, by the giving of sulfonamides, and by the use of plasma and other intravenous fluids. Autopsies and reports made several decades ago should be examined with special care as they may actually be more reliable than autopsies performed recently. Fortunately, a portion of the autopsies which I examined came from this earlier period.

Material

Analysis was made of the cases of burns which had been autopsied at Duke Hospital and at Johns Hopkins Hospital.†

Only those cases were selected in which burns or the complications of burns appeared to be the principal factor leading to death. In reviewing the cases at Duke Hospital, complete protocols were prepared and all microscopic sections and the clinical histories were thoroughly studied. In reviewing the cases at Johns Hopkins Hospital I examined slides of liver, spleen, adrenal, and kidney in all cases in which these sections were available, and made notes of each case, as indicated in the sample protocol which follows:

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Colored male, 3 years of age (autopsy no. 15592). Death 2 days after burn. Two-thirds to three-fourths of body surface involved. Gentian violet spray. Temperature and pulse rose very high. No infection demonstrated in sections of skin. Spleen showed early acute splenic tumor. Liver showed slight diffuse fatty change.

In interpreting the histologic changes, the duration of survival is of great importance (Table I), for when death occurs after only a few hours it is conceivable that cells have already been damaged physiologically without cytologically demonstrable evidence of such damage. On the other hand, when death occurs several weeks after burning, cells which were necrotic at first may have been replaced by regeneration. Also, burns may become infected and bacteremia may develop in patients who survive longer than several days, and the changes observed in the internal organs may be the result of the bacteremia and not of the

TABLE I

Duration of Survival in Fatal Burns

Death during:	No. of cases
1st day	37
2nd day	9
3rd day	9
4th day	4
5th day	0
6th day	4
7th day	0
2nd week	7
3rd and 4th weeks	12
Period beyond 4 weeks	14
Total	96

burn. Necroses in these older cases may be due to other complicating factors such as anemia and congestive heart failure.

Analysis of Table I showing duration of survival indicates that slightly more than one-third of the patients died during the first day, slightly less than one-third died during the remainder of the first week, and almost exactly one-third died after the first week. There were 26 cases in the most interesting period of all, that beginning with the second day and extending through the first week. It is during this period that deaths from burns occur with the least satisfactory explanations. Deaths during the first day are explainable on the basis of shock, especially when the burns are very severe, and deaths after the first week are usually explainable on the basis of complicating factors, but during the period from the second day through the first week primary shock has largely disappeared and infection usually has not developed.

LIVER

Hepatic necrosis was not mentioned prominently in reports of fatal burns published before 1925, *i.e.*, before tannic acid was used on burns. In Schjerning's [7] table published in 1884 showing the occurrence of pathologic lesions following burns, the liver is not even listed. Dohrn [8] found no changes in the hepatic cells. McCrae [9] saw no necrosis in 12 cases. Marchand [10] stated: "The liver shows no essential finding. In high grades of blood destruction increased secretion of bile can occur, as in other types of hemoglobinemia." Weiskotten,[6] reporting 10 cases, found foci of necrosis of liver cells in 2.

Since 1925, attention has been called to severe hepatic necrosis in fatal burns, but apparently the severe grades of necrosis have been due to the tannic acid which was applied to burned areas. Vogt,[11] in 1929, reported 8 cases of fatal burns and found no necrosis of hepatic cells. He mentioned fatty change in these cells, and an increase and degeneration of leukocytes in the hepatic capillaries. In 3 of his cases death had occurred before 1925. There is no information as to whether tannic acid had been used in the treatment of the cases in which death had occurred after 1925.

In 1938 Wilson, Macgregor, and Stewart [1] described hepatic necrosis of severe grade in fatal burns following survival periods of from 2 to 12 days. (A photomicrograph of liver from one of their patients who died 71 hours after a burn shows extreme necrosis with only a rim of viable cells about the periportal areas.) Tannic acid had been applied to the burns in many of their cases. In 1939 Belt [2] described the hepatic necrosis following burns as similar to the hepatic lesions of yellow fever. In his 4 cases in which tanning with tannic acid had been employed, death occurred between the second and fourth days of survival. The necrosis is described as mid-zonal, but the illustration indicates that exceedingly few viable hepatic cells remain either about the central vein or about the periportal areas. Further evidence of the relationship between hepatic necrosis and the tannic acid therapy of burns [3, 12, 13] is summarized in an editorial in *The Journal of the American Medical Association*.[14] Wells, Humphrey, and Coll [3] were apparently the first to realize that the tannic acid was responsible for the hepatic necrosis rather than the burns, and they supported their view by producing hepatic necrosis in rats by subcutaneous injections of tannic acid.

Erb, Morgan, and Farmer,[15] in 1943, reported that of 27 patients tanned with tannic acid and dying in the period between the 3rd and 19th day, only 3 failed to show hepatic necrosis. The hepatic necrosis

illustrated by them is of extremely high grade, involving the hepatic lobule for nine-tenths of the distance from the central vein to the periphery. In strong contrast, no case of hepatic necrosis occurred in their 20 patients in the untanned group, 7 of whom died between the 3rd and the 14th days, a period in which necrosis was an outstanding feature in the tanned group; and no hepatic necrosis was seen by them in patients who had died before the introduction of tannic acid therapy for burns.

Observations

Necrosis was noted in the cases which I examined, but with relative infrequency, as indicated in Table II. Moreover, the necrosis was usually not at all severe. In only 3 instances was it as much as 2 plus,

TABLE II

Liver in Fatal Burns

Time of death in relation to injury	No. of cases with sections of liver	No. with necrosis	No. with fatty change
1st day	32	1 (±)	6 (+++, +, +, +, ++, +)
2nd day	9	1 (±)	2 (+, +)
3rd day	8	3 (±, +, +)	1 (+)
4th day	3	0	0
6th day	4	1 (±)	0
2nd week	6	1 (+)	0
3rd and 4th weeks	11	2 (+, +)	2 (++, +)
More than 4 weeks	14	4 (++,++,±,++)	9 (+, ++, ++++, +++, +, +, ++, ±, +++)
	87	13	20

which indicated necrosis extending nearly one-half of the distance from the central vein to the periphery of the hepatic lobule. But all 3 patients had survived for more than 4 weeks, and necrosis could scarcely be thought of as the effect of the original burn, since cells originally rendered necrotic would have been removed unless, of course, a necrotizing influence from the burn continued to be present. Tannic acid had not been used in these cases.

In all 3 cases complications of the burns or other accessory factors explained the hepatic necrosis more reasonably than the direct effect of the burns. In the first case, a child of 1 year, there was purulent otitis media and thrombosis of cerebral veins. In the second case, a male, 66 years of age, there was thrombosis of periportal veins, pulmonary emboli, dilatation of the right side of heart, syphilis with gummata of lungs and testes and perforation of the palate, and bilateral lobular pneumonia. In the third case, a man, 52 years of age, a burn of the right arm extended to the bone and was treated at home for 11 days. Twenty-one days before death the patient was brought to the hospital

with thick exudate covering the arm. Phlebitis of the popliteal vein developed.

Five of the cases showed hepatic necrosis of a grade of 1 plus, indicating that necrosis did not extend more than a quarter of the distance from the central vein to the periphery of the liver lobule. Usually the extent was less. It occurred in 2 cases with death on the third day, in 1 case with death in the second week, and in 2 cases with death in the third and fourth weeks.

Analysis of necropsy and clinical data in these 5 cases indicated that in 1 case there was nothing but the burn to explain hepatic necrosis; in 1 case there were possible accessory factors, but the burn may have been the factor; and in 3 cases hepatic necrosis was explained best on complications such as infection or cardiac failure.

The following notes were made concerning the case in which there was nothing but the burn to explain hepatic necrosis:

Colored male, 41 years of age. Death on third day following burn in December, 1925.

Section showed central necrosis of the liver with polymorphonuclear neutrophils about the borders of necrotic cells. The central necrosis occurred in some areas of the section and not in others.

The anatomic diagnosis was: Burns. Central necrosis of the liver.

The clinical record indicated that the patient was burned over one-half of the body surface 3 days before death. There was no note indicating the presence of jaundice, and no evidence that tannic acid was ever applied, and there was a note that vaseline gauze had been used. The pulse rate was 100 to 130 per minute. Death occurred following urinary suppression.

Five cases showed probable hepatic necrosis, as indicated by a plus-minus sign. In the sections of liver from these cases there was mild condensation of the nuclear material in the cells closely surrounding the central veins, such as to suggest pyknosis, but no corresponding cytoplasmic change; or there was some other slight change of questionable significance.

In 2 of these 5 cases with equivocal necrosis there was no factor but the burn to account for the change noted microscopically.

When Table II is reconstructed with omission of the cases in which hepatic necrosis is better explained by complicating factors, it appears as in Table III.

Thus, hepatic necrosis of high grade did not occur as a direct result of burning. Necrosis of minimal grade was present in four instances in which the burn may have been the cause. It was noted with death on the first day in one instance (of plus-minus grade), and with death on the third day in three instances. Hence, minimal degrees of hepatic necrosis may apparently be caused by burns; and it seems probable that the changes observed were not present in the liver before the burns

occurred, as the nearly complete absence of necrosis in the large group of patients dying during the first day suggests.

How was the minimal necrosis produced? The untoward effects of therapeutic agents may have been responsible. Tannic acid was not applied in any of these 4 cases. (In another case, not included in the revised table, necrosis may have been due to tannic acid. This is discussed later.) Sulfadiazine spray was used in one. Plasma and other intravenous fluids might be responsible, since the older reports mention necrosis so infrequently. Other theories include the acute congestion of shock, absorption of toxic substances from the burned area, and throm-

TABLE III

Liver Necrosis in Fatal Burns
(Necrosis Due to Complicating Factors Excluded)

Time of death in relation to injury	No. of cases with sections of liver	No. with necrosis "due" to burn
1st day	32	1 (±)
2nd day	9	
3rd day	8	3 (+, +, ±)
4th day	3	
6th day	4	
2nd week	6	
3rd and 4th weeks	11	
More than 4 weeks	14	

bosis. No support for the last theory was obtained from microscopic study.

Hepatic Fat. Histologically demonstrable fat was noted most frequently in those who died on the first day and in those who died in the period beyond 4 weeks. When it was noted in those who died on the first day, the question arises as to whether the fat was present before the burn as a storage phenomenon or whether it indicates hepatic injury. This question cannot be answered without control studies. When the fat was noted in those who died in the period beyond 4 weeks, the question arises again as to whether the state of nutrition of the patient accounted for the fat or whether the fat indicated hepatic damage. In some instances in which the fat bordered the necrotic areas it seemed clear that it indicated hepatic damage, but in the numerous instances in which fat was present without necrosis the fat was not interpreted as an indication of hepatic damage.

Tannic Acid

Apparently the tannic acid therapy of burns never had any great vogue at Johns Hopkins Hospital or at Duke Hospital. Some of the Hopkins cases were autopsied before the advent of the tannic acid treatment, and it was possible to study these early cases with certain

knowledge that tannic acid was not utilized. Twenty-eight of the Hopkins cases occurred before 1924. Davidson's [16] paper, "Tannic Acid in the Treatment of Burns," appeared in August, 1925; and the cases which he studied occurred in and after May, 1924. Of the 28 cases, sections of liver were present in 21, all of which were normal except 2. The protocols of the 7 cases without sections indicated the probable absence of hepatic necrosis in these cases also. Of the 2 cases, 1 case, previously mentioned, showed 2 plus hepatic necrosis probably associated with secondary infection of the burn, death occurring 32 days after a small burn. In the other case there was questionable necrosis; and confluent lobular pneumonia with toxemia, or with cardiac failure, offered as satisfactory an explanation as did the burns for the slight changes noted in the liver. Hence, in a series of 28 cases from the period when tannic acid was not used there was no case of hepatic damage due to the direct effect of the burns.

In the cases at the Johns Hopkins Hospital after 1924 it was not determined in each instance whether tannic acid had been used, since analysis of the clinical records was impracticable. But in all those cases in which hepatic necrosis was observed microscopically the clinical record was thoroughly reviewed in attempting to make certain whether tannic acid had been used. In only 2 of the 13 cases of Table II which showed necrosis microscopically had tannic acid been used. In 1 of these, the child was treated with tannic acid compresses. He died on the second day and no condition other than the burns was discovered. The minimal necroses in this case may have been due to the absorption of tannic acid. In the other case a girl of 9 years was treated with tannic acid over a burn of more than half of the body surface sustained 44 days before death. The minimal necrosis of the liver could not have been due to the tannic acid, because of the long interval of time; and there were other factors, such as profound anemia, which could have produced the hepatic change. Hence there is one case in this series in which hepatic necrosis may have been produced by tannic acid.

The problem may be approached, also, by determining what the liver showed when it was known that tannic acid had been used. This was true in at least 2 of the cases at the Johns Hopkins Hospital. In 1, previously mentioned, death occurred on the second day. The equivocal necrosis may have been due to tannic acid. In the other, tannic acid had been applied to second degree burns of the back and buttocks of a colored boy of 18 months. Death occurred 12 hours or so after the burn. The liver appeared normal, but with such early death the general effects of tannic acid would probably not be histologically apparent.

Tannic acid had been applied to two of the burned patients autopsied at Duke Hospital. Death occurred 30 days and 44 days after burning and no necrosis or scarring was noted in either case. At such long intervals after the burn any original necrosis might have been replaced by regenerated liver cells.

Concerning tannic acid, then, the present series gives little information except in comparison with the series of others, such as those of Wilson, Macgregor, and Stewart,[1] Belt,[2] or Wells, Humphrey, and Coll,[3] in which tannic acid was used extensively and in which necrosis of high degree was noted when death occurred during the first few days after the burns were received. The comparison indicates that hepatic necrosis in the cases of these authors was the result of the tannic acid treatment rather than of the burns. Experimental studies of Wells, Humphrey, and Coll, of Baker and Handler,[17] and of others, show clearly that hepatic necrosis can be produced regularly in experimental animals by the application of tannic acid to a wound or by subcutaneous injection of tannic acid.

Splenic Nodules

Bardeen [5] described swelling and necrosis in the lymphoid nodules of the lymph nodes, peripheral lymphoid tissue, and spleen which he considered characteristic of burns and indicative of toxemia, just as similar changes in diphtheria were indicative of toxemia. Regarding the spleen he stated:

"The Malpighian bodies become enlarged from the swelling of their cells and from the subsequent degenerative and necrotic process which begins at the centre. Single cells and small groups of cells may be seen degenerating in all parts of the pulp, but well-marked focal areas of degeneration are confined to the centres of the Malpighian bodies."

These observations were made on the organs of five children who had been fatally burned. The children varied in age from 16 months to 8 years. The time elapsing between burning and death varied from 4 to 9½ hours. He commented on the fact that in the child who died soonest, and only 4 hours after the burn, the lymphatic lesions were well marked, but he did not suggest that the changes might have been present before the burn was sustained. In a footnote Bardeen [4] stated:

"Since working up the cases described above I have had the opportunity of studying the tissues from the bodies of two adults whose death was due to superficial burns. In each case lesions similar to those described above were found, but the lesions seemed less marked in the lymphatic tissue of the adults than they were in those of the children."

McCrae [9] did not find the constant presence of focal necrosis in the lymphatic glands, upon which Bardeen laid considerable stress.

Dohrn [8] did not note in his cases the full development of the changes described by Bardeen. He recognized that Bardeen described the changes in children and he questioned whether the changes were specific for burns.

Weiskotten [6] reported on 10 cases of burns, 5 in children and 5 in adults. Regarding the spleen he stated:

"Microscopically, in all of the cases of less than 3 days' duration there were found rather characteristic lesions in the lymph nodules. . . . There was apparent necrosis of the cells of the germinal centers evidenced by karyorrhexis. Endothelial leukocytes . . . were phagocytic for the necrotic cells and for the lymphoid cells of the nodules. . . . In many instances this process continued until the lymph nodule was represented by a large central area filled with phagocytic endothelial leukocytes surrounded by a narrow rim of lymphoid cells. These lesions apparently developed very soon after the burns were received, and were evident in all of the cases of less than three days' duration. In the cases of more than three days' duration, there were areas corresponding in distribution to the lesions described in the earlier cases. These areas were relatively homogeneous and eosin staining with occasional vesicular nuclei. At the periphery of some of these were seen occasional cells resembling the endothelial leukocytes seen in the earlier lesions. These appearances suggest that the areas represent the earlier lesions in process of hyaline degeneration and resolution or repair."

Lubarsch [18] considered the changes in the lymph nodules to be the most constant finding in uncomplicated fatal burns. He noted that the change occurred in the great majority of instances in children, and pointed out that in children the lymphatic tissue reacts especially vigorously in the most varied diseases. Vogt [11] stated that in children the foci were regularly present. Fender [19] was interested in the changes in the lymphoid nodules as indicating toxemia. He mentioned the similarity of the changes in infections and intoxications such as scarlet fever and diphtheria.

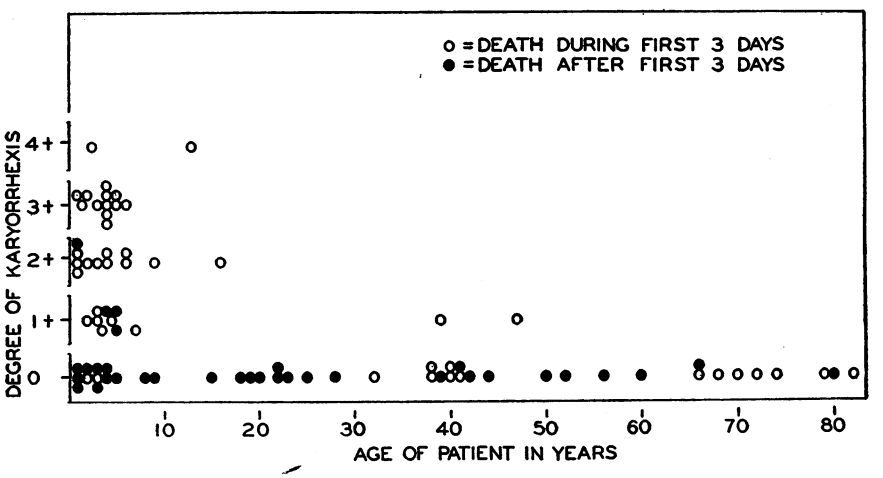
Observations

In the observations which I have made I have concentrated on a single, easily recognized feature of the changes described in the secondary centers (germinal centers) of splenic lymph nodules, or, more accurately, lymph cords. This feature is karyorrhexis (nuclear fragmentation). Usually when much karyorrhexis was present the secondary centers were large. The degree of karyorrhexis is expressed from 0 to 4 plus, varying from no observable karyorrhexis to the highest amount noted. If the degree of karyorrhexis so observed is correlated with the age of the patient (Text-Fig. 1) it is obvious that high degrees of karyorrhexis are noted only in the young and almost exclusively in persons less than 17 years of age. More than a 1 plus degree of karyorrhexis was not encountered in a single subject beyond adolescence.

In Text-Figure 1 the cases are divided into two groups depending on

whether the survival period was more or less than 3 days. It is noted that in only a single case with death after the third day was the degree of karyorrhexis as much as 2 plus. Thus the young (*i.e.*, those less than 17 years old) who died more than 3 days after receiving a burn failed to show the high degree of karyorrhexis which was exhibited by the young who died within 3 days.

The significance of these clear-cut results is difficult to evaluate, but several aspects may be discussed. It might be concluded that the burn is the cause of the high degree of karyorrhexis in the young. However, it may be that this degree of karyorrhexis was already present in the



Text-Fig. 1. Correlation of the age of the burned patient, duration of survival following burning, and the degree of karyorrhexis in the germinal centers of the splenic nodules. Each dot or circle represents a case. High degrees of karyorrhexis in the splenic nodules in fatal cases of burns occurred only in the young, *i.e.*, in those less than 17 years of age. In addition, high degrees of karyorrhexis occurred only in those who died during the first 3 days following the burn, regardless of age.

young, and that the burn which killed the child merely permitted the pathologist to see something normally present in the spleen. If this were so, it was also true that the condition present "normally," and during the first 2 days after the burn, disappeared some days later, possibly due to inanition, infection, or some other factor.

To try to determine the normal degree of karyorrhexis in the splenic nodules, sections of spleens were obtained from persons who had died within 24 hours after accidental injury such as an automobile accident, shooting, stabbing, strangulation, or suffocation. In many cases death was instantaneous. Only subjects at least 1 year of age were used.

In several thousand autopsies, 54 cases of such violent deaths were found, but unfortunately only 2 of these cases were young children

(5 and 3 years of age). These showed 1 plus karyorrhexis. Two plus karyorrhexis was shown by 2 adults, aged 21 and 45 years. None showed 3 plus or 4 plus karyorrhexis. Thirty-nine showed no karyorrhexis and among these there were no children less than 10 years of age. Hence one obtained the impression that normally the splenic nodules do not exhibit a high degree of karyorrhexis, but obviously the number of children in the series is too small for a conclusion. It would be desirable to examine a large series of accidental deaths in children, with death occurring soon after the accident, in an institution where such autopsies are available, in order to determine the degree of karyorrhexis present normally.

Karyorrhexis was observed within a few hours after a burn. Karyorrhexis of 3 plus degree was noted in a child who survived only 3 hours, and karyorrhexis of 4 plus degree was noted in a child who survived only 6 hours. Thus if the burn is the cause of the nuclear fragmentation the lesions develop with great speed. It may be that nucleated cells of the blood or of the tissues are damaged by the burn, just as red cells are,[20] and that particles of the injured nuclei are brought to the splenic nodules and deposited there. Or it may be that the cells of the lymph nodules are damaged by a toxic substance brought to them in the blood. Attempts to determine the origin of the nuclear particles by microscopic study were not successful. Some of the particles suggest the lobes of necrotic polymorphonuclear cells while others suggest pyknotic lymphocytes. Usually the particles are within the cytoplasm of macrophages. Occasionally the macrophages of the secondary centers of the splenic nodules also contain portions of red blood cells.

The failure to find karyorrhexis of high degree more than 3 days after receipt of the burn may indicate that sufficient time has elapsed to permit the macrophages to digest the nuclear material, or at least to destroy its property of absorbing the basic stain. This is in accord with the interpretation of Weiskotten.[6]

Kidneys

Sections of kidney from 88 of the cases were examined. A small number, only 9 cases, showed definite recent lesions. Infections, resulting from the burns, were present in the cases with renal lesions in which death occurred in the second week or later. These infections constituted a thoroughly satisfactory cause for the lesions noted. If these cases were excluded, only 4 remained in which renal damage was present and might have been a direct effect of the burn. In 1 of these 4 cases in which death took place 12 hours after the burn there were

hyaline droplets in the tubular epithelium, but diabetes was a complicating factor. In the 3 cases with death on the third day the renal changes might well have been due to the burn itself, but in all 3 cases there were complicating factors also, which might have been responsible for the changes observed. The type of damage and attendant circumstances in these 3 cases with death on the third day are given in the three succeeding paragraphs.

In the first case there was necrosis of the renal tubular epithelium of a moderate grade, with no obstruction of the collecting tubules. A third degree burn of four-fifths of the body surface had been sustained, hematuria had been present, and sulfadiazine spray had been used locally and plasma intravenously.

In the second case there was patchy necrosis of renal tubular epithelium. Epithelial cells were dislodged and had been caught in the tubules farther down. Hyaline droplets were present occasionally in the tubular epithelial cells. Extensive burns had been sustained and lobular pneumonia had developed.

In the third case there was minimal dilatation of the convoluted tubules. There was also focal necrosis of liver and hemorrhagic ileitis and colitis in this subject of 68 years.

No such spectacular lesion as that described by Brown and Crane,[21] bilateral cortical necrosis, was encountered in any of the cases in the entire series.

The cases at Johns Hopkins Hospital were examined before I knew about the importance of hemoglobinemia and hemoglobinuria in burns,[20] and I probably did not examine with sufficient care the contents of the tubules for the presence of hemoglobin casts. The lesion in the distal convoluted tubule and elsewhere in the kidney which has been described recently for the crush syndrome [22] and also in patients with burns [23] may have been overlooked.

The cases at Duke Hospital were re-examined for hemoglobin casts and changes in the distal convoluted tubules. Seven cases with patients surviving a short time were available, death occurring after 3, 12, 14, 22, and 40 hours, and 4 and 8 days, respectively. In 2 cases there were appearances suggesting hemoglobinemia, though this had not been established clinically.

The first of these was a woman, 39 years of age, who had received deep charred burns over 60 per cent of the body surface. Plasma (2300 cc.), whole blood (100 cc.), and cortin had been given. Death occurred 14 hours after the burn was received. At autopsy the bladder was empty. Blister fluid was pink as was much of the subcutaneous edema fluid. The intima of the aorta was stained intensely red. In the

blood vessels of the kidney distorted, shrunken, or conglomerated red cells occurred. The shrunken forms were identical to those described in the peripheral blood by Shen, Ham, and Fleming.[20] In the capsular spaces of the glomeruli eosin-staining material occurred which suggested hemoglobin. In an occasional collecting tubule there was eosin-staining fluid, débris, and rounded masses suggestive of hemoglobin.

In the second case, a child, death occurred at the end of 4 days. Burns were extensive and severe and had been treated with dry dressings. Oliguria and azotemia developed. In the distal convoluted tubules granular débris and masses with the eosin-staining qualities of hemoglobin were present, but there was no necrosis of the epithelium of the tubules. In a very rare collecting tubule débris which looked like hemoglobin was present.

In summary, even with these added considerations, renal changes in the series of burns were not impressive, and changes noted in patients dying in the second week or later were explained best on the basis of the secondary infection and septicemia which was usually present. In 3 cases, with death on the third day, it is possible that the changes were the direct result of the burns, but even in these cases there were complicating factors. Hemoglobin casts would undoubtedly have been found in some of the Hopkins cases upon re-examination.

Adrenal Glands

According to Weiskotten [6] the most prominent and characteristic of the necropsy findings in patients with burns are the changes in the adrenals. He described swelling, redness, and periadrenal edema with hemorrhage in all cases of more than 24 hours' duration. The weight of the adrenals in one of his cases was three times normal. Microscopically there were congestion and hemorrhage, and the gland cells were pale-staining and much swollen. Necrotic gland cells being invaded by polymorphonuclear and large mononuclear cells were not infrequent.

Observations

In the majority of cases the adrenal gland did not show arresting changes grossly, and the organ was usually described as normal, or congested, or as showing periadrenal edema.

I examined sections of the adrenal glands stained with hematoxylin and eosin from 68 cases. An analysis of the microscopic observations indicated the following: (1) Most of the cases showed no impressive change in the adrenal; (2) Congestion in and about the adrenal, periadrenal edema, and rarely periadrenal hemorrhage (not massive hemorrhage) were noted in several cases, especially during the first 3

days; (3) Necrosis was noted in 2 cases and was due to infection. It was thought that the congestion, periadrenal edema, and occasional periadrenal hemorrhage were probably features of shock and of the shifts of fluid which occur in burns. It is to be borne in mind, however, that changes in the adrenal of a functional metabolic nature could not be evaluated with any degree of refinement by simply looking at a section of adrenal gland stained with hematoxylin and eosin. Study of fat stains, granule stains, and quantitative methods might reveal changes.

Since the observations in the preceding paragraphs were made I have noted two pertinent references concerning adrenal lesions. Mallory and Brickley [24] reported focal necrosis of the adrenal in 2 cases in which death followed the Cocoanut Grove fire by 2 days in one instance and by 3 days in the other. They mentioned splitting of the cords of the outer portion of the cortex with accumulation of serous exudate in the space produced, pyknotic nuclei, acidophilic necrosis of adrenal cells, and infiltration of polymorphonuclear cells. Rich [25] has recently described a peculiar type of adrenal cortical damage associated with acute infections and has discussed the possible relation of this damage to circulatory collapse. The lesion consists of necrosis of isolated cells and a striking transformation of the solid cords of the zona fasciculata into tubular structures containing an inflammatory exudate.

In view of these observations, sections of adrenal were re-examined in cases autopsied at Duke Hospital with death occurring 3, 12, 14, and 40 hours, and 8 and 20 days following burns. In all of these cases, except in that with death on the 20th day, shrunken, dark-staining, apparently pyknotic nuclei were found occasionally in the cells of the cords of the zona fasciculata; and in 1 case, with death at 40 hours, some cells of the zona fasciculata had intensely eosin-staining cytoplasm in addition to pyknotic nuclei. Accumulations of inflammatory cells were not seen about the cells with intensely staining nuclei. I am unable to say whether actual necrosis was present or whether vagaries in staining accounted for the appearances observed. In the case in which death occurred 3 hours after the burn there was slight separation of the cells of cords of the zona fasciculata to form spaces, but this did not approach the tubule formation described by Rich [25] as characteristic of his cases with infections of various sorts.

Comment

Other organs than those previously mentioned showed changes but these were not subjected to analysis. Congestion and hemorrhage were frequently observed in the earlier deaths. Petechial hemorrhages of the epicardium and endocardium, lungs, stomach and duodenum, and else-

where were noted, as were occasional Curling's ulcers. Extensive hemorrhages into the lungs, with infarct-like areas, occurred in some cases. Congestion of many viscera, such as the spleen and liver, was noted in the cases in which death occurred after a short period of survival. The changes in the lymphoid nodules of the lymph nodes and gastrointestinal tract paralleled the changes in the splenic nodules. No definite or constant alteration was found in the brain. Mention should be made of necrosis and inflammation in the respiratory tract, which occurred from the direct inhalation of flames and fumes.

In the literature on burns, mention is made of the direct effect of heat on the internal organs,[26] with, for example, the production of large vacuoles or bubbles in the liver. Fat embolism has been reported.[10]

Nevertheless, the emphasis should be on the paucity of lesions in the internal organs following fatal burns. If the early changes are interpreted as those of shock and the slightly later ones as those of hemoconcentration, and if the changes in the blood cells and the hemoglobinemia in deep burns are recognized, there are possibly no additional morphologic alterations characteristic of burns other than the changes at the site of the burn. The liver usually shows no necrosis, the changes in the adrenals are possibly those of shock, and karyorrhexis in the lymphoid nodules occurs only in children. There is thus little support for the concept of a powerful burn toxin on the basis of pathologic studies.

Summary and Conclusions

Available for analysis was a series of 96 autopsies in which cutaneous burns or the complications of cutaneous burns were the chief cause of death. The series included 37 cases with death during the first day, 26 cases with death from the second to sixth day inclusive, and 33 cases with death after the first week.

Hepatic necrosis was usually absent, and when present could be explained more reasonably as a result of a complication of the burn, such as infection, then as a direct result of the burn. Necrosis of minimal degree was noted in 4 cases in which no factor but the burn was demonstrated as a cause. In this series of cases tannic acid treatment had not been used to any appreciable extent. In 28 cases from the period before the use of tannic acid there was no case of hepatic damage due to the direct effect of the burns. It was concluded that necrosis of the liver is not a lesion characteristic of burns.

Karyorrhexis of high degree occurred frequently in the lymph nodules of the spleen in those patients less than 17 years of age who died during the first 3 days following burning. Karyorrhexis was absent, or present in minimal degree, in the splenic nodules of those older

than 17 years. Moreover, when those less than 17 years of age survived more than 3 days, karyorrhexis was absent or present in minimal degree. While it could not be proved that the striking karyorrhexis present in the young who died during the first 3 days was not present before burning, it was thought that the karyorrhexis was probably the result of the burn and that it disappeared after the third day because of the digestion of the nuclear particles by phagocytic cells rendering them nonstainable with hematoxylin. It was concluded that changes in the splenic nodules were not fully characteristic lesions of fatal burns, since these changes were not present in adults.

Unequivocal changes in the adrenal and kidney were infrequent. The swelling, congestion, and occasional homorrhage in the adrenals in early deaths were attributed to shock. Hemoglobin casts were noted in the kidneys rarely.

In general, emphasis is placed upon the paucity of histopathologic alterations specific for burns and not attributable to shock, to the rarely occurring hemoglobinemia, or to secondary infection.

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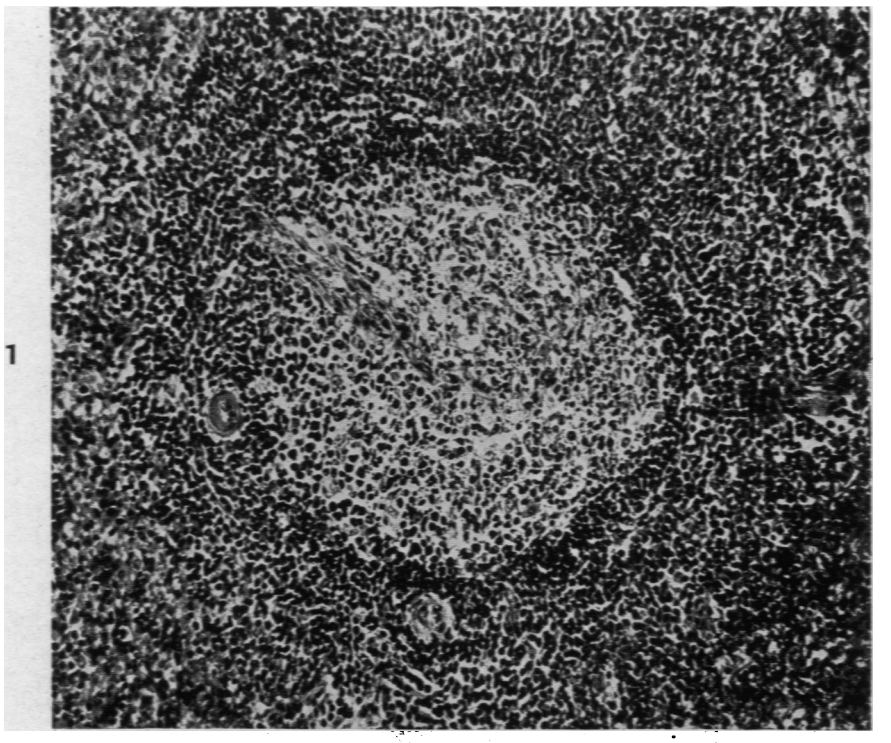
[*Illustrations follow*]

DESCRIPTION OF PLATES

PLATE 122

FIG. 1. Low-power photomicrograph of a splenic nodule from a child, 4 years of age, who survived 3 hours following a burn. The nodule has a large secondary center (pale) with a rim of lymphocytes about it. Hematoxylin and eosin stain. × 50.

FIG. 2. Oil-immersion field from the center of a secondary nodule of the same case as in Figure 1, showing karyorrhexis of 3 plus degree. Most of the nuclear fragments are within phagocytic cells. This case demonstrates that high degrees of karyorrhexis may be encountered as soon as 3 hours after a burn in those less than 17 years of age. Hematoxylin and eosin stain. × 1,458.



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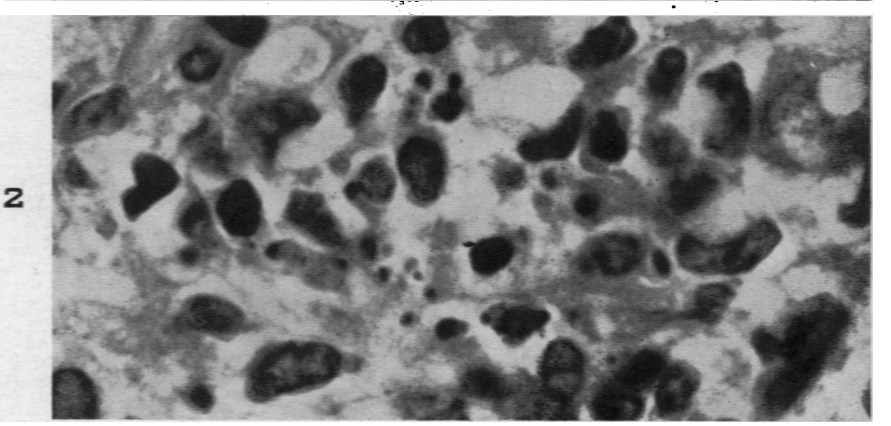
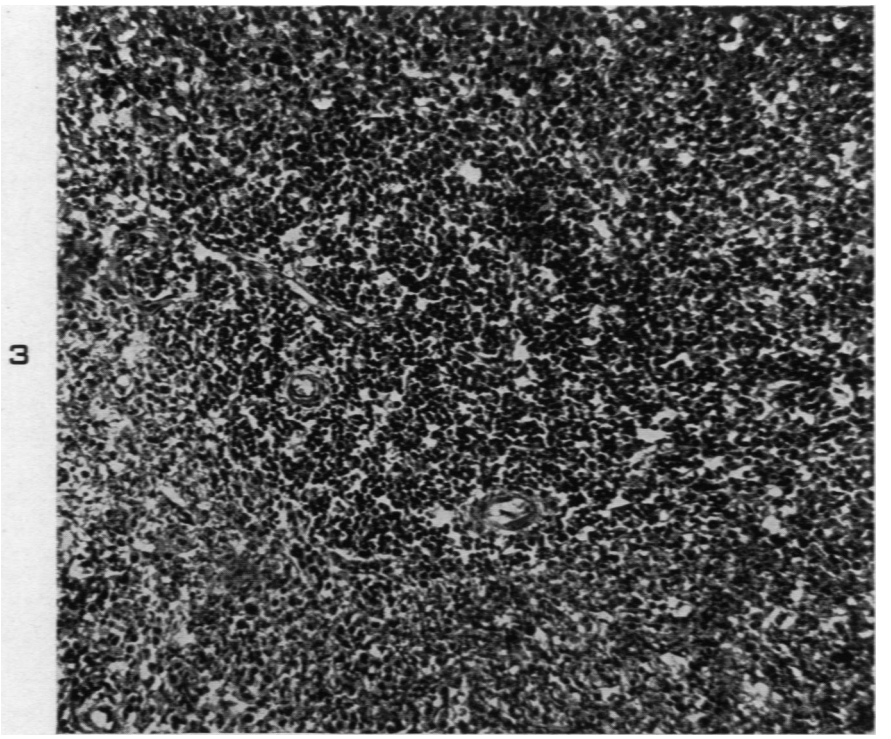


2

PLATE 123

FIG. 3. Low-power photomicrograph of a splenic nodule from a child, 3 years of age, who survived 20 days following a burn. The nodule contains no secondary center, and typifies the nodules throughout the section. Hematoxylin and eosin stain. × 50.

FIG. 4. Oil-immersion field from the center of the splenic nodule of the same case as in Figure 3. No karyorrhexis is present. This case conforms with the general experience that high degrees of karyorrhexis were not encountered in those patients less than 17 years of age if they survived more than 3 days following the burn. Hematoxylin and eosin stain. × 1,458.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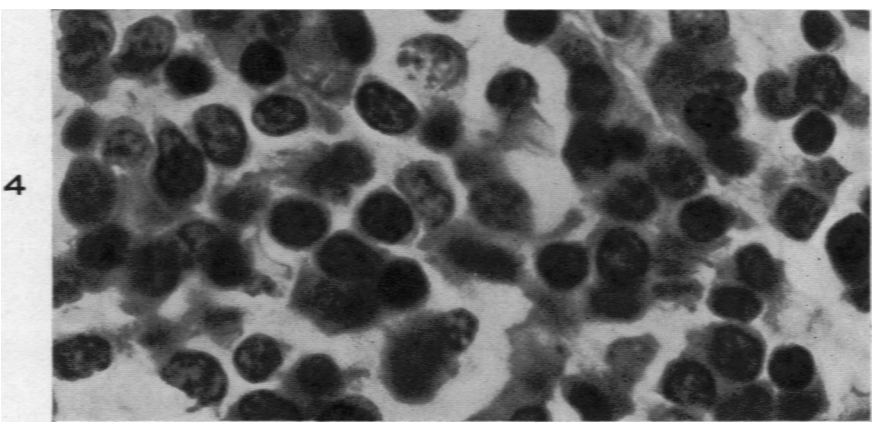
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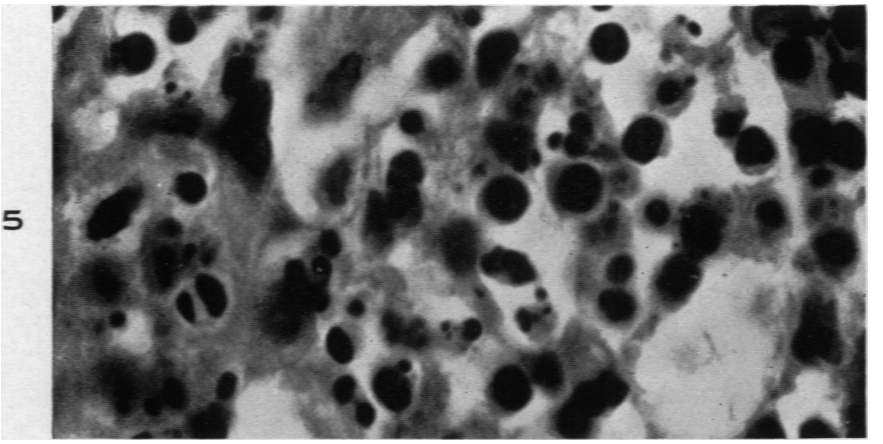
PLATE 124

FIG. 5. Mid-portion of a secondary center of a splenic nodule of a child, 6 years of age, who survived 22 hours following a burn. Karyorrhexis of 3 plus degree is present. As in this example, marked karyorrhexis is usual in young persons dying during the first 3 days following a burn. Hematoxylin and eosin stain. × 1,458.

FIG. 6. Center of a splenic nodule and edge of a secondary center from a child of 5 years who died 8 days following a burn. Karyorrhexis of 1 plus degree is present. As shown in this case, high degrees of karyorrhexis are not noted in young persons who survive more than 3 days following a burn. The photomicrograph also shows cells with abundant hyaline cytoplasm which may represent material previously in the form of nuclear particles, but which now fails to stain because of intracellular digestion. Hematoxylin and eosin stain. × 1,458.

FIG. 7. Center of a splenic nodule from an adult, 38 years old, who survived 12 hours following a burn. Karyorrhexis is absent. This conforms with the observation that high degrees of karyorrhexis were not observed in adults. Hematoxylin and eosin stain. × 1,458.



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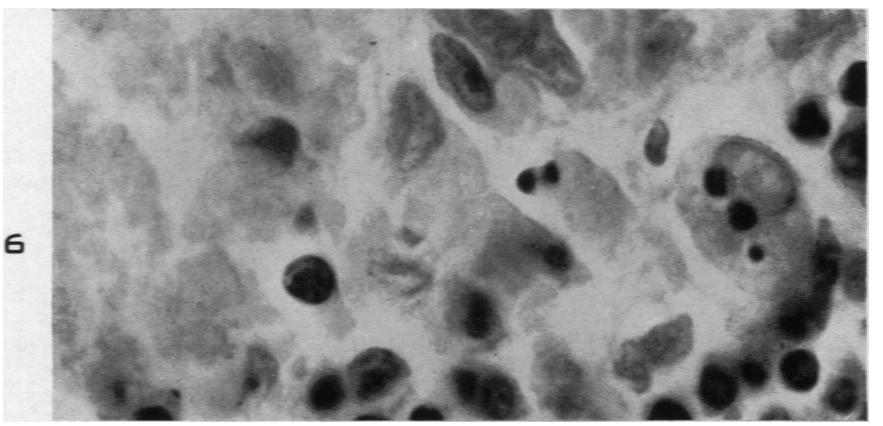

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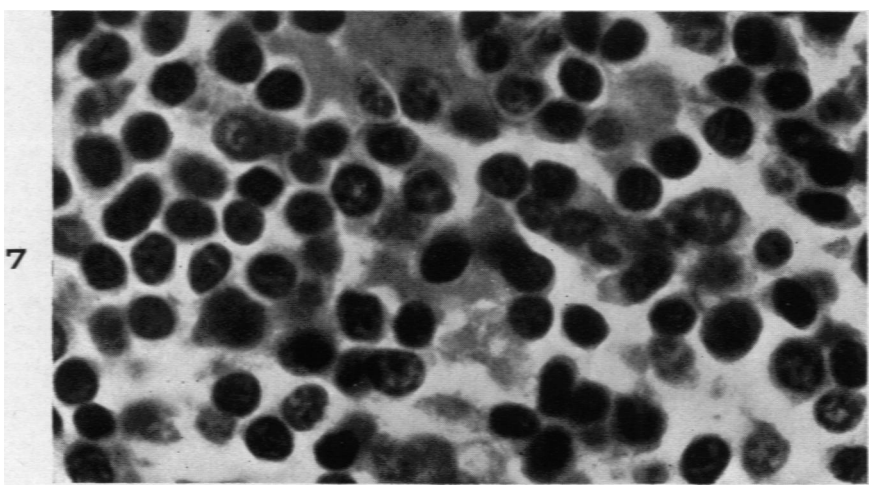

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