THE RATIONALE OF WHOLE BLOOD THERAPY IN SEVERE BURNS*

A CLINICAL STUDY

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INTRAVENOUS THERAPY is so well-established in the treatment of burns there is no longer reason to question its value, but there remains some question as to the best fluid to use. In 1923, Underhill demonstrated the value of sodium chloride solutions in the treatment of burns and, since 1938, blood plasma has been used on a large scale and has proved of value; recently, the publications of Rosenthal,¹ and Fox,² have renewed interest in electrolyte solutions.

The purposes of this paper are (1) to call attention to the red blood cell deficit in the burn patient soon after the burn has been received; and (2) to offer clinical evidence that whole blood may be given advantageously to severely burned patients in the presence of so-called hemoconcentration.

Clinicians have observed that many burn patients given plasma in adequate amounts will show by the fourth or fifth day a moderate to severe anemia. Harkins³ points out that Schrievers found in experimental studies in burns on rabbits an early reduction in the plasma volume accompanied by a decrease in the total circulating red cell mass. The excellent research of Moyer, Coller, Iob, Vaughan and Marty⁴ demonstrated that in the severely burned dog defibrinated whole blood was more effective in controlling burn shock than was plasma, especially if it was given in conjunction with orally-administered sodium chloride-bicarbonate solution.

THE RED BLOOD CELL DEFICIT IN BURNS

Between 1941 and 1944 we had collected a considerable body of blood volume data on severely burned patients. The initial blood volume determinations were made before any fluid had been given intravenously and at 18- to 24-hour intervals for four to five days. Our original interest in blood volume determinations in burn patients was aroused by doubt as to the reliability of estimates of plasma loss when calculated by formulae proposed by Elkinton, Wolff and Lee,⁵ and by Harkins⁶; this will be discussed in a later paper. We were further stimulated to reëxamine this blood volume data by the studies of Moyer, *et al.*, on the value of whole blood therapy in experimental burns. When calculations from these blood volume data were made for

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total circulating red cell mass in burn patients, it was found that in some of them there existed, soon after the burn had been received, a serious deficit in red cell mass. In nine calculations taken at random from the blood volume data of some of the more seriously burned patients it was found that the red blood cell deficit averaged around 40 per cent of the total volume in deficit. This is shown graphically in Chart I. It is evident that there may exist in the severely burned patient a serious red blood cell deficit and that this can only be corrected by the administration of whole blood. When only plasma was administered a serious secondary anemia rapidly developed.

We have confidence in the validity of these data on the red blood cell deficit in the severely burned patient for two reasons: (1) When intravenous fluid therapy consisted only of plasma, and redeterminations of the total mass of circulating red blood cells were made at intervals during the first 72 to 96 hours, there seemed to be little change in the size of this mass. If any change occurred, it was in the direction of a further decrease; and (2) if only plasma was given, and the initial data showed a smaller than normal circulating red cell mass, when the blood volume was returning to normal around the 72nd hour there occurred regularly a moderate to severe secondary anemia, which persisted until red blood cells were given.

Other than a deficit in the red cell mass soon after the burn is received the cause of the early anemia in burn patients has not been disclosed by any studies made by us. We do not believe intravascular hemolysis is responsible for the major portion of this red cell deficit because in many patients there was little or no staining of the plasma with free hemoglobin; we are of the opinion that the red cell deficit is due in the main to sludging or trapping of large masses of red blood cells in the capillaries in and adjoining the burned area. This view is supported by the work of Moritz⁷ who found quantities of iron in the skin of experimentally burned animals, amounting in some cases to around 30 per cent of the total circulating hemoglobin.

It might be stressed that hematocrit data do not necessarily indicate the extent of the anemia in burns, especially when plasma and red cells are lost in disproportionate amounts into the burned area. Further, some of the deficit in red cell mass, especially in children and women in our series, may have been the result of a preëxisting anemia. This view is supported by the findings of Dr. T. Stanley Meade,⁸ who has found a moderate to severe secondary anemia in approximately 50 per cent of the children examined by him in our local health clinics.

CLINICAL STUDIES OF WHOLE BLOOD THERAPY IN SEVERELY BURNED PATIENTS

The main purpose of this study was to evaluate whole blood transfusion* in the management of burn shock in the severely burned patient. Since our studies on red cell deficit in the burn patient (mentioned above) indicated that without blood volume data the hematocrit reading might give no indication of

^{*} By whole blood transfusions we mean "citrated blood"; 50 cc. 5 per cent sodium citrate is used as anticoagulant in each 500 cc. whole blood.

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red cell loss, it was decided to give whole blood transfusions to this series of patients regardless of hematocrit readings. We were encouraged to do this, despite the height of some hematocrit readings, by the report of Moyer, *et al.*, that scalded animals with hematocrit readings of 75 to 80 per cent could be given massive transfusions of defibrinated blood, and that these were compatible with life. Accordingly, whole blood transfusions were given in some cases when the hematocrit readings were as high as 65 to 67 per cent.

The general plan of a clinical experiment was to treat the patient's burn by pressure dressings and to give intravenous whole blood infusions of 500 to 1,000 cc. every six hours for the first 48 hours, along with enough saline and other fluids to keep up a urinary output of 50 to 100 cc. per hour. Every effort was made to have the patient take fluids by mouth rather than by the intravenous route. Fluids were given in the form of water, soft drinks, milk, or fruit juices. This required special nursing care, which was provided in most instances. No attempt was made to give large amounts of sodium salts, orally or intravenously, but with each whole blood transfusion 8 Gm. of sodium bicarbonate was given. Some patients who took fluids best in the form of soft fountain drinks, such as coca-cola, were allowed to have them. All patients were typed and given only type specific blood. At the suggestion of Dr. Philip Levine,9 all female patients were given Rh-negative blood until it could be demonstrated that this was unnecessary. For children one to five years of age the six-hourly infusions of whole blood were usually limited to 150 to 200 cc.; in all burned patients every effort was made to give whole blood to the amount necessary to keep the hemoglobin level above 100 per cent during the first four days of therapy. Penicillin. usually 100,000 units daily, was given to all patients.

In this series of 32 burn patients there have been three deaths: The first, an eight-year-old Negro child, was found in a burning house in which her mother and sister perished. The child was brought to the hospital about four hours after having been burned and was in a state of severe shock; the blood pressure being unobtainable. There were third-degree burns of approximately 60 per cent of the body surface, with severe burns of the face. When the bladder was catheterized no urine was obtained. The initial hematocrit was 67 per cent. She was given during the next eight hours approximately 1,000 cc. of whole blood and 1,000 cc. of saline. In four hours 470 cc. of urine was obtained. The child died following generalized convulsive seizures about eight hours after admission. At catheterization of the bladder after death 210 cc. of urine was obtained. The nonprotein nitrogen was 26 on admission and 40 shortly before death. It would appear that in this apparently hopelessly burned child, admitted in a state of severe shock, whole blood therapy at least resulted in a return of renal blood flow to well above that usually found at the shock level. The second death is that of a 57-year-old Negro male, with approximately 80 per cent body surface involved by thirddegree burns. He had been found lying in a bed that had caught fire, and had been apparently stuporously drunk at the time. On admission, he was

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unconscious, with a blood pressure of 70/50. He was given during the next four hours approximately 2,000 cc. of whole blood and equal quantities of normal saline, but died four hours after admission. The third death occurred in an 11-year-old burned child, 26 days after admission. This patient's treatment and course will be commented on in detail (Case 1).

CASE REPORTS

Case 1.-(Fig. 1, Chart 2): C. P., age 11, was admitted to the Medical College Hospital, January 5, 1945, after having suffered a severe burn. While standing in front of a bonfire his clothing became ignited. The flames were finally smothered by blankets. On admission to the hospital, there was a deep burn extending from the nipple line over the entire body down to the ankles. Sedation was secured with intravenous morphine gr. 4. The burned areas were cleaned with soap and water and dressed according to the pressure dressing technic. Fluid therapy was given as shown in Table I. During the first 24 hours the patient received 2,500 cc. of blood and adequate fluids by mouth so that a urine output of approximately 2,000 cc. was secured for that period. Reference to Chart 2 illustrates that this patient received whole blood transfusions despite the presence of what is considered severe hemoconcentration. During the second 48 hours he received an additional 1,000 cc. of whole blood and adequate fluids by mouth to maintain a good urinary output. The child was quite ill during the first four days of hospitalization, but by the 96th hour showed marked improvement. He was then able to take all necessary fluid by mouth and maintained daily a good urinary output. Penicillin was given every fourth hour, 10,000 to 15,000 units. The first dressing was done on the 12th hospital day, at which time the photograph shown in Figure I was made. At this dressing it was observed that sloughing would take place of the full-thickness of the skin from the ankles to the axillae. At this time, however, the child was in remarkably good condition. He was given whole blood transfusions to the amount of 500 cc. about every third day after the first four days. The hemoglobin levels, which were taken daily, never fell below 82 per cent, and generally were above 90 per cent. The plasma protein, while it was 5.4 per cent on the fourth day, steadily rose, so that by the tenth hospital day it was 6.2 per cent, at about which level it remained. In addition to the blood transfusions a daily intake of approximately 100-120 Gm. of protein was maintained. Although we despaired of ever securing enough skin for grafting, the child's condition appeared hopeful until January 29, the 24th hospital day, at which time he became irrational. Blood chemical studies were all within the normal range, the nonprotein nitrogen being at no time above 46 mg. per cent. It was noted on January 29 that the blood pressure was rising, and late on that day the readings were regularly 160/110, whereas previously they had been in the range of 110/70. Gradually a comatose state set in, and by January 30 the child could not be aroused. All attempts at plasma, whole blood, sodium chloride or sodium lactate therapy failed to change the condition. Despite every attempt at therapy the child died on January 31, 1945. A postmortem examination was secured. This examination showed the burned skin to involve approximately 60 per cent of the body surface. The autopsy revealed no adequate explanation for the patient's death ; since permission for examination of the brain could not be obtained, it is impossible to eliminate an encephalitis or degenerative cerebral lesion as a primary cause of death (see Walker and Shenkin¹⁰). Sections of the liver and kidneys showed no changes from the normal.

COMMENT: This burn patient represents one of the most serious we have treated, and was, indeed, a real test for the efficacy of whole blood transfusions for the management of burn shock. The fact that the child was kept alive for 26 days, with fairly normal levels of hemoglobin, plasma protein and







FIG. 3





F1G. 6



FIG. 1.—Case 1: C. P., taken on first redressing on the 12th hospital day. Full-thickness burns from ankles to nipple line.

FIG. 2.—Case 2: D. T., illustrating extent and depth of the burns of the legs. Figures 7, 8 and 9 show the extent of the burns in this patient of the left arm, thorax, abdomen and buttocks. FIGS. 3 and 4.-Case 3: H. R., illustrating extent of the burns. Photograph taken at first redressing. FIG. 5.-Case 4: W. H., taken at first redressing

FIG. 6.—Anterolateral portion of the thorax of badly burned child taken at the time of first grafting. The good state of nutrition is to be noted. This child received large and frequent whole blood transfusion at the time of entry.

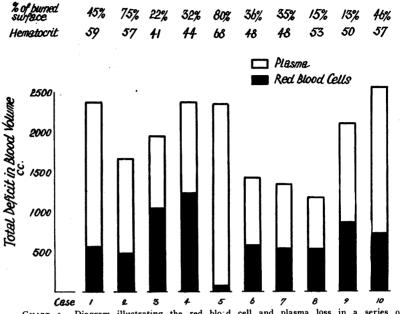
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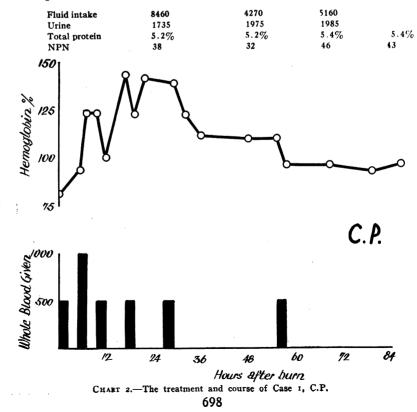
a	FLUID BALANCE SHEET FOR PATIENTS DISCUSSED			IN DETAIL IN TEXT	
	Oral				
Day	Water	Milk	Fruit Juice	Intravenous	Urine
Case 1. C. P. 1	1600	550	510	2500 blood 2000 saline	173 5
				1400 water 3 amp. sod. lact. 32 Gm, NaHCO ₃	
2	2445	710	?15	500 blood 500 saline 2 amp. sod. lact.	1975
3	1730	1040	90	8 Gm. NaHCO ₃ 500 blood 1500 saline 1 amp. sod. lact.	1985
			600	8 Gm. NaHCO ₃	
4 5	1420 1515	1640 2235	680 680		2745 1625
саяе 2. D. T.	1315	2235	000		1025
1	1560	••••	500	3300 blood 3000 saline 2500 water 2 amp. sod. lact.	1525
2	2370	720	790	32 Gm. NaHCO ₃ 2000 blood 2500 water 1000 saline 1 amp. sod. lact.	2010
3	3240	1050	200	32 Gm. NaHCO ₂ 500 blood 8 Gm. NaHCO ₂	1795
Case 3. H. R.					
1	1470	••••	400	2500 blood 1000 water 1000 saline 2 amp. sod. lact.	1900
2	360	••••	250	24 Gm. NaHCO3 1500 blood 3000 water 24 Gm. NaHCO3	2100
3	1210	200	650	500 blood 8 Gm. NaHCO ₃	1000
4 Case 4. W.H.	2460	360	380	3000 saline	1350
1	1860	300	660	2500 blood 500 saline 1 amp. sod. lact. 32 Gm. NaHCO3	2762
2	1860	360	500	1000 blood 16 Gm. NaHCO ₃	2400
3	1540	450	640	500 blood 8 Gm. NaHCO3	1900
4	1280	480	440		1200
5	1430	720	560	500 blood 8 Gm. NaHCO3	1300

TABLE I

BLOOD AND PLASMA DEFICIT IN BURNS



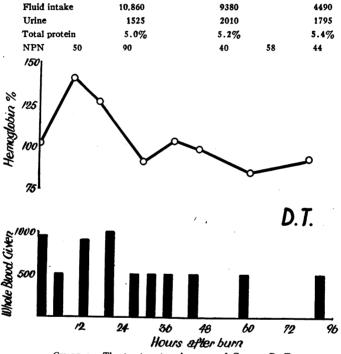
CHAR 1.—Diagram illustrating the red blo: d cell and plasma loss in a series of severely burned patients. Calculations were made on the basis of a normal person having a total blood volume of 80 cc. per Kg., and an hematocrit of 45%. Cases 2 and 5 died on the fourth and fifth days, respectively; the other patients survived. Case 5 was largely a second-degree burn.

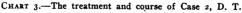


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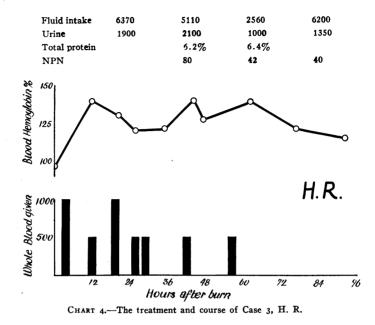
urinary output attest, we believe, to the value of whole blood transfusions in the badly burned patient.

Case 2.—D. T., white, male, age 27, was admitted November 18, 1944. In a fire which totally destroyed an automobile trailer (in which his wife and child perished), the patient suffered severe deep burns of left arm, thorax, trunk, buttocks and legs, as shown in Figures 2, 7, 8 and 9. On admission, the blood pressure was 115/70. Pressure dressings were applied rapidly, and intravenous blood and saline therapy begun. Thirty-three hundred cubic centimeters of whole blood was given during the first 24 hours, and 2,400 cc. during the second day. Whole blood was given in the presence of marked





hemoconcentration in this patient (Chart 3). Urine output was good, although the nonprotein nitrogen rose to 90 at the 12th hour, returning to 40 the next morning. Fluids were taken well by mouth, and on the third day a special high protein diet was started which the patient took well. The first redressings were made of the arms and chest on the 14th day, the buttocks and legs five days later. Grafting of the legs was done first on January 2, 1945. It is interesting to note that this extensively burned patient maintained a good hemoglobin level (never below 79 per cent during his six-month hospital stay); this we attribute to his excellent coöperation in taking a special high protein diet daily during his first five months of hospitalization and which will be discussed in a later paper. He was discharged June 3, 1945, after grafting and intensive physiotherapy, able to walk. He will return later for revision of a graft of the left popliteal space.



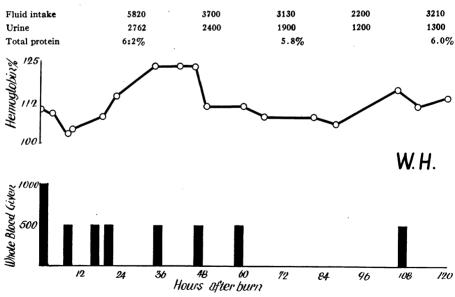
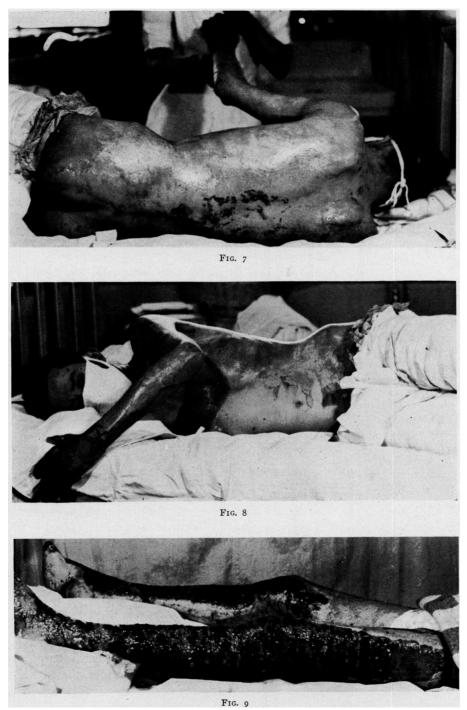


CHART 5.- The treatment and course of Case 4, W. H.

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FIGS. 7, 8 and 9.—Case 2: D. T., showing extent of burns. Figures 7 and 8 taken at first redressing on the 14th day. Figure 9 taken four weeks after the burn had been received. In extensive burns of this nature, it is our practice to redress only small portions of the burned surface at one session. **Case 3.**—H. R., a 34-year-old Negress, was admitted to St. Philip Hospital January 17, 1945. Her clothes caught fire while she was "throwing kerosene into the stove." Despite extensive burns as shown in Figures 3 and 4, the patient was in good condition on admission. Pressure dressings were applied, and the patient given whole blood transfusions as shown in Chart 4. She took fluids well, and maintained a satisfactory urinary output. Her clinical course was excellent; the first redressings were made on the 14th day, at which time photographs shown in Figures 3 and 4 were made. Although her hemoglobin levels were kept above 85 per cent during the first 29 days of hospital stay, and while she was taking well a special high protein diet, her clinical course was marred by the fact that vigilance relative to diet was relaxed, so that during the second month of hospital stay the hemoglobin dropped to 70 per cent. This was corrected by 1,500 cc. whole blood infusions and resumption of the special diet. Excellent healing occurred of all badly burned parts except the under portions of forearms; these were covered with split-thickness grafts.

Case 4.-W. H., an 18-year-old male Negro, who suffered burns of thorax and abdomen, hands and forearms, thighs, scrotum, and penis, was admitted to St. Philip Hospital January 6, 1945. He received his burns as a result of throwing motor oil on an open fire. On admission, the patient was in good condition, and pressure dressings were applied in the ordinary manner soon after entry. He was given 2,500 cc. whole blood during first 24 hours, and 1,000 cc. whole blood the second day (Chart 5). His hemoglobin remained in the neighborhood of 110 per cent after the first 48 hours. Healing of the burned areas was extraordinarily rapid, the photograph shown in Figure 5 being taken on first redressing on the 14th hospital day. Plasma protein levels never fell below 5.8 per cent, and after the 14th hospital day remained above 6.8 per cent. The special high protein diet was given starting on the fourth hospital day. During the first month of treatment the hemoglobin was consistently 100 per cent or above, although no more blood transfusions were given after the fifth hospital day. On February 2, 1945, the penis was covered with a dermatome split-thickness graft and "postage stamp" grafts, cut with the dermatome, were applied to the left thigh. The "take" was 100 per cent. The patient was discharged March 1, 1945, with complete recovery.

THE CLINICAL EVALUATION OF WHOLE BLOOD THERAPY FOR BURN SHOCK The besetting sin of clinical investigation can be preference for argument over observation

After treating several hundred burn patients, we find it difficult to compare the effectiveness of blood and so-called blood substitutes, one with another. It is, therefore, difficult for us to compare whole blood with plasma in the management of burn shock. For this reason some of the observations cited below concerning the value of whole blood in the initial treatment of the severely burned patient might best be termed "clinical impressions." They should not be construed as detracting from the value of plasma in burn therapy.

(1) Blood Hemoglobin Levels: In our experience, if fairly large amounts of whole blood are given to the burn patient during the first 48 hours "masked anemia" is not encountered, whereas in burn patients treated only with plasma this condition occurs frequently. It appears, therefore, that if whole blood is given in adequate amounts during the burn shock period secondary anemia will be prevented. This leads us to believe that secondary anemia in burn patients may be more easily prevented than treated. Volume 122 Number 4

(2) Plasma Protein Levels: When burn patients are given plasma alone, even in large amounts, it is not unusual to find low plasma protein levels on the fourth or fifth day. This is especially true if the burn is deep and extensive (above 40 per cent). On the other hand, in this series of burns treated with large amounts of whole blood the plasma protein levels were maintained at more nearly the optimum level (Cases I to 4). This may be due to improved blood flow through the liver during the burn shock period and, therefore, less liver anoxia in the whole blood therapy may be the maintenance of the liver in such a state that plasma protein production is carried on in a more nearly normal manner during the initial burn period. It should be remembered, however, that this group of patients received large and frequent transfusions.

(3) Urinary Output: As was noted in the detailed case reports, we have found it possible to maintain a good urinary output even when hemoconcentration appeared to be quite marked. It is evident from the nonprotein nitrogen figures that renal blood flow must have been maintained at a level adequate for good renal clearance. Difficulty on this score was encountered with only one patient (Case 5).

Case 5.—A 57-year-old colored female, M. T. [on whom we have previous clinical records indicating that she was suffering from hypertensive cardiovascular disease (B. P. 230/140, retinal changes Grade 3)], when she received a deep burn of approximately 25 per cent of the body surface on March I, 1945. She was treated with whole blood infusions totaling 2,500 cc. during the first 48 hours, and maintained a good urinary output for the first three days (1,900, 1,725 and 1,285 cc., respectively). Her hemoglobin levels ranged from 100 to 120 per cent during this time. On the fourth day, when her hemoglobin level was 106 per cent, the blood nonprotein nitrogen rose to 106, and her urinary excretion diminished to less than 600 cc. From then on she was given only approximately 2,000 cc. of fluid by mouth each day. By the seventh day the nonprotein nitrogen had come down to 46, and urinary excretion was good, and remained so.

An attempt should be made to induce the burn patient to take fluids and food (especially protein) by mouth, so that it is not necessary to give large amounts of fluid intravenously. The observations of Moyer, et al., emphasize this point forcibly. We have hesitated throughout our studies on burns to employ excessively large amounts of fluid by vein precisely for the reasons pointed out by Moyer. Conscious patients, given expert nursing care, will take adequate amounts of fluid by mouth, especially if given the type of fluid they desire. The first burn patient we treated with plasma in 1939, would take only one particular soft drink but drank six to eight bottles of it each 24 hours for the first two or three days. By letting patients have fluids of their own preference and at intervals according to their wishes, or after quiet but firm insistence by the nurse, it is usually possible to maintain a good urinary output throughout the 24-hour period, but when intravenous fluids are resorted to, one usually finds that good urinary output occurs only during and shortly after the fluid administration.

(4) Toxemia: Our clinical impression is that these burn patients treated

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with whole blood have shown less "toxemia" than did other patients treated with plasma or gelatine. This can only be an impression. The temperature and pulse curves of the four patients whose records were presented above are: Case I, C. P., for the first four days rectal temperature ranged between 100° and 102° F., pulse rate between 90 and 120; Case 2, D. T., for the first four days rectal temperature ranged 102° to 104° F., pulse rate consistently around 120; Case 3, H. R., for the first four days temperature ranged from 100° to 102° F., pulse rate 90 to 120; Case 4, W. H., rectal temperature first four days 100° to 103° F., pulse rate 100 to 110. The respiratory rates of all four patients averaged around 30 for the first four days. It should be recalled, however, that Case I, C. P., was at times irrational during the first two days and vomited small amounts at intervals during this time. One other patient, a badly burned four-year-old colored child, appeared to be quite toxic during the first four days of therapy.

(5) Healing of Burns: This is another problem that defies comparison of one series of burns with another because it is difficult to judge the exact depth of the burn in an individual patient, but, in general, burns caused by actual fire are deeper than those caused by hot water or steam. It may be significant, therefore, that in this series all patients were burned by fire. On the basis of our former experience one would have expected that more or less extensive grafting would be required in many of the patients in the present series; such was not the case.

We realize that no known therapy will convert a full-thickness burn into one that heals satisfactorily without grafting. Nevertheless, in burns with severe destruction of the tissues, which heal without grafting, there are several factors that might act to promote or retard epithelial growth. For example, if in a burned area viable epithelial cells are left at the base of hair follicles or sweat glands, healing may take place by outgrowth from these "hidden islands" if (1) the dressing is left undisturbed for long periods of time; (2) infection does not supervene; and if (3) proper nourishment is available to promote rapid growth in the residual epithelial cells.

We have been pleased with the rapidity with which growth of epithelium has taken place in burned areas that at first appeared of a depth and extent to require extensive skin grafting. We do not wish to overemphasize the importance of adequate amounts of whole circulating hemoglobin in the healing process but only with an adequate circulating red cell mass can oxygen and food, such as amino-acids, be carried to the zone of injury in sufficient quantities. With an inadequate number of red cells, healing cannot be rapid.

(6) Intravascular Clotting: An increased incidence of thrombosis in burn patients with hemoconcentration has been feared, and one might hesitate to give whole blood for this reason, but it is interesting to note that in this series of 32 patients, 29 of whom survived, there was no instance of thrombophlebitis or pulmonary embolus clinically recognizable.

Finally, it should be emphasized that whole blood has been used in this

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series of patients to determine whether it could be given safely to the burn patient in the presence of moderate to severe hemoconcentration. Our experience indicates that whole blood can be given safely under these conditions.

CONCLUSIONS

Blood volume determinations of severely burned patients made soon after the burn had been received indicate a decrease in total circulating red cell mass. It is believed that this initial loss of red blood cells may account for a considerable portion of the "masked anemia" that appears in the post-shock period in many burn patients.

Whole blood infusions have been employed for the management of burn shock in a series of 32 severely burned patients. Whole blood has been given in the presence of marked hemoconcentration. Apparently, whole blood can be given safely to burn patients with hemoconcentration. If adequate amounts of whole blood are given initially in severely burned patients, secondary anemia is regularly avoided.

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