PRIVY COUNCIL

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SPECIAL REPORT SERIES No. 249

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PREFACE

In the four years immediately preceding the war there were approximately 1,270 deaths per annum from burns and scalds in England and Wales, of which nearly half were at ages under 15. The many thousands of burned patients who did not die represent a formidable loss of man-power in industry and of school-hours. Many recovered with crippling deformities due to scarring.

In the present war, in which petrol engines, explosives and fire play so large a part, burns and scalds have become still more important, and their treatment one of the major problems of war surgery. At El Alamein, one in four of the battle casualties were of this nature, and all through the desert campaign, quite apart from actual fighting, serious accidental burns due to petrol were of common occurrence.

These injuries present many unsolved problems. It is not clear why damage to the skin—sometimes, in children, involving only a tenth of the body surface—should so often prove fatal. Nor has it been possible up till now to prevent septic infection of most of the deep burns—as well as many of the more superficial ones. Skin replacement by grafting procedures has greatly assisted healing, but the possibility of improved methods needs to be explored. Finally, there is a whole train of difficult metabolic problems created by the long continued suppuration and exudation from the burned surfaces, and by the destruction of tissues.

The need for investigation of all these questions has long been recognized—indeed many enquiries have been set on foot in years gone by—but progress has been slow. It has always been hampered by the fact that burns and scalds occur at irregular intervals and the patients are received into every general hospital. Nowhere in Britain had there hitherto been a concentration of patients together with a team of surgeons and laboratory workers with facilities for a prolonged systematic study.

At the Royal Infirmary, Glasgow, wards have for many years been set aside for the treatment of burns, and a larger number of these injuries is dealt with there than at any other hospital in the British Isles (about 1,000 fresh cases every year). In these wards, 10 years ago, Dr. Robert Cruickshank made an important contribution to the bacteriology of burns, showing that, in many instances, infection by haemolytic streptococci develops within a few days after admission to hospital and is by far the most serious complicating factor. He also observed—probably for the first time—that haemolytic streptococci were frequently present in considerable numbers in the air of the Burns Wards, whereas they were found only in small numbers in the general surgical wards and not at all (in his experience) in the medical wards of the hospital.

In view of the urgent need created by the war emergency to initiate further research on various aspects of the treatment of burns, the Medical Research Council, in agreement with the Managers of the Royal Infirmary, Glasgow, decided to appoint a junior surgeon to give whole-time assistance to Mr. A. M. Clark, the surgeon in charge of the Burns Wards, and to establish a laboratory team with a view to a preliminary bacteriological, haematological and biochemical survey of the problem. Mr. Thomas Gibson was appointed from February, 1942, to the surgical post, and Dr. Leonard Colebrook, of the Council's staff, undertook to direct the laboratory studies, and to co-ordinate these with the clinical observations. Professor J. W. S. Blacklock, Pathologist to the Royal Infirmary, kindly arranged laboratory facilities for Dr. Colebrook and his team, and himself supervised the pathological

investigations of the cases. A part-time grant was made to Dr. Alexander Brown for the haematological work, and for the general medical supervision of the patients. Dr. A. Bruce Anderson, in charge of the Biochemical Laboratory of the Royal Infirmary, undertook to supervise the work of Miss E. Semeonoff, who received a whole-time grant from the Council.

The present Report embodies observations made in 1942 and 1943 on some 400 in-patients with burns, and on nearly 2,000 patients with less severe burns who were treated as out-patients.

MEDICAL RESEARCH COUNCIL,
c/o London School of Hygiene and Tropical Medicine,
Keppel Street, London, W.C.1.

July, 1944.

CONTENTS

(Detailed Tables of Contents precede Parts I–VI.)

STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942-43)

GENERAL INTRODUCTION

BY

LEONARD COLEBROOK, M.B., B.S., F.R.C.O.G.
(Member of Scientific Staff, Medical Research Council).

The work covered by the reports forming parts of this monograph has dealt chiefly with two aspects of the burns problem—the control of infection and the treatment of " burns shock ".

Part I tells of an attempt to formulate the functions of an ideal first-aid treatment; calls attention to the danger of first-aid undertaken without regard to asepsis; recommends an antiseptic cream for use in certain limited circumstances; and sets out the results obtained in combined clinical and bacteriological trials of such a cream.

Part II, on the control of infection, challenges the tacitly accepted view that infection of deep burns is inevitable; and relates a serious effort to eliminate such infection in 330 cases. It emphasizes the large part played by cross-infection; describes the measures taken to prevent it, including the elimination of " reservoirs of infection " by penicillin and sulphonamides; shows the degree of success achieved by these procedures, and discusses the lines along which further progress may be expected. The need for further concentration of burned patients in specially staffed and equipped centres is stressed.

In Part III, on replacement therapy, attention is focused upon " burns shock", which is responsible for the majority of the deaths from burning. The authors proceed from the established fact that concentration of the corpuscular elements of the blood occurs early after burning, and attempt to show how far correction of that concentration, by transfusion of serum or plasma, will avert the advent of shock and subsequent death. By a series of graphs synchronizing the degree of haemoconcentration, changes of blood pressure, pulse rate and temperature, with the fluid replacement, they illustrate their conclusion that energetic intravenous fluid replacement is often able to tide the burned patient over the dangerous period, but that this procedure calls for constant clinical watchfulness and laboratory aids in carrying it out. They emphasize, in this connexion, that too rapid transfusion, or the transfusion of excessive amounts of fluid, carries its own grave risks, especially in young children: it may lead to severe transfusion reactions or to pulmonary oedema. A nicety of clinical judgment, with constant observation of the pulse rate and volume, blood pressure and skin circulation—and with frequent blood examinations—is required to strike the happy mean between inadequate and too liberal transfusion.

Part IV—on blood changes and blood pressure in burns—is supplementary to Part III. It provides data on the correlation of haemoconcentration with different degrees of burning. It also shows that changes of blood pressure are often an unreliable guide to the patient's progress, especially during the first few hours after burning. In addition, it traces the development of

anaemia in burned patients and supplies evidence that this is not merely the result of a compensatory dilution of the blood by return of fluid from the tissues. Striking changes in the fragility of the red cells in severely burned patients are also recorded, as well as some preliminary observations on the changes in the leucocyte counts after burns.

Part V presents a preliminary survey of some of the biochemical changes found in a series of 70 burned patients. It calls attention to the considerable loss of protein from the blood plasma, and the moderately increased nitrogen excretion and high bilirubin values, in such cases.

Part VI—on post-mortem findings in 30 fatal cases of burning—brings further support, although of a negative kind, to the current view that extensive central lobular necrosis of the liver is usually associated with tannic acid treatment. Apart from congestion and oedema of the brain, and some evidence of damage to kidney structures, post-mortem examinations brought few positive indications as to the pathological processes which lead to death in the early stages after burning.

STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART I.—THE FIRST-AID TREATMENT OF BURNS AND SCALDS*

BY

LEONARD COLEBROOK, M.B., B.S., F.R.C.O.G.

(Member of Scientific Staff, Medical Research Council)

THOMAS GIBSON, M.B., Ch.B., F.R.C.S.E.

(Working with a whole-time grant from the Medical Research Council)

AND

J. P. TODD, Ph.D., Ph.C.

(Professor of Pharmacy, Royal Technical College, Glasgow)

CONTENTS

INTRODUCTION

In any discussion about the management of burns and scalds, it is important to distinguish clearly between—

(*a*) treatment applied as a purely temporary measure at the scene of the accident, before the patient is sent to a hospital or doctor. This is strictly *First-Aid Treatment.*

(*b*) the formal treatment, carried out by a doctor or nurse, whether in the home, or the "surgery" or the hospital, where adequate facilities are available. This we have termed, at the suggestion of Sir Almroth Wright, the *Plenary Treatment,* to convey the idea of completeness.

(*c*) subsequent dressings, skin grafting procedures, etc.

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* A paper similar to this was published in the *British Journal of Industrial Medicine,* 1944, **1**, 99.

The present paper is concerned only with First Aid—and almost entirely with the local treatment of the burn. Civilian burns have been chiefly in mind, but the principles underlying treatment are the same for burns sustained on active service.

There is no agreed policy with regard to the initial treatment of burns. Owing to the natural urge on the part of the patient or his friends to do something (however ill-advised), it has been found that about 75 per cent. of civilian patients arrive at hospital with some kind of application to the burned area—olive oil, carron oil, flour, coagulant jellies, cold tea, sodium bicarbonate, an "ointment" or flavine, etc.—often covered with a dirty, or at least a non-sterile, piece of cloth. Frequently, pain has not been relieved by these applications—sometimes it has been increased; and the difficulty of removal of the semi-coagulated jelly, of the oil or caked flour, may well augment considerably the original trauma suffered by the burned tissues, thereby favouring the development of "shock". First-aid remedies of this kind, especially if applied, as they usually are, without aseptic precautions, may well do much more harm than good.

In view of the great importance of burns in the mechanized warfare of to-day, and their contribution to wastage in industry, we have attempted to formulate a simple first-aid procedure which would be generally applicable, and have a satisfactory scientific basis. An ideal first-aid procedure should—

(*a*) relieve pain promptly and, by so doing, cut off sensory stimuli which probably play some part in inducing "shock"

(*b*) prevent the arrival of pathogenic organisms—in particular of haemolytic streptococcus—on the burned surface; or, if this has already happened, destroy the bacteria or prevent their multiplication

(*c*) do no further damage to the already injured but still viable skin tissues, nor interfere with the natural anti-bacterial defence by leucocytes

(*d*) provide a dressing easily removed by gentle washing with a watery solution during the subsequent clean-up in hospital or the "surgery".

THE RELIEF OF PAIN

The problem of the relief of pain in burns was studied in two ways—

(1) by direct observation on small experimental burns in the human subject,

(2) by the application of creams containing analgesic agents to a series of accidental burns in factories and in the Burns Ward of the Royal Infirmary, Glasgow.

The experimental human burns were caused by a flat-bottomed copper tube through which water at temperatures of 55° to 60° C. was circulating (Leach, Peters and Rossiter, 1943). Light pressure with this tube on the forearm for 45–50 seconds gave a fairly uniform, manageable, second degree burn, which was more painful than burns caused by higher temperatures for a shorter period.

Observations on some 24 of these standard low temperature burns showed—

(i) that exposure to air caused pain and hot air increased it. The burned area, however, is partially anaesthetic (pin-prick test).

(ii) that cold water or any cold watery cream gave instantaneous relief (cooling effect) but this relief was usually short-lived and was followed by a variable amount of burning or throbbing, which lasted for an hour or more.

(iii) the application of local analgesics in a cream composed of :—

Cetyl trimethyl ammonium bromide (" Cetavlon ")	1 per cent.
Cetyl alcohol	5 per cent.
Linseed oil	25 per cent.
Water to	100 per cent.

sometimes afforded more relief than the cream alone, but the effect was not constant in different individuals. The local analgesics tested were :—

Orthocaine B.P. (" Orthoform ")	2 per cent.
Benzocaine	0·5 per cent.
" Percaine " (" Nupercaine ")	1 per cent.

The effect of these analgesic creams on accidental burns was similarly difficult to assess. At a Rolls-Royce factory, the medical officer and his surgery staff were definitely of the opinion that the cream containing orthocaine was superior to those with other analgesics, and to the same cream without any analgesic. He also reported that very satisfactory healing, with almost no sepsis, resulted when this cream was left on the burns as the sole treatment. At another factory (Messrs. C. & J. Weir, Ltd.) the medical officer and his assistants did not get such a clear-cut impression. In the Burns Ward at the Royal Infirmary, Glasgow, the relief obtained from application of the orthoform cream was also somewhat variable. (It was noted that many of the patients on arrival at hospital within half an hour to two hours of burning did not complain of pain.)

No toxic effects were observed from the use of these analgesics, but they were not applied to extensive burns. One of us (L. C.) was informed by Lieutenant-Colonel J. Barrett Brown, of the Medical Corps, U.S. Army, that such effects have been reported in America, particularly with " Percaine ".

THE PREVENTION OF INFECTION

One event is especially to be feared in connexion with every fresh burn, namely, infection of the surface by haemolytic streptococcus. If this does not occur, the great majority of superficial burns heal within 7–20 days ; if it does occur, the damage to tissues is usually increased, healing may be much delayed, and, if the burned area involves flexures, contractures are likely to result. In some cases, a spreading cellulitis or lymphangitis may develop and constitute a threat to life. The late deaths (after the fourth day) are not infrequently due to such an invasive infection. Staphylococcal infection of the fresh burn may also be troublesome and delay healing, but seldom has such serious consequences as infections due to streptococci.

Under the existing somewhat haphazard arrangements for first-aid treatment in burns, both these infections are very common. Table I shows the incidence of streptococcal contamination of 516 burns on arrival at the Glasgow Royal Infirmary (1942–43). Within the first 12 hours after burning, only 4 per cent. yielded haemolytic streptococci—and the proportion of positives was considerably lower for cases examined within three hours. After 12 hours the proportion of infected cases rises steeply.

TABLE I

No. of hours after injury	*No. of burns examined*	*Haemolytic streptococci present*
0–12	370	15 = 4 per cent.
12–24	39	9 = 23 per cent.
More than 24	107	45 = 42 per cent.

(Of all the minor burns treated in the out-patient department, 30 per cent. were infected with haemolytic streptococci at the patients' first visit to the hospital.)

The primary object of all first aid to burns should be the prevention of these streptococcal infections. It should seek, in the first place, to prevent the arrival of any streptococci on the burned surfaces; and, if they have already arrived there, it should seek to destroy them, or at least to prevent their multiplication.

How to prevent the arrival of haemolytic streptococci on the burned surfaces

Haemolytic streptococci are rarely found on normal human skin (see below) it follows, therefore, that those which infect burns must usually be derived from sources other than the patient's own skin.

Colebrook, Maxted and Morris Johns (1935) isolated haemolytic streptococci (group A) from the hands of 7 of a group of 181 factory workers, but the circumstances suggested that in some of these subjects the organisms might have come there from the respiratory tract. The same authors failed to isolate any group A strains from the perineum and thighs of 160 parturient women. Hare (1941) in Canada isolated only one group A strain from the hands of 248 students. Colebrook (1930) also showed that when haemolytic streptococci were experimentally dried on the skin of the hands they did not remain viable for more than a few hours.

It is not difficult to visualize the many sources from which burns may acquire these infecting cocci. Haemolytic streptococci are widely distributed in all human communities in the temperate zones, being associated with, and continually disseminated from, many common infectious processes, e.g., cellulitis and septic sores, erysipelas, impetigo, whitlows, scarlet fever and tonsillitis, otitis media and the chronic "*running* ears" of childhood, puerperal fever, etc. In addition, they are present in the naso-pharynx in many healthy "carriers" (5–30 per cent. of the population), who project them into their environment by coughing, sneezing, etc. Much less commonly, they proliferate in the noses of "nasal carriers", and these individuals are especially dangerous, because of the continual seepage on to handkerchiefs, clothes, hands, etc. From all these sources, haemolytic streptococci find their way into the air of public places and private houses; they remain viable for long periods in dust, and are freely disseminated by the sweeping of floors and the shaking of blankets and other bedding (Thomas, 1941; see also pp. 34 and 36, below). Finally, it should be noted that, although haemolytic streptococci cannot survive in the acid secretion of normal skin, they multiply very rapidly in the serous exudates of the burned surface and commonly persist there for long periods.

Clearly, it will not be easy to prevent the fresh burn from contamination from so many potential sources; and, without strict precautions, first-aid procedures may themselves provide the medium for such contamination. There can be little doubt that in the past they have often done so.

First-aid personnel treating burns should wear efficient masks, covering the mouth and nose, or, if these are not available, a clean handkerchief tied over the nose and lower half of the face may serve. The burned surface should be covered as soon as possible with a sterile cloth or, at least, a recently laundered clean towel. Blankets are seldom sterilized at the laundry, and therefore are very apt to be contaminated with pathogenic organisms, including haemolytic streptococci. They should on no account be allowed to touch the burned surface.

The hands of first-aid personnel should be carefully washed for at least two minutes, and then dried on a clean towel, before any treatment of the burn is undertaken.

If the burn is extensive and cannot be exposed without removal of clothes, the patient should be sent immediately to hospital, without any first-aid dressing of the injured surface.

How to deal with haemolytic streptococci which have already arrived on the burned surface

First-aid treatment should involve a minimum of interference with the burned surface, because the conditions will seldom be such as to allow of strictly aseptic procedure. For this reason, the burn should not be washed, nor should blisters be snipped.

The bactericidal or bacteriostatic agent employed should be in the form of a water-soluble cream which can be easily washed off during the subsequent plenary treatment, rather than a jelly or coagulant solution, such as tannic acid, which will be difficult to remove. Bactericidal dyes, such as gentian violet, although they may have advantages in some special circumstances—e.g., on small ships—are not recommended for general use, because they prevent the medical man who subsequently treats the case from forming an opinion as to the depth of the burn. They are also highly toxic to the already injured skin tissues, and cannot be washed off during the plenary treatment. They cannot be relied upon to sterilize the burned surface with certainty.

Of the anti-bacterial agents available at present, the new synthetic detergent, cetyl trimethyl ammonium bromide (" Cetavlon ") seems likely to be the most effective for the first-aid treatment of burns. Barnes (1942) showed that, in addition to its cleansing effect on normal skin, it was remarkably effective in getting rid of the " resident " organisms—apparently reaching those in the depths of sweat and sebaceous glands and hair follicles more successfully than the substances previously used as skin antiseptics. Our own experiments and those of Williams *et al.* (1942) have confirmed this, and also the fact that " Cetavlon " has a rapidly lethal action on haemolytic streptococci. Because of its toxic action on leucocytes and on cells in tissue culture (Barnes, 1942; Jacoby, 1943), it cannot be regarded as the ideal substance to apply to tissues of which regeneration is necessary, but in actual practice with burns the risk of any toxic effect has proved very slight. Apart from three instances of sensitization-dermatitis (see note below), no irritant effects have been observed among the 2,000 cases of burns to which " Cetavlon " has been applied in Glasgow during 1942–3 ; nor has it seemed to delay healing.

" Cetavlon " has, however, the disadvantage of being a potent protein precipitant, and thereby forfeits much of its anti-bacterial potency in presence of the serous exudate of burns. On the other hand, as shown in Table II, this anti-bacterial effect is by no means abolished by serum or blister fluid. Pending the discovery of an equally potent anti-bacterial substance which is free from its defects, " Cetavlon " appears to be the most suitable disinfectant for first-aid application to burns. By virtue of its powerful detergent properties, it will remove most of the detachable organic material from the burned surface and surrounding skin, and thereby greatly facilitate the destruction of bacteria. Moreover, it is compatible with sulphonamides, so that these two types of anti-bacterial agent can be combined in a first-aid cream.

Such a combination seemed desirable for two reasons: (1) because the bacteriostatic effect of the sulphonamide would reinforce that of the " Cetavlon," and (2) because sulphonamide was likely to be more effective than " Cetavlon " in controlling an infection by haemolytic streptococci which had already invaded the tissues, e.g., in burns several hours old when first seen.

Several such combined creams were prepared for trial at the Glasgow Royal Infirmary by one of us (J.P.T.). The one found most satisfactory ("No. 9 Cream") had the following composition :—

Cetyl trimethyl ammonium bromide	1 gramme
Sulphanilamide	10 grammes*
Castor oil	25 „
Beeswax	1·8 „
Wool fat	1·8 „
Cetyl alcohol	5 „
Glycerin	10 „
Water	45·4 „

"No. 9 Cream" is prepared as follows :—Mix the castor oil, beeswax, wool fat and cetyl alcohol at as low a temperature as possible. Dissolve the "Cetavlon" in the water with the aid of heat ; mix with the oil etc. at about 60° C., and stir till set. The sulphanilamide is then rubbed up with an equal weight of glycerin, the two together comprising 20 per cent. of the final product. This sulphanilamide-in-glycerin is then incorporated in the cream and thoroughly mixed. A Peerless Mixer with bent arm at slow speed has given the best results, but the preparation can be made by hand, although not quite so well.

This cream cannot be heated to sterilize it, but it may be regarded as self-sterilizing for the ordinary non-sporing pathogens. Samples experimentally contaminated with *Staphylococcus aureus*, *Proteus* and *Ps. pyocyanea* have always been found free from viable organisms after 24 hours. It is possible that spores of pathogenic clostridia, including *Cl. tetani*, might survive in it (this point is being investigated), but the risk of such contamination may be regarded as extremely small. When the cream is to be kept for long periods, 0·2 per cent. of chlorocresol should be added to it, to prevent any growth of moulds.

Tests *in vitro* with No. 9 Cream and various first-aid remedies in common use

To find out how much bactericidal or bacteriostatic effect was to be expected in the presence of a copious exudate of blister fluid on the surface of a burn, tests were carried out as follows :—

1 c.c. volumes of blister fluid (if available), or of serum, were inoculated with staphylococci and haemolytic streptococci, and then vigorously shaken with a large loopful (40 mg. approx.) of the cream or other first-aid remedy. Viable counts were made (with adequate dilution, but without chemical neutralization of the bactericidal agent) before the addition of the test substance,

---

* Recent batches of No 9 cream have contained only 3 per cent of sulphanilamide. This reduction was decided upon when it was found that a toxic dose of the drug might sometimes be absorbed from extensive burns dressed with the 10 per cent. cream. (Contrary to our expectations, this excessive absorption occurred in patients with deep, heat-tanned burns, rather than in second degree burns.) Excessive absorption from a 3 per cent. cream would be very unlikely. Even if as much as 300 grammes were used for a single application, it would contain only 9 grammes of sulphanilamide. Only part of this would be absorbed, and its absorption would be spread over several hours ; part would seep away into the dressings after solution in the exudate ; and some would probably remain undissolved. On the other hand, 3 per cent. of sulphanilamide is probably more than enough to give the desired prophylactic effect.

and again after 24 hours incubation with it at 37° C. Typical results are shown in Table II :—

TABLE II

	Staphylococcus aureus		*Haemolytic streptococcus*	
	Before incubation	*After incubation*	*Before incubation*	*After incubation*
Experiment 1				
Blister fluid alone	80,000	18 million	19,000	13 million
Blister fluid + " Tannafax " (Tannic acid + phenol 0·5 per cent.)	80,000	2 million	19,000	600,000
Blister fluid + No. 9 Cream	80,000	0	19,000	0
Blister fluid + " Triofax " (Gentian Violet 1 per cent. + Brilliant Green 0·1 per cent. + Euflavine)	80,000	0	19,000	0
Blister fluid + Gentian Violet Jelly (G.V. 1 per cent. + " Merthiolate " 0·02 per cent.)	80,000	0	19,000	0
Experiment 2				
Serum alone	300,000	10 million	150,000	15 million
Serum + tannic acid + acriflavine 0·1 per cent.	300,000	2 million	150,000	0

In this experiment, No. 9 Cream, " Triofax " and Gentian Violet Jelly gave the same results as in Experiment 1.

It is seen that—

(*a*) in blister fluid alone *Staphylococcus aureus* and haemolytic streptococcus multiplied freely. (This is not the case with some of the non-pathogenic " micrococci " normally resident on the skin.)

(*b*) in the presence of No. 9 cream and the dye-jellies used, these organisms were killed off.

(*c*) in the presence of tannic acid, phenol (0·5 per cent.) had no antiseptic action, while acriflavine (0·1 per cent.) also was largely neutralized, allowing staphylococcus to grow out, although streptococcus did not.

By this test, No. 9 Cream appears at least as satisfactory as the jellies containing bactericidal dyes, and it has the important practical advantage over these, that it can be readily washed off for the plenary treatment, allowing the medical man to estimate the depth of the burn.

It is recognized that these tests as performed *in vitro* do not reflect exactly what would happen on the surface of a fresh burn, because they take no account of any fixation of the antiseptic agent by the tissue cells of the burned surface. Other observations, which will be reported on a later page, showed that washing over a fresh burn (i.e., one not more than 24 hours old) with " Cetavlon " solution usually reduced the bacterial contamination of the surface from a matter of " thousands " to nil or almost nil. We think it may be presumed that a similar effect will be obtained with No. 9 Cream.

Clinical trials of first-aid creams

Following upon these tests in the laboratory, observations were made upon two series of cases of minor burns at the Glasgow Royal Infirmary, in order to determine, if possible, how far the application of the creams was preventing infection by haemolytic streptococci.

Series I.—Two creams were used, viz., No. 9 as described above, and a simpler one, " Cetavlon Cream ", containing no sulphanilamide. (Its composition was : Cetyl trimethyl ammonium bromide 1 gramme, cetyl alcohol 5 grammes, linseed oil 25 grammes, water 69 grammes.)

Consecutive patients, with burns not severe enough to necessitate admission to hospital, were treated as follows at their first attendance: A moist swab (A) was rubbed over the burned surface for subsequent bacteriological examination. Blisters, if present, were not opened nor epithelial debris removed; nor was any attempt made to clean up the burned surface in order to remove the substances previously applied—caked flour, "Vaseline", semi-coagulated jellies, etc. After his burn(s) had been dressed with one of the two creams, covered with gauze, wool and a bandage, the patient was told to report next day at the out-patient burns clinic. Here a second swab (B) was taken for bacteriological examination, and the burn then received its full or plenary treatment*—blister skin being removed, the surface gently cleaned with "Cetavlon" solution and a sulphanilamide dressing applied. Eighty-two patients were treated in this way with "Cetavlon Cream" and 62 with "No. 9 Cream".

The clinical results of these trials were very satisfactory; the dressings had been comfortable from the first in the great majority of cases, and the burned surfaces were usually either healed or almost healed when the patients came back after one week.

The bacteriological evidence as to the control of haemolytic streptococcus (H.S.) infection is shown in Table III:—

TABLE III

	"Cetavlon Cream"	*"No. 9 Cream"*
Group 1.—Cases in which cream was applied within 24 hours of the injury—Total 119—		
Did not become infected with H.S.	66	42
H.S. present in first and second swabs	2†	4†
H.S. present in first swab but did not persist ..	0	1
Became infected with H.S. after application of cream	4‡	0
	72	47
Group 1a.—Cases belonging to Group 1, but in which the second swab was taken *more than 24 hours after injury*—Total 68—		
Became infected with H.S after application of cream	4‡	—
Approximate number in which H.S. infection *was to be expected* after 24 hours (see Table I) if cream had not been applied	20 to 30	
Group 2.—Cases in which cream was applied 24 hours or more after the injury—Total 25—		
Did not become infected with H.S.	6	6
H.S. present in first and second swabs	2	8§
H.S. present in first swab but did not persist ..	0	0
Became infected with H.S. after application of cream	2‖	1¶
	10	15

* It should be made clear that the procedure described above was adopted only to obtain evidence as to its efficacy in preventing infection by streptococcus. If this object had not been in view, the plenary treatment would have been carried out at the first visit to hospital

† Of these 6 patients, 3 had been burned 21 hours or more before the cream was applied, so that invasion of the tissues had probably begun.

‡ One of these burns had been covered with lanolin and another with flour, which may have prevented effective contact of the cream.

§ These patients had been burned respectively for 27 hours, 2 days (2 cases), 3 days (2 cases), 3½ days, 5 days and 7 days.

‖ One of these burns was covered with ointment, the other had a heavy coagulant dressing of gentian violet, which probably prevented satisfactory contact of the cream.

¶ This is open to doubt; the first swab gave a confluent growth of staphylococcus, in which a few haemolytic streptococcal colonies could easily have escaped detection.

The data in Table III suggest the following tentative conclusions :—

(1) That the temporary dressing of the burns with cream in the 68 cases of Group 1a did to some extent prevent their becoming infected with haemolytic streptococci. In view of the figures in Table I, it seems reasonable to suppose that many more than four of these 68 cases would have been so infected after 24 hours if they had been left alone. (It must, however, be admitted that *any* sterile dressing would have had some protective effect.)

(2) That the creams as applied were not usually successful in getting rid of the haemolytic streptococci already present on the burned surfaces at the time of the first swab. The failure to get rid of them in 6 cases out of 7 should, however, be viewed in the light of the footnote to Table III. It may well be that we should have had more success if all the patients had been burned only a short time, and if the burns had not been smeared with " white ointment ", " Vaseline ", jellies, etc., before the cream was applied. The failure to eliminate haemolytic streptococci from the burns to which our creams were applied late, i.e., more than 24 hours after injury, did not surprise us, as Barnes had previously shown that " Cetavlon " did not reduce the bacterial count of a granulating surface, and our own experience with definitely infected burns had confirmed this many times. Once the streptococci have invaded the tissues, " Cetavlon " is probably of little or no use.

Series II.—In this series of 104 minor burns, only " No. 9 Cream " was used and the procedure was modified slightly, in the hope that we should get still better control of infection. The various applications made before the patient came to hospital were removed as far as possible. A swab (A) was then taken for bacteriological examination. Blisters were usually emptied (but blister skin was *not* cut away). The burned areas were washed over with " Cetavlon " solution, and No. 9 Cream was applied for periods varying from 12–48 hours. The second swab (B) was then taken and the usual plenary treatment carried out.

The burns of 73 patients were free from streptococci when they first came to the hospital (A swab), and none had acquired them when the B swab was taken 20–40 hours later—with two exceptions, for which there was a sufficient explanation. One of these was a boy who did not reappear for seven days after the first-aid treatment was applied; the other, a child which pulled off its dressing before it came back for the second swab.

Of the 31 patients who already had haemolytic streptococci in the A swab, 8 had lost them before the second swab was taken—presumably as a result of the first-aid treatment. Of the remaining 23, who did not lose their streptococci, 20 had been burned more than 24 hours before they came to hospital and 2 of the others were burned 16 and 20 hours, respectively, before treatment.

These results certainly suggest that the cream and the " Cetavlon " solution as used were effective in holding off streptococcal infection in this series of burns.

Commentary upon these clinical trials

1. We do not claim to have proved conclusively that the first-aid procedures adopted have prevented infection by streptococci, although we think that the findings point to a large measure of success and warrant a more extended trial of the methods used.

2. A random series of hospital patients, some of whom have been burned many hours or even days before, and have had diverse applications, cannot yield clear-cut results. Future comparative trials of first-aid remedies should be made on fresh burns which have had no previous treatment.

3. Medical officers of large industrial organizations, e.g., foundries where many minor burns occur, in collaboration with a bacteriological laboratory, could obtain valuable data by comparison of cases treated with No. 9 or other antiseptic cream, with other cases treated with similar cream without the antiseptic.

Note on sensitization to " Cetavlon "

In the course of this work, we have encountered three instances of severe vesicular dermatitis apparently induced by the application of " Cetavlon ". In two of these, the condition developed after the " Cetavlon " cream had been in contact with the burned areas for several days (12 days in one case); in the remaining case, a solution of " Cetavlon " had been applied to the skin on three occasions, and the dermatitis developed seven days after the third application. In all three patients, the condition cleared up within 2–3 weeks, after becoming more or less generalized and associated with some degree of systemic disturbance. A scratch test with a 1·5 per cent. solution of "Cetavlon " gave a definite positive result in all three subjects after the dermatitis had cleared up. A similar test with potassium bromide in two of the cases gave a negative result. Potassium bromide by mouth in one case produced a slight eruption.

One of the patients has had two recurrences of the dermatitis at intervals of several months—one of them definitely induced by accidental contact with " Cetavlon ".

These three are the only cases of dermatitis we have met in a total of more than 2,000 burns to which " Cetavlon " has been applied at the Glasgow Royal Infirmary. We are informed by Dr. R. G. Macfarlane that a 1 per cent. solution of " Cetavlon " has been used for cleansing the skin of some 2,160 blood donors in the West of England, and that no dermatitis therefrom has been reported to date.

CONCLUSIONS

1. The avoidance of infection by haemolytic streptococcus should dominate first-aid policy for all but very severe burns. In the latter, measures for the preservation of life will often have to take precedence over local treatment of the burns.

2. For most small burns which are accessible, e.g., of the hand or forearm or head, first-aid at the scene of the accident should usually be limited to covering the injured skin with a recently laundered clean towel, or, better, if it is available, with a sterile cloth. (Wherever burns are likely to occur, such cloths should be kept ready, previously sterilized in an oven and stored in a tin.) With the burn thus covered, the patient should be sent at once to the factory " surgery ", or to a hospital or a private doctor.

In all severe or extensive burns, no first-aid should be attempted other than keeping the patient warm and giving morphine if required. Immediate removal to hospital is the first consideration.

3. When quite superficial small burns are treated at home or when, in the case of more severe burns, the plenary treatment cannot be carried out without considerable delay, it is recommended that the burned area, and the skin around, should be freely smeared with a water-soluble cream containing 1 per cent. of cetyl trimethyl ammonium bromide and 3 per cent. of sulphanilamide. This cream should be applied with a knife blade or spoon, previously sterilized by dipping for two minutes in boiling water. The burn should not be washed before the cream is applied, nor should blisters be snipped.

This first-aid treatment must be carried out with due precautions against the transfer of streptococci to the burned surface. Thus the operator's hands must be thoroughly washed and dried; and he should wear a gauze mask or a clean handkerchief over his mouth and nose.

After being smeared with the cream, the burn should be carefully wrapped in sterile lint and a bandage, or in a recently laundered clean towel.

On no account should blankets be allowed to come into direct contact with the burn (because they are often heavily contaminated with pathogenic organisms).

4. The cream should not as a rule be left on the burn for more than two days, as there is a slight risk of its inducing a dermatitis if left longer.

In special cases—e.g., in a small ship, or in shipwrecked persons—this small risk will be of no account in comparison with the much greater risk of infection if the burn is not treated.

5. The inclusion of a local analgesic in the first-aid cream is not recommended —for the following reasons :—

(*a*) It is unlikely to give sufficient relief for the pain of a severe burn, which will usually require morphine.

(*b*) The pain of many small burns is so transient as to need no analgesic.

(*c*) The relief of pain by local analgesics is at best uncertain, and often short-lived.

(*d*) There is some risk of toxic effects from the use of local analgesics on a large burned area in susceptible individuals.

ACKNOWLEDGMENTS

Our thanks are due to Mr. A. M. Clark, in whose Department this work was carried out; and to Dr. M. L. Thomson, Mr. W. C. Cawston, Sister Donald and Sister Bertram, who undertook much of the routine work; to Dr. A. Tracy and the volunteers collected by him who submitted to experimental burning; and to Dr. E. Collier who helped in the clinical trials of local analgesics.

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STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART II.—THE CONTROL OF INFECTION IN BURNS AND SCALDS

BY

LEONARD COLEBROOK, M.B., B.S., F.R.C.O.G.

(Member of Scientific Staff, Medical Research Council)

A. M. CLARK, M.C., M.A., Ch.M.

(Surgeon to the Royal Infirmary, Glasgow)

THOMAS GIBSON, M.B., Ch.B., F.R.C.S.E.

(Working with a whole-time grant from the Medical Research Council)

AND

J. P. TODD, Ph.D., Ph.C.

(Professor of Pharmacy, Royal Technical College, Glasgow)

CONTENTS

INTRODUCTION

Aseptic repair of the superficial " blister burn " is universally regarded as the proper aim of treatment, and is commonly attained by several different procedures.

Aseptic repair of deeper burns, involving the whole or the greater part of the dermis, has been commonly regarded as an impracticable ideal. To attain it will certainly prove a very difficult matter.

The coming of the sulphonamides, of penicillin and of propamidine, has given us new power over the two micro-organisms—haemolytic streptococcus and staphylococcus—which constitute the chief threat to the burned patient. These drugs, and the gradual awakening of surgeons during the last few years to the sinister influence of hospital infections, have created a new situation, and compel us to ask how far it is now possible to go towards attaining aseptic repair of the deep burn, with all its far-reaching benefits—quick healing with a minimum of pain, avoidance of contractures and keloid scars, as well as of many late deaths which formerly resulted from sepsis.

The present report describes the beginning of such an inquiry—based on the study of some 1,530 burns. Although it has manifestly come far short of complete success, it does, we think, give a clear indication that success is not unobtainable—at least with the majority of deep burns.

HISTORICAL BACKGROUND

Special wards have for many years been reserved at the Glasgow Royal Infirmary to deal with the very large number of patients with burns and scalds applying for treatment (200–300 per annum requiring admission, as well as about 1,000 with minor burns, treated as out-patients).

The many varieties of treatment employed in these wards during the past hundred years have been reviewed by Dunbar (1934), and the more modern methods by Clark & Cruickshank (1935) and Clark (1939). Coagulation dressings (tannic acid), which had been in use for several years, gave place in 1940 to " open " methods designed to discourage bacterial growth and avoid sticking. With these ends in view, a neutral and stable cream, freely miscible with water, was devised by one of us (J. P. T.), incorporating sulphanilamide (1 per cent.) in a base containing lanette wax SX and cod liver oil (see p. 27). The application of this cream, previously spread on sheets of gauze, was a simple matter; the patients so treated were comfortable and their burns did not need re-dressing for several days. Healing was very satisfactory and there seemed to be less septic infection than there had been with coagulant or other dressings. Bacteriological records, however, showed that the burned areas were very commonly infected (or, at least, infested) by haemolytic streptococci and staphylococci, and sometimes by other organisms.

For two months before the present investigation started Dr. R. D. Stuart had made a systematic examination of all cases in the wards—a swab being taken on admission and at subsequent dressings. This showed that, of the 26 cases admitted without haemolytic streptococci, no fewer than 21 (83 per cent.) acquired that organism in the burned areas. It was usually present when the dressings were first changed, on about the third or fourth day. During the previous summer (1941), Dr. Stuart had found 52 per cent. of the 51 cases examined so infected when they were examined 3–6 days after admission. Six years earlier (1935), Cruickshank, working on patients in the same wards, reported that 66 per cent. of them had haemolytic streptococci in their wounds 3–6 days after admission, as compared with 11 per cent. at the time of admission. In the same paper he made the important observation that the " dust of the burns ward contained numerous haemolytic streptococci ", while plates exposed in a medical or general surgical ward gave respectively no growth, or a scanty growth, of that organism.

Provision by the Medical Research Council and the Royal Infirmary of additional personnel and facilities for a systematic investigation of this problem of streptococcal infection of burns has enabled us to carry out the work here reported.

BACTERIOLOGY AND EPIDEMIOLOGY OF BURNS AND SCALDS

It is not our intention to deal with these problems here in any detail, but only to call attention to such aspects as have clinical importance.

Routine procedure.—Cultures were made on blood agar plates from each of the burned areas (by means of cotton wool swabs) :—

(*a*) on admission, before cleaning up,

(*b*) at almost all subsequent dressings.

(For nine months, cultures were also made immediately *after* the initial cleaning-up—see pp. 25 and 26).

Incubations were aerobic except occasionally, when there was reason to suspect the presence of anaerobic bacteria. In all, some 3,420 swabs were bacteriologically examined ; the average number from each in-patient being about 10.

The swarming of *Proteus* on so many of the plates created a special difficulty, as it prevented the detection of other pathogens. To avoid this, we made duplicate plates at first, covered with melted agar (Fry, 1932) and then flooded before incubation with absolute alcohol for one minute and dried (Butcher's modification—see Spooner, 1941). This, however, involved a considerable wastage of medium. The following procedure was devised by Mr. W. C. Cawston (who has been responsible for most of the bacteriological examinations) to eliminate this wastage of medium ; and it has since become our routine method. A strip about 6 mm. wide is cut out of a blood agar plate, separating off one-third of its surface. The swab under investigation is planted on both sectors, and the smaller sector is treated by the modified Fry technique described above, care being taken that the melted agar does not spill over into the ditch. (If it does so, it can easily be removed with a sterile knife blade.) On one half of the larger inoculated sector a drop of 1–3,000 gentian violet solution is sometimes spread, to suppress growth of staphylococci and diphtheroid bacilli. This may enable haemolytic streptococci to be detected when they would otherwise be missed (Garrod, 1933 ; Fleming, 1942).

Findings.—Broadly speaking, the infections of burns in this country resolve themselves into :—

(i) *The coccal infections of the first week (haemolytic streptococcus and Staphylococcus aureus).*

(ii) *The abundant, mixed coccal and bacillary infections of the second to the fourth weeks (deep burns), while necrotic tissues are separating.*

(iii) *The later, mainly coccal, infections of the granulating period.*

Depending upon the opportunities for cross-infection, the flora of these three periods will be less or more distinct.

(i) The Coccal Infections of the First Week

These are of great importance, not only to the individual patients but also to the community and the hospital services, because they so frequently convert a simple " blister burn ", capable of healing in 14 days, into a deeper lesion which heals only by granulation in a much longer time. We feel that the importance of preventing this by proper first-aid and plenary* treatment needs to be strongly emphasized.

* For the connotation of " plenary " treatment, see p. 5.

It is not perhaps generally realized why and how a burned surface so readily becomes infected. In the process of burning at temperatures above 90° C., most bacteria present on the actual surface of the skin will usually be destroyed. (Swabs taken within an hour or two frequently yield no growth.) But in many instances organisms such as staphylococci and diphtheroid bacilli, which are believed to be normally present in the ducts of sebaceous glands and hair follicles, may escape destruction by the heat, and will soon find their way on to the surface—along with blister fluid, which begins to exude as early as 15 minutes after burning (unless the skin tissues have been heat-tanned). Other organisms, too, not normally present on the skin, are often conveyed to the fresh burn from the respiratory tracts of well-meaning friends or first-aid personnel, or by the non-sterile blankets and dressings with which the burned surfaces are too commonly covered. Of these, the haemolytic streptococcus is by far the most important.

Example.—R.F. was burned in a factory explosion. Four hours later, an abundant pure culture of haemolytic streptococcus was isolated from one of her burned hands. Within three-quarters of an hour of the accident, her hands had been soaked with acriflavine and efficiently covered with sterile dressings. On inquiry, it transpired that, in order to combat the " primary shock " of the injury, blankets had been thrown over her. These blankets had come from the factory ambulance station and were never sterilized. They may well have been used not long before for cases of tonsillitis, scarlet fever, or cellulitis.

The blister fluid of a burn constitutes an excellent culture medium for staphylococcus and haemolytic streptococcus, and for that reason it is not uncommon to obtain abundant cultures of these organisms within a few hours of burning (see Table IV, p. 26.) Our records during the past year include three cases in which haemolytic streptococci were cultivated from a fresh burn within three-quarters of an hour of the injury, and others in which they were obtained within 1, 3, 4 and 7 hours, respectively. *Staphylococcus aureus* was still more frequent in these early cultures.

Among 37 strains of haemolytic streptococci isolated from fresh cases on arrival at the hospital, there were 11 different Griffith types. No one type was predominant. Fourteen strains could not be typed.

Transmission of Haemolytic Streptococci in the Wards

As already stated, Dr. Stuart's investigation during January and February, 1942, made it clear that the " hospital " transmission of streptococci to uninfected burns was very frequent at that time. We expected to find a considerable mixture of different strains, but that proved not to be so. One strain (Griffith's type 4) was clearly predominant, and was being acquired by nearly all new cases.

There was little doubt that this dissemination was due in part to the covering of the fresh burns on admission with unsterilized blankets, and in part to faulty dressing technique. This strain quickly ceased to spread when these faults were corrected, but it was not finally eradicated until the wards were fumigated with formalin six months later. Since then, there has been evidence of spread of other types to a few cases, e.g., of type 12 in November and December, 1942; of type 11 in January and February, 1943; and of another type in March and April, 1943—but no one type has become predominant at any time.*

* For the typing of these and many other strains, 257 in all, we are greatly indebted to Dr. Dora Colebrook and Dr. Stuart Elliott of the Streptococcal Research Laboratory of the Medical Research Council in London. Without their identification of types, we should have missed the fundamental fact that one strain was predominant in the ward at the beginning of the investigation and was being conveyed in part by blankets; and we should have arrived at many false conclusions subsequently.

It is not clear how these later infections were transmitted. Some of them were probably due to dust falling on the wounds during dressings (for evidence in support of this, see p. 34). In other cases, the infections were probably due to imperfect sealing off of the dressings, or to interference with them by the patients.

There has been no obvious indication that any of the infections were due to transfer of streptococci from the respiratory tracts of the patients, staff or visitors, but that possibility certainly cannot be excluded—indeed, in view of the evidence from other sources, e.g., puerperal fever work (Smith, 1931 ; D. C. Colebrook, 1935 ; L. Colebrook, 1936, etc.), it is probable that such infection has played some part. There were only two cases of haemolytic streptococcus tonsillitis among the staff or patients during the 15 months under review. Routine throat swabs could not be taken, owing to pressure of work, but on one occasion when type 4 streptococcus was prevalent on the burned surfaces, swabs of the throats of all patients and staff failed to discover that strain in any individual. Two nurses were removed from the ward because they were persistent throat carriers, but there was no evidence that their streptococci were acquired by any of the burns.

Sensitivity of the Streptococcal Strains to Sulphonamides

Our experience suggests that the development of " fastness " to sulphonamides (and probably to other compounds) is likely to create considerable difficulties in the future treatment of burns by chemotherapeutic agents.

The chief findings have been as follows :—

(1) A sulphanilamide-resistant type 4 streptococcal strain was completely predominant among the cases in the wards when our investigation began—following 12 months of routine treatment by a 1 per cent. sulphanilamide cream.

(2) For a few months after this strain had been eliminated, resistant strains were isolated only sporadically but, during the last three months, three resistant types have again assumed a clear predominance, namely, types 3, 4 and 6.

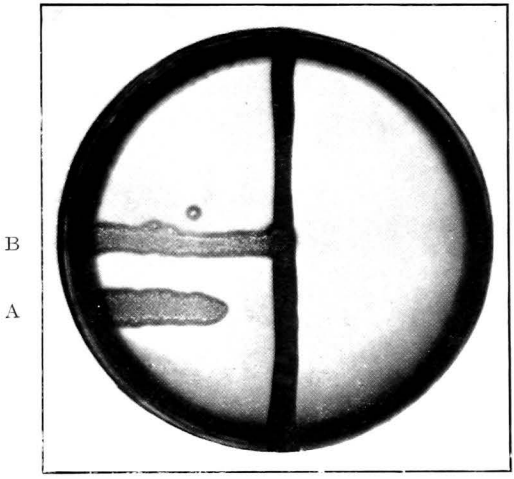
(3) Of 37 fresh strains isolated from patients on admission, 33 were typically sensitive to sulphanilamide (20 mg. per 100 c.c.) and 4 resistant. Two of the latter came from patients who had had local sulphonamide treatment for a few days before the strain was isolated ; they might possibly have become resistant in that time. The other two came from patients who, so far as is known, had had no sulphonamide treatment, but their strains may, of course, have been acquired from somebody who had been so treated.

(4) In three instances we have obtained evidence that the streptococci changed from sulphonamide-sensitiveness to sulphonamide-resistance during continuous treatment by sulphonamides. The degree of sensitiveness was gauged by the blood-agar ditch test (Fleming, 1941 ; Colebrook and Francis, 1942)—the ditches being filled with sulphanilamide-agar, 20 mg. per 100 c.c.

McK.—Burned February 25th.
Treated with sulphanilamide cream from February 25th till March 17th.
Strep. isolated March 5th was inhibited to a distance of 12 mm. (Fig. 1—A)
Strep. isolated March 17th was not inhibited at all (Fig. 1—B). (The serological identity of the strains isolated on March 5th and 17th, respectively, was not proven in this case, as neither of them could be typed.)

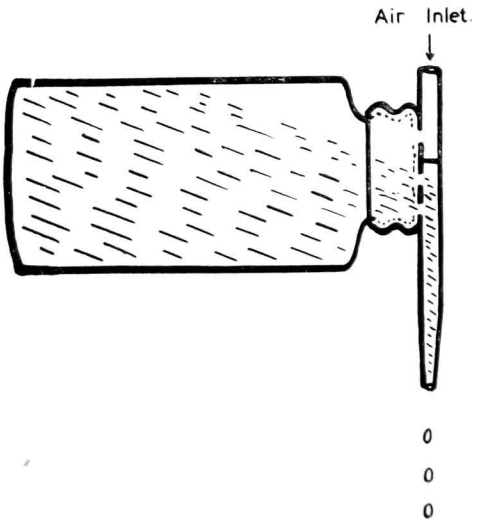
J.G.—Burned November 20th.
Treated off and on with sulphanilamide cream and powder till April 4th
Strep. isolated February 23rd (type 11) was inhibited to a distance of 15 mm.
Strep isolated March 21st (type 11), after six applications of sulphanilamide powder, was not inhibited at all.

FIG. 1



SULPHANILAMIDE
20 mgm. per 100 c.c. agar.

FIG. 2



A third case was that of a nurse with a septic finger, treated by oral sulphanilamide for a week, and local for three weeks.

Strep. isolated August 15th (type 11), after two days' treatment, was inhibited to a distance of 28 mm.

Strep. isolated August 27th (type 11) was inhibited to a distance of 13 mm.

Strep. isolated September 12th, after completion of treatment, was not inhibited at all.

It is probable that a similar change from sensitiveness to fastness would have been detected in the streptococci from other cases if we had systematically sought for it, but, as our primary aim has been to rid the wards of infection, we have usually eliminated the streptococci at an early stage by the application of penicillin or propamidine.

(5) The strains resistant to sulphanilamide (20 mg. per 100 c.c.) showed considerable differences in their sensitiveness to other sulphonamides (Colebrook, 1943). None of them was resistant to sulphathiazole at a similar concentration, and only two at a concentration four times weaker.

Sensitivity of the Streptococcal Strains to Penicillin

We have met with no group A haemolytic streptococcus so far which is not sensitive to penicillin *in vitro* (ditch test on blood agar, the ditch being filled in with agar containing 0·45 Oxford units of penicillin per c.c.—and kept in the refrigerator overnight before planting). Forty-nine strains in all have been tested in this way, including 27 which were resistant to sulphanilamide 20 mg. per 100 c.c. The degree of inhibition was remarkably uniform, but differences might have appeared if we had tested against a lower concentration of penicillin.

The *in vivo* test (application to infected burned areas) has also been applied to about 60 strains, including many of the 49 tested *in vitro*. In every instance the streptococcus has disappeared under treatment—but in a few it reappeared after some days or longer. In some of the latter cases the reappearance was probably due to re-infection from another area, or from another patient.

There has been no indication so far that any strain has become resistant to penicillin, but judgment on this point must be reserved, as we have not systematically sought for evidence of such a change.

Two strains of non-haemolytic streptococci of faecal type were tested *in vitro* and proved only slightly sensitive as compared with the group A haemolytic strains.

Coliform bacilli and *Proteus* have all proved insensitive to penicillin, both *in vitro* and *in vivo*.

Infections by Staphylococci—and their Transmission

Staphylococci have given rise to comparatively little acute or serious sepsis, and their influence upon the rate of healing in burns has been much less evident than that of haemolytic streptococci. Unlike the streptococci, too, they have seldom, if ever, been responsible for the failure of grafting operations.

It has not been possible to trace the source of these staphylococci. Many were probably derived from the patients' own skin ; others may well have been air-borne. (Plates exposed in the wards during dressings have usually yielded some *Staphylococcus aureus*—see Table VI, p. 34). Some strains were no doubt transmitted during dressings.

(ii) The Mixed Infections of the Sloughing Period

In addition to the coccal infections, which often persist through this period, diphtheroid and coliform bacilli* of various types, *Proteus* and *Ps. pyocyanea*, if

* The differentiation of a number of coliform bacilli isolated from some of our cases is not yet completed, but it is evident that they form a heterogeneous group—including *B. coli communior*, *B. lactis aerogenes*, Morgan's bacillus and some of the paracolon group.

transmitted to the burned area, will proliferate freely. In many instances' these infections are accompanied by irregular fever and increasing anaemia, and, although other clinical signs of infection may not be present, it seems justifiable to regard at least the gram-negative organisms mentioned as true pathogens in relation to burns. How far they actually invade the tissues is not known. The presence of agglutinins to *Proteus* in the serum of infected patients has recently been described (Sonnenschein, 1943). Dr. R. D. Stuart, of this laboratory, has sought for similar evidence of antibody reactions to some of the coliform bacilli we have isolated, but so far without success.

Transmission of Proteus, Ps. pyocyanea and coliform bacilli

In considering the conditions which allow of the invasion of burned surfaces by these organisms, the following facts should be borne in mind :—

(*a*) These organisms are rarely found on human skin, except as temporary contaminants, e.g., in the perineal region. When experimentally implanted on the skin, *Proteus* disappears within half to one hour (Colebrook, 1930). Recent unpublished experiments have shown that the same applies to *Ps. pyocyanea*. In 285 consecutive swabs taken from fresh burns on admission, neither *Proteus* nor *Ps. pyocyanea* was isolated on any occasion—and coliform bacilli only rarely.

(*b*) These organisms are not found in the normal throat or nose.

(*c*) They do not multiply readily in fresh serum or blister fluid, but will do so when this has lost its anti-tryptic power or has been " corrupted " (Wright, 1919) by the disintegration of leucocytes.

(*d*) They are often present in the air of the burns wards—and particularly in the near neighbourhood of patients whose burns are infected by them (see Table VI, p. 34).

(*e*) They have been found much more frequently among burns treated in the wards than among those treated in the out-patients department.

Of 243 in-patients (October, 1942–October, 1943), 22·6 per cent. acquired *Proteus* and 16·9 per cent. *Ps. pyocyanea*.

Of 243 out-patients treated in the same period, a growth of *Proteus* was obtained from only 5 per cent., and of *Ps. pyocyanea* from 2·4 per cent.

(The validity of this comparison is, however, open to question, since the burns of the in-patients were swabbed much more frequently, and the number of in-patients with sloughs was also much higher.)

It appears probable that the high incidence of these infections in hospital wards—particularly in wards full of burned patients—is attributable chiefly to faulty dressing technique and/or to transmission by dust.

(iii) The Later Infections of the Granulating Period

The bacterial flora during this time is usually much less abundant and less mixed than in the sloughing period. When the granulations are flat, and of healthy type as judged by the naked eye, and discharges are not allowed to accumulate, they usually yield only a moderate growth of staphylococci. The absence of a few haemolytic streptococci cannot, however, be assumed, and it should always be verified, if possible, before undertaking a grafting operation. When, on the other hand, the granulations are pale and oedematous, and the exudate is more abundant, haemolytic streptococci will often be found, along with *Proteus*, coliform bacilli or *Ps. pyocyanea*. Spontaneous changes in the flora are common in these circumstances.

It is probable that such transient bacterial populations represent a surface infestation rather than a true infection of the tissues.

(iv) Tetanus

No case of tetanus has occurred in our experience, and no prophylactic treatment has been given.

THE INVESTIGATION AND "DRIVE" AGAINST STREPTOCOCCAL INFECTION

The situation with which we had to deal in February, 1942, presented the following features:—

(1) Dissemination of haemolytic streptococci was evidently the hard core of the infection problem in the Burns Unit at the Royal Infirmary. Most of the burns in the ward were already infected with a single strain (Griffith's type 4); and the majority of new cases were acquiring this strain during the first 48 hours after admission.

There was little doubt that these infections were responsible for most of the acute febrile disturbance of the first ten days, and for much of the subsequent delay in healing.

(2) It was not feasible to suspend all admissions and close the wards while they were cleaned and fumigated. Moreover, 14 per cent. of new patients were already infected with haemolytic streptococci on admission.

(3) There were no facilities for segregating patients already infected with streptococci.

Taking these circumstances into account—and remembering that haemolytic streptococci are particularly well adapted for growth in the exudate of fresh burns—we decided that an attack upon these infections would need all our resources; it would be unwise to rely upon antibacterial drugs alone.

We therefore formulated a comprehensive plan of attack, in which the following were the chief items:—

(i) Strict precautions during the first stage of treatment, i.e., from the moment of the patient's entering hospital till the burns were cleaned up and dressed.

(ii) Initial sterilization of the whole burned area and surrounding skin.

(iii) Application of a bacteriostatic dressing, which would not require to be changed frequently.

(iv) Efforts aimed at the prompt elimination of haemolytic streptococci from any wounds found to be infected with these organisms.

(v) Measures for the prevention of cross-infection—including a strict dressing technique; control of dust and "disinfection" of wards; masking and routine swabbing of the staff; sterilization of blankets and other bedding, etc.

The procedure adopted under each of these headings is described below.

(i) Precautions during the First Stage

The first few hours following the admission of a burned patient to hospital constitute the period of his greatest danger, from the points of view both of "shock" and of infection. More often than not he arrives with his burns uncovered, or inadequately covered; because he is cold, he is covered with blankets, which in most hospitals are never sterilized and are in consequence frequently infested with streptococci and other pathogenic bacteria. (Cultures made from blankets just returned from the laundry, February, 1942, yielded on two occasions the same strain of streptococcus, type 4, as was present in most of the wounds.) In the process of removing the patient's clothes (often very dirty) it will be impossible to avoid some contamination of the burned surfaces; and during the subsequent cleaning-up and dressing processes, these surfaces will again be exposed for an appreciable time to an atmosphere laden with dust carrying streptococci, staphylococci, coliform bacilli, etc., derived from other burns in the ward. These risks are all increased a hundredfold if, as often happens, the patient arrives in a restless, irritable condition, throwing himself about the bed, disturbing whatever dressings there may be on the burn, and perhaps vomiting.

As already stated, the freshly burned surface, with its abundant exudate, provides ideal conditions for the rapid multiplication of serophytic organisms such as staphylococcus and streptococcus.

The precautionary measures we have adopted to meet these risks include the following :—

(*a*) The patient's clothes are removed, and the plenary treatment carried out, in a reception room kept for that purpose. Traffic in and out of this room is reduced to a minimum. (Ideally, of course, clothes would be removed in one room and the plenary treatment carried out in an adjoining room, but available accommodation at the Infirmary has not permitted this. The ventilation of these rooms should preferably be by filtered air from the outside—led in by an induction fan—and provision should be made for the frequent sterilization of the air, e.g., by ultra-violet light or by " aerosols ", or a bactericidal vapour. This has also not hitherto been possible at the Infirmary.)

(*b*) Only sterilized blankets are used to cover the patient (see pp. 36 and 37).

(*c*) The standard of asepsis during the plenary treatment is as strict as in the operating theatre, except that overshoes have not been used. Masks, head covers and sterile gloves are worn by the dresser, and the patient himself is masked. The burned surfaces are dealt with one at a time, and exposed for the shortest possible period. " No-touch " technique, and dry instruments, are used throughout.

(*d*) If " shock ", or the threat of it, calls for postponement of the plenary treatment for some hours, the burned areas receive only a provisional treatment as follows :—

Blisters are snipped and a trickle of " Cetavlon " solution is run over the whole surface, which is then covered with sheets of gauze, previously spread with a bactericidal and bacteriostatic cream (First-aid Cream No. 9—see p. 10) ; these, in turn, are covered with wool and a bandage. Such patients are retained for treatment in a separate " shock-room " for a period varying from 15 hours to three days.

(ii) Initial Sterilization of the Burned Area and Surrounding Skin

The experimental work of Colebrook (1930), Colebrook and Maxted (1933), Price (1938) and others has shown how difficult it is to get rid of the " resident flora " of the skin (staphylococci and diphtheroid bacilli, in particular) by means of soap and water, or with soap followed by any of the chemical agents generally employed in the past, e.g., alcohol, iodine, salts of mercury, hypochlorites, etc. It appears that none of these agents reaches the organisms in the depths of the sebaceous glands and hair follicles. Until 1942 no method was known whereby any large area of skin could be rendered even approximately sterile (i.e., if a sufficiently severe test for sterility was employed, such as rubbing a piece of moist gauze over five or more square inches, and inoculating all the fluid expressed from the gauze).

Progress in this direction was, however, claimed by Barnes (1942), who reported that a new wetting agent, cetyl trimethyl ammonium bromide (CTAB or " Cetavlon "), which has the properties of a soap but also considerable bactericidal power, when applied to human hands rendered them almost completely sterile. Similar success was obtained by one of us (L.C.) on several occasions, using a 2 per cent. solution of this compound—only one or two colonies being grown from the whole hand after three minutes' soaking in this solution. On the basis of his observations, Barnes suggested the use of this substance (in 1 per cent. solution) for the cleansing of burns, and we have now used it on some 1,530 cases. For several months, we employed a 1·5 per cent. solution but, as this was sometimes painful if left on for more than two or three

minutes, and particularly if the burns were more than 24 hours old, we have recently reverted to using a 1 per cent. solution. (It should be noted, however, that the cleansing power of the 1·5 per cent. solution is considerably greater than that of the 1 per cent. solution.)

In about 200 cases we have taken swabs from the area before and after this cleansing with "Cetavlon", being careful to wash away all traces of the solution with sterile saline before taking the second swab. (Very often both swabs have proved sterile, but when there has been delay in the patient's coming to hospital, the first swab has often yielded a more or less abundant culture of skin organisms, including some air-borne spore-bearing types, and often haemolytic streptococci.) As shown in Table I (p. 7), it was found that 42 per cent. of patients coming for treatment more than 24 hours after the burning injury had already become infected with haemolytic streptococci.

Typical results of cleaning up the burned area (and surrounding skin) in a series of cases are shown in Table IV.* It will be seen that complete, or almost complete, sterility was usually obtained, except in the cases where haemolytic streptococci were already present in large numbers on an area burned more than 24 hours previously. In such cases, after the cleansing with "Cetavlon", the streptococci, although reduced in numbers, were not usually eliminated. (We have not tried a more prolonged application of the "Cetavlon", i.e., for more than five minutes.) It may be assumed that in cases of this kind the streptococci have invaded the tissues well below the actual surface, and that the detergent does not penetrate to them.

It is probable that penicillin, being more diffusible, may be more successful in these circumstances, but we have not yet put it to this test.

The actual procedure of cleaning-up has been as follows:—

A sterile mackintosh sheet and a sterile towel are placed under the burned area. This area (but *not* the surrounding unburned skin) is first gently but thoroughly mopped with gauze soaked in 1 per cent. "Cetavlon" solution, in order to remove dirt and to sterilize the surface of any blisters before they are opened. This sterilizing process should take at least two minutes. The unburned skin for six inches round the burned area is next thoroughly cleansed with the solution, care being taken that the washings run away from, not over, the burned area. (A sterile nail-brush may with advantage be used for this unburned skin, as it is found that a more complete sterilizing effect is obtained in that way; the nail-brush should *not* be used on the burnèd surface.) This skin-cleansing done, the blisters are opened with sterile scissors and all the loosened epithelium, along with the clotted blister fluid and débris, is removed. Finally, the whole raw area is very gently mopped again with "Cetavlon" solution. The whole procedure for any one area should not take more than a few minutes, if the skin is not badly soiled with sticky material.

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* Since this work was done, it has been shown in America (Valko and Du Bois, 1944) that the organisms apparently killed by short exposure to certain cationic detergents ("Zephiran" and cetyl pyridinium bromide) can be revived by treatment with high molecular anions, e.g. sodium dodecyl sulphate. Similarly, Colebrook, in unpublished experiments, has recently found that the bactericidal effect of "Cetavlon" *in vitro* can be considerably reduced by the addition of this anionic substance, and, in conformity with that observation, that the great apparent reduction of viable organisms cultivable from the skin of the hands after soaking in "Cetavlon" is no longer obtained if the hands so treated are dipped within a few minutes in sodium dodecyl sulphate.

In the light of this new finding, it will be necessary to re-investigate the apparent high degree of sterilization of burned surfaces shown in Table IV, when these surfaces are freely soaked, say 10 to 20 minutes after treatment by "Cetavlon", with sodium dodecyl sulphate.

There is at present no reason to suppose that any body constituent will act like sodium dodecyl sulphate in reversing the bactericidal effect of "Cetavlon". Pending further evidence, it may therefore be assumed that, when burns are carefully cleansed with "Cetavlon", *and this is not washed off*, the bactericidal effect shown in Table IV will be obtained.

General anaesthesia has not been necessary for any adult patient, and has been considered undesirable. Under the routine dose of morphine given to patients with severe burns, the cleaning-up process has usually caused little or no pain. The pain is sometimes greater if the burn is more than 24 hours old, or if the "Cetavlon" is used for more than five minutes. Rectal pentothal has been tried occasionally for small children who were badly frightened and so restless as to make the cleaning-up and dressing difficult. We have not yet sufficient experience to express any opinion on its value.

TABLE IV

Results of bacteriological examination of burned areas—

(*a*) *Before cleaning with "Cetavlon"* (1·5 per cent. solution)

(*b*) *After this had been washed off with sterile saline.**

Patient's Serial No.	*Burned area*	*Interval between burning and cleaning (approx.)*	*Aerobic culture on blood agar plates*	
			Before cleaning with "Cetavlon"	*After cleaning with "Cetavlon"*
20	L. leg ..	24 hours	H.S.—uncountable	0
22	Chest ..	1½ hours	600—staph., diphd., sarc. ..	0
34	Chin ..	1½ hours	277—staph., diphd., sarc. ..	0
40	L. thigh	3 hours	1,500—staph., diphd., sarc. ..	1 col. staph.
40	L. arm..	—	2,000—staph., diphd., sarc. ..	0
41	R. leg ..	6¼ hours	300—staph., diphd., sarc., plus a.s.b.	0
41	L. leg ..	—	5,000—staph., diphd., sarc. ..	0
44	R. arm	8 hours	2,000—staph., diphd., sarc. + micrococci.	0
42	L. arm	10¾ hours	Uncountable—coliform and strep.	0
43	R. arm	7¾ hours	2,000—colif. and tetrads... ..	0
43	L. arm	—	1,000—colif. and staph.	0
47	L. leg ..	1¾ hours	2,000—staph., diphd., sarc. ..	0
2	R. leg ..	—	2,000—staph., diphd. and N.H.S.	3 cols.
52	Face ..	2¼ hours	400—staph. and micrococci ..	0
51	R. arm	4¼ hours	Uncountable—strep. virids., staph., G-bac.	3 cols. N.H.S.
51	Face ..	—	Uncountable—staph., etc. ..	0
49	L. arm	3¼ hours	500—N.H.S. and staph.	0
27	Buttock	2 days ..	Uncountable—H.S.	Many H.S.
28	Face ..	3 days ..	Uncountable—H.S. and staph. ..	Many H S.

H.S. = haemolytic streptococci; N.H.S. = non-haemolytic streptococci; sarc. = sarcina; diphd. = diphtheroid bacilli; a.s.b. = aerobic spore bearer; G-bac = Gram-negative bacilli.

Toxic effects of "Cetavlon".—In our report on the first-aid treatment of burns and scalds (p. 14) we have referred to three cases of sensitization to "Cetavlon" which resulted in a troublesome vesicular dermatitis, developing about 10 days after the first application. One of these patients had recurrences at intervals of several months after transient contact with "Cetavlon". No further

* In order to make sure that the absence of growth usually obtained after cleaning with "Cetavlon" was not due to traces of this substance carried over to the culture plates (in spite of washing with saline), a small portion of the agar surface was often inoculated with a suspension of staphylococcus or streptococcus. In no case did these control areas fail to grow normally.

cases of dermatitis have occurred, although we have continued to use the drug, so that the incidence rate still stands at 3 cases in about 1,530.* In two of the three subjects there had been prolonged exposure to "Cetavlon".

Further evidence regarding the toxicity of "Cetavlon" for human skin has recently been produced by Williams *et al.* (1943). Forty-two normal subjects applied a 1 per cent. solution to the hands twice or thrice daily for periods varying from two to three weeks. In a few cases some chapping of the hands resulted, but nothing more. Patch tests gave no evidence of sensitization by repeated exposure to the drug.

(iii) Application of a Bacteriostatic Dressing

Although, as shown in Table IV, cleansing of the burn with "Cetavlon" appears to achieve complete sterility in many cases, we cannot be certain of that result in all, especially when the skin has been heat-coagulated on the surface but not in the depths; nor in cases where the burn is several hours old before it is cleaned up. Moreover, it may well happen that staphylococci or other serophytic organisms from the surrounding skin will sooner or later find opportunity to multiply in the exudate soaking into the dressings—and thence will reach the burned surface. When the burn involves parts of the body which cannot be completely sealed off by dressings (e.g., the face and perineum), such infection of the surface will occur early and is likely to be heavy.

Our aim, therefore, has been to apply a dressing which will both assist the natural defensive mechanism (chiefly leucocytic) in suppressing any bacterial growth on the burned surface, and be innocuous to the regenerating tissues. Such a dressing could well be left undisturbed for a week or two. It should afford relief to the burned patient in three ways: (*a*) by its cooling effect, and by the exclusion of air, it should ease the burning pain of the first hour or two; (*b*) by preventing infection, it should eliminate most of the inflammatory pain of the succeeding days; and (*c*) by avoiding the "sticking" of dressings to the injured surfaces, it should eliminate most of the pain and mental distress associated with re-dressing.

One of the sulphonamide drugs, incorporated in an oil-in-water type of base, seemed the preparation most likely to meet these requirements. A suitable cream of this kind had been devised by one of us (J.P.T.) early in 1941. The original formula contained 1 per cent. of sulphanilamide in a base composed of lanette wax SX, cod liver oil and water. With slight modification, it has proved itself through two years to be admirably suited to our purpose. Being a smooth preparation, of neutral reaction, it provides a vehicle which holds the sulphonamides (or other substances, if desired) in stable suspension, and permits of their ready release into the serous exudate of the burn. Thanks to the glycerin with which the sulphonamides are dissolved or emulsified, it also does not dry out on keeping; and the glycerin, to a large extent, helps to avoid sticking of the dressings. (The first dressing is the most liable to stick, owing to clotting of the serous exudate in the meshes of the gauze.)

The modifications of the original cream introduced during 1942–43 have been as follows:—

(1) Cod liver oil was replaced by castor oil—partly to conserve supplies of the former for nutritional purposes, and partly because cod liver oil, in the presence of sulphanilamide, was prone to undergo a brownish discolouration at the surface exposed to air. Its odour was also somewhat unpleasant, and probably attracted flies.

* Since this report was drafted, 620 additional cases have been treated, and no further instance of dermatitis has been encountered.

(2) The sulphanilamide content was increased from 1 per cent. to 10 per cent., when it was found that we had to deal with relatively resistant streptococci and we wished to obtain a greater bacteriostatic effect.

The absorption of sulphanilamide from creams of this strength (10 per cent.) was generally not excessive, but in one case with a very extensive deep burn a blood level of about 30 mgm. of the drug per 100 c.c. was registered, and the patient became "light-headed" but survived (see p. 184). In another case, a child with an extensive deep burn, in whom unfortunately the blood sulphonamide level was not determined, also probably absorbed a dangerous amount of the drug, since death occurred with agranulocytosis after three weeks (see pp. 161–2).

These two experiences taught us that, contrary to our expectations, sulphanilamide can be readily absorbed through the leathery heat-coagulated tissue of a deep burn; and that, in such cases, if the burn is extensive, it is wise to employ a cream weaker than 10 per cent. A simple calculation showed that a 3 per cent. cream could hardly yield a dangerous amount of the drug, since, even if as much as 300 gm. of cream were used (for an adult) and all the sulphanilamide were absorbed, the total absorption would amount to only 9 gm., and it would be spread over a number of hours.

For a time, therefore, we used a 3 per cent. sulphanilamide cream for all extensive burns, retaining a cream with 10 per cent. of sulphanilamide for the rest. Later, we employed a sulphathiazole cream (3 per cent.), in the expectation that, by reason of the much lower solubility of this drug, it would never be absorbed in any large amount. It seemed probable, too, that it would exert a greater and more prolonged bacteriostatic effect—particularly upon strains of streptococci resistant to sulphanilamide (Colebrook, 1943). As to whether the bacteriostatic effect has been greater or more prolonged, we are unable, at present, to offer any definite evidence.

During the last three months, our routine dressing (in over 100 cases) has been with a cream containing both sulphanilamide and sulphathiazole (3 per cent. of each), which is more economical than using several different creams, and is likely to combine the advantage of a rapid liberation of sulphonamide (sulphanilamide) into the exudate of the burn with the prolonged action of sulphathiazole.

The sulphonamide absorption and excretion in two patients with extensive burns, which were dressed with this mixed cream, is shown in Table V. Similar but less complete investigations of absorption and excretion have been made in three other patients with smaller areas burned. The values obtained were in all cases less than those shown in Table V.

This mixed cream has given very satisfactory clinical results and is now recommended for the routine plenary treatment. The details of its present composition, and method of preparation, are as follows:—

Mixed Sulphonamide Cream for Plenary Treatment

Formula:

Sulphanilamide	3 gm.
Sulphathiazole	3 gm.
Glycerin	10 gm.
Castor oil	25 gm.
Lanette wax SX	10 gm.
Water	49 gm.

Preparation

Heat 25 gm. of castor oil to 70° C. and add 10 gm. of lanette wax SX. When the wax is completely melted, add water (49 c.c., previously heated to 65° C.), with gentle stirring to avoid incorporation of air. Heat the whole to 100° C. for at least 30 minutes to kill off non-sporing pathogens, and shake as it cools. Rub up the sterile sulphanilamide and sulphathiazole powders, 3 gm. of each, in a sterile mortar with 10 gm. of glycerin. Heat to 65° C. for 2 hours and then mix slowly with the base. Store in a sterilized jar and keep always covered.

Notes

(*a*) The final product will remain a perfectly smooth cream indefinitely in temperate climates. It will freeze solid at low temperatures and part of the sulphanilamide will come out in the form of large crystals. On cooling after exposure to the heat of the tropics, or in the holds of ships during hot weather, the cream may become slightly "rough" for the same reason, i.e., a minor degree of crystallization, but this will not be enough to make it unsuitable for use on burned surfaces. (Such roughness after mild heating will necessarily occur with any cream containing more than 1 per cent. of sulphanilamide, whatever the base.)

(*b*) It should be noted that the cream as prepared is not self-sterilizing. The usual aseptic precautions should therefore be taken in using it. Samples prepared in the dispensary at the Royal Infirmary have been repeatedly examined by aerobic and anaerobic culture, and have invariably been found free from contamination by bacteria or moulds. Where, however, the cream is to be kept for long periods, the addition of a preservative, such as chlorocresol, 0·2 per cent., would be advisable.

(*c*) Where many burns have to be dealt with, it will be found convenient and time-saving to have the cream previously spread on sheets of gauze, approximately 6 in. by 12 in., which are stored (folded) in a sterile jar. (Preparation of these sheets must, of course, be carried out with strict asepsis; they are best prepared in flat sterile trays—the personnel being masked and the whole procedure done in an atmosphere as free as possible from dust.)

Lanette wax SX has been obtained from Messrs. Ronsheim & Moore, Ann Boleyn Walk, Cheam, Surrey.

TABLE V

Absorption of Sulphanilamide from Extensive Fresh Burns

1. Mrs. J., aet. 62: Clothes caught fire 5 p.m., July 19th, 1943. Second and third degree burns of abdomen, neck, left arm and both legs. Total area = 21 per cent. of body surface.

Date	*Dressing*	*Blood sulphde. (free) (mg. per 100 c.c.)*	*Urine sulphde. (gm. in 24 hours)*	
			Free	*Total*
July 19th, 5.30 p.m.	Sulphde. cream (3 per cent.) ..	—	—	—
9.30 p.m.	—	1·0		
July 20th, 9.45 a.m.	—	0·7	Specimens not obtainable	
2.0 p.m.	—	0·6		
July 21st, 9.0 a.m. ..	—	0·4		
July 22nd	Sulphde./S-thiazole cream (3 per cent. of each).	—	—	—
July 23rd, 9.0 a.m.	—	6·8	0·78	1·09
July 24th	—	4·0	1·22	1·58
July 25th	—	1·5	0·83	1·52
July 26th	—	—	0·28	0·54
July 27th	—	—	0·15	0·29
July 28th	—	—	0·11	0·22
July 29th	—	—	0·05	0·09
July 30th	—	—	0·08	0·15
July 31st	Mixed cream as above	—	—	—
August 2nd ..	—	6·2	—	—
August 4th	—	1·8	—	—
August 15th ..	—	trace	—	—

2. P.G., aet. 6½: Fell into boiling water 2.30 p.m., July 26th, 1943. Extensive third degree (and some second degree) burns involving whole trunk and part of thighs. Total area = 45 per cent. of body surface.

Date	*Dressing*	*Blood sulphde. (free) (mg. per 100 c.c.)*	*Urine sulphde. (gm. in 24 hours)*	
			Free	*Total*
July 30th	Sulphde./S-thiazole cream (3 per cent. of each).	Specimens could not be obtained.	(Specimens could not be collected for first week.)	
August 3rd	—	—	0·42	0·55
August 4th	—	—	0·27	0·37
August 5th	—	—	0·22	0·27
August 6th	—	—	0·21	0·29
August 7th, 11 a.m.	Mixed cream as above	—	0·17	0·23
August 8th, 12 noon	—	6·1	1·33	1·92
August 9th	—	—	1·02	1·54
August 10th ..	—	—	0·61	0·80
August 11th ..	—	—	0·25	0·33
August 12th ..	Mixed cream	—	—	—
August 13th ..	—	—	1·26	1·64
August 14th ..	—	—	0·59	0·89

The plenary dressing is usually left untouched for 7–10 or even 12 days unless the affected area is such that some amount of contamination is unavoidable, e.g., around the mouth and nose, or the perineum and buttocks.

The occurrence of some fever, even to 102°, during the first two to three days is in itself no indication for changing the dressing, for we are convinced that such fevers are frequently reactions to injury (comparable to those which follow simple fractures—Cuthbertson, 1932) rather than to infection. If, however, the burned part is unduly painful, and the patient's general condition suggests an acute infection (which has seldom happened in recent months), we undo the dressing to make a bacteriological examination, and to see if there are clinical signs of such infection.

Care is taken, in finishing these dressings, to make sure that the wool covering extends well beyond the gauze at every point, and that it is firmly bandaged. There is little doubt that many burns become infected (especially in small children) because of too little attention to these last details—permitting access of dust or dirty fingers.

Oral administration of sulphonamides.—Our reasons for preferring local to oral administration of sulphonamides as a routine practice are discussed on p. 44 below.

In a few instances, where a patient was admitted with an acute febrile infection due to streptococcus, or where such an infection developed after admission, sulphanilamide or sulphathiazole was given for a few days by mouth, in the usual dosage, such systemic treatment being combined with local application unless the latter was contra-indicated by suppuration or sloughs. We have seen no reason to change this procedure.

Subsequent dressings.—Many second-degree burns are healed when the first dressing is removed. If they are not, and the wound is clinically uninfected (not infrequently it is bacteriologically sterile), it is immediately re-dressed with sulphanilamide cream on gauze sheets, without any washing of the surface; this dressing, in turn, is left for a further five to seven days.

Healing seems to be rather slow if the cream is used for more than 15–20 days on end, and in such cases it is sometimes advisable to change to zinc lotion or paraffined tulle and moist saline dressings, or, in some cases, to leave the wound dry with no dressing at all.

If deep sloughs are present, but without clinical signs of infection, when the first dressing is removed, we proceed as above till the sloughs are separated, about 18–30 days after the injury; skin grafting is then performed as soon as possible, if a bacteriological examination shows the surface to be free of haemolytic streptococci and the granulations are healthy. When haemolytic streptococci have been present, we have been able to eliminate them within a week by four applications, at intervals of 48 hours, of penicillin cream or of propamidine (see below), before skin grafting is performed.

If infection supervenes in a case with deep sloughs, the continued application of sulphonamide cream is unlikely to be effective—partly because the drug is neutralized by pus and the breakdown products of necrotic tissue, but also because the bacteria which usually predominate at this time (*Proteus*, coliform bacilli, etc.) are relatively insensitive to sulphonamides. Frequent applications of a hypochlorite solution, such as "Eusol", at this stage have appeared to hasten the separation of sloughs—probably by liberation of proteolytic ferments from disintegrated leucocytes, as suggested by Wright and Colebrook (1921) in connection with hypertonic salt solution.

(iv) Elimination of Haemolytic Streptococci and Staphylococci from Burns already Infected

About 14 per cent. of all burn cases admitted to the wards, and 30 per cent. of those treated as out-patients, are already infected with haemolytic streptococci (and many with staphylococci) when first seen; others have acquired these infections during treatment, in spite of our precautions. Daily powdering with sulphanilamide, and covering with moist gauze, will usually get rid of haemolytic streptococci within a few days from granulating surfaces which are free from sloughs and are not suppurating freely (Colebrook and Francis, 1941). A 30 per cent. sulphanilamide cream, changed every second day, was also successful in similar circumstances. Less frequent application of the weaker sulphanilamide creams recently employed (10 per cent. and 3 per cent.) has sometimes, but not always, been followed by rapid disappearance of streptococci.

Within the last year, however, we have shown that the most certain method of eliminating haemolytic streptococci (and also staphylococci) from burned surfaces is by means of penicillin applied as a cream, using a base similar to that employed for sulphonamides (Clark *et al.*, 1943). This cream has been prepared as follows:—

Penicillin Cream: Preparation—

The base.—This is prepared as for sulphonamide cream (p. 29).

Penicillin.—Dissolve penicillin powder (either sodium or calcium salt) according to its unitage in sterile distilled water to make a solution of about 800 Oxford units per c.c. Of this solution, add 5 c.c. to 30 gm. of the base; mix thoroughly. The final strength is about 120 units per gramme of cream.

This cream retains its activity with but little impairment for 15 days at room temperature, and for four weeks at least in the refrigerator at + 2° C.

In 41 out of a series of 54 burns infected with haemolytic streptococci which were treated with the penicillin cream (76 per cent.), these organisms disappeared from the wound within five days and did not reappear. This effect was seen in several instances even when the cream was applied to acutely infected wounds with adherent sloughs. No case was met with in which the drug was without effect on the streptococci. Seven of the patients were infected with streptococci which had persisted on the burns under treatment by sulphanilamide cream, and which were also found to be resistant to sulphanilamide *in vitro* (20 mgm. per 100 c.c.). These streptococci were eliminated by penicillin from the burns just as promptly as the sulphonamide-sensitive strains.

In the same paper, we reported on the application of propamidine —the new aromatic diamidine compound (4 : 4 diamidinodiphenoxypropane dihydrochloride),—to a series of 34 burns. This was applied in a concentration of 0·1 per cent. in Mumford base (Lanette wax SX hard paraffin and technical white oil), the applications being repeated, as in the case of penicillin, four times at 48-hour intervals. From 21 of the 34 cases, haemolytic streptococci disappeared within a few days, but there was a small minority (eight cases) in which this preparation appeared to be without effect. Healing was usually very good, both with penicillin and with propamidine, and no toxic effects were observed. (*Caution.*—Little is known at present about the absorption of propamidine from burned surfaces, but its use on extensive burns may possibly prove to be dangerous.)

It would be difficult to exaggerate the importance of this new power to control acute infections by haemolytic streptococci (and often staphylococci), and to eliminate these organisms at will from burned surfaces. It means that we can promptly check the destructive process which so often in the past has converted the burn with partial skin loss, capable of epithelial regeneration, into one with complete loss of the epithelial tissues and consequent great delay in healing—with opportunity for contractures. In the later stages, by removal of streptococci, we can greatly accelerate spontaneous healing; and where grafting is required, we can eliminate the chief obstacle to success.

More important still, in the long run, will be the effect on streptococcal infection as a whole, in centres where many burns are treated. Each patient whose burns are quickly freed from streptococci ceases to be a reservoir from which infection can be transmitted to other cases. In our own wards, this has meant that we have usually had only three or four streptococcal wound carriers at any one time, instead of the 15 to 20 with which we were confronted at the beginning of the investigation. And it seems likely that we have by no means reached the limit of what is possible in regard to the control of these reservoirs of infection.

In conclusion, as a practical recommendation, we suggest—(*a*) that, until penicillin becomes more generally available, propamidine should be employed for the rapid elimination of haemolytic streptococci from all burns of small or moderate size, due watch being kept for possible toxic effects; (*b*) that, where bacteriological facilities are not available for the detection of streptococcal infections, it would seem advisable to make such applications of penicillin or propamidine a routine procedure before skin-grafting or plastic repair operations.

(v) Measures for the Prevention of Cross-Infection

Special attention has been directed to the following :—

A.—The Technique of Ward Dressings

In default of a room set aside for this purpose with appropriate equipment, all dressings have been done in the wards by a dressing team using the " no-touch " technique, more or less as described in " The Prevention of ' Hospital ' Infection of Wounds ", *Medical Research Council War Memorandum*, No. 6, 1942.

In order to get through the work (usually 6–12 dressings—some of them large), it has been found convenient to use a dressing team of four, comprising :—

The Dresser (Doctor or Sister).

The Trolley Nurse (or Sister), who touches nothing infected, and hands everything to the Dresser with Cheatle forceps.

The " Cutter-down ", who cuts bandages before the trolley arrives, but does not remove the dressings. She also places a sterilized mackintosh sheet under the part to be dressed. (*This plan is not recommended for general adoption*, but has been used to save time.

It may lead to exposure of a wound before the dressing team arrives—especially in restless children—and so may favour infection from the air or transmission of infection by flies, etc.).

The " Runner ", who moves the bin for dirty dressings to the bedside, brings sterile instruments from the sterilizing room and takes them back when soiled for re-sterilizing. (This combination of functions is admittedly open to criticism, and its institution may perhaps have been a mistake. It was almost impossible to avoid, owing to shortage of nurses. The employment of an ambulant patient to move the bin was considered at first, but found impracticable, as frequently there was no such patient available.)

In addition, there is a nurse stationed in the sterilizing room, who first equips the trolley with its sterile instruments, etc., and subsequently washes and re-sterilizes the soiled ones.

The Dresser wears the same pair of rubber gloves throughout—washing them in " Cetavlon " (1 per cent.), and drying them on a fresh towel after the dressing of each separate wound. (For a time, the Dresser used ungloved hands but, owing to a spread of *Ps. pyocyanea* and *Proteus* infection, we have reverted to the use of gloves.)

The Cutter-down washes her hands in water between each case.

The sterile instruments are kept dry, and covered.

Sticking of dressings.—Most of the sulphonamide cream dressings come off easily, but occasionally (when there has been much exudation into them and this has clotted) there may be some difficulty—particularly at the first change of dressing. To moisten them when this occurs, we have employed a saline dripper, devised by Mr. T. W. Pearce, of Park Prewett Hospital, Basingstoke, (see Fig. 2, facing p. 20) instead of the chemical wash bottle described in the *M.R.C. War Memorandum No. 6.* Being of sturdy construction, it can be put bodily into the sterilizer with its contained saline, and will deliver only drips, or a steady small stream at will. If saline is to be used for this purpose, it is essential that it should be freshly sterilized each day.

B.—The Disposal of Soiled Dressings

As covered containers were not available, we have been compelled to use ordinary open enamel pails, which are emptied into larger (covered) bins. This procedure is not satisfactory—in particular, it lends itself to dissemination of infection by flies, and by the hands of nurses who have to handle the pails. (If dressings were done in a special room, a chute could be provided to carry away the soiled dressings to a corridor, from which they could be removed at intervals to the destructor.)

C.—Sterilization of Limb Baths

This has been done in a steam-heated tank, the bath being first emptied into a sluice.

D.—Sterilization of Full-Sized Bath

Very few patients have been treated in a bath, as the sulphonamide cream dressings have seemed to give more satisfactory results, with much less trouble and less risk of cross-infection. Chemical sterilization of the baths with lysol, as described in *M.R.C. War Memorandum No. 6*, has been used when required.

E.—Avoidance of Infection by Dust

Preliminary investigations to find out the magnitude of this danger were carried out as follows :—

Experiment 1

Plates of nutrient agar, or of blood agar, were exposed in the wards for 1–2 hours during the period of morning dressings. Usually, one was placed on a table in the centre of the 10-bedded ward (average distance five yards from the actual dressings) ; another, on the

floor near the door. The findings summarized in Table VI indicate that the concentration of pathogens in the air *at a distance from the beds* was not very high, except in the case of *Staphylococcus aureus* on two occasions.

Experiment 2

To test the opinion that a higher concentration of pathogens would be found in the immediate vicinity of patients with infected burns, we exposed agar plates on five occasions during bed-making, within two yards of a bed whose occupant's wounds had been constantly infected with *Proteus*.

That organism was grown on eight plates out of ten exposed.

In connexion with these results, it should be borne in mind that the burned areas exposed during dressings are often many times greater than the area of the plates.

TABLE VI

(*Showing Results of Exposing Plates in the Wards for Two Hours*)

(i) *Blood Agar Plates*

Number exposed	Haem. strep. *present on*	Proteus *present on*	Ps. pyocyanea *present on*
52 (on 26 days)	5* (only one or two colonies)	12	0†

* Three strains were of the same serological type as strains recently isolated from burns in the ward.

† There may have been some non-chromogenic strains which were not detected.

(ii) *Ordinary Agar Plates*

(For detection of *Ps. pyocyanea* and *Staphylococcus aureus*.)

Number exposed	Ps. pyocyanea *present on*	*Number exposed*	Staph. aureus (*coagulase* +) *present on*
46 (on 23 days)	3* (Three colonies on one occasion, one colony on the other two).	49 (on 25 days)	40†

* Two positives in Ward 41, where there had been three patients with the organism in their burns. One positive in Ward 40, where there had been one patient similarly infected.

† On two successive days there were 150 and 350 colonies on the plates, respectively; on all other occasions, there were only a few colonies—usually less than 10. No explanation of this difference was forthcoming.

It is evident, therefore, that every exposure of a burned surface involves an appreciable risk of direct infection by dust. We have sought to minimise this risk by the following measures:—

(*a*) Blankets, which contribute a large part of the ward dust, are sterilized after the discharge of each patient, see p. 37. (In ideal circumstances, the sterilization would be done immediately a patient lost the streptococci, *Proteus*, *Ps. pyocyanea* or other pathogen with which his wounds had been infected; but this has not been possible in war-time, owing to shortage of laundry staff. The dissemination of fluff from blankets would also be avoided, to a large extent, by their treatment at each laundering with white oils, as suggested by van den Ende and Thomas (1941).)

(*b*) Free ventilation of the wards is encouraged at all times when dressings are not being done, in order to reduce the concentration of pathogens in the air. (Unfortunately, the blackout and blast protection walls have seriously interfered with free ventilation and sunlight. All windows have had to be kept closed during blackout hours, to prevent escape of light.)

(*c*) Spindle oil has been rubbed into the ward floors every third week, in order to " mat up " dust and prevent its dissemination by sweeping (van den Ende *et al.*, 1940).

(*d*) Sweeping of ward floors is, whenever possible, concluded an hour before the commencement of dressings, in order to allow dust to settle. (Owing to shortage of ward cleaners, this has not always been possible.) In ideal circumstances, sweeping would be done with a suction vacuum cleaner of which the exhaust is known to be reasonably free from bacteria.

(*e*) Windows are kept closed during the dressings, and unnecessary traffic in the wards at these times is forbidden.

(*f*) Only one burn is exposed for dressing at a time.

(*g*) Each ward has been fumigated on at least one occasion with formaldehyde vapour, as recommended by Fry (1941). (After the room had been sealed completely, 100 gm. of paraformaldehyde for every 2,000 cubic feet of air space was burned off, using 60 c.c. of methylated spirit. Streptococcus- and pyocyaneus-infected filter papers, exposed in covered dishes during this process, have always proved sterile. On one occasion, the dishes were placed respectively inside a hair mattress and in a bed completely covered with the usual bedding. Sterility was achieved even in these circumstances.)*

We did not succeed in eliminating the type 4 haemolytic streptococcus with which the wards were originally infested, until this fumigation was carried out. Ideally, we consider that such fumigation should be carried out at least once every two months in wards housing burned patients.

F.—Transfer of Infection from the Respiratory Tract

Owing to pressure of work, the systematic bacteriological examination of throats and noses of all patients and staff on entry to the wards, and at intervals thereafter, could not be carried out. Since January, 1943, however, a throat swab has been taken from all new nurses.

A single swabbing (tonsils) of all the staff and patients during the early months, when type 4 streptococcus was predominant in the wards, did not reveal that organism in any instance.

The routine measures adopted have included :—

(*a*) Masking of all the staff (medical and nursing), and also visitors, while dressings are being done. The mask used has consisted of four layers of fine mesh gauze, with a piece of paper inset to cover the mouth.

(*b*) Masking of patients while their wounds are being dressed.

(*c*) Reporting of all respiratory tract infections in patients or staff, and immediate swabbing with a view to detection of streptococcal infection (those who give positive swabs are isolated or sent off duty, according to circumstances).

(*d*) Transfer of nursing staff if any throat swab yields a predominant or abundant culture of haemolytic streptococci—or if repeated swabs always yield a few of these organisms. (Actually, only three nurses during 15 months have had to be transferred because they were carriers.)

(*e*) Avoidance of talking during dressings.

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* Since the above was written, stringent tests have shown that, if blankets are *heavily infected* with dried pus or blood plus pyocyaneus, formaldehyde sterilization is not always effective.

G.—Avoidance of Infection from other Sources

(*a*) *Hair.*—Cotton caps, completely covering the hair, are worn by the Dresser and other members of the dressing team.

(*b*) *The clothes.*—Sterile gowns are worn by all taking part in dressings. Before the daily round of routine dressings, a sterile gown is put on by each member of the dressing team. (In ideal circumstances, the gown worn by the Dresser should be changed before each dressing, because of the possibility that infected fluff derived from contact with the bedding or dressings of a previous case might fall on to an uninfected burn; the larger the burned area of the previous case, the greater the chance of such transfer by way of the Dresser's gown. Owing to the war-time shortage of laundry staff, however, we have had to compromise on this ideal procedure and change the Dresser's gown only after he has dealt with obviously infected or extensive burns, which could not be dressed without a probable contamination of the gown.)

Against the transfer of infection by unseen particles of dry fluff the use of oiled gowns should give additional security.

(*c*) *Bed-pans.*—Attempts to secure a bed-pan sterilizer were unsuccessful, and for some months we had not even a tank in which the pans could be chemically sterilized. (As there have been many burns involving the buttocks, there is little doubt that infection has sometimes been conveyed in this way.)

(*d*) *Dolls and toys.*—Instructions have been issued that dolls and toys are not to pass from child to child, without intermediary sterilization; and, to ensure this, they are tied to the cots. Fumigation of fluffy dolls in the formalin chamber of the Glasgow Corporation Public Health Department has been carried out at intervals, through the co-operation of Dr. R. J. Peters.

(*d*) *Blankets.*—At the commencement of this investigation, it was ascertained that many burns were becoming infected with haemolytic streptococci within a few hours after admission to the ward. It seemed probable that this infection was derived, in some cases at least, from the blankets which were thrown over the patients on arrival, while their freshly burned surfaces were completely exposed. This led us to enquire into the treatment of the blankets in the process of laundering. We discovered that, in order to avoid shrinking and felting, the blankets were simply treated with warm soap solution (not above 42° C.), then rinsed and dried in warm air. *They were never heated at a temperature which would kill haemolytic streptococci or other pathogens.* Haemolytic streptococci of the type prevalent in the burns ward were, in fact, isolated on two occasions from clean blankets in the linen store. (Subsequent enquiry at a number of other hospitals in England and Scotland elicited the fact that the procedure outlined above is quite usual in hospital laundries. There can be little doubt that this is a serious source of hospital infections, and that too few people are aware of it.)

Experiments with artificially-infected blanket material showed that haemolytic streptococci and *Ps. pyocyanea* could be killed, without damage to the blanket, in two ways:—

(1) By exposure of the blanket (unfolded) to formaldehyde vapour for 24 hours. This, however, would necessitate a large sealed chamber.

(2) By low pressure autoclaving for a short period.

For several months, all blankets from the Burns Ward have been autoclaved for 20 minutes at 5–7 lb. pressure (after blowing off steam). Infected test samples have always proved free from haemolytic streptococcus and *Ps. pyocyanea.*

(*f*) *Mattresses.*—These are sterilized in an autoclave at 120° C. for one hour, after each patient is discharged; or, if this sterilizing procedure is found to be harmful, the mattresses may be autoclaved at 5 lb. for 20 minutes.

RESULTS OBTAINED

In order to determine the extent of our success in controlling infection, it would be desirable to ascertain precisely what proportion of the burned areas treated became "infected"; and to contrast that figure with others relating to earlier periods in the Burns Unit of this Infirmary, or with those of other observers reporting large series of burns.

Such a comparison cannot be made, partly because of the difficulty of judging in many cases as to whether there was a definite infection of tissues (see p. 22), and partly because adequate data are not available, either for earlier periods at the Royal Infirmary or, so far as we are aware, for other large series of burns treated elsewhere.

Analysis of our records does, however, give some indication of the progress made, and it may serve as a base line by which to register further progress in the future. It may conveniently be presented under four headings:—

(i) The incidence of severe, and of fatal, septic infection.
(ii) The mean daily temperature curve during the first 20 days.
(iii) The incidence of hospital infection by haemolytic streptococci.
(iv) General impressions with regard to infection and healing.

The duration of hospital treatment has not been studied, because it was evident from the beginning that the very heterogeneous material included in a burns clinic—and various special circumstances, such as the transfer of cases to another hospital, the fortuitous admission of cases already grossly infected, etc.—could not provide data of any value for a statistical analysis. In future studies aiming at an appraisal of the therapeutic procedures, it will be essential to include a follow-up of all cases to the time of complete restoration of function. There is often a long interval between discharge from hospital and such complete recovery.

(i) The Incidence of Severe, and of Fatal, Septic Infection

The outstanding impression left by all the 282 cases treated as in-patients from the beginning has been the rarity of acute septic infection. Only 20 passed through an acute suppurative phase due to streptococcal infection, and one due to staphylococcal infection. Four of the streptococcal cases followed grafting operations—the streptococcus being apparently acquired in the operating theatre. In only one case, a child of two years, did the infection constitute a serious threat to life.

We are particularly impressed by the fact that, in all these 282 cases treated from the beginning, there has not been a single instance of spreading cellulitis or erysipelas, or lymphangitis, or of a scarlatiniform rash. Only one patient developed a generalized infection by haemolytic streptococcus.

In only three instances have we seen pus locked up under an eschar. One patient with a deep burn over the internal malleolus of the tibia developed a septic arthritis of the ankle joint.

The 21 cases of acute infection referred to above all occurred in patients with deep burns, and some degree of infection persisted through the period of separation of sloughs. In addition, there were 25 other cases of deep burns,

which passed through a " dirty " phase during the sloughing period, when cultures yielded usually an abundant growth of coliform and diphtheroid bacilli, *Proteus*, staphylococci and, at times, *Ps. pyocyanea.* We recognise frankly that we have been unsuccessful in controlling or preventing these infections, which have been partly responsible for death in several instances. In most cases they caused some irregular fever and some suppuration, but usually no signs of acute infection (swelling, redness, pain, or ulceration of wound edges).

Fatal infections.—Among the 1,530 patients treated (330 in-patients, 1,200 out-patients), there has been only one death from infection by haemolytic streptococci, and none from staphylococcal infection.

(We have felt justified in excluding the case of Mrs. B., aged 68, who died 74 hours after receiving a deep burn of the abdomen, thighs and hands—26 per cent. of the body surface. A swab from one only of her burned areas 24 hours after admission yielded some haemolytic streptococci, but her temperature did not rise at that time, nor were there any clinical signs of acute infection. The clinical condition was that characteristic of fatal burns—prostration, leading to coma, with hyperpyrexia during the last few hours of life. A blood culture was not performed. Autopsy revealed extensive arteriosclerosis and did not suggest a generalized infection.)

The only other fatal result for which septic infection may have been in some part responsible was that in a mentally defective dumb girl, with a deep burn of thighs and buttocks (22 per cent.); who had intermittent fever for seven days and then died in coma with jaundice. Her burns at the time of death were in the " dirty ", sloughing stage, and yielded cultures of coliform bacilli and staphylococci. Haemolytic streptococci were not grown from any of the 10 swabs examined. Autopsy gave no indication that death had been due to generalized infection.

Two other patients, both young children, died from pulmonary complications associated with fever, but without any evidence of sepsis of the burned areas. Blood culture from one of them during life gave a growth of *B. faecalis alkaligenes* (which was not present on the burned area). Lung puncture in the other child, immediately after death, yielded a non-haemolytic streptococcus. At autopsy, in each case, atelectasis was a prominent feature (p. 200).

(ii) Mean Daily Temperature during the First Twenty Days

There seems to be little doubt that a rise of temperature during the first 24–36 hours after burning may be, and often is, purely an expression of reaction to injury, rather than an indication of infection. (Swabs from the surface of the burn at the time of this fever, and at the first dressing a few days later, have, on more than one occasion, yielded no growth.)

On the other hand, prolongation of fever beyond 48 hours—or a rising temperature after the first fall to normal—is usually indicative of an infection of the burned surfaces, though in young children it may indicate a superadded respiratory tract infection.

It seemed probable, therefore, that the mean daily temperature of sufficiently large groups of patients receiving different treatment would afford a useful pointer to the amount of infection occurring in those groups.

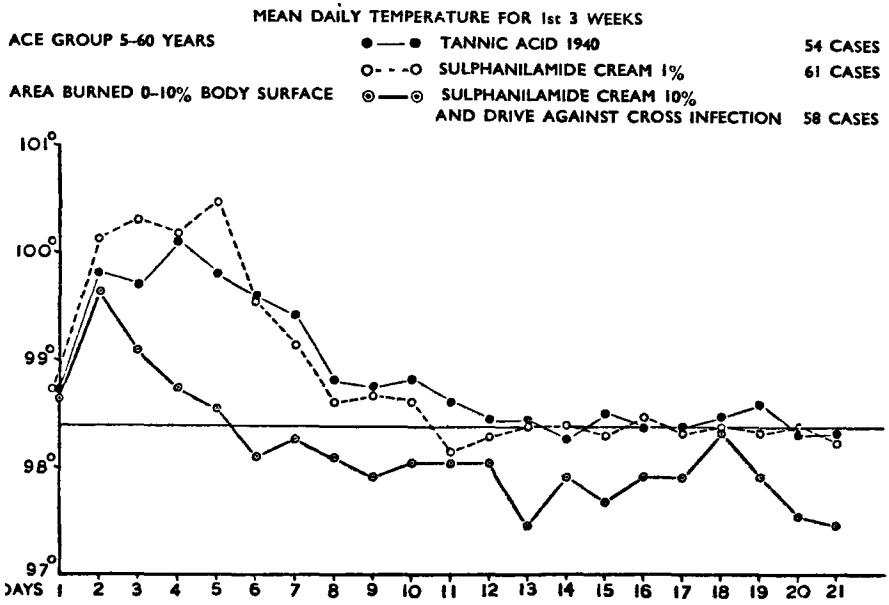
The composite chart (Fig. 3) shows such an analysis of the temperature records of three groups of 55–60 cases of burns each. In order to avoid the extremes of life, and to obtain sufficiently large numbers, we have chosen all patients admitted during three distinct periods, falling into the age group 5–60 years, and having burns not greater in extent than 10 per cent. of the body surface (the great majority had burns of 4–10 per cent.). The three groups of cases comprise respectively :—

(*a*) 54 treated with tannic acid during 1940.

(*b*) 61 treated with 1 per cent. sulphanilamide cream (lanette wax SX and cod liver oil base), from February, 1941 to February, 1942, without any special effort to control hospital infection.

(*c*) 58 treated with 10 per cent. sulphanilamide cream (lanette wax SX and cod liver oil or castor oil base), from February, 1942 to February, 1943—plus an intensive drive against hospital infection, and the use of penicillin in some of the cases.

FIG. 3



Skin temperatures were taken throughout, in the axilla when possible.

It will be seen that the mean temperatures of the third group of patients during the first 24 hours are not very much lower than those of the other groups—as was to be expected if fever at this time is chiefly a reaction to injury; there is, however, a striking difference between the third and the other two groups in respect of the time taken by the temperature to fall to normal level (six days and 12 days, respectively). The subsequent level was also decidedly lower in the third group, indicating a relative absence of late febrile disturbances.

While this improvement in the mean temperatures during the last period indicates definite progress in the control of infections, we cannot be sure how far that progress has been due, respectively, to the initial cleansing with cetyl trimethyl ammonium bromide, to the bacteriostatic influence of the sulphonamide cream, or to the various measures adopted for the prevention of hospital infection. It seems probable that all have contributed.

(iii) The Incidence of Hospital Infection by Haemolytic Streptococci

Eighty-three of the 282 patients (30 per cent.) admitted without haemolytic streptococci acquired them at some time during their stay in hospital. The distribution of these cross-infections, month by month, is shown in Fig. 4.

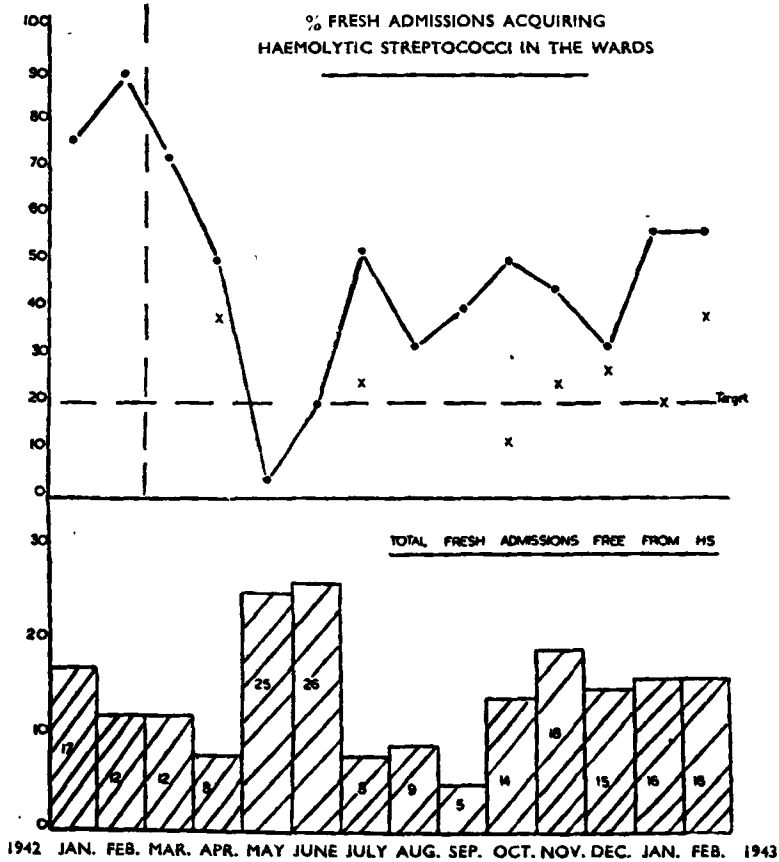
Swabs were taken from each burned area on the patient's arrival in the ward (before the burned surface was cleaned) and at each subsequent dressing. It is unlikely, therefore, that we failed to detect a fresh infection in any patient.

The graph shows three outstanding features :—

(1) That during the months of January and February, 1942, (before the drive against cross-infection had begun) an average of 83 per cent. of the patients whose burns were free from haemolytic streptococcus on admission became infected with that organism in the ward.

(2) That during May and June, 1942, after a few weeks of intensive effort—including the education of nurses, drastic revision of the dressing technique, removal of blackout curtains and other sources of dust, etc.—the cross-infection rate was reduced to 4 per cent. and 20 per cent. respectively (average 12 per cent.). (It should be noted that this reduction was achieved while the ward was exceptionally busy, the admission rate being higher than for any other two-monthly period in 1942.)

FIG. 4.



x Percentage figure corrected by omission of cases whose infection by streptococci was considered excusable, e g children who interfered with dressings, face burns which could not be effectively covered, etc

(3) That we did not succeed in keeping down the cross-infection rate to this low level, although it has been very much lower than the rate for January and February, 1942. Some of these infections were not clinically important, since they occurred in the later stages of healing, but the total number gives a valuable indication of the infective risk to which fresh cases are exposed.

By way of commentary upon these findings, we wish to make the following points :—

(*a*) We began the drive against cross-infection under a very heavy handicap. Not only were almost all the patients' burns infected with haemolytic streptococci (giving abundant opportunity for repeated transfer), but these cocci were all insensitive to sulphanilamide.

(*b*) The striking fall during May and June shows that hospital infection *can be prevented*—given the right conditions (see discussion below).

(*c*) In considering the difficulty of completely eliminating cross-infection from any Burns Unit, two circumstances must be taken into account. Firstly, that there is likely to be always a steady influx of cases already infected with haemolytic streptococci on admission (in Glasgow it was about 14 per cent.) ; these may infect the dust of the wards, bedding, etc., before the cocci can be eliminated from their burns ; they also provide opportunity for cross-infection by dressings, social contacts, etc. Secondly that, in a few cases, anatomical and other considerations make it almost inevitable that some infection should occur (at any rate under present conditions). We have in mind here the burns of the face, which cannot be completely protected from dust or dirty fingers ; and also burns involving the buttocks, upper thighs and/or perineum. Aside from auto-infection of such cases, however, the prevention of cross-infection has been almost impossible without adequate facilities for the sterilization of bed-pans, which we have not had.

The influence of these " excusable " cases on the monthly incidence of cross-infections is indicated on the graph (Fig. 4) by the sign " x ".

We attribute our failure to maintain a lower level of infection after June chiefly to the following features :—

(*a*) The constant change of nurses in the ward. To meet the requirements of training, all the nursing staff, except the sister, have been changed after two months in the ward, and often after much shorter periods. This arrangement has had three unfortunate consequences. For the first week or two of each new nurse's turn of duty, she has been imperfectly aware of the detailed precautions devised to prevent cross-infections. Secondly, it has not been possible to keep up the level of enthusiasm reached during April, May and June, 1942. Moreover, owing to the continual infiltration of new nurses, it proved impossible to provide regularly the simple course of instruction in the laboratory which, it was hoped, would make the nurses, to some extent, " microbe-conscious " and enable them to do their work with understanding. This education of the nurses, we consider to be an essential feature of any serious attempt to maintain the high standard of ward work which alone can eliminate infection from burns.

(*b*) With the coming of summer, followed by an unusually mild autumn and winter, the presence of flies has been a difficulty which we have not been able to overcome. (The wards are situated on the ground floor, over a tunnel conveying main hot water supplies, and, under war-time conditions of diminished ventilation, they are often unduly hot.)

There can be little doubt that wound infection has often been transmitted by flies (Shooter and Waterworth, 1944).

(*c*) For want of a room set aside for that purpose, all dressings have had to be done in the open wards, where the dust has frequently been found to be infested with haemolytic streptococci, staphylococci and *Proteus* (see above).

(*d*) We have been unable to reserve a special room exclusively for the plenary dressing on admission to hospital.

(*e*) Although blankets have been sterilized by heat for several months past, wartime conditions have not permitted us to do this as often as was desirable, or to treat them with white oil as recommended by van den Ende and Thomas (1941), or to prevent the dissemination of fluff.

(*f*) Owing to shortage of sterile gowns up till March, 1943, it was sometimes necessary to do plenary and other clean dressings with gowns which had been used for infected cases.

(*g*) As noted in (*b*) above, the ventilation of the wards, owing to war-time regulations, has often been seriously inadequate. Also, on account of blackout arrangements, blast walls and overshadowing by other buildings, the wards have had no direct sunlight. Fumigation of the main wards has been possible on only one occasion during the 15 months. There has therefore been every opportunity for the survival of pathogens in the dust, and cross-infection at some period has been almost inevitable for patients with multiple burns, or burns which had to be dressed many times.

(iv) General Impressions with regard to Infection and Healing

Impressions gained from heterogeneous collections of cases are notoriously untrustworthy. Nevertheless, we wish to record our belief that the rarity of acute invasive infection in this large series of burned patients represents a notable advance on results obtained by earlier methods.

Where infection has been avoided or controlled, the healing of superficial burns has, in general, been rapid. We have seen no evidence that any constituent of the creams used has retarded epithelial regeneration in such cases. The effect of prolonged treatment by the creams on deeper tissues is perhaps more doubtful; it requires further investigation.

There is little doubt that covering by skin grafts is the best treatment for the raw surface in the later stages, and that any preliminary treatment of such surface which, by eliminating infection, makes for good results in skin-grafting will, in the long run, contribute most to rapid healing of the deep burn.

The difficulty of following up many of our patients, owing to war conditions, makes it impossible to give reliable data as to the incidence of contractures. In only 9 cases out of 1,530 treated is it known that contracture requiring surgical interference has developed. The incidence of keloid scars has also been very low. Only 6 patients up to date (three months after the period of investigation) are known to have developed them.

It is probable that the true figure for both contractures and keloid will be somewhat higher.

The Incidence of Infection by Organisms other than Streptococci

It will be noted that we have dealt above only with hospital infections by haemolytic streptococci. There have, of course, been many other such infections which it was not possible to study in the same detail. Infection by *Proteus* was acquired by 55 (22·6 per cent.) of a group of 243 in-patients; and *Ps. pyocyanea* by 41 (16·9 per cent.). The spread of *Ps. pyocyanea* infection has been intermittent; for six months we had none.

We do not doubt that a much larger measure of success will be achieved against these, as well as the streptococcal infections, when the optimal conditions are provided, and when the reservoirs of potential infection are sufficiently reduced by appropriate chemotherapeutic remedies.

The control of " hospital " infection is the central problem in the treatment of the burned area: and it is not insoluble.

COMMENTARY AND DISCUSSION

In this section, we wish to bring out certain points which have not been dealt with in the preceding pages. They may conveniently be presented in the form of answers to questions :—

(i) *What evidence is there that the growth of bacteria on the burned surfaces was effectively checked by the sulphanilamide or sulphathiazole creams ? Which of these drugs has proved the more effective for that purpose ?*

The fact that haemolytic streptococcus was able to establish itself on the burned surfaces of 83 cases (30 per cent.), in spite of local treatment by sulphonamide creams, suggests at first sight that these chemotherapeutic agents can have had very little bacteriostatic or bactericidal effect. Certainly their effectiveness has been less than we had hoped.

Two factors have probably been responsible for this. First, the predominance of a sulphonamide-insensitive strain in the wards when the investigation started. No less than 36 of the 83 strains which were acquired in the course of treatment were found to be insensitive to sulphanilamide *in vitro* (20 mgm. per 100 c.c.). Some of these cocci were sensitive to much higher concentrations of sulphanilamide (100–200 mgm. per 100 c.c.), but it is unlikely that they would have been exposed to such a high concentration for any prolonged period after the application of the cream. The evidence at present available suggests that neither daily powdering by sulphanilamide (Colebrook and Francis, 1941) nor less frequent application of sulphonamide creams will usually suffice to prevent infection by sulphonamide-resistant streptococci.

Secondly, it may well be that in many cases the sulphonamide was in some measure inactivated by the presence of necrotic tissue and/or purulent exudate on the burned surfaces. Such inactivation has been demonstrated *in vitro* by King and Henschel (1939), by McLeod (1940) and by Fleming (1941). Most of the 47 patients whose burns became infected by sulphonamide-sensitive streptococci had necrotic tissue in their injuries; and in about half the cases the infection occurred between the tenth and thirtieth days, i.e., at a time when the sloughs were separating and there was a certain amount of purulent exudate. (Since saprophytic bacterial growth at such times is often copious, and several widely different species of bacteria have been shown to produce substances antagonistic to sulphonamides (Stamp, 1939; McLeod, 1940; Woods, 1940; Green and Bielschowsky, 1942), this also may have played a part.)

Notwithstanding our failure in these 83 patients to keep the burns free from streptococcal infection throughout the whole period of their healing (five of them became infected only at a late stage when it was of little consequence), we still have a strong impression that the bactericidal effect we hoped for has to a large extent been achieved both by sulphanilamide and by sulphathiazole. At the first change of dressing, after 7–10 days, the burns are almost invariably clean, without any sign whatever of clinical infection; and bacteriological examination usually gives only a scanty growth. In several instances, the burns have remained bacteriologically sterile for 10–14 days.

To get convincing evidence in support of this impression, it will be necessary to make a careful bacteriological follow-up of a number of cases treated, after identical cleaning-up, with one of the sulphonamide creams or with the base without the sulphonamide principle. This we have not yet done, because, in the conditions under which we have worked, it seemed unjustifiable to dispense with any presumed aids against infection. It is hoped to carry out such an investigation in the near future, and to compare the bacteriostatic effects (if any) with those obtained by means of penicillin applied in a similar base.

There is, of course, the possibility that, even when the burns do become infected with haemolytic streptococci in spite of the local application of sulphonamides, these drugs may diminish the invasive capacity of the cocci. The demonstration of such an effect in animal experiments has been claimed (Horsfall, 1942). It might well explain the rarity of acute inflammatory conditions in our patients.

(ii) *Why was the local application of sulphonamides considered preferable to systemic administration?*

Two considerations dictated this policy.

(*a*) The sulphonamides were used primarily as insurance against infection by haemolytic streptococci, and the time of onset of that infection was quite uncertain—it might be during the first 24 hours or at any time in the first three weeks—depending upon the opportunities for transmission of the organisms. Clearly, it was undesirable to maintain an effective concentration of the drug in the blood-stream for two to three weeks, on the off-chance that infection might occur. Such prolonged administration involves an appreciable risk of serious toxic effects.

(*b*) We wished to have a high concentration of the bacteriostatic principle in the exudate bathing the burn, in order to suppress growth of any relatively insensitive organisms as well as the highly sensitive strains of haemolytic streptococci. With the more soluble drug, sulphanilamide in particular, it was reasonable to hope for local concentrations reaching 500 mgm. per 100 c.c., for some hours at least, as compared with 5–10 mgm. per 100 c.c., which is all one can expect from oral administration.

(iii) *What are the special merits—and defects—of the method of treatment here described?*

In the nature of things, the treatment of a severe burn must be largely a compromise. We are dealing with injured tissues which cannot, as a rule, be removed surgically. The primary aim should be to protect them from infection while they are being replaced by regenerated normal tissues.

The treatment here described has certainly not fully achieved that aim, but we believe it represents some progress towards it. It is essentially an "open" method—unfavourable to formation of sealed-off "dead spaces" round any necrotic tissue. In these "dead spaces", with their accumulating products of tissue autolysis, any bacteria which have survived the cleaning up process will sooner or later find conditions favourable for multiplication, and will induce suppuration. That we believe to be the fundamental disadvantage of all coagulant or "closed" methods of treatment.

The treatment used in our patients has the added advantage of being *simple*. Provided the burn is not extensive and does not require active measures to combat "shock", the injured surface can be dealt with in a small hospital, or on board ship, or even in a private house, if the conditions permit of aseptic procedure. No general anaesthetic is required, nor special equipment. The sulphonamide cream is soothing; patients are usually comfortable as soon as the dressing is applied. Their burns are usually not disturbed thereafter for a week or more. Not infrequently we have seen children playing with their toys and dolls on the day following a burning injury; and we have seen them submit to re-dressing on about the tenth day without any fright or pain.

At the same time, the burn is readily accessible for re-dressing at an earlier stage should circumstances require it.

The method has three chief drawbacks :—

(*a*) It does not prevent excessive fluid loss during the first 48 hours after burning. This loss can, however, be made good by plasma or serum transfusions.

(*b*) It does not, in its present form, effectively control infections by coliform bacilli, *Proteus* or *Ps. pyocyanea*, during the stage of separation of sloughs. This defect, however, is probably shared equally by all methods of treatment hitherto available.

(*c*) The policy of infrequent dressings, even when there is no sepsis, inevitably entails a certain amount of odour, and this, in turn, attracts flies, especially in hot climates.

(iv) *Is it likely that, with great extension of sulphonamide therapy, sulphonamide-fastness among haemolytic streptococci will become so common as to defeat the policy of bacteriostatic dressings?*

This question cannot receive a definite answer at present. In two instances we have seen streptococcal strains change, under treatment of the burn by sulphonamide cream, from typical sensitiveness to fastness (20 mgm. sulphanilamide per 100 c.c.), the serological type remaining the same. In another instance, the same change occurred while the patient was having both oral and local treatment with a sulphonamide. In all these cases the development of sulphonamide-fastness seemed to be a slow process, taking about three weeks or more to become established, but further observations on this point are required.

It is significant also, in this connexion, that in at least two surgical centres where many streptococcal cases are assembled, and local sulphonamide treatment is a routine procedure, resistant strains have become predominant in the wards and have given rise to a number of unfortunate "incidents" (chiefly sepsis following operation). The centres in question are the Plastic Surgery Wards in charge of Sir Harold Gillies at Basingstoke (see report by Francis, 1942) and the Glasgow Burns Unit at present under consideration. (In a third centre, viz. the Plastic Surgery Unit under Mr. Rainsford Mowlem at St. Albans, a spread of type 13 strains of haemolytic streptococcus in some 15 wounds was reported by Spooner (1941). Several of these strains were sulphonamide-resistant.) So far as we are aware, these are the only centres in which systematic investigation of the infecting streptococci has included observations on their sulphonamide-sensitiveness or resistance.

The danger of a considerable extension of sulphonamide-fastness appears, then, to be very real. It may call for abandonment of the local use of sulphonamides in the routine treatment of burns. In any event, the policy of excluding hospital infections should be vigorously pursued, together with the prompt elimination of streptococcal infections, when they do occur, by penicillin or propamidine, or by other effective chemotherapeutic agents which may become available in the future.

(v) *In what directions should we look for further progress in the control of infections in burns?*

Although a large part of this report has been devoted to the chemotherapeutic attack, it seems to us unlikely that this will ever suffice by itself to guard the great majority of burns from infection throughout the long weeks of healing. We must also limit the opportunities for such infection by all the means in our power. We must work out a system of preventive measures, analogous to those of the operating theatre but appropriate to the different conditions obtaining in wards.

As a preliminary to that task, we shall do well to consider—

(*a*) what are the essential conditions for the elimination of cross-infection in the wards? and

(*b*) is the establishment of those conditions a practicable aim?

Many of the conditions which we regard as essential have already been mentioned, or hinted at, in the description of our procedure given above (pp. 23–27), e.g., strict techniques of dressings, elimination of dust, application of a bacteriostatic dressing, sterilization of blankets, bed-pans, etc. Some of these require further discussion, as also do certain larger questions of future policy with regard to the burned patient.

It appears to us axiomatic that the great majority of patients with burning injuries should, in future, be treated in centres specially staffed and equipped for the purpose—not scattered as heretofore in the ordinary surgical wards of general hospitals, where their treatment has too often been entrusted to relatively inexperienced staff.

It is not proposed to discuss here in any detail the design, organization and equipment of such special burns centres, but we would suggest that the following features merit special consideration:—

(1) An adequate surgical staff. The care of badly burned patients makes considerable demands on the surgeon's time and skill, both during the shock period and later. It should be the responsibility of a whole-time surgical officer, with more experience and authority than the average house-surgeon.

(2) Active and continuous collaboration in the control of infection, between the surgical staff and the nursing staff on the one hand, and the bacteriologist on the other. Facilities for haematological and biochemical investigation will also be required.

(3) A nursing staff sufficiently stable to permit of the maintenance of an exceptionally high standard of aseptic ward technique. There should also be a "pool" of nurses trained in the work of the centre, from which additional help can be drawn in times of stress. The interest of all the nurses should be stimulated by some practical instruction in applied bacteriology.

(4) Provision for the dressing of all cases in an atmosphere free from dust and, so far as possible, from pathogenic bacteria. The most appropriate process of air conditioning for this purpose has still to be decided. Apart from filtration of dust particles, it will probably be necessary to employ some form of sterilization of the incoming air. This problem is at present being investigated.

The question of siting burns centres, if possible, outside cities, so that the wards may be freely ventilated with clean air, and the patients may get direct sunshine while their wounds are healing, will also need careful consideration.

(5) The exclusion of flies from the wards.

There remains the question whether the establishment of such special centres is practicable—or even necessary? We believe it to be necessary, because it will not be feasible to maintain the conditions outlined above—nor the exceptionally high standard of ward technique required—in the surgical wards of every general hospital. And we believe it to be no more impracticable than it has proved to adopt the strict aseptic and antiseptic ritual now employed in every operating theatre. Once we have learned how to combat the dust evil effectively, have included enough applied bacteriology in the training of doctors and nurses to make them microbe-conscious in their daily work, and have also gained the power to control infections by the gram-negative organisms,

it will certainly be found much less troublesome and expensive to secure healing of the badly burned patient in 3–8 weeks without infection than in as many months with infection. This should lead to a considerable saving of life and man-power, and the functional results as regards the burns will be correspondingly good, for contractures and deformities will be avoided, as well as (we believe) much keloid growth.

The partial success we have had in eliminating cross-infection from wards full of burned patients has convinced us that much greater success in this respect is attainable. It is a matter of establishing the right conditions, of working out the necessary régime of ward hygiene, of progress in chemotherapy, and of taking trouble.

A second big problem also awaits solution—that of dealing with the severe protein depletion or other profound metabolic disturbance which so often now kills burned patients after three to six weeks, and probably greatly delays healing in those who survive.

The large number of burning injuries, both in peace and war—and the high incidence of sepsis among them at present—make these problems of considerable national importance.

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STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART III.—REPLACEMENT THERAPY IN BURNS SHOCK

BY

THOMAS GIBSON, M.B., Ch.B., F.R.C.S.E.

(Working with a whole-time grant from the Medical Research Council)

ALEXANDER BROWN, M.B., Ch.B, M.R.C.P.E., F.R.F.P.S.G.

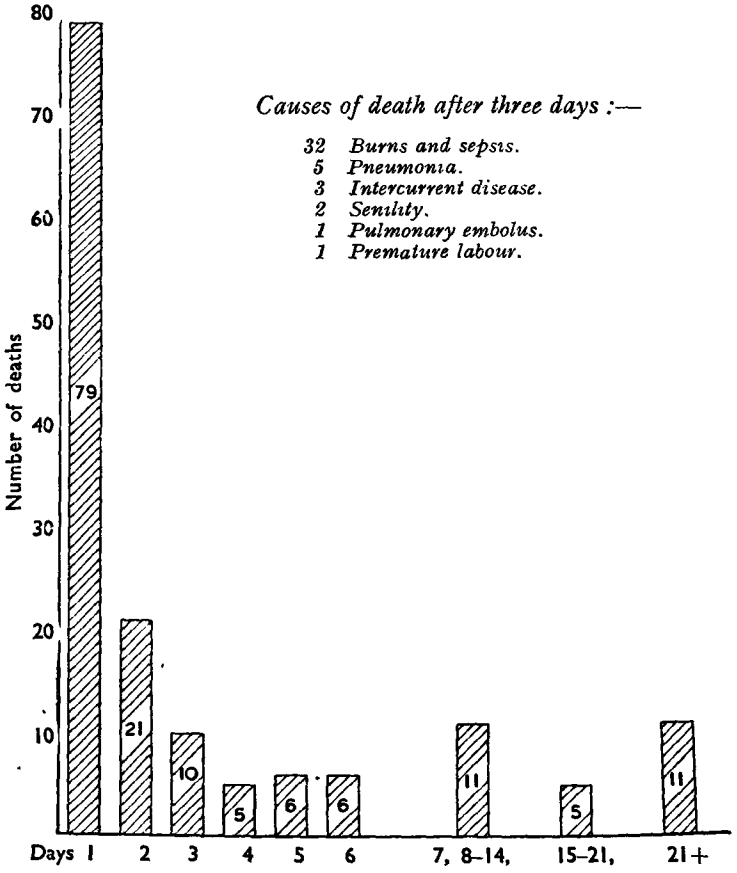
(Working with a part-time grant from the Medical Research Council)

CONTENTS

INTRODUCTION

The general reaction following severe burns— the so-called " Burns Shock " —still remains the most important single factor influencing the mortality in this type of injury. Analysis of the records of the Glasgow Royal Infirmary Burns Unit for the years 1937 to 1941 inclusive (Fig. 5), reveals that, in a series of 1,200 admissions, 49 per cent. of the deaths occurred within 24 hours of the burn, and 72 per cent. within three days. Only 4 of the patients received plasma or serum intravenously.

FIG. 5



Analysis of 154 (12·8 per cent.) deaths occurring in 1,200 consecutive cases of burns—Royal Infirmary, Glasgow, 1937–41.

THE TERM " BURNS SHOCK "

The sequence of physiological derangements which leads so often to death within the first three days of burning is still far from being fully understood. Pending more precise knowledge, it may conveniently be referred to by the comprehensive and somewhat vague term " burns shock." This condition is quite distinct in its clinical manifestations from the acute circulatory collapse of " primary shock," which may (but, in fact, seldom does) occur shortly after burning, just as it may after any other injury. The clinical features of " burns shock " as we have seen it will be described later in this report.

THE AETIOLOGY OF BURNS SHOCK

A number of different theories have been put forward in recent years to account for burns shock. Some workers, following Underhill and his colleagues (1923), have emphasized the loss of fluid from the circulating blood, with the resultant concentration of the cellular elements and a progressive anoxaemia of the tissues; others have invoked a variety of different toxic products thought to be derived from the burned tissues; others, again, have attributed the fatal issue to excessive sensory stimuli from the burned area. Deficient functioning of the adrenal apparatus has also been invoked as a possible cause.

Discussions of these different, and even divergent, views have been published by Wilson, Macgregor & Stewart (1938), Harkins, Conrod & Romence (1942), Rossiter (1943), and others.

SCOPE OF THE PRESENT INVESTIGATION

In our study of burns shock in patients admitted to the Glasgow Royal Infirmary during 1942–43, we have concentrated attention chiefly upon the loss of fluid from the blood-stream, upon the physiological changes associated with it, and upon the effect of replacing the fluid lost, by transfusion.

Apart from post-mortem observations, which will be reported in a later paper (p. 192), we have not investigated the question of adrenal function or the possible influence of toxic products derived from the burned tissues.

During the period of the investigation, 350 patients were admitted to the burns unit, but naturally only the more severe cases needed transfusion. The detailed observations in the present paper relate mainly to 62 patients (cases 1—62, Appendix I, pp. 203–206) in whom transfusion was given for the prevention or treatment of burns shock.

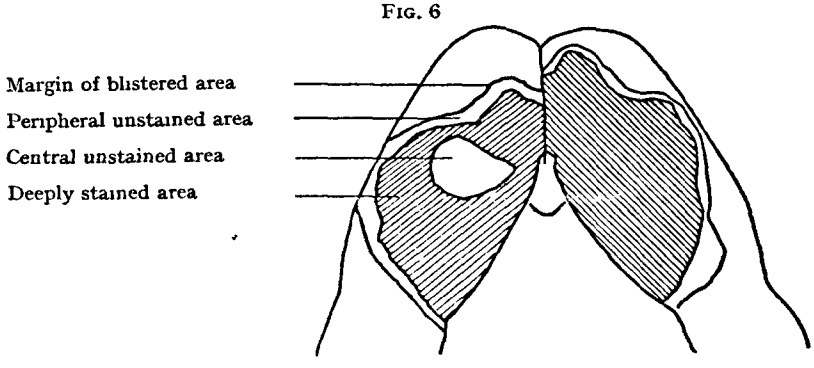
OBSERVATIONS RELATING TO CAPILLARY PERMEABILITY AND TO FLUID LOSS

Capillary Permeability—Experiments with Kiton Fast Green

It was thought that variations in local capillary permeability to dyes of high molecular weight, distributed through the blood-stream, might be used to differentiate deep avascular burns from more superficial lesions. The dye, Kiton fast green, had previously been used by Sorsby (1939) for demonstration of ocular lesions. It was administered to four of our patients only, since one showed severe vomiting immediately following its use, and it was felt that the possible toxic effects precluded its use in early cases of burns. The results obtained, however, were sufficiently striking to be put on record. The findings in the following case are typical:—

Case No. 6.—Admitted one hour after burning, the patient was found to have extensive blister burns on the back of both thighs. After cleansing, when all blister epithelium had been removed, 8 c.c. of the dye were

FIG. 6



injected intravenously. The whole burned area became stained within a few minutes a brilliant green colour, with the exception of two areas—a small central area which before the injection had appeared avascular, and the periphery of the blistered area, which, for a variable width, remained unstained. Erythematous burns at the margin of the blistered area were unstained (see Fig. 6).

The subsequent course of the different areas was instructive. The brilliantly stained areas were found to be of partial skin loss; the central unstained area was deeper, and practically of whole-thickness loss; the peripheral unstained area was healed after 10 days—i.e., it was a superficial, rather than a deep blister-burn.

The results in the other three cases examined corroborated these findings — namely, that in burns involving partial skin loss, the increase in capillary permeability is greater than in superficial blister burns.

Amount of Fluid Loss in Burned Patients

The large loss of fluid from the surface of an extensive burn in man is so well recognized as to need no emphasis. It is no exaggeration to say that the fluid escaping from the burned surface often "soaks the bed", and may amount to several litres during the first three days. Whether the amount lost into the tissues is more or less than that lost from the surface cannot be stated with any assurance (we have no means of determining it in human beings), but there is no doubt that it is often very large. (For relevant observations on experimental burns in animals, *see* Harkins, 1935; Keeley, Gibson & Pijoan, 1939; Leach, Peters & Rossiter, 1943; and Rossiter, 1943.)

From the practical point of view of the treatment of shock, the estimation of haemoglobin or of red cell volume has provided a sufficiently accurate indirect estimate of the fluid lost by all routes, although, for scientific purposes, it could not, of course, give accurate data, owing to our ignorance of the blood picture before burning. Generally speaking, the amount of fluid required to correct haemoconcentration has varied roughly with the extent of the burning.

Increased Capillary Permeability throughout the Body

The experimental work of Simonart (1930) with animals, suggested that there was an almost immediate dilatation of capillaries, and a general increase of capillary permeability, after burning. He obtained evidence of haemoconcentration occurring within a few minutes.

Whether an analogous general dilatation of capillaries after burning occurs in man is not known. In our experience, haemoconcentration has often begun to develop within 1–2 hours (assuming a normal corpuscular volume before burning), but its onset is sometimes apparently delayed beyond that time. There has been no detectable effusion into tissues remote from the burned area in our patients. While the possibility of a slight general increase of capillary permeability should be borne in mind (pp. 134–5), it seems probable that the large external fluid loss, and the local loss into the tissues of the burned area, play the major parts in inducing haemoconcentration.

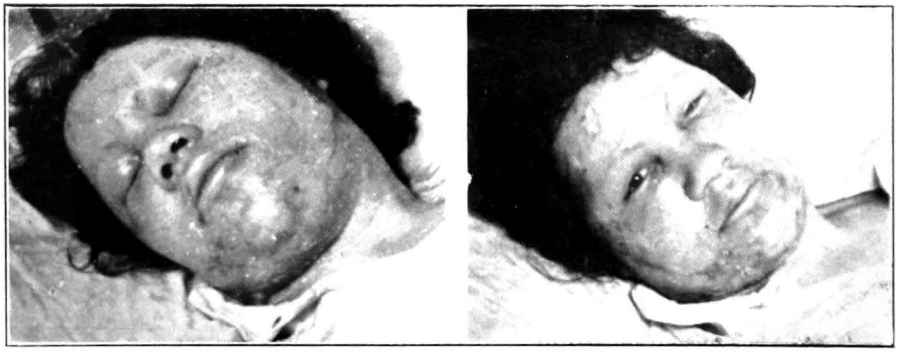
Duration of Increased Capillary Permeability

The observations on experimental low temperature burns in human beings reported on p. 6 showed that oedema of the tissues was already visible to the naked eye 20–30 minutes after burning. Superficial burns of the face in a number of patients have given a striking illustration of this rapid onset of increased capillary permeability, and also of its decline. In several cases the oedema has been sufficient to close the eyes completely. The photographs in Fig. 7 show well the increase of oedema up to 15 hours, and its commencing re-absorption after 18–20 hours.

FIG. 7

Changes in oedema after superficial burn of face

A.—3 hours after burning. B.—8 hours after burning.



C.—15 hours after burning. D.—24 hours after burning.

There can be little doubt that the reduction in the oedema which enables the patient with a badly burned face to open his eyes marks the onset of recovery of the capillaries, and the cessation of fluid loss into the tissues. Plasma therapy in severe burns is accordingly required chiefly during the first 20–30 hours after burning; and often it has been found that there is no longer haemoconcentration after that time. In cases of extensive superficial burning, however, there may still be copious loss of fluid externally up till about 60 hours after the injury, and this may result in persistence, or even increase, of the haemoconcentration, which calls for a large fluid intake, although it has seldom, if ever, given rise to pronounced symptoms, or required additional transfusions of plasma or serum.

FLUID REPLACEMENT THERAPY

Plasma or serum has been given in all cases by the continuous intravenous drip method. In a few instances this was followed by glucose-saline, as explained later. Whole blood has not been used in the " shock period," as our primary aim has been to correct haemoconcentration.

In selecting cases for treatment by fluid replacement, for several months we were guided chiefly by the haematocrit reading on admission, the blood pressure and pulse-rate, and the patient's general condition, rather than by the severity of the burning. The patient was watched for a few hours, and replacement therapy was not started until there was a rise in the haematocrit reading, a fall in blood pressure and a rising pulse-rate, or a deterioration of the general condition.

This policy was gradually changed as we came to realize that, if the haemoconcentration and signs of derangement of the central nervous system (increasing drowsiness, etc.) were allowed to develop over a period of several hours, there was little hope of overtaking the pathological processes by fluid replacement.

In recent months, therefore, our decision to start transfusion has been influenced much more by the severity and extent of the burns, and by the time already elapsed before admission, than by the haematocrit reading or the blood pressure, though these and other factors still need to be taken into account. Plasma or serum is now given early and in adequate quantity, to *prevent* undue haemoconcentration. This change of plan appears to have been justified by results. (For further details, see the Commentary on p. 67.)

Types of Fluid Used

Normal Citrated Plasma

This has been supplied to us by the courtesy of Professor J. P. Todd, of the Glasgow and S.W. Scotland Blood Transfusion Service. The plasma was obtained from a pool of several samples, some separated from the cells early and some only after a period of 1–2 weeks.

Ether Extracted Concentrated Serum

This was supplied by the N.W. London Blood Supply Depot. The protein content varied between 13·5 and 16 gm. per cent.

Dried Serum

This was prepared by the Medical Research Council's Serum Drying Unit at Cambridge, by the spin-freeze-high-vacuum-sublimation RG process of Greaves. This serum is separated within 24 hours, and is derived from a mixture of bloods of groups A, AB and B in proportions approximate to those in the general population. Relatively little group O blood is used. The bacteriological control is strict: no batch which on culture shows more than 100 organisms per cubic millimetre before filtration, is filtered, and only sterile material is dried.

At first, liquid plasma was used almost exclusively. In 7 patients reactions were noted, characterized by rigor and pyrexia. Some degree of pyrexia, however, is commonly seen in patients with extensive burns during the first 24–48 hours, even in the absence of transfusions, and some minor reactions may have been unrecognized (see Charts Nos. 1 and 2, pp. 72 and 73). In each instance, the reaction ceased shortly after the transfusion had been stopped or the offending bottle changed. In two cases, the reactions were very severe and may have contributed to the fatal result (see Charts Nos. 12 and 18, pp. 85 and 92). The presence of clots in the plasma favoured the occurrence of reactions. In 5 cases in which the fluid causing the reaction was examined bacteriologically, the fluid proved to be sterile. Ether extracted serum was used with good results and few reactions. On one occasion, however, ether anaesthesia was induced in an adult by administration of 400 c.c. of ether extracted concentrated serum in 20 minutes : ether was noted in the patient's breath, and the bottle itself smelt strongly of ether. Recovery in this case was uneventful, but the product was used very seldom thereafter, owing to the frequent need for rapid administration of large amounts of fluid.

Reconstituted dried serum was used extensively and proved to be the most useful product. Only one reaction was noted in the administration of over 300 bottles for the treatment of burns shock. Used, however, in concentrated form (2–3 times), as a source of proteins in the later stages of three cases of severe burns, it produced in each patient a rigor and pyrexia. In burns shock it has been used almost entirely in normal concentration.

Concentrations higher than normal have been used for 4 patients. In 2, as an alternative to normal concentrations, twice concentrated serum was used. The amounts required were, as far as could be ascertained, similar to what would have been expected if normal concentration had been used. In one case (No. 47), increasing concentrations up to four times normal were used in an attempt to withdraw fluid from the oedematous tissues into the blood-stream, with no appreciable effect. In the fourth case (see Chart No. 12, p. 85), three times the normal concentration was given, in an attempt to reduce the cerebral oedema which had been found post-mortem in cases with severe mental upset. No improvement was noted.

During the second half of the period of investigation, glucose has been added, in the strength of 15 gm. per 400–500 c.c. of plasma or serum, as a measure aimed at controlling the repeated vomiting in severely burned patients. It has been of little value in this respect (see below).

Routes of Administration

Arm Veins

The veins of the antecubital fossae were generally the most easily accessible and the most satisfactory, but in many cases of severe burns they could not be used and other routes had to be tried.

Saphenous Veins

The long saphenous vein as it runs anterior to the medial malleolus is very constant in position and easily cannulated ; and the ankle usually escapes burning even in very extensive cases. As a route for plasma or serum administration, however, this vein proved unsatisfactory : spasm of the walls occurred to such a degree that considerable extra pressure was required to maintain a flow of fluid at the desired rate. This extra pressure could easily be applied by the use of a Higginson's syringe attached to the air inlet of the bottle, but after a few hours such pain developed in the line of the vein that some other route of administration had to be sought. Attempts to relieve the spasm were of no permanent value. Massage of the vein, when tolerated, had only a slight effect ; injection of 1–2 c.c. of 2 per cent. procaine into the

drip was beneficial in some cases, but only for 1–2 minutes; and application of warmth locally was ineffective. Venous spasm was encountered in arm veins, but never to a degree sufficient to interfere with the transfusion. Use of the saphenous veins at the ankle was finally abandoned, as it did not allow of the rapid administration of sufficient fluid. Interference with transfusion by venous spasm was encountered only when plasma or serum was being administered. It was not encountered in the use of glucose-saline.

External Jugular Vein

When both elbow regions were burned, this vein proved a useful site for intravenous therapy. The wall of the vein is firmly attached to the deep cervical fascia, which it pierces at the root of the neck and by which it is held patent. Spasm was not encountered in any of the six patients in whom this route was used. Exposure of the vein was usually simple, but, owing to the poor support given by the lax tissues in the neck, kinking of the vein over the end of the cannula occurred on several occasions. This was best prevented by stitching down the cannula to skin as high on the neck as possible, and by keeping the head turned to the opposite side.

Bone Marrow

Transfusions into the sternal marrow were tried in four cases when superficial veins were difficult of access. The results were unsatisfactory. The rate at which fluid would run in was limited at first to a fast drip and, over a period of 5 to 6 hours, the rate gradually slowed until it stopped (see Chart No. 26, p. 105). Pressure was of little value in increasing the rate of transfusion. In one case, an attempt to re-start the transfusion through a second sternal puncture failed, since all the fluid leaked through the first puncture; this difficulty was overcome by making a fresh puncture in the manubrium sterni, the first two having been in the body of the sternum.

Regulation of Dosage and Rate of Flow

The ideal at which we have aimed is the restoration of the blood volume to its normal level as soon as possible after injury, and its maintenance at that level until further fluid loss has ceased. Until, however, repeated accurate direct estimations of blood volume in burns shock are possible, other indirect criteria on which dosage may be based, must be used. We have been guided chiefly by (*a*) changes in the degree of haemoconcentration (or dilution); (*b*) changes in blood pressure and/or pulse-rate; (*c*) the patient's age and general condition. Of these, variations in the blood picture have, in our experience, proved the most accurate and useful guide; the other criteria, apart from age, were depended on only in cases where venous blood samples were not obtainable. Recent evidence that capillary blood is also reliable for this purpose has enabled us to use it almost exclusively in regulating dosage.

Blood Examinations

On all possible occasions, a specimen of venous blood was collected into a heparinized tube (p. 116) as soon as the patient was admitted to the ward. In the majority of cases, haematocrit readings were used as an index of changes in plasma volume, and complete estimations made at leisure on the samples. Later, when a simple, accurate and rapid photo-electric method of estimation of haemoglobin became available, this was preferred. Further samples of blood were withdrawn during the first 48 hours, as often as was considered necessary for control of plasma administration. In many cases of extensive burns, it was difficult to obtain more than one sample of venous blood. At first, fluid administration was controlled in such cases by blood pressure and pulse-rate observations. These were found insufficiently reliable (see below) and, subsequently, estimations were made on capillary blood. A capillary

haematocrit tube was used, or the haemoglobin concentration was estimated. In spite of evidence that the plasma-cell ratio in capillary and venous bloods may differ, especially in the initial stages, when capillary stasis is marked, these estimations on capillary blood were of great value.

Estimations of Blood Pressure

These were made with the Baumann apparatus or with the dial manometer and cuff employed by Grant. (A small cuff was obtained for children from Messrs. Down Bros., Ltd.)

Owing to frequent involvement of the upper arms in the burning injury, observations of blood pressure often could not be made. When available, they often proved of value, especially in patients from whom samples of venous blood could not be obtained. Sometimes, however, the blood pressure proved misleading, since it was apt to be higher than normal for a few hours after burning (for evidence on this point, and a summary of the changes associated with different degrees of burning, see p. 136). In general, it was found that changes in the degree of haemoconcentration provided a more reliable index of the need for fluid replacement than changes of blood pressure.

ACCESSORY MEASURES ADOPTED DURING THE SHOCK PERIOD

General Measures

Morphine was given in full doses immediately on admission, and the patient was undressed, put to bed between sterile blankets (the burns being covered with sterile towels), and removed to the " shock-room." This room, specially reserved for shock cases, is treated with the same respect for asepsis as a surgical theatre. The temperature is thermostatically controlled at 70–75° F. Higher temperatures (80–85° F.) were used in the early stages of the investigation, but the patients complained of discomfort, and there was no evidence that the slight reduction in temperature was harmful. In addition, the ability to lose heat is greatly diminished in cases with extensive skin loss: too high a room temperature may lead to hyperpyrexia.

Local Measures

The practice of dealing fully with the local lesion before measures had been taken to treat or prevent shock was held responsible for the poor results obtained in some cases treated early in the investigation, and was abandoned thereafter for the great majority of patients. As a rapid preliminary to administration of fluid, it was found better, therefore, to snip the blisters and to cover the burns with " No. 9 Cream " (see p. 10), without any attempt at cleansing. The local treatment was completed 24–36 hours later, when the patient's condition had improved. In a few cases, plenary dressing was carried out shortly after admission, but only after fluid administration had been begun, and when the patient's general condition was sufficiently satisfactory; these cases were adults with burns of about 20 per cent. of the body surface.

Treatment of Repeated Vomiting

Severe thirst was a constant symptom in extensively burned patients. They clamoured continually for drinks to relieve it but any attempt to satisfy the demand with more than a mouthful of water was usually followed by vomiting. Incorporation of glucose in the transfusion was suggested by Dr. Janet Vaughan (1942), in order to lessen the sickness, but it had no appreciable effect. The vomiting could be prevented or relieved only by efficient nursing and by restricting the fluid given by mouth. At first, 2–3 drs. of water, glucose and soda-water, or a proprietary glucose drink, were given. If no untoward result occurred, the dose was cautiously increased until 1–2 ozs. were given at a time. Weak tea, or milk and water, could then be given and, later, whole

milk. Twenty-four hours after the burn it was generally possible to give fluid freely by mouth. In the event of recurrence of vomiting within the first 24 hours, it was found best to reduce the fluid intake by mouth until vomiting ceased.

It seems illogical to restrict fluids in patients with severe fluid loss, but our experience has been that large amounts of fluid given by mouth are regurgitated and not retained in cases of burns shock, and the only method we have found of relieving the vomiting is by stringent rationing of oral fluids. It therefore becomes all the more important to carry out replacement by the intravenous route.

Glucose-Saline Transfusions after the First 24 Hours

A greater or lesser degree of oliguria is present in all cases of severe burns, even when adequate replacement therapy has been given. Recurrent sickness, and the need for controlling fluid intake by mouth in the severely burned, no doubt aggravate this. In extensively burned patients where oliguria was marked, it was therefore our custom to continue the "drip" for the second 24 hours after burning, or even longer, using glucose-saline solution (5 per cent. glucose in normal saline), in place of plasma or serum; or, alternatively, to administer glucose-saline per rectum. The dosage aimed at was 4–6 pints in 24 hours in the adult, and correspondingly smaller amounts in children.

RESULTS OF PLASMA AND SERUM THERAPY

Sixty-two cases of burns were considered sufficiently severe to require intravenous plasma or serum. In the presentation of the cases, they have been divided into two broad age groups:—

1. Children up to 12 years of age.
2. "Adults" over 12 years of age.

Further sub-divisions have been made on the basis of the approximate extent of the burn (see Appendix II, p. 210), and six groups are presented as follows:—

Group 1	—Children, mild burns	..	5–10 per cent. of body surface.
,, 2	—Adults, ,, ,,	..	5–20 ,, ,, ,,
,, 3	—Children, medium burns	..	10–20 ,, ,, ,,
,, 4	—Adults, ,, ,,	..	20–30 ,, ,, ,,
,, 5	—Children, severe burns	..	Over 20 ,, ,, ,,
,, 6	—Adults, ,, ,,	..	,, 30 ,, ,, ,,

Further sub-division of the child groups according to age would be interesting, but would be of little value in this series, because of the relatively small number of cases.

Throughout Tables VII–XIII, below, the following abbreviations are used to designate the different degrees of burning:—

B.B. = Simple blister burn.
P.S.L. = Partial skin loss.
W.S.L. = Whole skin loss.

In the diagrams indicating the extent and depth of burning (Charts Nos. 1–30), the following notations are used:—

 = B.B. (Blister burning).

 = P.S.L. (Partial skin loss).

 = W.S.L. (Whole skin loss).

Group 1 : Children—mild burns (age 0–12 years : extent of burn 5–10 per cent.).

This group comprises 5 patients (Table VII). Plasma transfusions were given in 4, because symptoms of shock had developed. The fifth child received plasma prophylactically, because the burns were apparently deep though small in extent. The 3 cases recorded in Charts Nos. 1–3 (pp. 72–74) demonstrate the rapidity of the response to intravenous therapy. Thirty-five other children with burns of similar extent were observed ; in none was there any apparent need for transfusion, and no symptoms of shock developed. No deaths occurred in this series.

TABLE VII

No.	*Name*	*Age*	*Area (per cent. of body surface)*	*Site*	*Amount of intravenous fluid given (c.c.)*	*When started* (Hours after burning)	*When finished* (Hours after burning)	*Adequacy*	*Notes*
1	M.S.	4½	8	Both buttocks, P.S.L. and W.S.L. Right hand, P.S.L.	1,600	26	30½	+	Not given until evidence of shock present
2	M.L.	6	7–8	Multiple small areas, B.B. and P.S.L.	1,100	16½	18½	+	Not given until evidence of shock present.
3	J.D.	8	5	Left thigh, P.S.L. and W.S.L.	1,600	5	14	+	Not given until evidence of shock present.
4	T.R.	2	9	Right arm, W.S.L.	800	3	12	+	Given because of low blood pressure.
5	T.B.	5	7	Axilla and back, W.S.L.	1,000	2	15	+	Given prophylactically.

Summary of Group 1

The majority of children with burns of 5–10 per cent. of the body surface did not require replacement therapy, but careful watch had to be kept for the occasional case which did ; considerable improvement followed plasma therapy in these patients.

The difficulty in interpreting the rise in temperature during the shock phase is well illustrated in two cases : in one, the rise in temperature coincided with the transfusion ; in the other, it had almost reached its peak before transfusion was given.

Group 2 : Adults—mild burns (age over 12 years : extent of burn 5–20 per cent.).

This group comprises 14 patients, 4 of whom received plasma after evidence of shock had developed. This evidence was either a falling blood pressure or haemoconcentration. In no case was there any clinical upset beyond slight vomiting. Only one death occurred—in an elderly man who had been burned during a hypertensive cerebral attack, and who died in a second attack 12 hours after the first. He had suffered only a small burn. Details of these cases are given in Table VIII.

TABLE VIII

No.	Name	Age	Area (per cent. of body surface)	Site	Amount of intravenous fluid given (c.c.)	When started (Hrs. after burning)	When finished (Hrs. after burning)	Remarks
6	D.R.	29	12	Buttocks and thighs, P.S.L.	1,000	20	27	At 20 hours: B.P. 96/68, Haematocrit 58·5 per cent.
7	D.S.	19	15	Chest and back, P.S.L.	800	15½	20	Haematocrit at 15 hours—52 per cent.
8	G.M.	20	16	Breast, arm, thigh and abdomen, W.S.L. and P.S.L.	1,600	8	14	At 8 hours: Haematocrit 53 per cent., B P. 86/50.
9	Mrs. Br.	31	16	Scattered areas on trunk, arm and thigh, W.S.L.	2,700	12	25	At 12 hours: Haematocrit 55 per cent., B P. 95/70.
10	J W.	66	6	Face, neck and shoulder, W.S.L.	800	3	5	Given prophylactically. Died
11	M.B.	32	6	Hands and face, B.B. and W.S.L.	1,000	2	6	Given prophylactically.
12	A.S.	32	8	Hands, face, B.B. and P.S.L.	1,500	4	12	Given prophylactically.
13	M.F.	30	10	Hands, face, legs, P.S.L. and W.S.L.	1,600	4	13	Given prophylactically.
14	Mrs. Be.	27	10	Back and shoulder, W.S.L.	2,500	2	16	Given prophylactically.
15	J.S.	37	10	Trunk, axilla and arm, W.S.L.	1,100	4	12	Given prophylactically.
16	A.G.	31	15	Back and arm, P.S.L. and W.S.L.	1,200	—	—	Given prophylactically.
17	J.D.	45	15	Arms and face, W.S.L. and P.S.L.	1,400	10	22	Given prophylactically.
18	Mrs. D.	31	16	Thighs and buttock, W.S.L. and B B.	3,000	4	16	Given prophylactically.
19	F.C.	51	19	R. leg, W.S.L. ..	3,600 (+1,000)	1	26	Given prophylactically.

The amount of fluid required varied from 1 to 3 litres, and roughly with the severity of the burn. The courses of 3 of the cases are illustrated in Charts Nos. 4–6 (pp. 75–77). The first was a typical case given fluid after the development of shock; the second was given fluid as a prophylactic measure; and the third demonstrates the large amount of fluid which may be required with a burn involving 20 per cent. of the body surface.

Nine further patients with burns of similar extent were observed. Slight haemoconcentration occurred in most of them, but no symptoms of shock were observed. They received no intravenous fluid and, within 3–4 days, evidence of haemoconcentration had disappeared. Typical blood readings in 5 of these cases are shown in Table IX :—

TABLE IX

Case	*Area (per cent. of body surface)*	*Site*	*Haematocrit Readings*			
			1st day	*2nd day*	*3rd day*	*4th day*
J.S. (No. 72)..	8	Face, arms, B.B. and P S L.	46	48	48	44·5
J.M (No. 73)	12	Forearms, face and neck, B.B. and P.S.L.	48	49	46·5	45
G.M. ..	10	Forearms and face, B.B. ..	46	48	—	43
J.McC (No.80)	16	8 per cent. P S.L. arms, face.	47·5	50	50·5	43
D N (No 79)	16	6 per cent. P S L. arms, face.	51·5	—	53	49

Summary of Group 2

Adult patients with burns of 5–20 per cent. of the body surface frequently did not require intravenous fluid. The probability of their requiring it increased with the extent of the burn, and it seemed advisable to administer fluid as a prophylactic to patients with burns of 15 per cent. or more of the body surface. Those burned less severely could be watched, and given transfusions if the need became evident.

Group 3 : Children—medium burns (age 0–12 years : extent of burn 10–20 per cent.).

This group comprised 10 patients (Table X). The majority were very young, and observations on haemoconcentration were in many cases too few, since samples of venous blood were difficult to obtain. It was realized that young patients are more sensitive to inadequate or excessive doses of plasma than are adults, and that frequent haemoglobin or haematocrit readings are essential. Capillary blood was found useful for this purpose when venous samples were not obtainable. Without such repeated observations, the tendency was to give an excessive amount of fluid, and it seems likely that this error was partly responsible for two of the deaths which occurred. The course of each of these fatal cases is shown in Charts Nos. 11 and 12 (pp. 83 and 85). The third death which occurred in this series was of a young child subject to recurring fits. Conscious at first, he began to have cyanotic convulsions lasting about 2–3 minutes. When first seen by the authors, eight hours after burning (the burns had previously been cleaned and dressed), he was practically unconscious, fits were recurring every 5–10 minutes, the blood pressure was 65/50, and the pulse rate 200. Intravenous plasma was started at once, and two pints were given in three-quarters of an hour. Some degree of pulmonary oedema followed; oxygen was administered, but cyanosis and respiratory distress continued and death occurred 2½ hours after plasma injection was begun. It seems probable that an excessive amount of plasma, given too rapidly and inducing pulmonary oedema, was a contributory cause of death.

TABLE X

No.	Name	Age	Area (per cent. of body surface)	Site	Amount of intravenous fluid given (c.c.)	When started (Hrs. after burning)	When finished (Hrs. after burning)	Remarks
20	M.W.	6	10	Thighs, W.S.L. and P.S.L.	1,900	1	8	Excessive transfusion (Chart 11). Died.
21	R.L.	6	10	Shoulder, chest, P.S.L. and W.S.L.	1,200	2½	10	Adequate transfusion. Recovered.
22	I.M.	9	12	Forearm, thighs, W.S.L. and P.S.L.	1,000	10	24	Adequate replacement. At 10 hours: haematocrit 43 per cent., B.P. 95/40. Recovered.
23	M.D.	2	15	Back and buttocks, B.B. and P.S.L.	1,900	4	35	(Chart 9.) Recovered.
24	M.C.	9/12	15–20	Chest, arm and thighs, W.S.L. and P.S.L.	500	3	6	Adequate replacement. Recovered.
25	M.H.	5	12	Side and buttocks, W.S.L. and P.S.L.	1,400	26	39	At 26 hours: Haematocrit 52 per cent.; B.P. not readable. Recovered.
26	J.K.	4½	12	Thigh, buttock and legs, W.S.L. and P.S.L.	1,600	13	21	At 15 hours: B.P. 80/70. Pale and apathetic. Recovered.
27	McA.	2	13	Chest, shoulder, P.S.L.	1,300	8	11	At 8 hours: B.P. 64/50. Recurrent fits. Died.
28	McE.	8	14	Thigh and legs, W.S.L. and P.S L.	2,350	24	30	At 24 hours: B.P. 65/60, haematocrit 54 per cent. Drowsy and irrational. (Chart 12). Died.
29	J.L.	1½	18	Back and buttocks, P.S.L. and W.S.L.	540	6	10	At 5 hours: B.P. 70/?, haematocrit 48·5 per cent. Recovered temporarily. (Died on 36th day)

Charts of six patients are reproduced (pp. 79–85). Charts Nos. 7 and 8 show the development of shock in cases not given plasma prophylactically, and the beneficial results of plasma therapy. Charts Nos. 9 and 10 show the results of giving plasma prophylactically and more or less adequately. Charts Nos. 11 and 12 are of two of the fatalities; in both these patients it seems likely that excessive amounts of serum were given—in one "prophylactically," and in the other after definite evidence of shock had appeared; in the latter

(Case 28), however, a severe transfusion reaction following the injection of plasma may have contributed to the fatal issue (p. 86). The details are appended in the protocols.

Summary of Group 3

In children, even more than in adults, it has been found essential to control the dosage of plasma by repeated examinations of the blood. By closer observations in this way on the progress of the patients in the early stages, it seems probable that the fatality rate in Group 3 might have been reduced.

Group 4 : Adults—medium burns (age 12 years and over : extent of burn 20–30 per cent.).

There were 10 cases in this group (Table XI), with 1 death in the shock phase. This occurred in Case No. 33, a senile patient, in whom transfusions were mistakenly stopped after 12 hours because of a normal blood reading. Symptoms of restlessness, delirium and disorientation occurred during the second day, with repeated vomiting ; death occurred in coma on the third day, when there was hyperpyrexia of 105° F. It seems probable that fluid replacement was inadequate.

TABLE XI

No.	*Name*	*Age*	*Area (per cent of body surface)*	*Site*	*Amount of intravenous fluid given (c.c.)*	*When started* (Hrs. after burning)	*When finished* (Hrs. after burning)	*Remarks*
30	Mrs. K.	21	20	Thighs, buttocks, arms and back, W.S.L. and P.S.L.	2,200	5	25	Inadequate transfusion. (Chart 15) Recovered.
31	M.H.	22	22	Back, axilla, arm, W.S.L.	1,600	5	44	Inadequate transfusion. (Chart 13.) Recovered.
32	T.W.	49	26	Face, arms, legs, P.S.L. and W.S.L.	3,400	6	41	Inadequate transfusion. (Chart 14.) Recovered.
33	Mrs. D.	68	26	Neck, trunk, thighs and hands, W.S.L. and P.S.L.	2,700	2	12	Transfusion probably discontinued too early. Died on 3rd day.
34	W.W.	39	20	Face, arms, back, B.B. and P.S.L.	3,600	4	22	Adequate transfusion. Recovered.
35	J.T.	?68	20	Chest, arm, W.S.L.	4,400	2	23	Adequate transfusion. (Chart 17.) Recovered temporarily. (Died on 21st day.)
36	A.B.	37	26	Back, arms, face, W.S.L. and P.S.L.	2,200	3	25	Adequate transfusion. Recovered.
37	D.M.	12	22	Abdomen, thighs, arms, W.S.L. P.S.L.	3,200	4	26	Adequate transfusion. (Chart 16.) Recovered.
38	M.B.	19	22	Buttocks, thighs, W.S.L.	4,420	2	26	Adequate transfusion. Recovered temporarily. (Died on 8th day.)
39	J.K.	19	26	Back, face, hands, legs, B.B., P.S.L. and W.S L.	3,540	5	24	Adequate transfusion. Recovered.

It was our custom in the early stages of the investigation to carry out the plenary dressing on admission, before beginning replacement therapy. This procedure was invariably accompanied by a fall in blood pressure, and also by an increase in haemoconcentration. Five cases are charted in detail (Charts Nos. 13-17, pp. 87, 91). In three of these patients, who received inadequate amounts of plasma or serum, the effect of initial cleansing, and of delay in transfusion, is shown. The other two cases are typical of those receiving adequate transfusions.

Summary of Group 4

Amounts of intravenous fluid between 2½ and 4½ litres may be necessary in this group for adequate replacement. Plenary dressing is best delayed until the second day, although it may safely be carried out in some cases in the first 24 hours, *provided that replacement therapy has been begun beforehand.*

Group 5 : Children—severe burns (age 0–12 years : extent of burn over 20 per cent.).

We have treated 12 patients in this group, 7 of whom died (Table XII). Inadequate control of plasma therapy was common to all the fatal cases. As the extent of the burn increases, so do the difficulties in replacement therapy and, with young children, these difficulties are considerably greater than in adults burned in similar degree. Blood pressure readings and venous blood samples are usually almost impossible to obtain, and cannulation of a vein, from being a simple surgical procedure, becomes an exceptionally difficult feat. Unfortunately, too, in children the need for haste in commencing replacement therapy is much greater than in adults, and evidence of mental upset—apathy, restlessness, delirium, etc.—occurs much earlier and more severely. In young children extensively burned, an hour wasted in setting up the " drip " may completely jeopardize the chances of survival. In our early cases, spasm of the saphenous vein, by delaying adequate early replacement, had a similar effect. The use of capillary blood for the haematocrit and haemoglobin readings has been of value in this series, and charts are given of two cases in which it was used to control the dosage of intravenous fluid (Charts Nos. 23 and 24).

Charts of six patients are reproduced (pp. 92–102); two of the cases charted were fatal in the shock period and four recovered either permanently or temporarily.

Summary of Group 5

There are two outstanding points in regard to plasma therapy in this group. The first is that transfusions must be started as soon as possible : the harmful effects of even a short delay have been shown. Secondly, adequate control over the dosage is essential. Great care must be exercised in assessing dosage. Severely burned children are particularly sensitive to either insufficient or excessive intravenous fluid replacement.

The amounts of fluid which may be termed " adequate " vary considerably, and a volume in excess of the patient's plasma volume is usually necessary.

Group 6 : Adults—severe burns (age over 12 years : extent of burn 30 per cent. and over).

There are 11 patients in this group (Table XIII). With one exception, the first six who were treated died. Profiting by experience, however, we were able to carry out adequate replacement therapy in the last 5 cases, with successful results. The burns were almost all deep and coagulated, due to clothes catching fire, but with transfusion it was possible to control shock in these extensive cases.

TABLE XII

No.	Name	Age	Area (per cent. of body surface)	Site	Amount of intravenous fluid given (c.c.)	When started (Hrs. after burning)	When finished (Hrs. after burning)	Remarks
40	McF.	2	20	Face, arms, back, P.S.L. and W.S.L.	800	3¾	12	Transfusion thought to have been inadequate. Died.
41	McG.	4	28	Arms, buttocks, thigh, W.S.L. and P.S.L.	2,650	3	20	Transfusion inadequately controlled. Died.
42	B.B.	2 2/12	29	Chest, back, arms, neck and face, P.S.L. and W.S.L.	1,500	6¼	11+	Transfusion probably begun too late. Died.
43	M.S.	6	35	Abdomen, thighs, arms, W.S.L.	2,250	3	24	Transfusion probably inadequate in early stages. (Chart 18) Died.
44	N.W.	2	40	Face, chest, arms, legs, W.S.L. and P.S.L.	1,900	1½	24+	Transfusion probably inadequate in early stages. Died.
45	J.M.	6	75–80	Trunk, arms, legs, W.S.L.	1,500	2	3	Excessive amounts given too rapidly. Pulmonary oedema occurred, with death at 11 hours.
46	McD.	10	80	Trunk, arms, legs, W.S.L.	6,600	1½	28	Adequate transfusion in first 24 hours. (Charts 19 and 20). Died on 4th day.
47	M.F.	2	22	Abdomen, thighs, arm, W.S.L.	1,000	4	12	Adequate transfusion. Recovered.
48	S.T.	7	40	Chest, abdomen, thighs, arm, W.S.L. and P.S.L.	3,600	3	22	Adequate transfusion (Chart 22). Recovered.
49	E.R.	9	40	Abdomen, thighs, arm, W.S.L.	2,200	4	13	Adequate transfusion, but stopped too early (Chart 21). Recovered temporarily. (Died on 31st day)
50	M.L.	3	44	Trunk, thighs, legs, arm, W.S.L. and P.S.L.	3,200	2½	32½	Adequate transfusion (Chart 23). Recovered.
51	P.G.	6½	45	Trunk, thighs, arms, W.S.L. and P.S.L.	3,400	1½	22½	Adequate transfusion (Chart 24). Recovered temporarily. (Died on 43rd day.)

The deaths in the shock phase were all associated with inadequate fluid replacement, while Case No.53 was further complicated by auricular fibrillation and congestive heart failure. The amounts given to Case No. 56 (totalling 7,600 c.c.) may appear adequate, but in the first 8 hours after burning only a little over 1 litre was given, due to spasm of the saphenous vein, and, during this period, a complete plenary dressing was carried out. The burns in this case were of the blister burn and partial skin loss type, due to boiling water, and were undoubtedly painful. Although the external jugular vein was cut

TABLE XIII

No.	Name	Age	Area (per cent. of body surface)	Site	Amount of intravenous fluid given (c.c.)	When started (Hrs. after burning)	When finished (Hrs. after burning)	Remarks
52	T.M.	14	31	Neck, trunk, arms, thighs, W.S.L. and P.S.L.	2,300	2	27	Transfusion probably inadequate (Chart 25). Died.
53	Mrs. Ba.	68	33	Trunk, thighs, arms, W.S.L. and P.S.L.	2,000	4	18	Inadequate transfusion + cardiac decompensation. Died.
54	W.N.	40	40	Chest, both arms, W.S.L. and P.S.L.	2,900	3	35	Transfusion probably inadequate (Chart 26). Died.
55	Mrs. C.	50	75	Trunk, arms, thighs, face, W.S.L. and P.S.L.	3,600	4	15½	Inadequate transfusion. Died.
56	T. McM.	51	75	Trunk, arms, legs, W.S.L. and P.S.L.	7,600	1	22 (Death)	Only inadequate amounts could be given in first 8 hours after burning. Died.
57	R.B.	44	47	Trunk, arms, thighs, W.S.L. and P.S.L.	3,600	1½	22	Adequate transfusion. Recovered temporarily. (Died on 37th day.)
58	J G.	25	40	Trunk, arms, thighs, W.S.L.	5,600	3½	20	Adequate transfusion (Chart 28). Recovered.
59	J M.	14	40	Trunk, buttocks, thighs, W.S.L.	2,200	20	32	Adequate transfusion. Case not seen until 20 hours. Recovered.
60	Mrs. R.	41	45–50	Trunk, arms, thighs, W.S.L.	7,200	2½	32	Adequate transfusion (Chart 30). Recovered temporarily. (Died on 64th day)
61	Mrs. A.	37	50	Trunk, arms, thighs, P.S.L. and W S L.	3,600	3	24	Adequate transfusion (Chart 27). Recovered temporarily. (Died on 16th day.)
62	W.W	14	50	Head, trunk, arms, legs, P S.L. and W S L	6,400	1	23	Adequate transfusion (Chart 29). Recovered

down upon after 8 hours, and 6 litres of fluid given rapidly, no improvement resulted, the patient became restless, delirious and later comatose, and died. We have now abandoned completely the practice of carrying out the plenary dressing in the early stages in such cases.

Case No. 59, that of a mentally defective girl, aged 14, is rather an anomaly in this series. She was first seen 20 hours after injury, no treatment having been carried out. There was no evidence of mental upset. The haematocrit reading was 58 per cent. and the blood pressure 85/55. 2,200 c.c. of plasma were apparently adequate at this late stage, and no further evidence of shock developed.

Charts and other details of 6 patients are reproduced (pp. 103–113). In the cases recorded in Charts Nos. 25 and 26, the fatal results were associated with inadequate transfusions, and they illustrate the unsuitability of either the saphenous vein or the sternal bone marrow as a route for rapid replacement therapy. The remaining 4 cases illustrate the enormous amounts of fluid which may be required in the first 24 hours to effect recovery from the shock phase.

Summary of Group 6

This group demonstrates more clearly than any other the value of adequate fluid replacement in burns shock. The following points emerged :—

(1) No attempt should be made to perform the plenary dressing in the first 24 hours. A first-aid dressing only should be applied rapidly, and plenary treatment be delayed until the second or third day.

(2) Plasma or serum therapy must be started at once and large amounts given rapidly. A delay of a few hours in the initial stages may prove fatal.

(3) As much as 7 or 8 litres of intravenous fluid may be necessary in the first 24 hours for a severely burned adult.

(4) The following approximate time schedule is suggested for an adult requiring such a large infusion (subject, of course, to guidance by blood examinations and to his general condition). First pint in 20 minutes ; second in 40 ; third in 60 ; fourth and subsequent pints in about 2 hours each.

Only the arm veins, the external jugular, or perhaps the femoral vein will permit of this. The importance of maintaining a satisfactory drip is obvious.

(5) Adequate fluid replacement probably prevented death from burns shock in 6 patients.

CLINICAL OBSERVATIONS ON BURNS SHOCK

Symptoms of burns shock in the majority of cases described above were much influenced by the administration of large amounts of fluid. In patients who received fluid only after evidence of shock was apparent, the symptoms observed were seldom those usually regarded as typical of surgical shock. In children, mental upset—characterised by drowsiness, restlessness, delirium and, rarely, convulsions—was the predominant feature. Haemoconcentration was a constant finding, and was associated with a fall in blood pressure and with a rapid pulse rate. In adults, mental upset was rare. In a patient with very extensive burns, given only morphine to relieve pain and restlessness, stupor gradually developed and, after a short period of coma, death occurred ; no rise of temperature above normal was noted. This early onset of stupor and coma

may have been due, at least in part, to the morphine. Two patients, who had little pain and received little morphine, remained alert and rational, with almost no general upset, until within half an hour of death.

Inadequate transfusion therapy in severe cases had little effect on general symptoms. A phase of initial well-being was followed after 6–18 hours by stupor, with occasional restlessness, and then by coma. In this group, a rising temperature was a common feature in the terminal stages, and in several cases skin temperatures of 106–108° F. were recorded. Vomiting was frequent and severe. Death followed in all patients in whom even mild haematemesis occurred.

Adequate transfusion therapy greatly influenced the general symptoms following severe burns. In patients so treated, even with burns up to 50 per cent. of the body surface, no mental upset was noted, and, with still more extensive burns, all those who received sufficient plasma to produce and maintain normal blood levels from an early stage survived the first three days after burning. Treated in this way, a girl of 10 years survived for four days a third degree burn involving 80 per cent. of the body surface. Adequate administration of plasma did not, however, influence the frequency and severity of vomiting, nor did it prevent oliguria in the shock period.

The term " toxaemia " has been applied by some authors to the general upset following burns. It was used by Wilson *et al.* (1938) to describe a syndrome of vomiting, mental upset, hyperpyrexia and circulatory failure which occurred chiefly in children and usually 12–15 hours after burning. The use of such a term implies knowledge of some aetiological factor, and some relation between the syndrome and central necrosis in the liver was suggested. Harkins (1942) also stressed the association of " toxaemia " and liver damage—with jaundice, oliguria, and demonstrable decrease in liver function—occurring 24–72 hours after burning. While certain of the symptoms described by these authors under the heading of " toxaemia " have been observed in our series of patients, the great majority have failed to appear even in the most severe cases given adequate transfusion. Jaundice has not occurred in any case, and the level of plasma bilirubin has not approached that at which clinical jaundice might be expected. In no case of a patient dying *during the shock period* has there been any post-mortem evidence of hepatic necrosis. The cases of Wilson *et al.*, and of Harkins, were treated with tannic acid, and it seems probable, in view of recent evidence (Wells, Humphrey & Coll, 1942 ; Erb, Morgan & Farmer, 1943) that some differences in the shock syndrome seen in the present series have been due to the fact that tannic acid was not used.

COMMENTARY ON RESULTS

Types of Fluid Used

Dried serum proved to be the most satisfactory form of fluid for replacement therapy. Plasma was almost as good, but caused a higher incidence of reactions. Ether extracted concentrated serum should not be used for rapid replacement, unless complete freedom from ether is guaranteed. We have no reason to believe that there is any advantage in giving concentrated plasma or serum. It did not appear to have any effect in withdrawing fluid from the oedematous tissues. Alterations in the osmotic pressure of the patient's plasma are perhaps relatively ineffective during the period of increased capillary permeability.

Type of Patient requiring Replacement Therapy

Not all patients with burns require fluid replacement, and the majority show little evidence of shock. On what grounds, therefore, are we to decide when plasma or serum transfusions should be given? With very extensive burns,

involving 25 per cent. or more of the body surface, the need is usually self-evident, and haemoconcentration can often be observed within an hour or so of burning. With burns of lesser degree, however, evidence of fluid loss may be absent in the early stages, although it may develop later. In such cases, we feel that it is wrong to wait until evidence of shock has developed. We have noted carefully, therefore, the progress of patients with burns of smaller extent, in an attempt to find a critical level at which it would be possible to divide cases of burns into two groups—those requiring replacement therapy and those for whom no anti-shock measures are required.

These levels have been taken at :—

In "adults" (*i.e.* patients over 12 years of age)—15 per cent. of the body surface.

In children up to 12 years of age—5–10 per cent. of the body surface, depending on the age.

Patients with burns of greater extent than these areas are therefore given transfusions as early as possible, whether evidence of shock is present or not. With borderline cases, and in patients with burns involving slightly less than these areas, careful note is taken of the blood pressure, pulse rate and haemoglobin reading or haematocrit, and the transfusions are started if any untoward signs develop.

No doubt, with such empirical levels, patients are sometimes transfused who would recover equally well without replacement therapy, but such criteria are helpful for clinical use, in view of the danger of waiting until shock has developed before beginning transfusions. In our view, they represent the minimum levels; patients with burns of lesser extent are unlikely to develop shock.

Assessment of Dosage

Since the introduction of plasma and serum transfusions for the treatment of burns shock, numerous attempts have been made to devise formulae for calculating the amounts required in any given case. Black (1940), Elkinton, Wolff & Lee (1940) and Harkins (1942) have produced formulae based on evidence of haemoconcentration. Such formulae carry the tacit assumptions (*a*) that the patients' blood levels were normal before burning, (*b*) that the calculated amount of the fluid transfused will be retained in the circulation, and (*c*) that a single estimation of haemoglobin or packed cell volume gives a useful indication of the ultimate requirements of the case. None of these assumptions is justifiable. In an anaemic patient, blood estimations may give no indication whatever of haemoconcentration (see Case 61, Chart No. 27). The fact that amounts of plasma or serum exceeding 7 litres have been required in 24 hours (Case 60, Chart No. 30) indicates that the fluid transfused leaves the vessels in the same way as does the patient's own plasma. As long, therefore, as fluid loss continues, fluid must be replaced, and repeated blood observations are necessary to control the dosage accurately. In cases of extensive burns (Group 6), it has been shown that for fluid replacement to be effective, the development of haemoconcentration must be anticipated and prevented. With adequate treatment, there should be no evidence at any time of haemoconcentration to which the formulae cited may be applied.

A more rational method is the First Aid Method of Harkins (1942), in which the amount of intravenous serum or plasma required is assessed on the basis of surface area (50 c.c. for every 1 per cent. of the body surface burned, or 1 pint of plasma for every 10 per cent.). We consider these amounts to be too small. The following table, compiled from Groups 4 and 6, in which

adequate amounts of fluid were given, compares the actual amounts required with those calculated from Harkins's formula :—

Group 4

Case No.	*Fluid Requirement. Estimated (Formula of Harkins).*	*Actual.*
34	1,000 c.c.	3,600 c.c.
35	1,000 c.c.	4,400 c.c.
36	1,100 c.c.	2,200 c.c.
37	1,100 c.c.	3,200 c.c.
38	1,100 c.c.	4,420 c.c.
39	1,300 c.c.	3,540 c.c.

Group 6

Case No.	*Fluid Requirement. Estimated (Formula of Harkins).*	*Actual.*
57	1,750 c.c.	3,500 c.c.
58	2,000 c.c.	5,700 c.c.
60	2,500 c.c.	7,200 c.c.
61	2,500 c.c.	3,400 c.c.
62	2,500 c.c.	6,400 c.c.

While the area of the burn gives a rough indication of the amount of fluid required, the age of the patient is also of great importance. The depth and site of the burn may also be factors. Deep burns require relatively more fluid than superficial, and burns about the thighs and buttocks more than burns elsewhere. With so many variables involved, it seems unjustifiable to base the dosage on any mathematical formula. Dosage can be assessed only while the transfusion is being given, the rate being adjusted to produce and maintain a normal blood level. The following points must be stressed :—

(1) Transfusion should be begun as early as possible, and given sufficiently rapidly to restore the blood volume to its presumed original level. In hospital practice, the initial blood examination should, when possible, be more than a simple haemoglobin estimation (or P.C.V.). Estimation of M.C.V. and M.C.H.C. will reveal the majority of cases in which some allowance should be made for a previously low blood level (see Brown, *infra*, pp. 114 *et seq.*).

(2) The rate of transfusion throughout the shock period must be controlled by repeated blood estimations. If venous blood cannot be obtained, capillary blood should be used: it is sufficiently accurate for therapeutic purposes.

(3) In the absence of blood readings, the blood pressure and pulse rate may be used as criteria, but are much less reliable.

(4) Plasma or serum can be given too rapidly or in too great an amount, particularly in children. A fatal pulmonary oedema, with frothing at the mouth, occurred in two such patients, and was almost certainly due to the transfusion: good judgment and constant observation (with frequent blood examinations) are required to strike the happy mean between inadequate and too energetic fluid replacement. The special danger of inducing pulmonary oedema by transfusion in patients who have inhaled hot gases or irritant vapours must also be borne in mind.

(5) Transfusions should be continued for at least 24 hours after burning in severe cases. On no account should they be stopped before this period because of a normal blood reading. In the majority of cases fluid loss is still occurring and considerable haemoconcentration may develop.

(6) It is often an advantage to continue with glucose-saline infusions after the 24-hour period. If fluid loss is still occurring, plasma or serum is easily substituted.

Management of the Transfusions

We believe that the life of the extensively burned patient depends to a large extent on the proper care and maintenance of the transfusion in the early stages. Fumbling with a badly set up " drip " in the first few hours after burning may waste valuable time and jeopardize the patient's chance of survival. It seems worth while, therefore, to stress the following points which we have learned from experience :—

(1) Unless there is no alternative, avoid cutting down on an arm vein through a burned area. The oedema which develops from the burn is sufficient partially to occlude the vein, and greatly diminishes the rate at which fluid can be infused.

(2) The usefulness of the external jugular vein for transfusion therapy must be stressed. Even when the neck is burned, the tissues there are so lax that the resulting oedema does not occlude the vein.

(3) Always cut down upon the vein, and tie in a cannula. The simple insertion of a needle is not satisfactory for transfusions which must last for 24 hours in patients inclined to restlessness: the usual result is that the point of the needle pierces the deep wall of the vein and the fluid leaks into the tissues. It is also wise to stitch the cannula to the skin, rather than to fix it with adhesive tape. The stitching causes little pain and anchors the cannula securely.

(4) Don't waste time tinkering with a drip that won't run. Abandon it and cut down elsewhere.

(5) The transfusion, and the patient, must be under the constant supervision of a competent nurse, who is responsible for seeing that the flask is never completely empty, and must call the medical attendant immediately if any stoppage occurs.

The Value of Replacement Therapy

An absolute proof of the value of plasma replacement therapy in burns shock is lacking, because of the absence of a suitable control series. A frequent criticism, and one which it is difficult to refute, is the statement that the patients would have recovered equally well without serum or plasma transfusions. This criticism is particularly applicable to cases in the " mild " and " medium " sub-groups, and is no doubt justifiable in some. In all the groups, however, we have had examples of the development of burns shock when replacement therapy had either been delayed or had been inadequate, and some of the more instructive of these cases are detailed. It should be emphasized, too, that plasma or serum replacement therapy does not aim simply at preventing death. It should be used with the broader purpose of preventing shock, of relieving capillary stasis and promoting local capillary recovery.

The evidence for the value of plasma or serum in the " severe " groups is much stronger. The almost complete absence of shock manifestations in patients with burns of 40–50 per cent. of the body surface, in whom replacement was adequate, is an eloquent tribute to the therapeutic usefulness of this treatment of burns.

There were 17 deaths during the shock period in the group of 62 patients here considered (fatality rate 27 per cent.), but this figure by itself means little, since naturally only the more severe cases were selected for transfusion. On the whole series of 350 burned patients admitted to hospital during the period of the investigation, the fatality rate was 9.7 per cent.

SUMMARY

1. Observations relating to the duration of fluid loss after burns have been described. They suggest that 24–30 hours is the usual period. This is further corroborated by observations on haemoconcentration. Replacement therapy, therefore, should be continued for at least 24 hours.

2. The results in a series of 62 patients treated with plasma or serum transfusions are detailed. These show that—

(*a*) Much larger amounts than hitherto recommended are often necessary.

(*b*) Dosage cannot satisfactorily be calculated by formulae, but should be assessed by repeated blood estimations while the transfusions are being given.

(*c*) Special attention should be directed to the control of replacement therapy in children.

(*d*) Adults with burns of over 15 per cent. of the body surface, and children with burns of over 5–10 per cent., require transfusions in amounts sufficient to replace the fluid lost and to prevent haemoconcentration.

(*e*) In most cases, local treatment during the shock period should consist only of a first-aid dressing. Complete cleansing and dressing should be postponed until the second or third day.

(*f*) Almost complete control of burns shock may be obtained by adequate replacement therapy, begun as soon as possible after burning.

ACKNOWLEDGMENTS

It is with pleasure that we acknowledge our indebtedness to Mr. A. M. Clark, Surgeon-in-Charge of the Burns Unit, Royal Infirmary, Glasgow, for permission to carry out this work; to Dr. Leonard Colebrook for his enthusiasm and co-operation; to Professor J. P. Todd, of the Royal Technical College, Glasgow, and Dr. Janet Vaughan, of the N.W. London Blood Supply Depot, who have kindly sent us supplies of plasma and serum, and given much helpful advice; to Professor J. W. S. Blacklock, Pathology Department, Royal Infirmary, Glasgow, for his co-operation and help with post-mortem studies; to Dr. A. B. Anderson, Biochemical Department, Royal Infirmary, Glasgow, for his assistance with the biochemical aspect of the problem; to Sister Donald and a succession of nurses, who by their care and attention have made adequate replacement therapy possible; and to our resident House Surgeons, Drs. M. L. Thomson, A. Foster and M. Whittet, without whose help and co-operation much of this work could not have been done.

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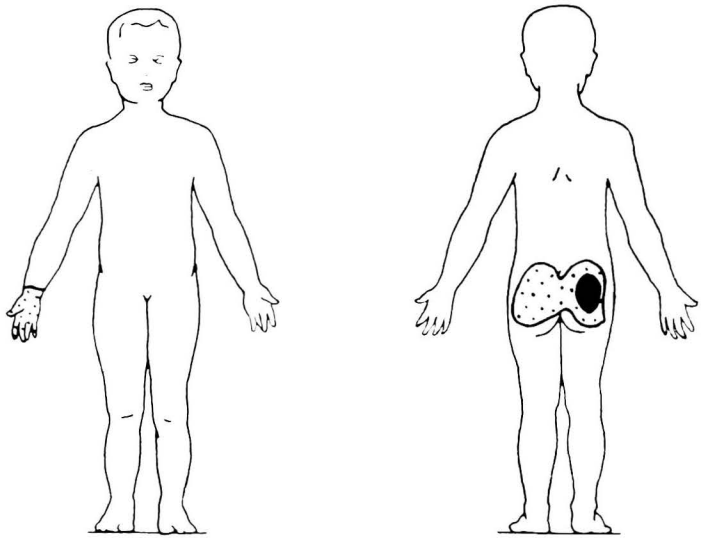
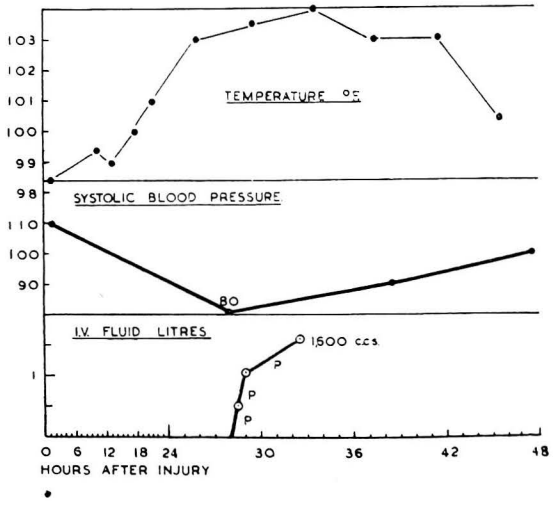
CHART NO. 1

Case No. 1.—Female, aged 4½ yrs. Extent of burning—8 per cent.





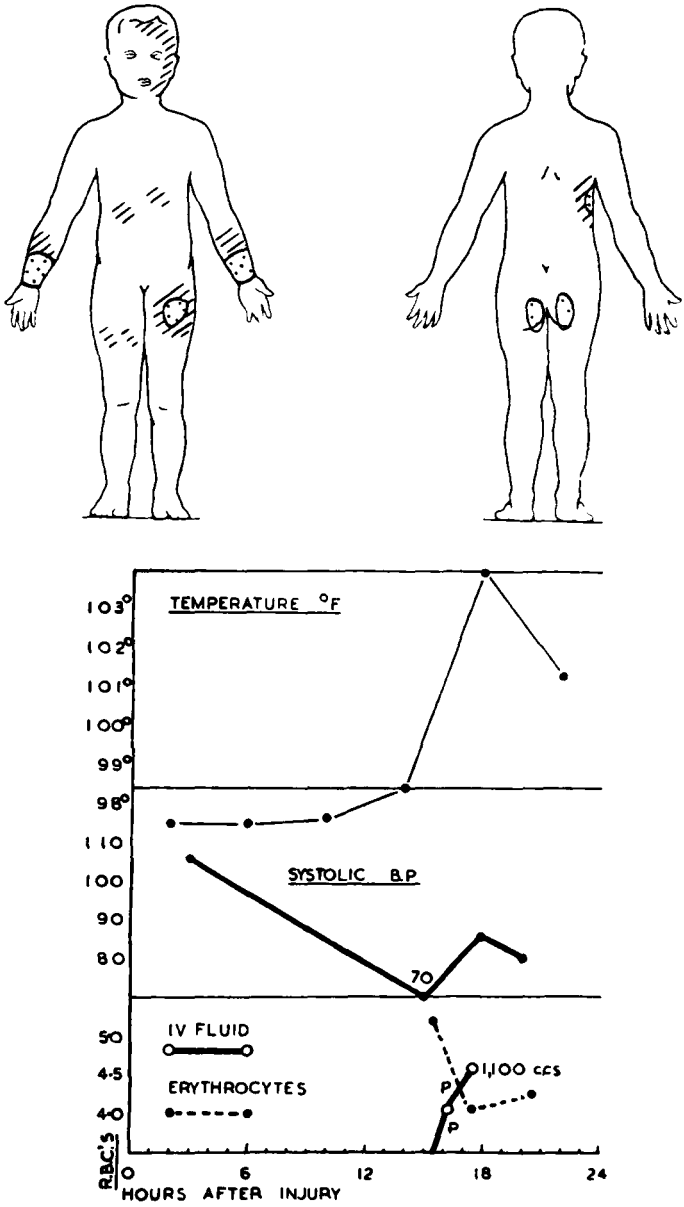
Case No. 1

No shock present on admission, and full dressing carried out. At 28 hours the child appeared *in extremis* and was almost unconscious. Pulse impalpable, respirations rapid. There was an immediate improvement after the first pint of plasma had been given; she became conscious and rational. The improvement was maintained and complete recovery ensued.

Note.—Considerable rise in temperature *before* plasma transfusion.

CHART No. 2

Case No. 2.—Female, aged 6 yrs. Extent of burning—7–8 per cent.



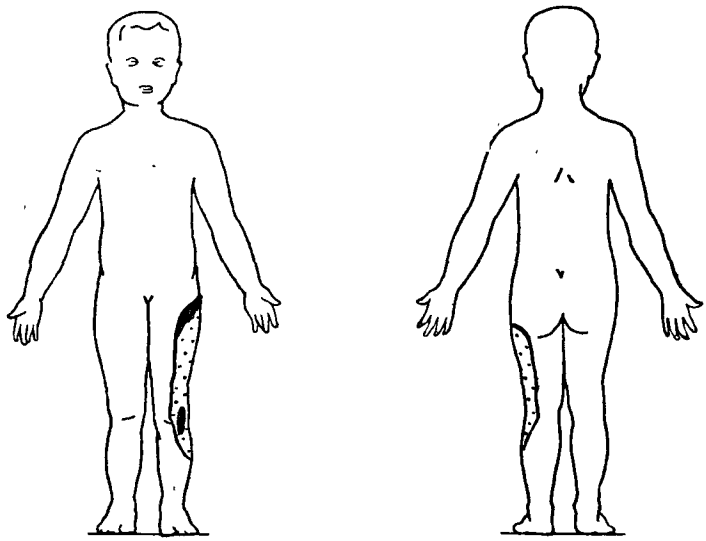
Case No. 2

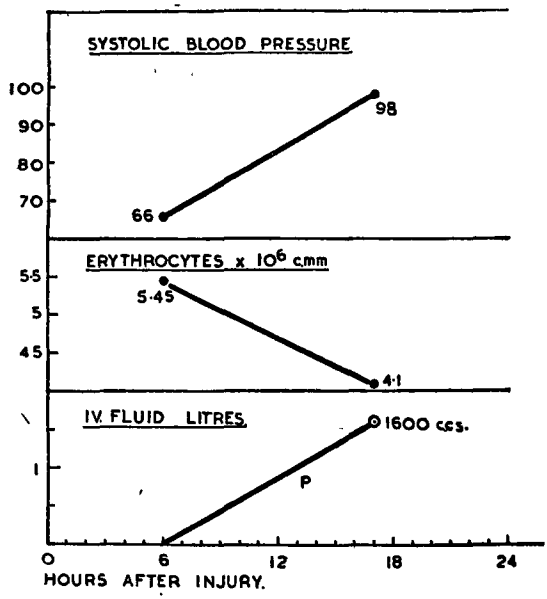
No evidence of shock on admission. 15 hours later—non-co-operative, irresponsive; and blood pressure low. Following transfusion of plasma, much improved clinically, " sitting up in bed asking for a drink ".

Note.—Rise of temperature coinciding with transfusion.

CHART No. 3

Case No. 3.—Female, aged 8 yrs. Extent of burning—5 per cent.



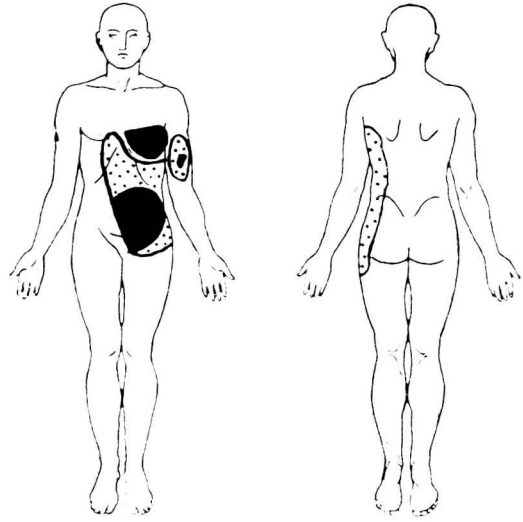


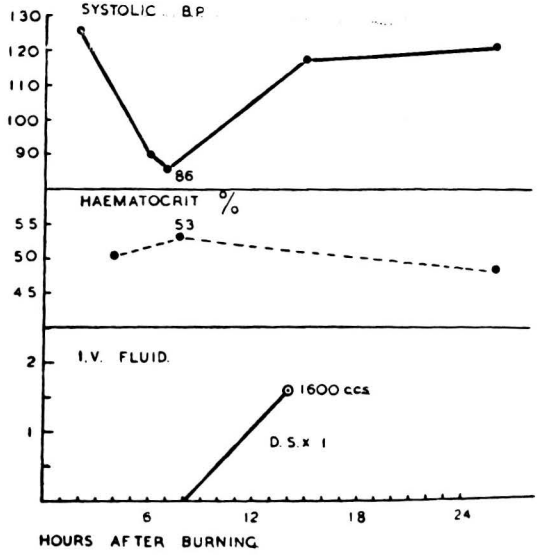
Case No. 3

When the child was first seen by the authors, six hours after injury, the plenary dressing had been performed and she was sleeping quietly; her colour was good, and her limbs were warm. Plasma therapy was started because of the low blood pressure and the slight degree of haemoconcentration. The beneficial results of this treatment are shown.

CHART No. 4

Case No. 8.—Female, aged 20 yrs. Extent of burning—16 per cent.



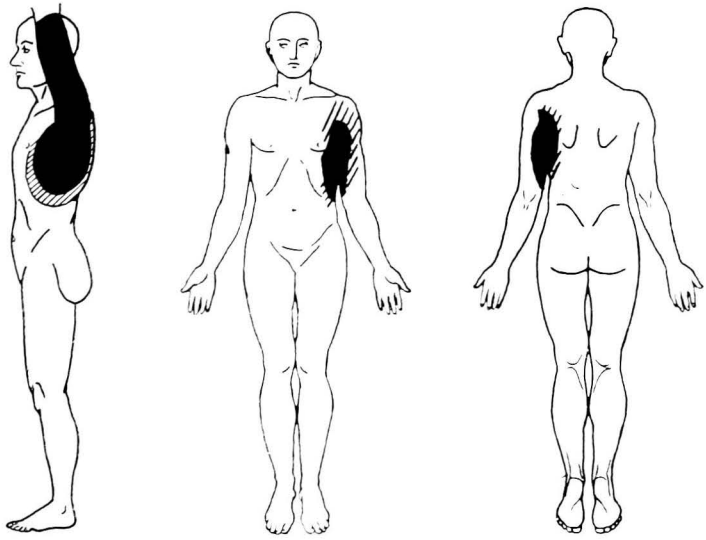


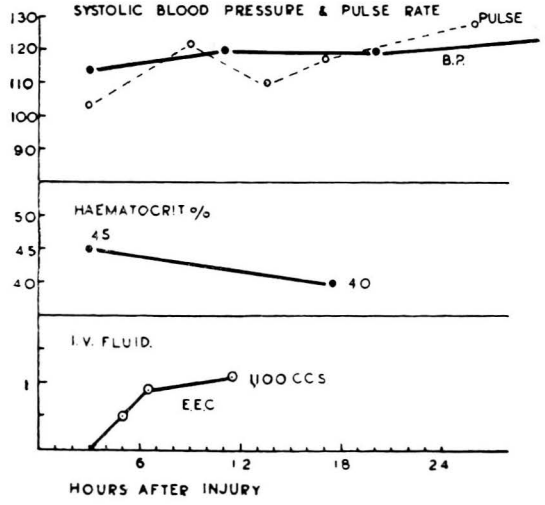
Case No. 8

Plenary dressing carried out on admission. This was followed by a considerable drop in blood pressure, and, in view of the increasing haemoconcentration, intravenous serum administration was begun.

CHART No. 5

Case No. 15.—Male, aged 37 yrs. Extent of burning—10 per cent.



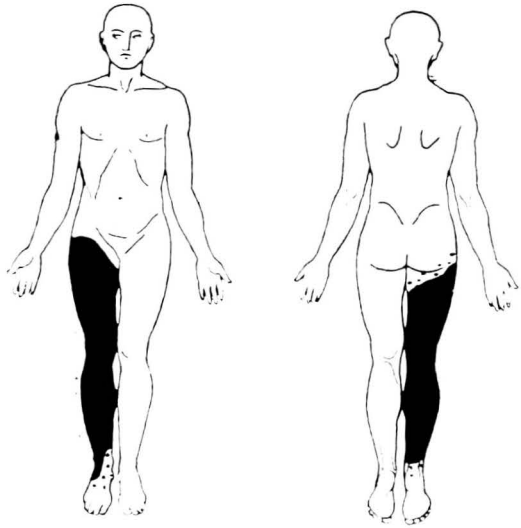


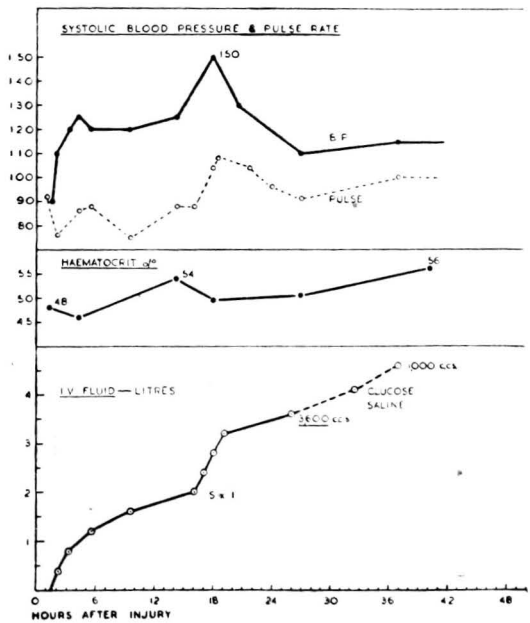
Case No. 15

Replacement therapy given prophylactically, because of the depth of the burn. The patient was slightly under the influence of alcohol on admission. The second dose (600 c.c.) of ether extracted concentrated serum (E.E.C.) was given by the sternal route ; it at first ran in rapidly, and then slowed down until the flow ceased. Symptoms of shock were absent throughout.

CHART No. 6

Case No. 19.—Male, aged 51 yrs. Extent of burning—19 per cent.





Case No. 19

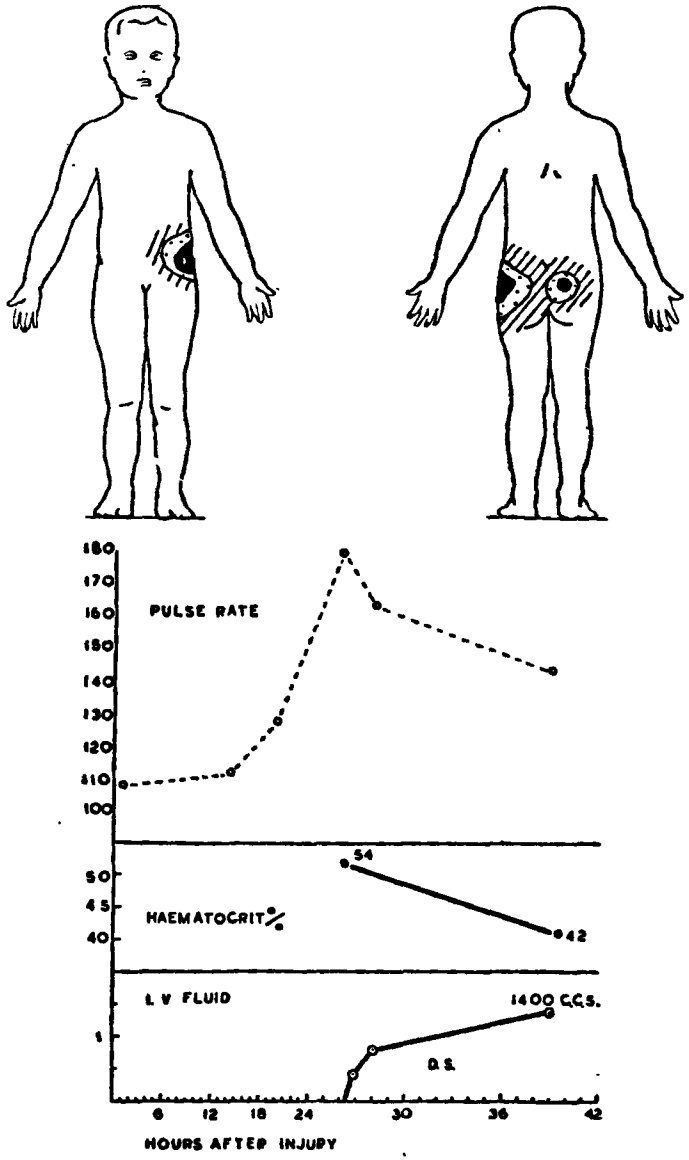
One of the few cases in which evidence of primary shock was present on admission—low blood pressure and patient cold, pale and shivering. The burns were dressed with No. 9 Cream (p. 10) and serum transfusions were begun at once (one hour after burning). Very large amounts of serum wer

Case No. 19—contd.

necessary to control the haemoconcentration, considering the extent of the burn. The relationship between the rate of transfusion, the degree of haemoconcentration and the blood pressure is well demonstrated. The haematocrit reading falls and the blood pressure rises on each occasion when the rate of transfusion is increased, and these rise and fall, respectively, when the rate is slowed. Haemoconcentration continued to occur in this patient after the transfusions of serum had been stopped at 26 hours, and haemoconcentration was not controlled by the further transfusion of one litre of glucose-saline, which was given because of repeated vomiting.

CHART No. 7

Case No. 25.—Female, aged 5 yrs. Extent of burning—12 per cent.

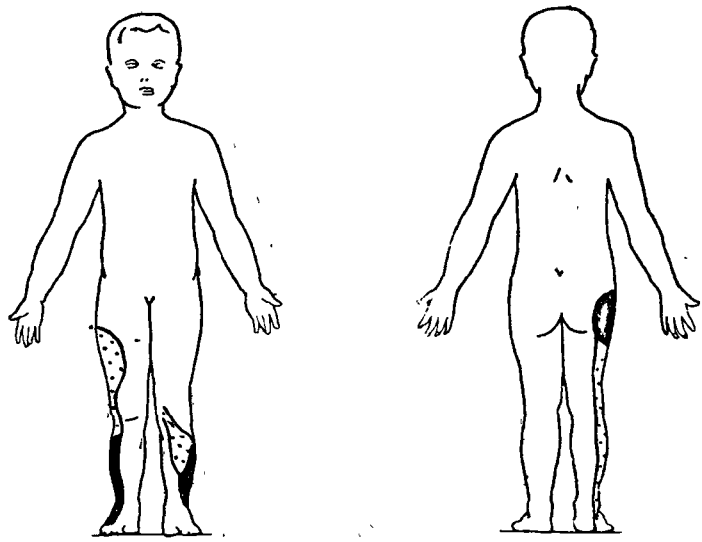


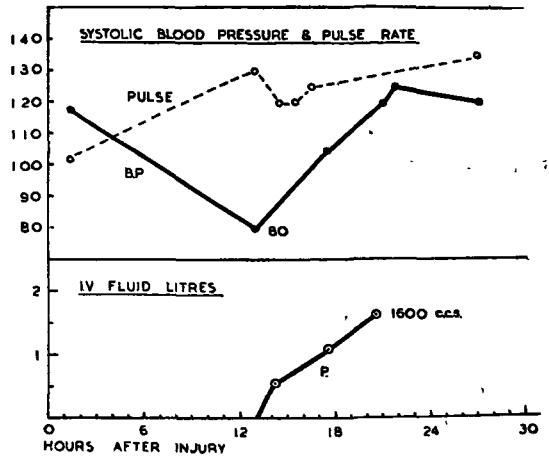
Case No. 25

Development of shock before plasma therapy was begun. Plenary dressing carried out on admission. The first evidence of shock appeared about 20 hours after burning, when there was some vomiting of bile-stained fluid. By 28 hours there had been repeated vomiting, the child was drowsy, semi-conscious and unresponsive. The pulse was very feeble and the blood pressure could not be recorded. The extremities were cold. The haematocrit reading was 54 per cent. 1,400 c.c. of fluid were given intravenously in the next 12 hours. Her general condition improved and she became rational. The pulse rate fell, and the haematocrit reading was reduced to 42 per cent.

CHART No. 8

Case No. 26.—Male, aged 4½ yrs. Extent of burning—12 per cent.



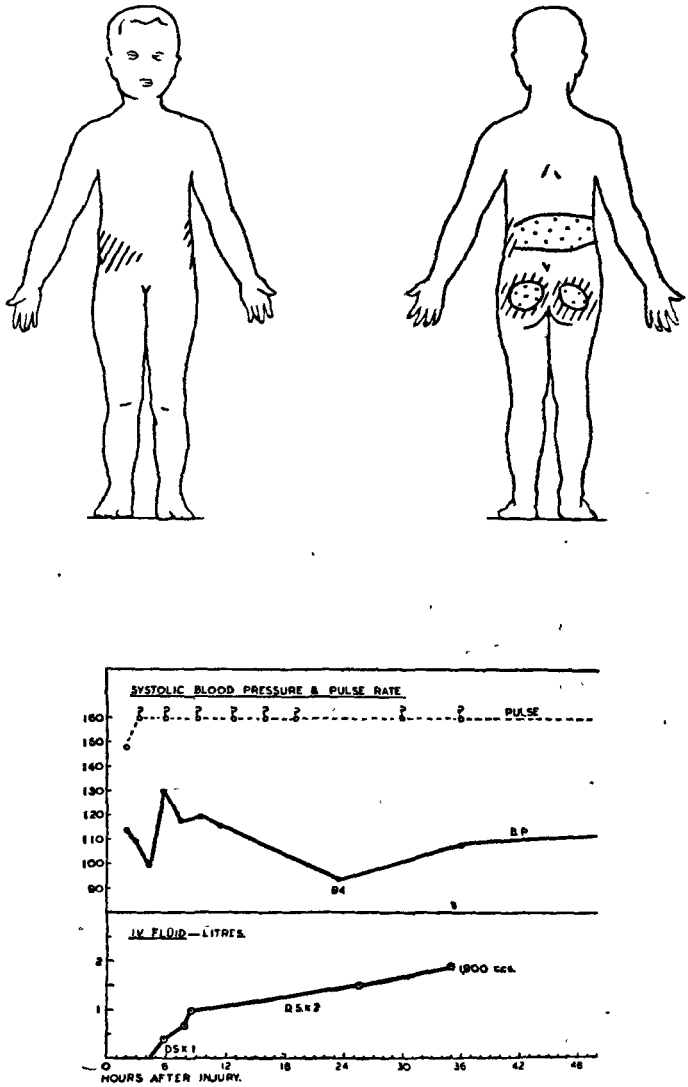


Case No. 26

Development of shock before replacement therapy. The plenary dressing was carried out on admission, at which time there was no evidence of shock. Twelve hours later, the child was extremely pale, with slight trace of cyanosis in the lips. The pulse was weak and irregular; the extremities were cold. Systolic blood pressure had fallen to 80 mm. Hg. 1,600 c.c. of fluid were given intravenously in the next eight hours. There was considerable improvement in colour; the pulse became stronger, and the blood pressure returned to a normal level. Convalescence was uneventful.

CHART No. 9

Case No. 23.—Female, aged 2 yrs. Extent of burning—15 per cent.

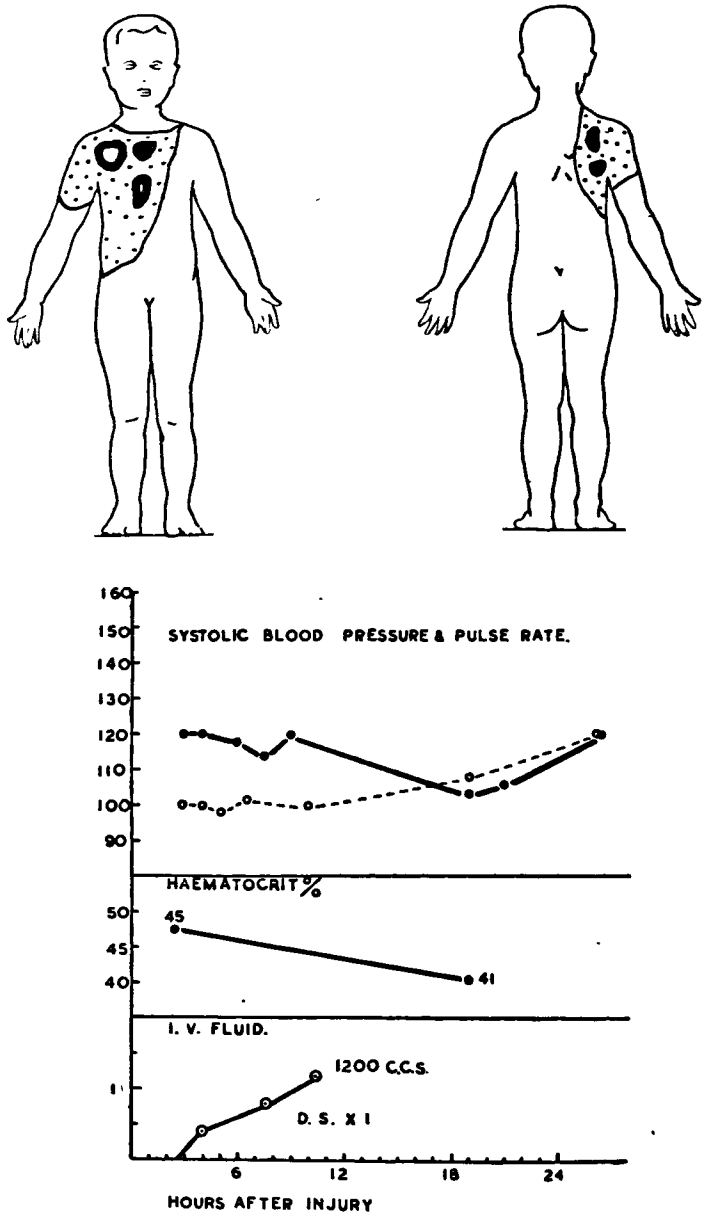


Case No. 23

Prophylactic administration of twice-concentrated dried serum. The pulse in this case was extremely rapid throughout. There were insufficient blood controls, however, of the haemoconcentration. The blood pressure was kept at a fairly normal level. The patient recovered.

CHART No. 10

Case No. 21.—Male, aged 6 yrs. Extent of burning—10 per cent.

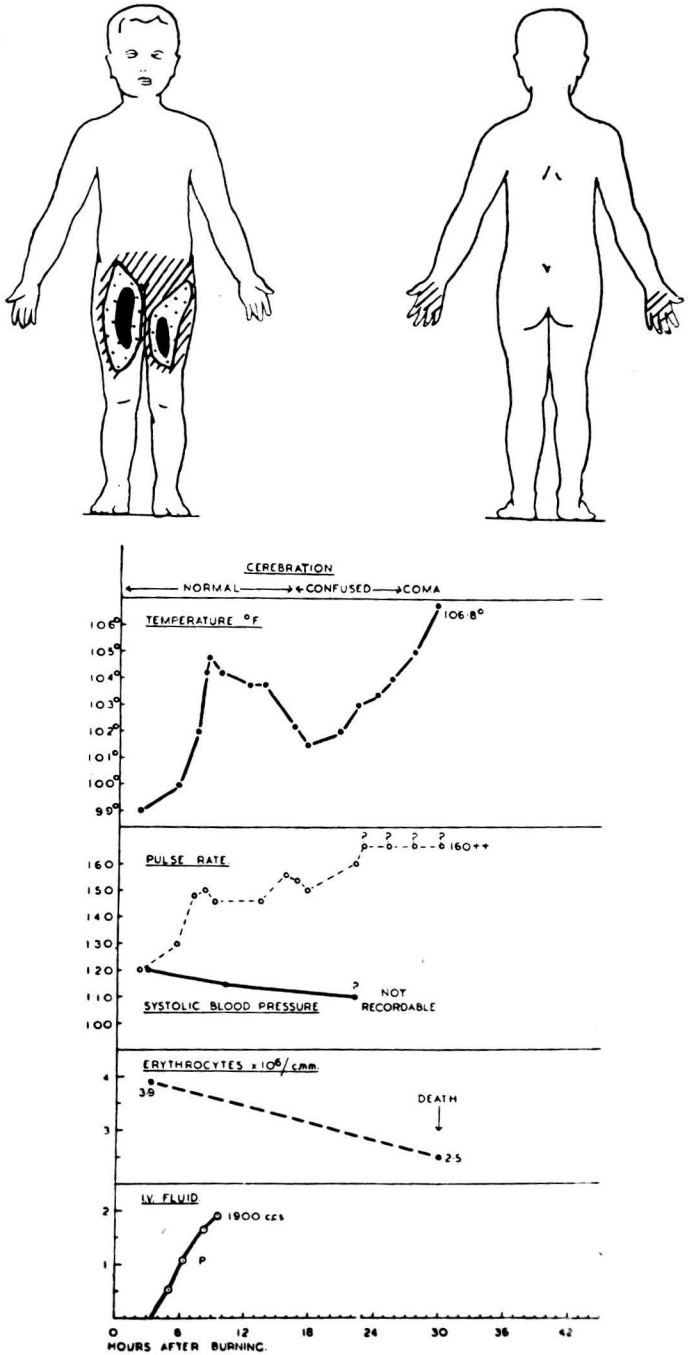


Case No. 21

Prophylactic administration of dried serum. The amounts were probably given rather too rapidly—note the slight fall in blood pressure after the transfusions were discontinued. Sufficient was given, however, to control the haemoconcentration.

CHART No. 11

Case No. 20.—Female, aged 6 yrs. Extent of burning—10 per cent.

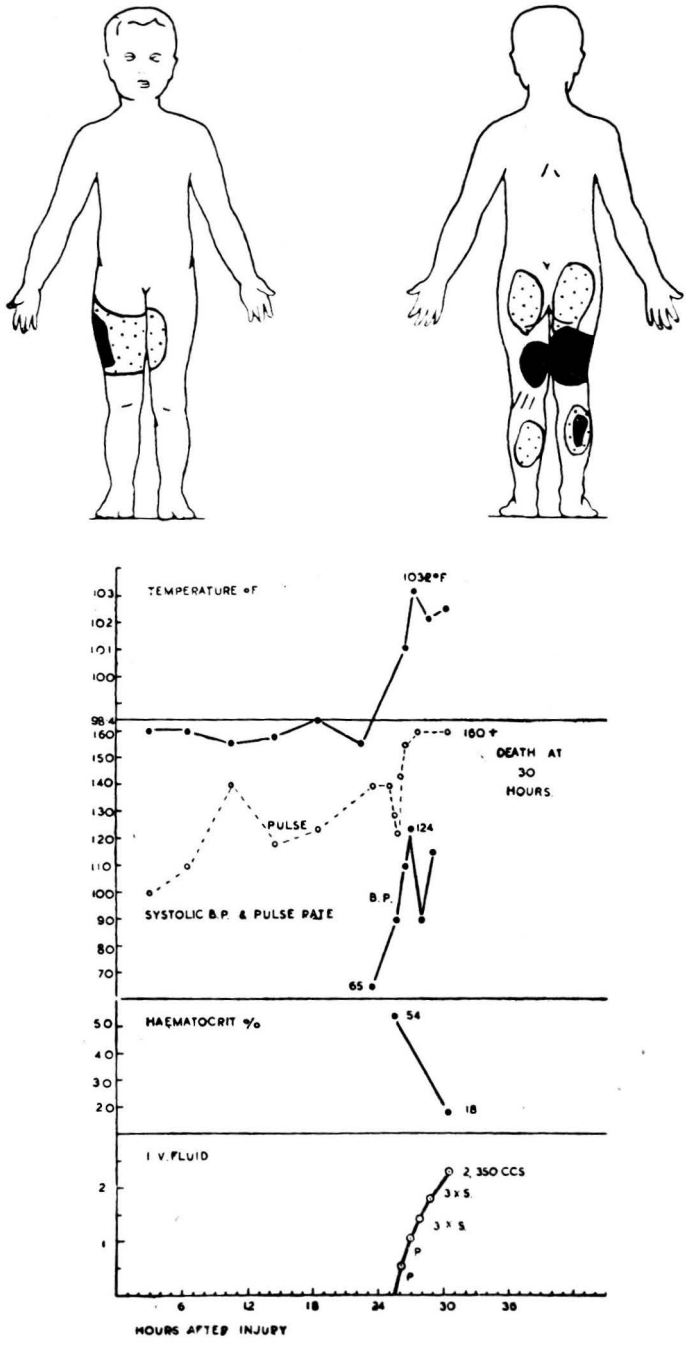


Case No. 20—contd.

Excessive administration of plasma. Plenary dressing carried out on admission. Almost two litres of fluid were given in the next six hours. There was no rigor, but the temperature rose abruptly to 104·8° F. The blood pressure fell, and the pulse rate rose. The child became mentally confused about 15 hours after burning, then delirious and restless. The respiratory rate was very rapid (50 per minute). The temperature, after a temporary fall, continued to increase until death. Heart blood removed post-mortem suggested excessive haemodilution, but there are considerable doubts as to the accuracy of this final estimation. Ante-mortem clot in the heart may upset red cell distribution.

CHART No. 12

Case No. 28.—Female, aged 8 yrs. Extent of burning—14 per cent.

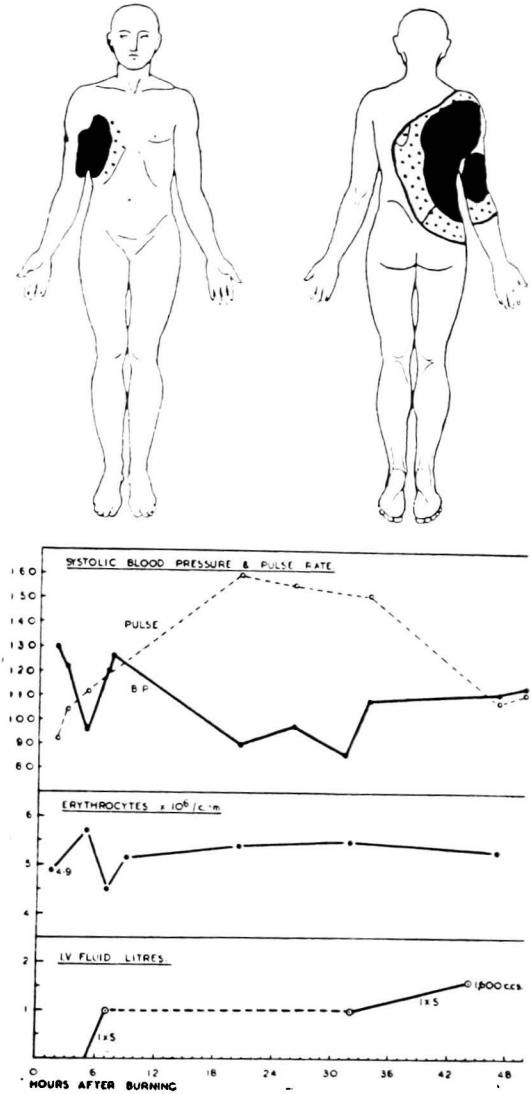


Case No. 28—contd.

Burn of rather similar extent to Case No. 20. It was decided, in view of the reaction to plasma in the latter case, not to administer it here, at least until shock had developed. The child remained well for almost 24 hours, when she was found to be collapsed, restless and disorientated. The blood pressure had fallen to 65 mm. Hg. One litre of plasma was given intravenously, and this led to a considerable rise in blood pressure and a temporary fall in the pulse rate. The temperature rose, also, to 103° F. Since the chief post-mortem finding in similar cases had been cerebral oedema, she was given three-times-concentrated serum, in the hope that the oedema might be reduced and the symptoms of cerebral irritation relieved. No such effect occurred, however, and the child died 30 hours after burning. A blood sample removed at death showed that very gross haemodilution had occurred.

CHART No. 13

Case No. 31.—Female, aged 22 yrs. Extent of burning—22 per cent.



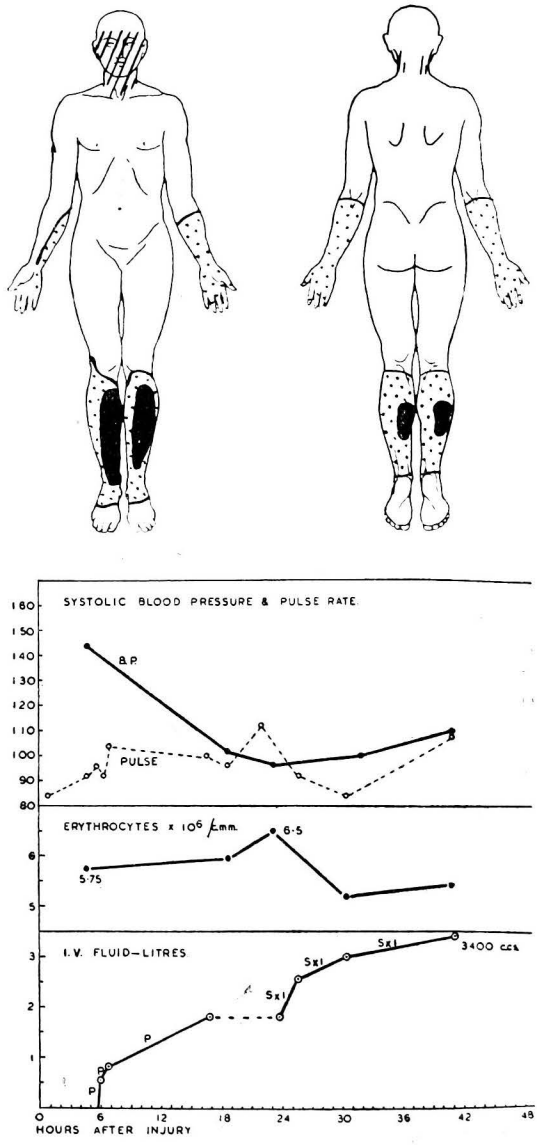
Case No. 31

Inadequate transfusion. Plenary dressing carried out between 2 and 3 hours after burning. This was followed by a considerable fall in blood pressure and a rise in pulse rate. One litre of dried serum was given between 5 and 7 hours, with temporary improvement in the blood pressure and haemoconcentration. Because of the normal blood findings, and the apparent well-being of the patient, it was (wrongly) decided to discontinue the transfusion. A steady fall in blood pressure and a rise in pulse rate followed this, and there was an increase in haemoconcentration. A further 600 c.c. of serum, given between 32 and 44 hours, caused considerable amelioration of these symptoms, and the patient recovered.

Note how very little haemoconcentration occurred between 20 and 30 hours showing that loss of fluid had more or less ceased by that time.

CHART No. 14

Case No. 32.—Male, aged 49 yrs. Extent of burning—26 per cent.

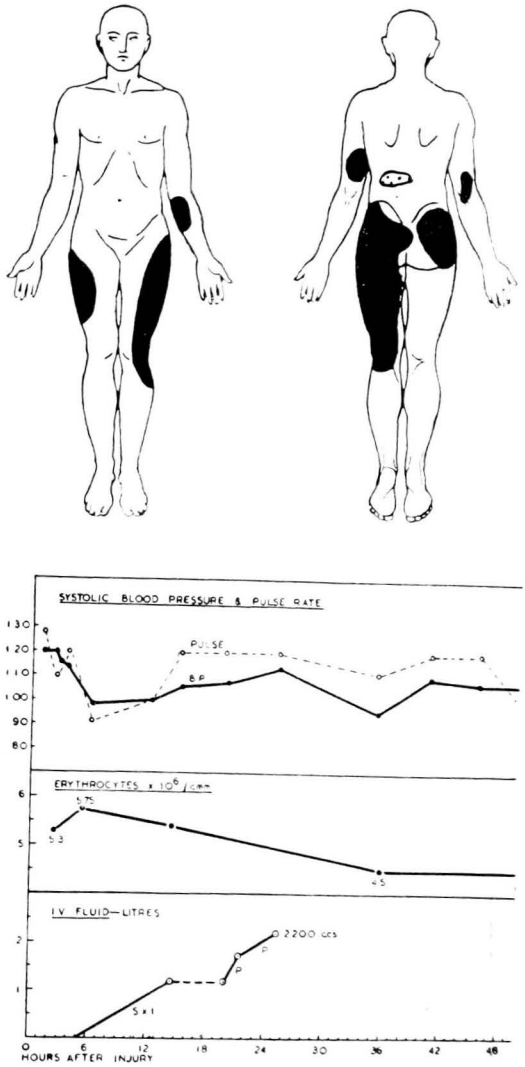


Case No. 32

Inadequate transfusion. Plenary dressing carried out between 2 and 4 hours. 1,800 c.c. of plasma were given until 17 hours; it was insufficient to control the haemoconcentration, and there was a considerable fall in blood pressure during this period. Further haemoconcentration occurred rapidly, and transfusion of dried serum was started at 24 hours. 1,600 c.c. were given, and this corrected the haemoconcentration and controlled the fall in blood pressure.

CHART No. 15

Case No. 30.—Female, aged 21 yrs. Extent of burning—20 per cent.

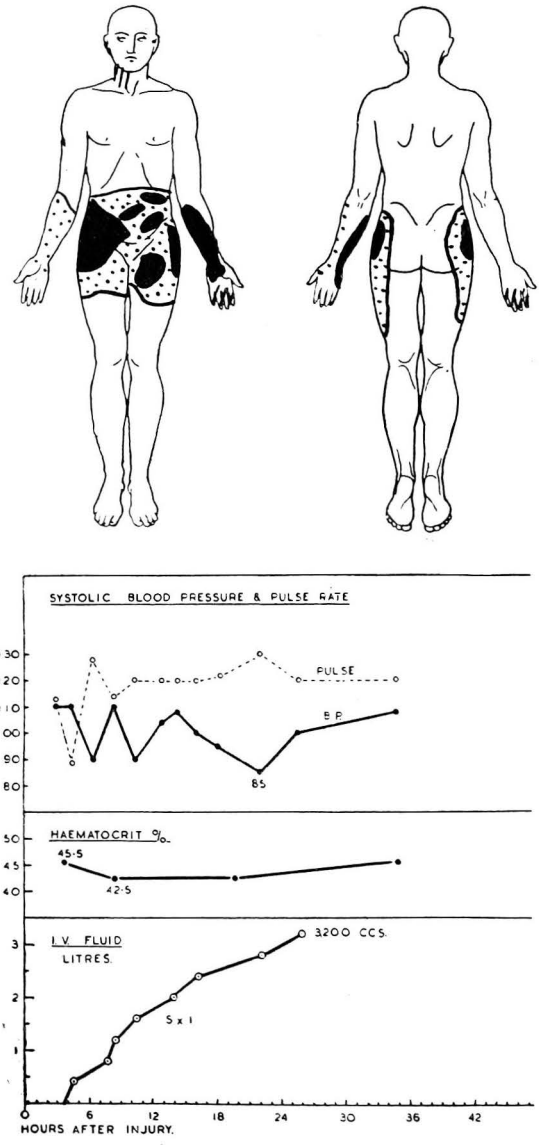


Case No. 30

Inadequate transfusion. Plenary dressing, carried out from 3 to 4½ hours after burning, was followed by a fall in blood pressure and an increase in haemoconcentration. 2,200 c.c. of serum and plasma were given between 5 and 25 hours, and were sufficient to control both the haemoconcentration and the blood pressure; the fluid should have been given more rapidly to start with, however, since little change was noted until about 14 hours after injury. The transfusion in this case was given via the saphenous vein at the ankle, and spasm prevented its being given more rapidly.

CHART No. 16

Case No. 37.—Female, aged 12 yrs. Extent of burning—22 per cent.



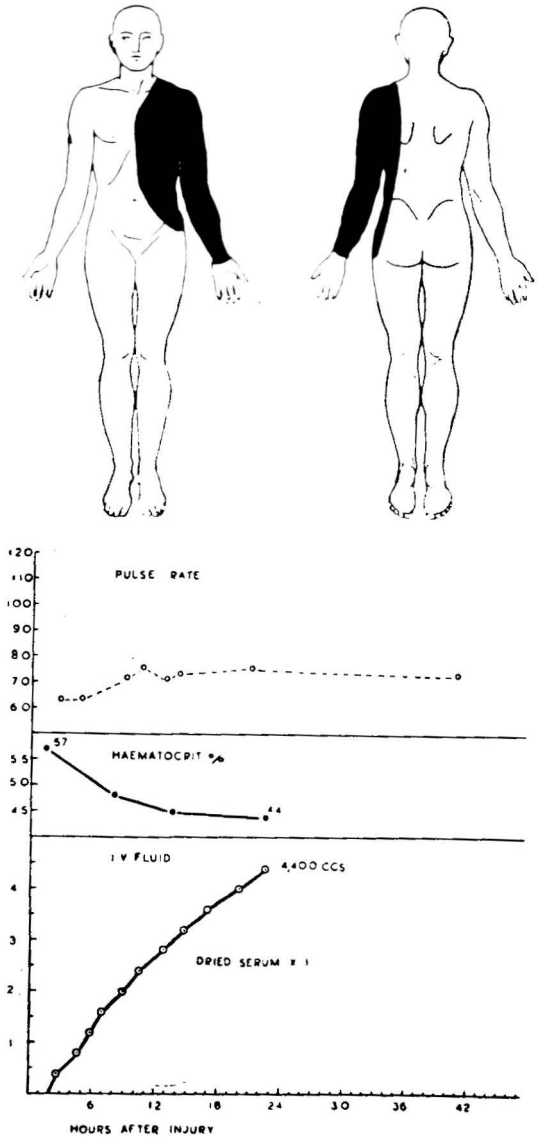
Case No. 37

Adequate transfusion. Burns simply covered with first-aid dressing on admission, and plenary dressing postponed till second day. The amount of fluid given was adequate in controlling the haemoconcentration, but considerable fluctuations occurred in the blood pressure.

Note the rise in blood pressure each time the rate of fluid administration was increased. The pulse rate remained fairly constant throughout at 120 per minute.

CHART No. 17

Case No. 35.—Male, aged 68 yrs. Extent of burning—20 per cent.

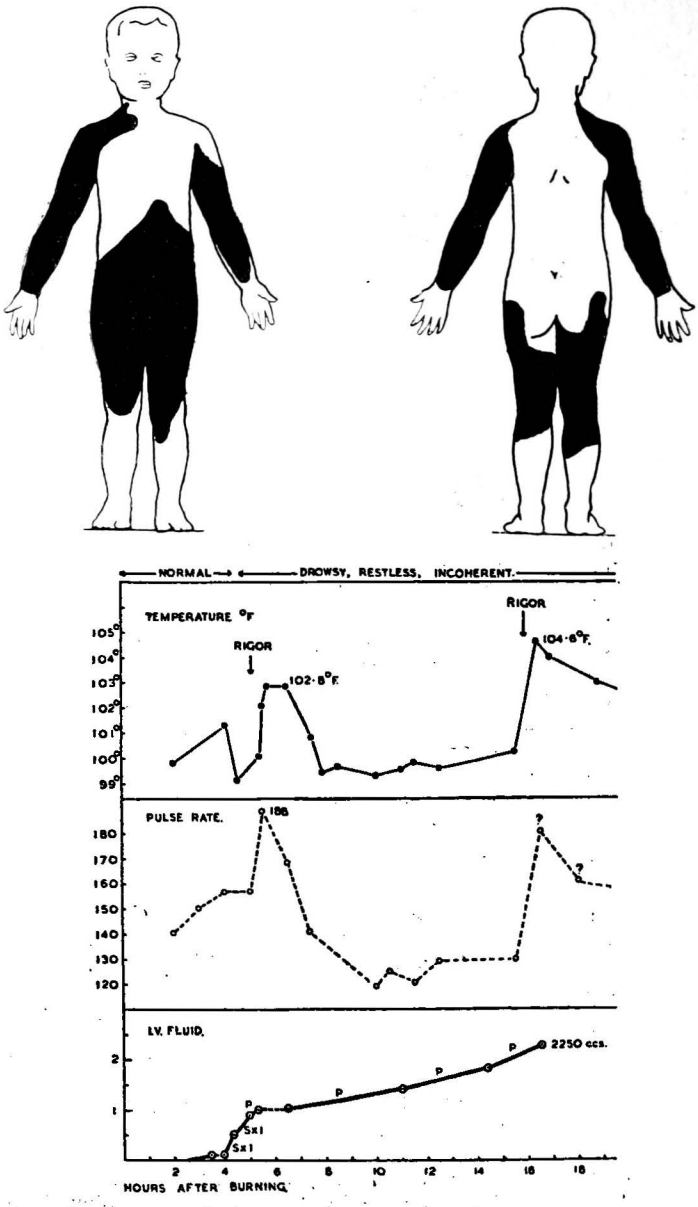


Case No. 35

Adequate transfusion. On admission, the burns were given a cursory cleansing with " Cetavlon " and covered with 3 per cent. sulphathiazole cream. This cleansing lasted only 10 minutes. 4,400 c.c. of serum were required for adequate control of the haemoconcentration, and the pulse rate remained steady throughout below 80 per minute. No blood pressure readings were available. Note the considerable increase in haemoconcentration which had developed within 1½ hours of burning. Slight increase in haemoconcentration occurred after transfusions had been stopped, showing that fluid loss had not quite ceased in this case by 24 hours after burning.

CHART No. 18

Case No. 43.—Female, aged 6 yrs. Extent of burning—35 per cent.



Case No 43

Fatal case. The transfusion was first attempted via the saphenous vein at the ankle, but would not run, because of spasm. Four hours after burning, therefore, the external jugular vein was cut down upon, and transfusion of serum started. Already by this time, however, the child was drowsy and wandering in her speech, and it is probable that the initial delay had been

Case No. 43—contd.

already too long for ultimate recovery. 400 c.c. of normal strength serum were followed by 400 c.c. of twice normal strength, in an attempt to reduce the probable cerebral oedema. These were followed by a bottle of plasma, but, after about 100 c.c. had run in, the child developed a severe rigor and the transfusion was stopped. When the rigor had ceased, transfusion with a fresh bottle of plasma was resumed very slowly. A further reaction, again accompanied by rigor, occurred with the third bottle of plasma, and the transfusion was stopped. Although there was some improvement in the pulse rate during the transfusion, the child's mental condition deteriorated, and death occurred at 31 hours, the temperature at that time being 107° F. Only the first 20 hours are recorded on the chart. The inadequacy of the replacement therapy here probably lay in the initial delay, but the transfusion reactions following injections of plasma may have contributed to the fatal outcome.

CHARTS Nos. 19 and 20

Case No. 46.—Female, aged 10 yrs. Extent of burning—80 per cent.

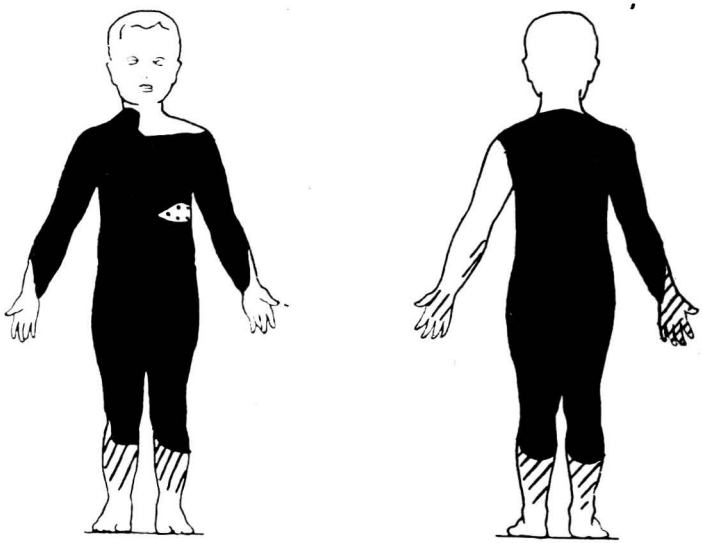
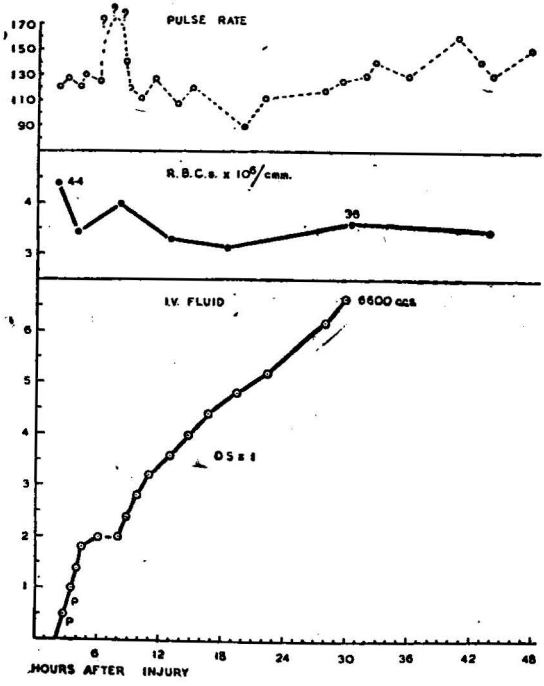


CHART No. 19



Case No. 46

Fatal case. The burns at first sight appeared hopeless, but a determined effort was made at replacement therapy, with initial success. Over 6½ litres were required to control the haemoconcentration, and the fluid was administered via the external jugular vein. Between 6 and 8 hours after

Case No. 46—contd.

burning, the cannula connection became loose and the fluid leaked into the bed. During this time the child's general condition deteriorated markedly. She became pale, apathetic and collapsed, and the pulse was impalpable, but, on recommencing the transfusion, these signs cleared up completely. Chart 19 shows the progress until death on the fourth day. The good general condition following the re-starting of transfusion—the child was speaking and behaving normally—was maintained until about 36 hours after burning, when she became confused, restless and apathetic. The pulse rate rose, and she became comatose on the fourth day, and died with a temperature of 108° F.

Total fluid intake diminished very rapidly after the first day, partly due to vomiting and partly due to the child's mental condition. No haemoconcentration occurred after the first 24 hours. The blood urea at death was 232 mgm. per 100 c.c.

CHART No. 20

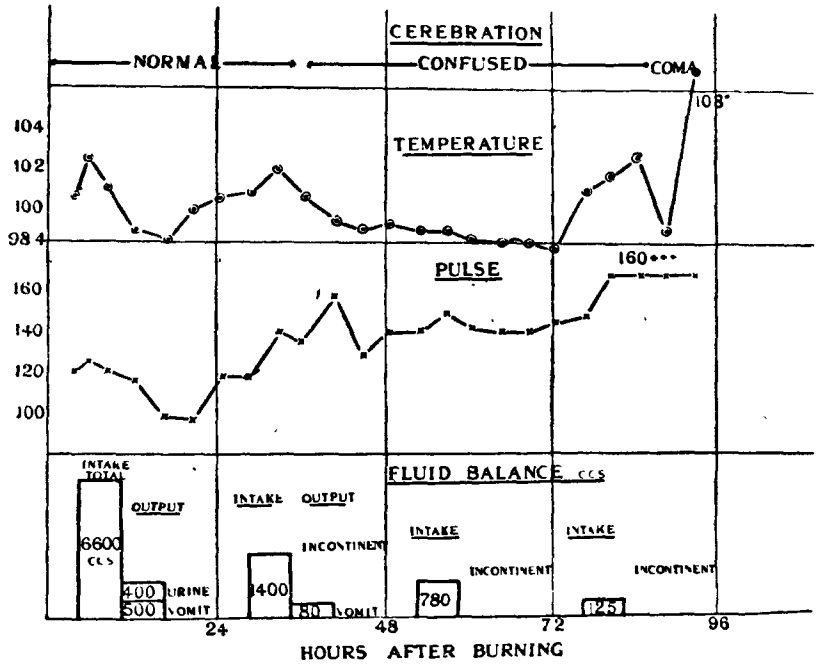
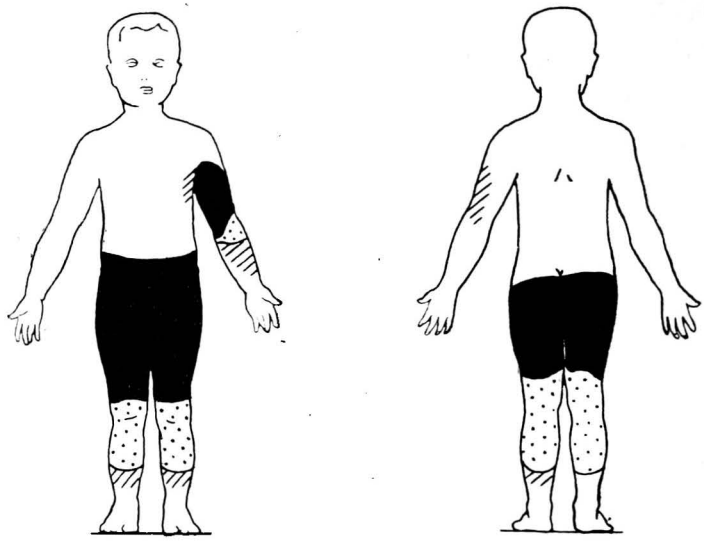
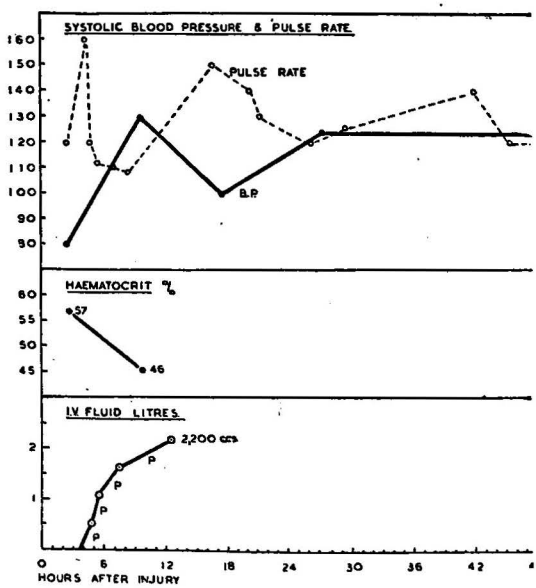


CHART No. 21

Case No. 49.—Female, aged 9 yrs. Extent of burning—40 per cent.





Case No. 49

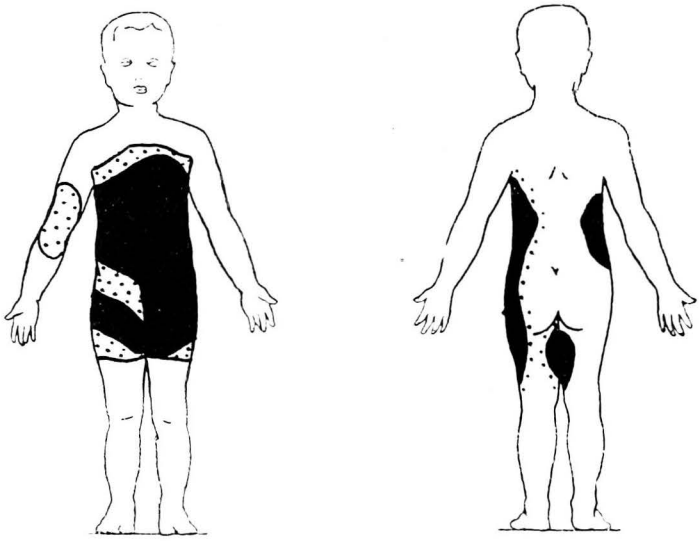
Fluid replacement almost adequate. Considerable haemoconcentration was present on admission at 2½ hours, but was rapidly corrected by the transfusion of 2,200 c.c. of plasma, given until 12½ hours. Because of the normal blood reading at that time, transfusions were stopped. This was followed by a fall in blood pressure and a rise in pulse rate up to 18 hours, but these changes

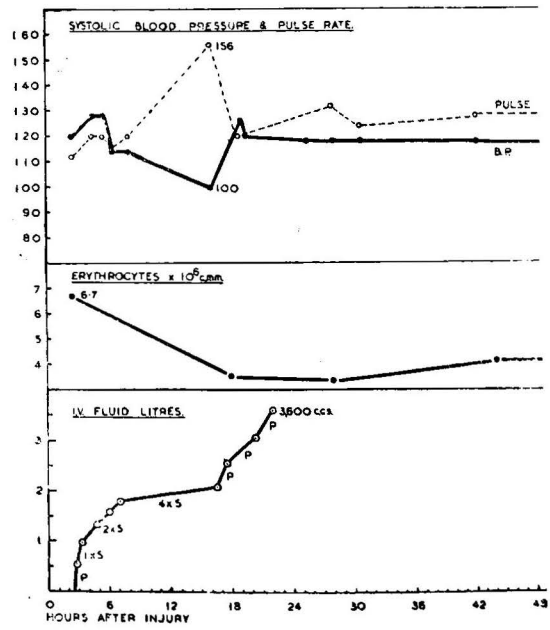
Case No. 49—contd.

were not sustained and the blood pressure and pulse rate had returned almost to normal by 28 hours. Transfusion in this case should have been continued for a further four or five hours. The return to normal of the pulse rate and blood pressure between 18 and 28 hours suggests that capillary loss had more or less ceased, and that re-absorption was taking place. There were unfortunately no further venous samples of blood available to corroborate this. The child showed no evidence of mental upset throughout the shock period.

CHART No. 22

Case No. 48.—Female, aged 7 yrs. Extent of burning—40 per cent.





Case No. 48

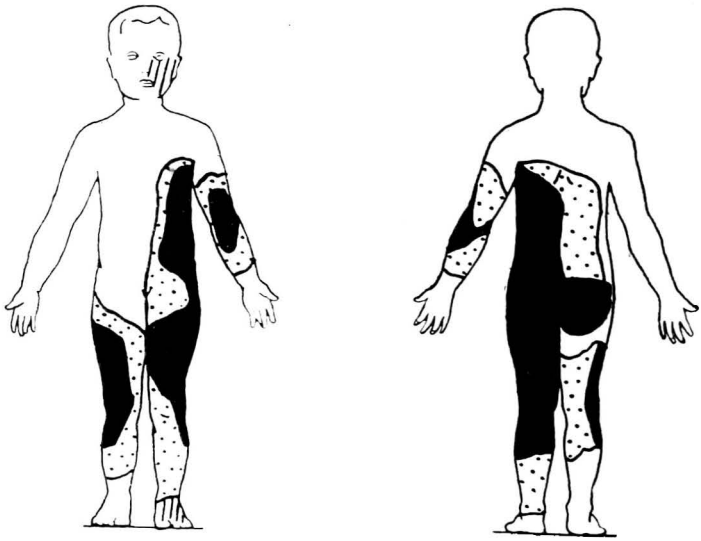
Fluid replacement almost adequate. Transfusion was started at 2½ hours, by giving one pint of plasma rapidly. It was then decided to use increasing concentrations of dried serum, to see if fluid would be withdrawn from the oedematous tissues. During the period when the four-times-concentrated

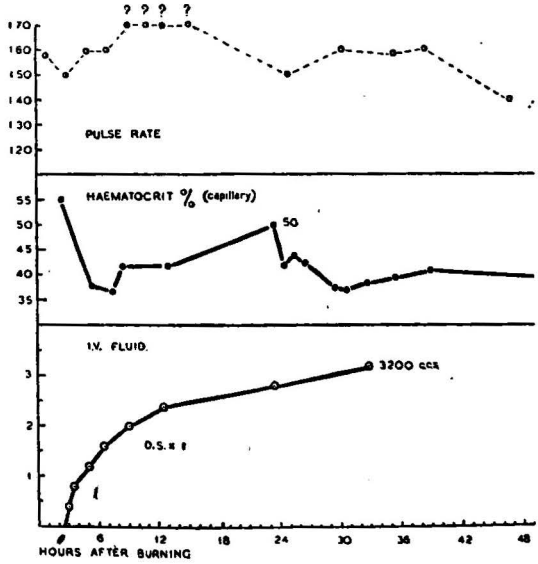
Case No. 48—contd.

serum was being given slowly, however, there was a fall in blood pressure and a rise in pulse rate, and it seemed evident that fluid required to be replaced as well as protein. More rapid transfusions of plasma were therefore resumed, and the blood pressure and pulse rate returned to normal levels and remained so. There was little evidence of mental upset throughout this period, but while the four-times-concentrated serum was being given slowly, the child became restless and appeared rather dazed. These symptoms cleared up soon after rapid transfusion of plasma had been resumed.

CHART No. 23

Case No. 50.—Male, aged 3 yrs. Extent of burning—44 per cent.



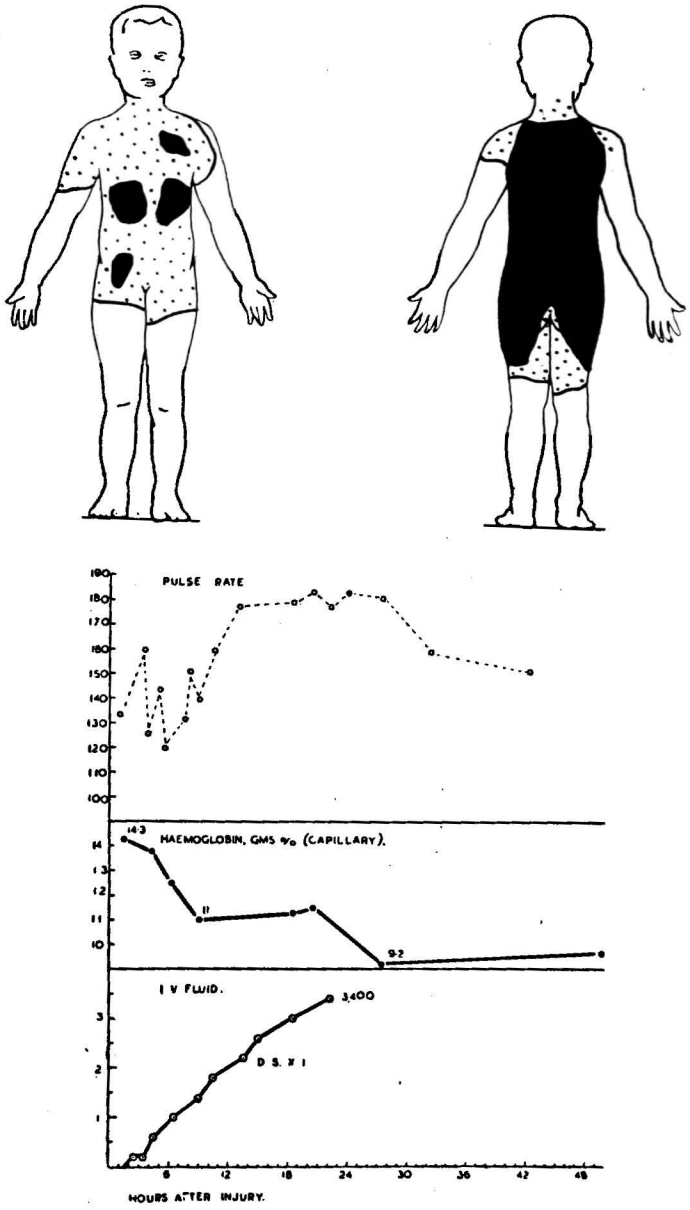


Case No. 50

Adequate replacement. Capillary blood was used for the estimations throughout in this case, and it afforded an excellent control of the dosage of fluid. 3,200 c.c. were required. Between 12 and 20 hours the child was restless and confused mentally, but these symptoms had cleared up completely by 24 hours. This mental change was also accompanied by increased haemo-concentration. He made a good recovery.

CHART No. 24

Case No. 51.—Male, aged 6½ yrs. Extent of burning—45 per cent.



Case No. 51

The child was extremely restless on admission, and difficulty was found in cannulating a vein. Shortly after the first transfusion had been set up, the child tore the cannula from the vein; a second attempt had then to be made,

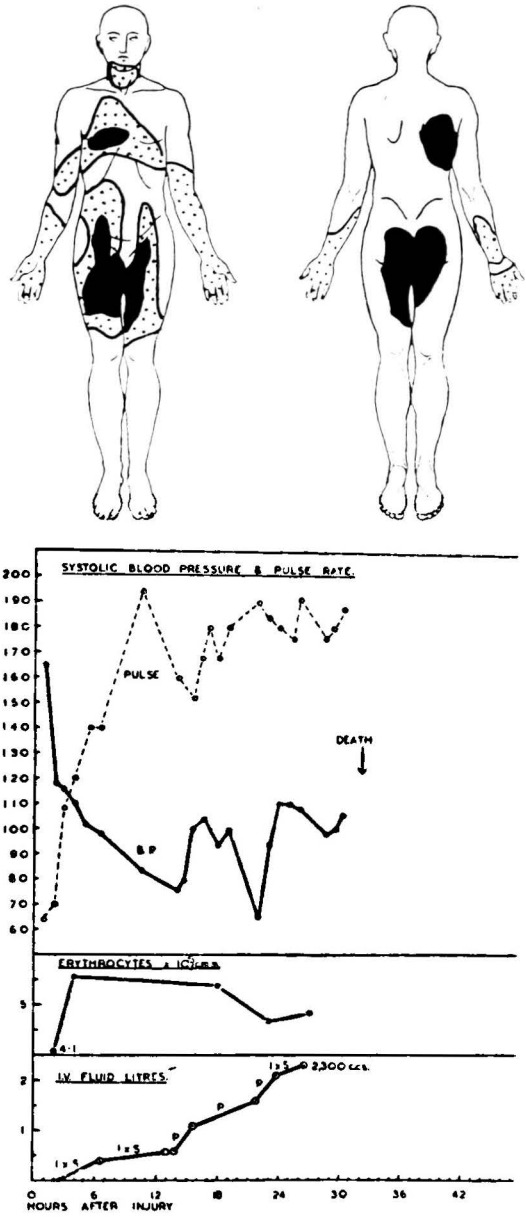
Case No. 51—contd.

and replacement therapy was not begun until four hours after injury. Already, by this time, he was drowsy but restless, not very coherent but responding to questions. Sufficient fluid was given to control the haemoconcentration within the first 24 hours, 3,400 c.c. of dried serum being required. The pulse rate became extremely rapid after about 14 hours, and remained so until almost 30 hours after burning. During this phase, he was drowsy and restless in turns, at times delirious, and quite unresponsive to questioning. Recovery was not expected but, during the second day, the child's mental condition improved somewhat, and by the third day he had become rational and less drowsy, though complaining of very severe pain, and but little interested in his surroundings. During the third and fourth days, glucose-saline transfusions were given per rectum at a rate of 2½ pints per day.

This is the only case in which we have seen good (though temporary) recovery after marked evidence of mental upset was present. The child survived for six weeks, and died from septicaemia and hypoproteinaemia.

CHART No. 25

Case No. 52.—Male, aged 14 yrs. Extent of burning—31 per cent.



Case No. 52

Replacement probably inadequate. Fluid was given via the saphenous vein at the ankle, and only about half a litre had run in by 13 hours. During this period, marked haemoconcentration occurred, the blood pressure—which was abnormally high on admission—fell to 76/50, and the pulse rate became

Case No. 52—contd.

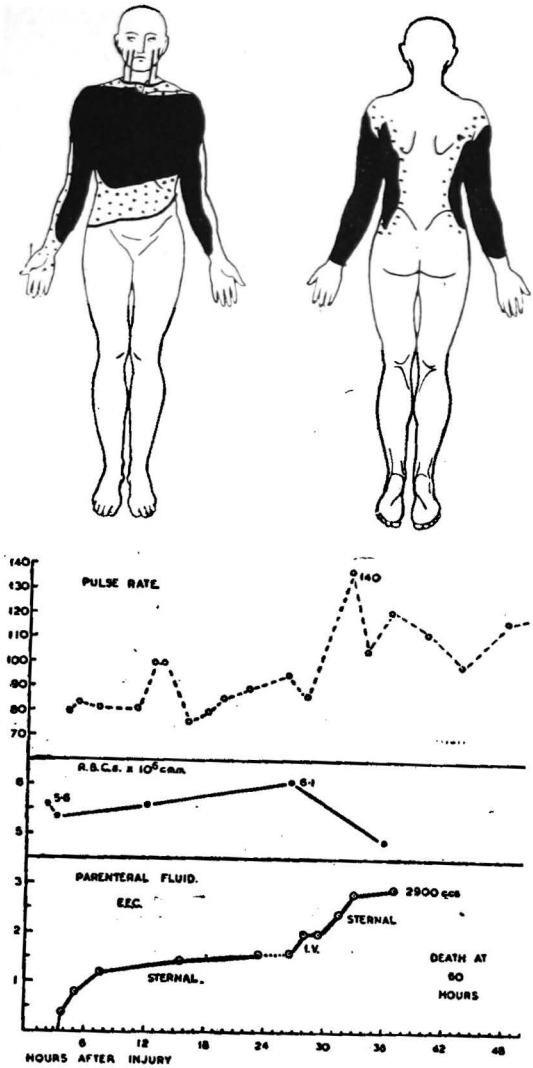
extremely rapid and difficult to count accurately. The patient was drowsy and apathetic, and muttering in his sleep. Although fluid was given rather more rapidly in the next 12 hours, no improvement in the mental condition occurred. He became extremely restless, with convulsive movements; became comatose about 28 hours, and died 32 hours after burning. The haemoconcentration was corrected in the later stages, and there was an improvement in the blood pressure each time the rate of transfusion was increased, but the pulse rate remained unaltered.

Inadequate transfusion in the first 12 hours after burning may have been responsible for death in this case. Cannulation of the external jugular, instead of the saphenous vein, might well have saved him.

Note.—Plenary dressing was carried out in this case immediately the transfusion had commenced.

CHART No. 26

Case No. 54.—Male, aged 40 yrs. Extent of burning—40 per cent.



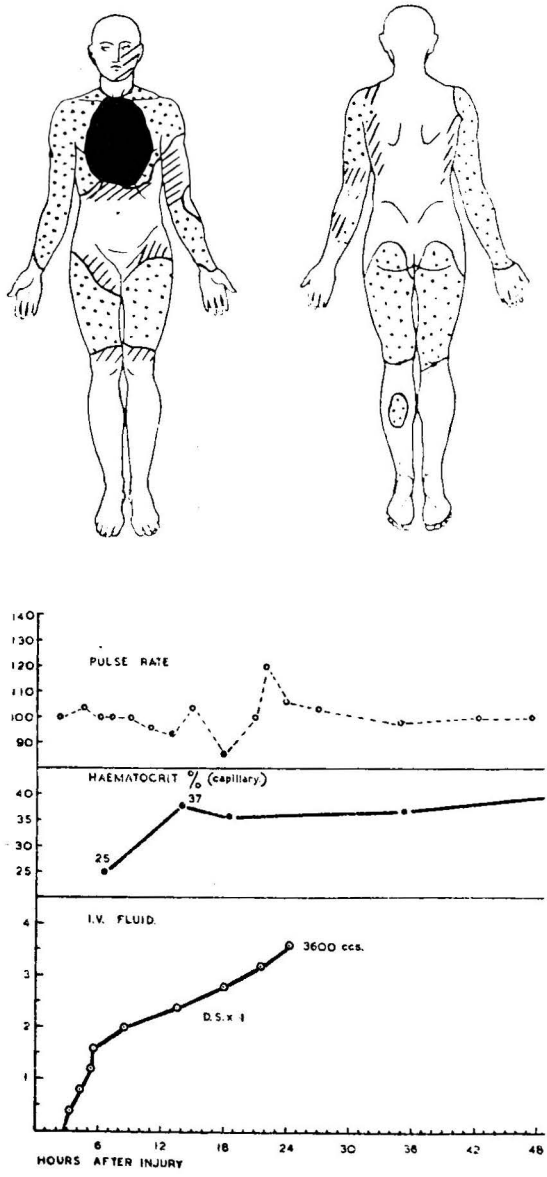
Case No. 54

Replacement probably inadequate in first 24 hours. Because of deep burns on both arms, the fluid was given in this case via the sternal route. Insufficient could be given rapidly enough, and the fluid stopped running after about 16 hours. An attempt to give fluid via the saphenous vein later failed, because of spasm, and the sternal route was again tried, with similar results to the first. Haemoconcentration was eventually controlled by about 36 hours. By this time his colour was poor, his speech was not coherent and he was difficult to rouse. He became delirious about 44 hours after burning, passed into coma about 50 hours and died 60 hours after burning.

Note.—The burns were dressed temporarily with 10 per cent. sulphanilamide cream at 3 hours, but no attempt at a plenary dressing was made.

CHART No. 27

Case No. 61.—Female, aged 37 yrs. Extent of burning—50 per cent.



Case No. 61

Adequate replacement. In view of the extensive nature of the burns, fluid was given rapidly on admission, without waiting for blood readings. Haematocrit measurement at six hours, however, gave a reading of 25 per cent. Allowing for an error in using capillary blood, it seemed that either excessive amounts of fluid had been given, or that the patient had been previously suffering from anaemia. Comparing this case with similar ones in the group,

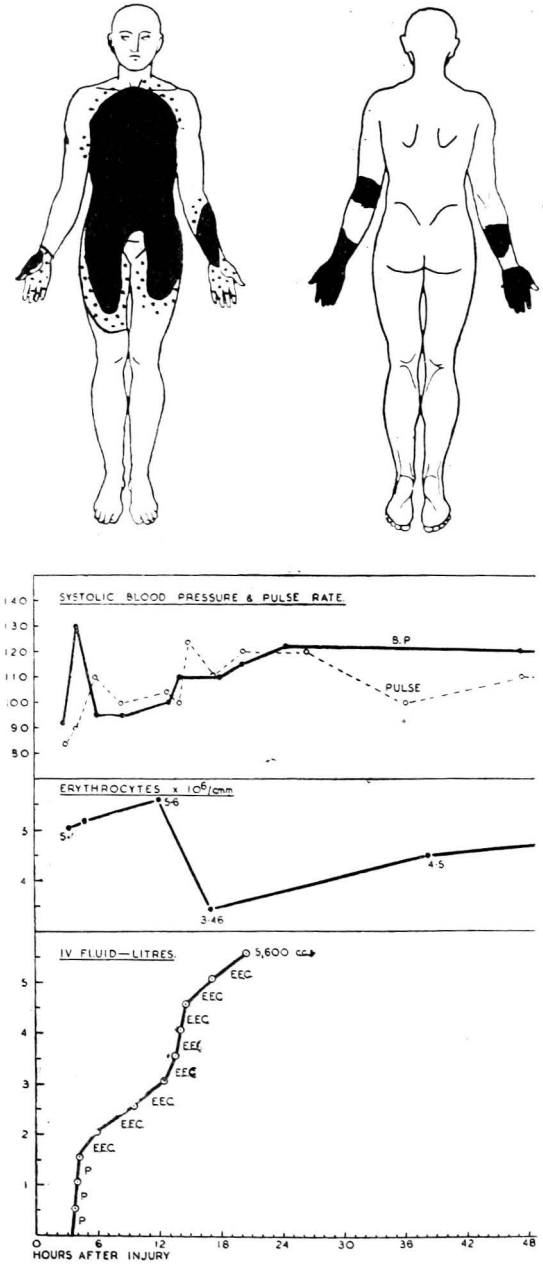
Case No. 61—contd.

it seemed probable that anaemia was at least partly a factor, and transfusions were continued, though at a rather slower rate, and the blood level stabilized at a haematocrit reading of 36 per cent. The pulse rate never rose above 120 throughout, and, though sickness was marked, there was no evidence of mental upset during the first two days. Complete recovery from the shock phase ensued, but death occurred on the 16th day.

Note.—Only a first-aid dressing was applied on admission, and the plenary dressing was postponed until the second day.

CHART No. 28

Case No. 58.—Male, aged 25 yrs. Extent of burning—40 per cent.



Case No. 58

Adequate replacement. 5,600 c.c. were required in this case. Compare the chart especially with that of Case No. 52. There was a gradual rise in blood pressure during the first 24 hours, and thereafter it remained more or less normal. In spite of the administration of three litres of fluid in the first

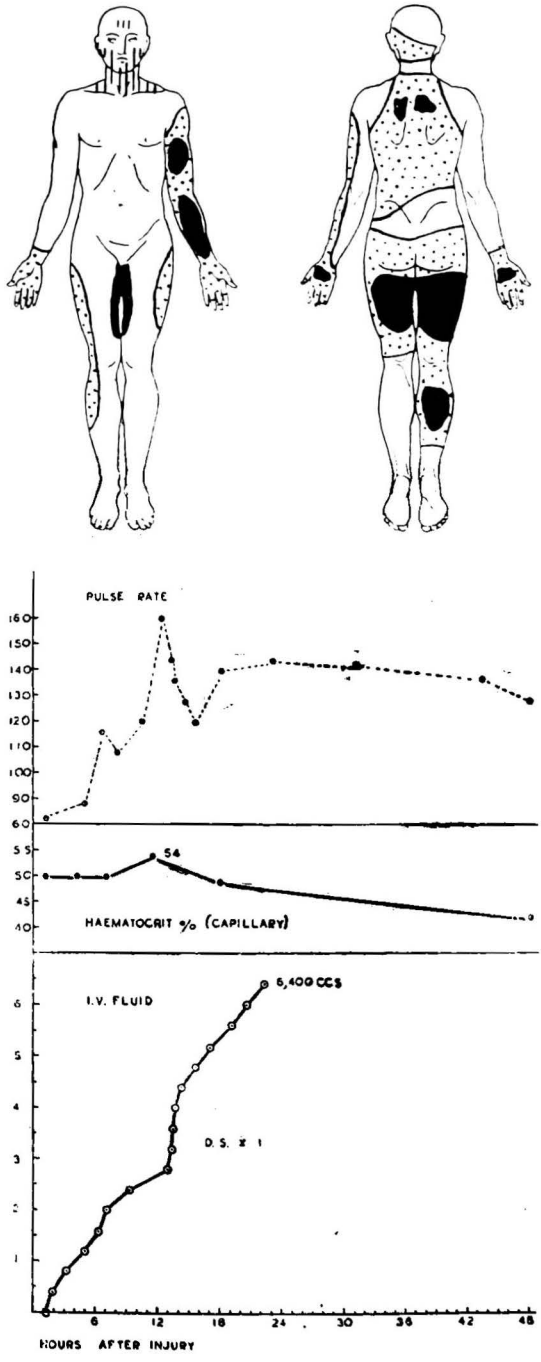
Case No 58.—contd.

12 hours, haemoconcentration actually increased. Fluid loss, however, was apparently diminishing considerably after that period, since a further two litres of fluid caused haemodilution. The drip was stopped shortly after this, and the blood returned slowly to a normal level. There was no evidence of mental upset until the third day, when the patient became rather delirious, and at this time there was a tinge of cyanosis about the lips. His blood-sulphanilamide was then 31 mg. per 100 c.c., and this was probably responsible for the mental changes. Complete recovery ensued.

There was no attempt to clean and dress the burns during the shock period; a first-aid dressing only was applied.

CHART No. 29

Case No. 62.—Male, aged 14 yrs. Extent of burning—50 per cent.



Case No. 62

Adequate replacement. 6,400 c.c. of dried serum were necessary to control the haemoconcentration. Note that, although more than five litres had been

Case No. 62—contd.

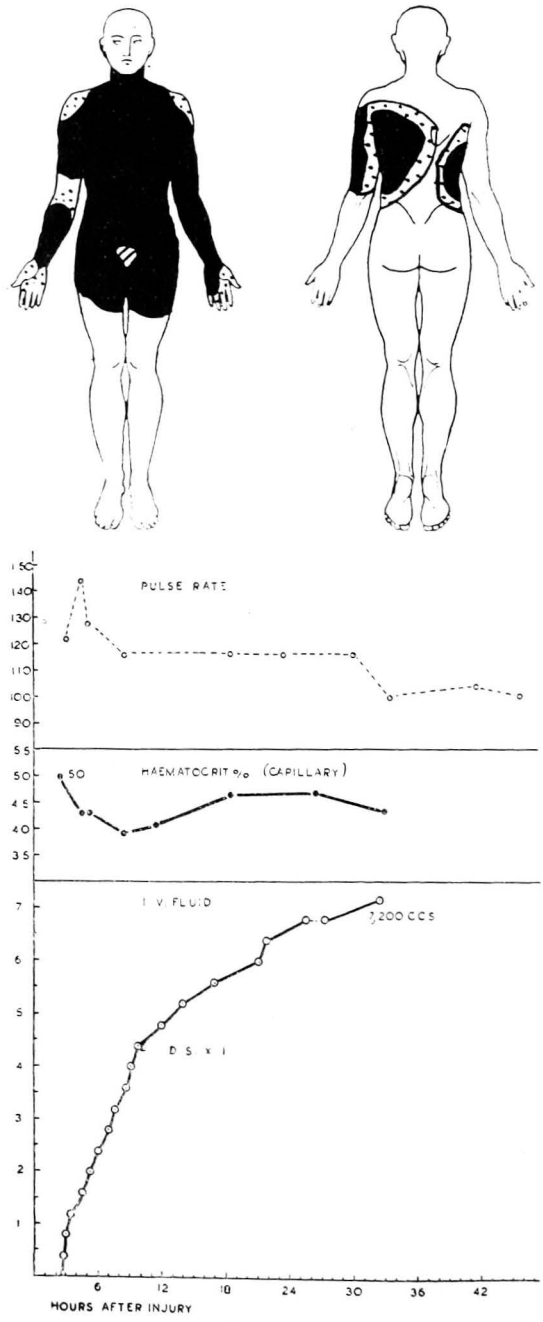
given by 18 hours after burning, the haematocrit reading was practically the same as it had been on admission. In other words, the patient had actually lost more than five litres of fluid during that period.

About 12 hours after burning, the patient appeared pale and apathetic, his pulse rate had risen to 160 per minute, and haemoconcentration had increased. It was found that fluid had been running in more slowly than had been intended, because of spasm in the arm veins. The fluid was therefore pumped in rapidly, and this was followed by an immediate fall in the pulse rate and by a lowering of the haemoconcentration. The mental condition improved, and complete recovery ensued.

Note.—Only a first-aid dressing was applied on admission. Plenary dressing was postponed until the second and third days.

CHART No. 30

Case No. 60.—Female, aged 41 yrs. Extent of burning—45–50 per cent.



Case No. 60

Adequate replacement of fluid. Very large doses—7,200 c.c. of dried serum—were required to control the haemoconcentration in this case. Except for vomiting, which was troublesome during the shock phase, the patient

Case No. 60—contd.

showed no general symptoms of shock. The pulse rate, after the eighth hour, was steady and below 120. Glucose-saline infusions were continued per rectum during the second and third days, to control dehydration. This patient remained very well for the first two weeks after burning. Thereafter, her condition gradually deteriorated—with the exposure of a very extensive raw area involving the greater part of the trunk, both thighs and both arms—and death occurred in the tenth week.

Note.—Only a first-aid dressing was applied on admission. Plenary dressing was postponed until the second and third days.

STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART IV.—BLOOD CHANGES AND BLOOD PRESSURE IN BURNED PATIENTS

BY

ALEXANDER BROWN, M.B., Ch.B., M.R.C.P.E., F.R.F.P.S.G.

(Working with a part-time grant from the Medical Research Council)

CONTENTS

INTRODUCTION

Although reference to changes in the erythrocyte count after burning injuries had been made on several occasions before the report of Underhill and his colleagues (1923), these authors were the first to stress the profound change in the red cell : plasma ratio (haemoconcentration) which follows severe burns.

They noted that this change appeared to vary with the severity of the burn, and that haemoglobin values nearly twice the normal might be recorded in some instances. This concentration of the blood has been regarded as due either to loss of fluid from the circulation into the tissues around the injury (Underhill, 1930; Blalock 1934), or to a more general and widespread permeability of the capillaries (Moon, 1942).

The development of anaemia in burned patients, at a somewhat later stage, has been the subject of much less discussion, though attention has been directed to haemolysis and haemoglobinuria in reports on the Cocoanut Grove disaster (Cope and Rhinelander, 1943).

Leucocytosis is a common and early finding after burns. Locke (1902) recorded its occurrence within an hour of injury, and his findings support the view of Dorrance (1932) that a leucocytosis of 50,000 p. c. mm. or over in the shock period is a very unfavourable sign.

Objects of the present Investigation

A systematic enquiry has been made into these various blood changes in a large series of cases of burns.

In particular, it seemed desirable both to ascertain how closely haemoconcentration was dependent on the severity and extent of the burn, and to investigate the rate of occurrence and the duration of this process. It was felt that the information so gained would be of great value in the correction by transfusion of the changes in blood volume which occur soon after burning.

Investigation has also been made into the origin of the anaemia which has been found to occur particularly after severe burns, so as to find out whether it is a true anaemia or only an apparent anaemia due to excessive haemodilution accompanying the return to the circulation of fluid from the oedematous tissues around the burn. The possibility of pathological red cell destruction has also been examined in some detail..

In relation to haemolysis, studies in red cell fragility have been made, and with these have been correlated changes in red cell size, the occurrence of changes in plasma bilirubin and, in a few cases, the occurrence of intravascular haemolysis associated with haemoglobinuria.

It was thought that observations on the reticulocytes might give some indication of marrow activity. Changes in the white cells and in platelets have also been investigated.

Finally, since a falling blood pressure is so commonly associated with the fully developed condition of " burns shock," it was desirable to ascertain how close was the relation between the alteration in blood pressure and the development of haemoconcentration; and how far the changes in pressure could be relied upon as a guide to prognosis and treatment.

The Clinical Material

Only patients admitted to hospital have been studied. They comprise a series of cases of both sexes with burns varying in extent from 1 per cent. to 90 per cent. of the body surface, and for descriptive purposes have been grouped as follows :—

Group I ..	.. Burns involving 1–5 per cent. of the body surface.*
Group II ..	.. Burns involving 6–15 per cent. of the body surface.
Group III ..	.. Burns involving 16–30 per cent. of the body surface.
Group IV ..	.. Burns involving over 30 per cent. of the body surface.

* For details of individual cases cited in the text—i.e. age, sex, site and degree of burning, ultimate fate, etc., see Appendix I (p. 203). An account of the method of calculating the extent of burning is given in Appendix II.

METHODS

General Considerations

Samples of blood were obtained by venepuncture in almost all cases. Where results recorded were obtained, instead, from capillary samples, attention is drawn to this fact in the report. For the withdrawal of blood from a vein, a dry sterile needle was used. The blood was collected in a heparinized tube without the use of a syringe, temporary stasis being induced. Examinations were made with the least possible delay, almost always within an hour of bleeding. An automatic shaker was used prior to sampling.

Except when special reasons to the contrary exist, throughout this study haemoglobin concentrations have been charted. In the great majority of cases red cell counts and haematocrit determinations were also made on the same sample of blood; in the remaining patients, apart from those from whom only capillary samples were obtained, the red cell counts were omitted. In regard to the assessment of haemoconcentration or anaemia, there was no significant difference between the values obtained for red cell counts and haematocrit or haemoglobin determinations. In the report by Gibson and Brown no burns shock (page 49 above), the blood changes in the shock period are frequently expressed in terms of red cell counts, as clinicians are more familiar with these than with the haematocrit or with haemoglobin values expressed in grams per cent. In the present report, however, preference has been given to haemoglobin values, because they are the most accurate of the three estimations.

In cases described here in which only capillary blood was obtained, estimation of haemoglobin was carried out, or a capillary haematocrit tube was used.

Haemoglobin*

At the beginning, the estimations in a few cases were performed by the alkaline haematin method (Cohen and Taylor, modified by Wu, Peters and van Slyke, 1932), comparison being carried out in a Duboscq colorimeter. Almost all the results recorded here were obtained by the use of a photoelectric colorimeter, using carboxyhaemoglobin as the pigment, and a Chance-Watson green filter. Throughout the work, the same 10 ml. pipette, delivering 9·998 ml. at 20° C., was used for 0·4 per cent. ammonia, to which was added 0·1 ml. of blood. The same apparatus was used in calibrating the instrument, a normal blood of known oxygen capacity (van Slyke method) being obtained for this purpose.

In the case of capillary samples, 0·05 ml. of blood was delivered directly from the skin puncture into 5 ml. of ammonia.

Throughout the investigation, the instrument was checked against oxygen capacity, and by the insertion of a neutral screen. No significant variation in sensitivity was found to occur. In recording serial estimations on samples of venous blood, differences of 0·2 gm. Hb. per cent. or more are regarded as significant, on the basis of a very large series of estimations performed in duplicate.

Haematocrit

The packed cell volume was estimated from a sample of venous blood by use of the Wintrobe haematocrit tube. When only capillary blood was available, a heparinized teated capillary pipette was employed to transfer the blood from the needle puncture to the capillary haematocrit tube. An angle centrifuge was used, the specimen being spun at about 3,000 revolutions per minute for 30 minutes.

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* The abbreviation "Hb." will be used for haemoglobin in the rest of this report.

Platelets, Reticulocytes, and White Cells

As a limited amount of time was available for the work, the method of Salter (1941) was used for these estimations. It was found to be satisfactory, but satisfaction appears to depend on the suitability of the cresyl blue employed. (Some samples of the stain produce turbidity when mixed with the cyanide and render the method quite useless.) Platelets were found to persist numerically unchanged for several hours at room temperature, and no difficulty was experienced in counting them unless there had been difficulty in obtaining blood from the vein.

Quantitative Erythrocyte Fragility (Saline)

The various dilutions of saline used in this test were prepared as stock solutions from sodium chloride of analytical purity, and checked by titration. The range of strengths employed varied from 0·24 per cent. to 0·72 per cent. NaCl, by steps of 0·02 per cent. Five ml. of the respective saline solutions were added to a series of centrifuge tubes, and then to each of these was added, by means of a microburette with a ground and vaselined tip, an equal volume of blood (0·1 ml.). A similar amount of blood at the beginning, and again at the end, of the manipulation, was added to 10 ml. of distilled water to provide standards equivalent to 50 per cent. haemolysis. The contents of the tubes were mixed by inversion, and allowed to stand not less than 15 minutes at 20° C. and not more than two hours at 20° C., or 24 hours at 0° C. The tubes were then centrifuged, and the supernatant solutions compared with the standards in a Duboscq colorimeter.

Comparison of the two standards revealed that, in the short time taken to add the blood to the saline solutions, no appreciable error occurred due to red cell sedimentation in the burette.

Blood Pressure

Blood pressure readings were obtained by use of a mercurial sphygmomanometer in adults. An instrument of the dial type, with a special 2-in. cuff, was used for infants and children (Messrs. Down Bros., Ltd.). The readings in this instrument were checked from time to time against the mercury manometer.

Blood Volume

In many aspects of this study, blood volume determinations would have given valuable information but, as no technical assistance was available and time was limited, this extra work could not be undertaken.

HAEMOCONCENTRATION* AND SHOCK

In attempting to assess the significance of Hb. levels in relation to burns, isolated estimations are valueless, both because of lack of knowledge of the pre-burn level and on account of the wide range of values obtained in apparently healthy individuals. The only possible exception to this is the occurrence of a value much above normal. Serial blood examinations are necessary, and the times at which these should be made are conditioned by the rate at which changes may be expected to occur.

In the first part of this report, changes in Hb. concentration are regarded as indicating changes in plasma volume, a rising Hb. concentration as indicating Hc. due to loss of plasma. The questions of inequality of distribution of red cells, and of the addition of red cells to the circulation from reservoirs such as the spleen, are discussed later. The occurrence of haemolysis, and the excretion

* The abbreviation " Hc." will be used for haemoconcentration in the rest of this report.

of Hb. by the kidneys, are also factors which interfere with the assessment of changes in blood volume on the basis of Hb. estimations; they are factors encountered only in very severe and extensive burns.

In the shock period—i.e. in the first 72 hours after burning—Hc. may occur with considerable rapidity, and it may continue for a few hours or for almost three days. At the end of this variable period, the red cell values begin to fall. In the severe cases reported here, frequent blood samples were obtained during the first 48 hours, because they were necessary to control the administration of serum or plasma. In the majority of the milder cases, less frequent observations were made, and in some it is impossible to demonstrate a rise in Hb. and Hc. Often, however, a definite fall on the second or third day justified the assumption that some degree of Hc. had probably occurred.

The blood values obtained after the shock period cannot be used to indicate the probable pre-burn levels because, as is shown later, these values may have been subnormal.

HAEMOCONCENTRATION—GROUP I. (Burns 0–5 per cent. of body surface.)

Magnitude of Haemoconcentration

This group is represented by males of ages from 16 to 60. None was given transfusion and none developed symptoms of shock. In the majority, a distinct cycle of changes in Hb. level occurred during the first week, but little alteration is recorded during the first 72 hours (Fig. 8). These changes in some cases are regarded as beyond experimental error, but, since they do not exceed the daily variations found in normal subjects (Brown, Chisholm and Goodall, 1944), they cannot be regarded as necessarily related to the burn.

This absence of change in the first 72 hours, or in the first week, is not representative of the Group, for in some cases, in which paucity of readings during the first 24 hours precluded their being considered at this stage, much more obvious changes occurred during the first week. Three examples of this are shown in Fig. 9. Case No. 68 is of special interest, in that changes of the magnitude seen here surpass those found in many patients much more extensively burned.

Duration of Haemoconcentration

In all the cases in this Group, any tendency to Hc. was seen during the first 12 hours and a fall was apparent by the second day.

Blood Pressure

Of the patients in this Group, Case 67 (Fig. 8) showed a blood pressure of 155/80 on admission at 3 hours after burning. The systolic pressure rose to 160 mm. Hg at the fourth hour, and by the ninth hour a slight fall had occurred (140/80). A final systolic level of 120–130 mm. Hg was reached by the 21st hour, and was maintained until the patient's discharge on the 9th day. In this case, the rising blood pressure occurred during the phase of Hc. In Case 65, though the initial reading of 108/70 was well within normal limits, a final systolic level of 95–102 mm. Hg was reached at the 9th hour and maintained till dismissal. Such a finding was encountered in all groups. In Case 88 no significant change in Hb. levels was recorded (Fig. 8); a B.P. of 118/80 at 1 hour after burning was unchanged fifteen hours later.

Summary

In Group I, changes in blood levels probably indicating slight Hc. occurred during the first 72 hours after burning. In the cases recorded, these changes were closely similar, but the total magnitude of the changes occurring in the

HAEMOCONCENTRATION
Burns 0–5 per cent. body surface

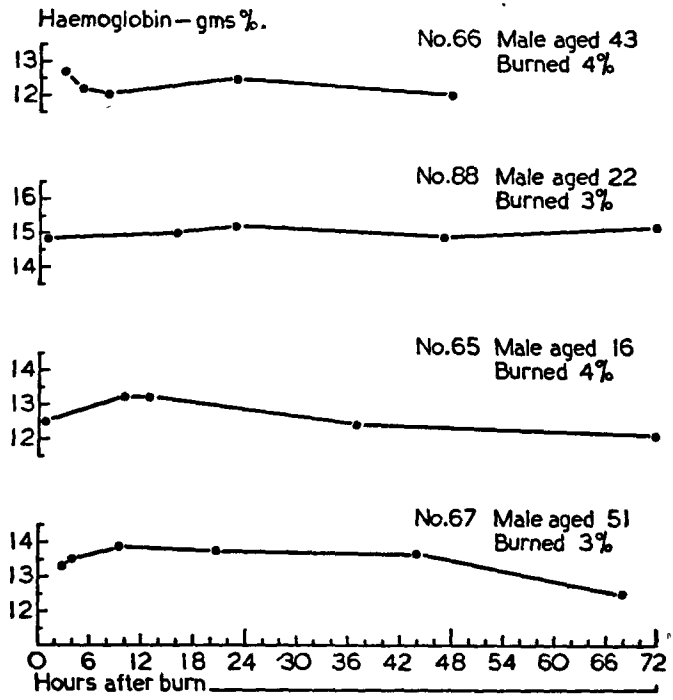

FIG. 8

HAEMOCONCENTRATION
Burns 0–5 per cent. body surface

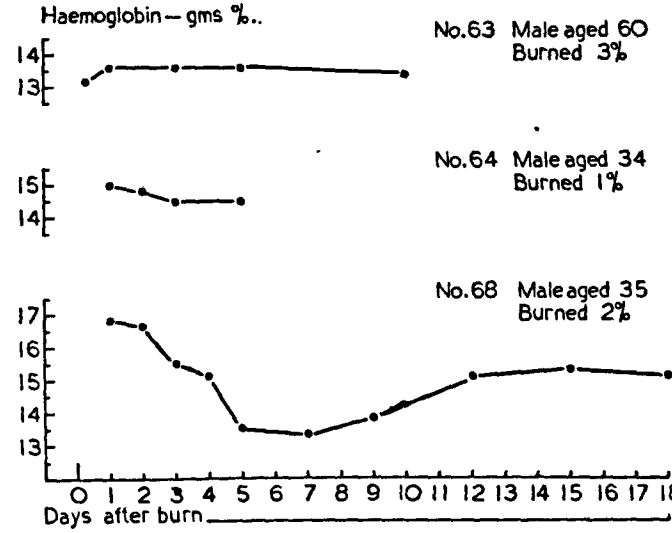

FIG. 9

first week bore little relation to the extent of the burn ; and it may be that the changes recorded here in the short period of our study are not entirely representative of this Group.

Blood pressure (B.P.) readings above normal, both absolutely and, in many cases, relatively, have been encountered in the first few hours. The high blood pressure may occur at the same time as Hc.

HAEMOCONCENTRATION—GROUP II. (Burns 6–15 per cent. of the body surface.)

The majority of the cases to be described in this Group are included to illustrate the changes in Hb. level immediately following injury. In some, B.P. is correlated with these changes, and in a few only B.P. readings are reported. No case developed symptoms of shock.

Magnitude of Haemoconcentration

In the study of Hc., the cases have been divided into two groups—5 patients who received serum transfusion, and 6 who did not. The latter will be considered first.

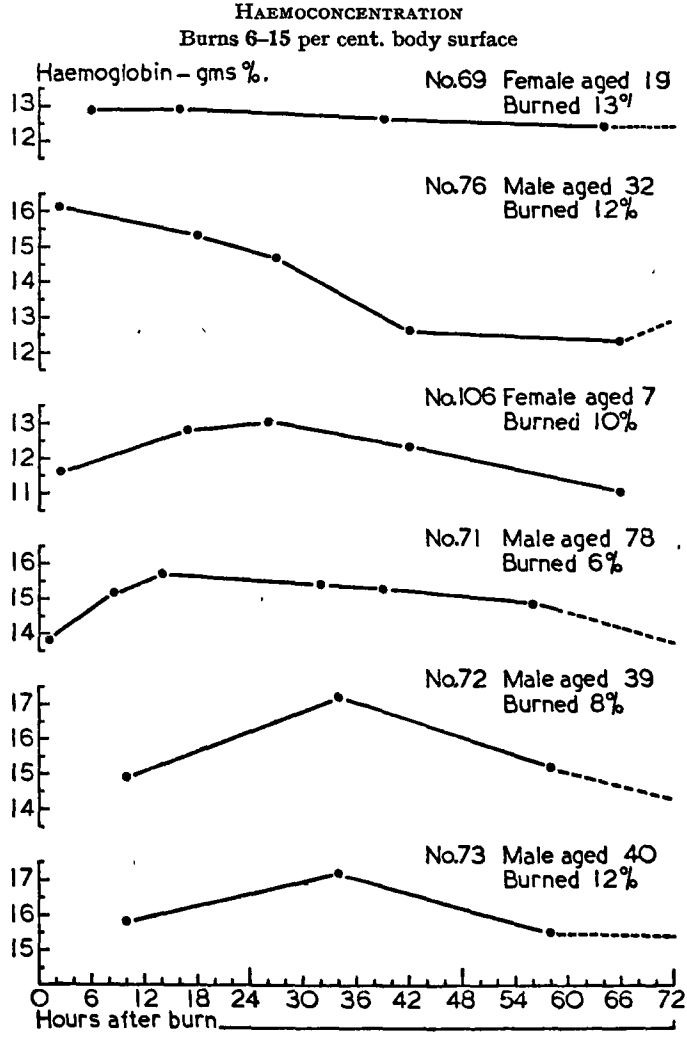

FIG 10

Reference to Fig. 10 reveals that the blood changes in Group II are more definite than those in Group I. But the magnitude of the changes varies considerably, and the variation is not related only to the extent of the burn. In comparison with those in other cases, the changes in Case 69 are conspicuous by their absence, in spite of the extent of the burn, while relatively minor burns (Cases 71 and 72) are associated with very significant Hc. Attention is again drawn to Case 68 (Fig. 9) and to Case 69 (Fig. 10). In the latter, no change occurred in Hb. levels during the 15 days following the burn.

HAEMOCONCENTRATION

Burns 6–15 per cent. body surface

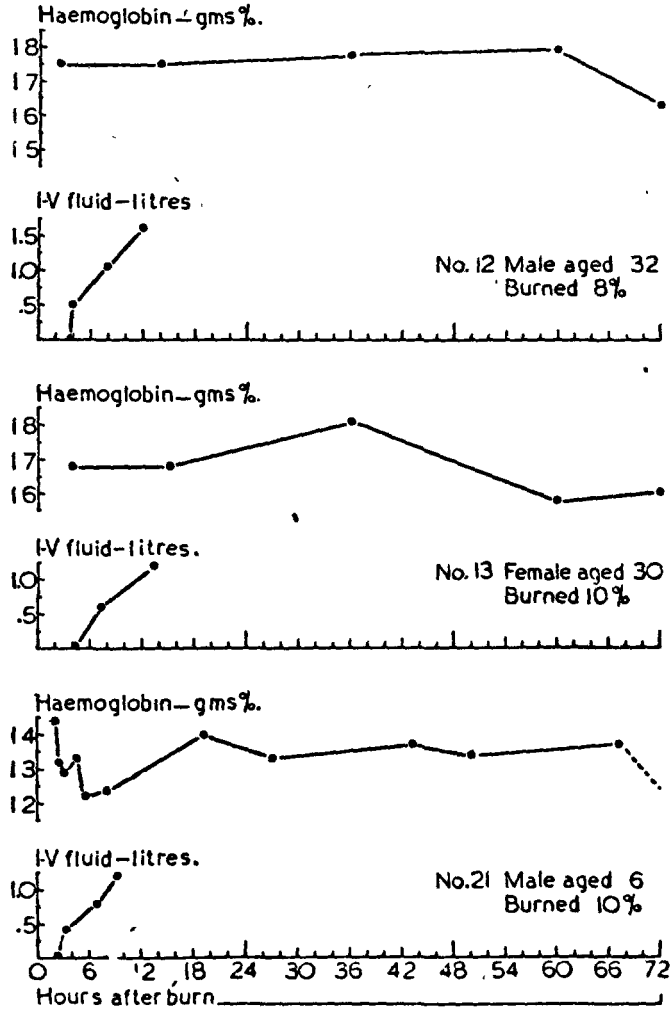

FIG. 11

Burns 6–15 per cent. body surface

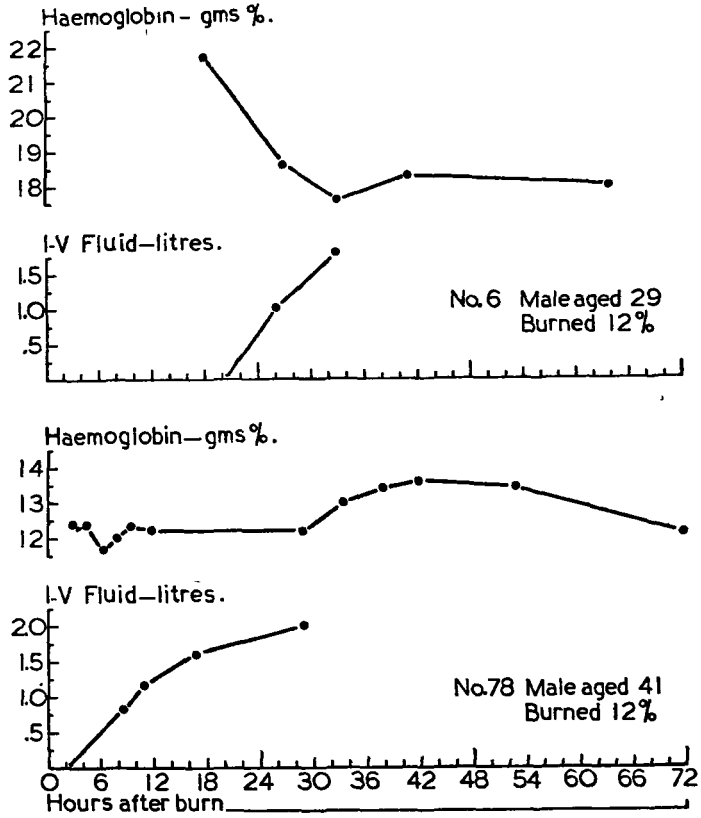

FIG. 12

The changes in Hb. levels in the shock period are viewed more closely in patients transfused. Cases 12 and 13 (Fig. 11) are similar in many respects. The subjects were of the same age, though of different sex, and the burns differed little in extent. Given like amounts of fluid in the same period after the burn, the two patients showed very similar Hb. curves. In these two cases, administration of serum at a rate of 3·0 and 3·2 ml. per minute for 9 and 8½ hours, respectively, in the first 12 hours, was accompanied by absolute maintenance of Hb. levels, and presumably also of plasma volume. In both, however, as soon as administration of serum ceased, there was a slight tendency, more marked in Case 13, for the Hb. to rise.

In Case 21 (Fig. 11), a child of 6 years, administration of serum at about the same rate (2·9 ml. per minute for 7½ hours in the first 12 hours) resulted in haemodilution, previous levels being rapidly regained after cessation of transfusion.

In Case 6 (Fig. 12) marked Hc. was present at 18 hours. Administration of serum at a rate of 2·3 ml. per minute from 20 to 33 hours sufficed to produce marked haemodilution, and to restore a Hb. level on the high side of normal.

In Case 78 (Fig. 12), during the first 12 hours, transfusion of 2·2 ml. of serum per minute maintained steady Hb. values. In the following 17 hours, with administration of 0·75 ml. per minute, these levels remained unchanged. When transfusion was discontinued, the Hb. level rose to a maximum at 42 hours and then slowly declined.

These findings are summarized in Table XIV. It is evident that fluid requirements tend to be greater in the first 12 hours after injury.

TABLE XIV

Patient		*Fluid Transfused*			
	Extent of Burn	*First 12 hours*		*Second 12 hours, etc.*	
Case No.	*(per cent. of body surface)*	*Rate ml./min.*	*Effect on Hb.*	*Rate ml./min.*	*Effect on Hb.*
12	8	3·0	Level maintained	None	Slight rise.
13	10	3·2	Level maintained	None	Slight rise.
6	12	None	Marked elevation	2·3	Marked fall.
78	12	2·2	Level maintained	0·75	Level maintained.

Duration of Haemoconcentration

Reference to Fig. 10 reveals that in the cases not transfused, maximum Hb. levels were recorded at 2¼ to 36 hours after burning. The chart shows the limits within which this is an accurate estimate. Case 76 shows an unusual reaction, with a rapid fall from a maximum level of 16·05 g. Hb. per cent. at 2½ hours to 12·4 g. per cent. at 66 hours. Subsequently, a steady rise to a level of 15·1 g. per cent. occurred, with stabilization at this level from the 8th day. If this last level indicates even very approximately the patient's normal level, Hc. must have been of rapid onset and short duration.

It is evident also, from Figs. 11 and 12, that there are great differences in the duration of progress of Hc.—60 hours in Case 12; 42 hours in Case 78; and about 36 hours in Case 13.

Administration of serum to a normal individual may produce haemodilution which, when transfusion is stopped, will be followed by a rise in Hb.—" haemoconcentration "; but in the three cases just cited (12, 13 and 78), from the commencement of the transfusion, no haemodilution was produced. It seems highly probable, therefore, that the subsequent rise in Hb. in these patients indicated continuation of plasma loss from the circulation.

Blood Pressure

Blood pressure records in this Group (Table XV) show a number of cases in which a high initial level and a subsequent fall occurred in the first few days, or in which a normal or slightly low B.P. was recorded on admission. Several patients showed a rise in B.P. in the first 48 hours.

In Case 69, a steady level was maintained during the first 3 days. No explanation is available for the higher reading on the 4th day. Case 71 shows a rise from 130/90 at 1 hour to 150/100 at 13¾ hours, and to 160/100 at 32 hours. The rise accompanied the process of Hc. in a phlegmatic elderly male. In Case 75, the highest B.P.s recorded occurred at 1 and 5 hours (blood values were not determined until the 17th hour). Case 76 showed a pressure of 150/90 at 2½ hours, when the highest recorded Hb. occurred (Fig. 10). In Case 106, little definite change in blood pressure or Hb. is recorded. Case 117 shows a rise in B.P. on the 2nd day, associated with little alteration in Hb. A relatively high B.P. was recorded 24 hours after burning in Case 118, and 1 hour after burning in Case 119.

Among those transfused, Cases 12 and 13 showed no upset in B.P. In Case 21 relatively high readings were obtained during the first 12 hours. These high levels were never again recorded during the period of hospitalization. In Case 26, the initial B.P. readings were low and administration of fluid was accompanied by a rise. The initial high reading in Case 78 occurred on admission, when the patient was drowsy and under the influence of morphine,

TABLE XV

GROUP II.—BLOOD PRESSURE READINGS

(Systolic and diastolic, in mm. Hg)

(*a*) No transfusions given

Case No.	*Days after burning*								*Remarks*
	0	1	2	3	4	5	6	7	
69	108/68	108/58	104/65	106/65	114/60	108/60	108/60		Minimal change in Hb. (Fig. 10.)
70		120/74	128/80	124/78	128/74	124/70	120/70	122/80	Moderate Hb. change.
71	130/90 ..... 150/100	160/100							Definite Hc. with rise in B P. (Fig. 10.)
75	112/72 ..... 110/72	96/66	98/64	98/60	100/60		102/62	100/62	Marked Hb. change.
76	150/90								Marked Hb. change. (Fig. 10.)
106	112/64	110/64	110/70	100/72	106/80	95/72	108/76	106/78	Slight blood change. (Fig. 10.)
117	104/68	120/72 ..... 128/85	116/72	114/72	105/72	94/70	102/68	94/68	Practically no Hb. change.
118		116/70	100/68	98/65		100/68			No bloods examined.
119	125/70	110/70	110/70		108/70				No bloods examined.

TABLE XV—*continued*

(*b*) Transfused

Case No.	Hours after burning								Remarks
	3	6	9	12	15	18	21	24	
6	108/72	106/72			96/72	100/72	110/74		Transfusion begun at 20 hrs. P.C.V. 58·5 per cent., Hb. 21·8 g. per cent. at 18 hours.
12	130/30			125/76					Very little change. (Fig. 11.)
13	120/48								(Fig. 11.)
21	120/75	118/78	115/78			104/68	106/70		B.P. established ultimately at 100/72–106/75. (Fig. 11.)
26	108/78			90/68	112/70	120/78	120/80	116/76	
78	170/90	145/100	150/90	148/98	138/85				No excitement at all. Ultimately established at 145/100–140/85.

and no excitement was apparent. It is probable that in this case the initial Hb. level of 12·4 g. per cent. represented Hc., for the patient was found to be iron-deficient, due to chronic loss of blood from haemorrhoids, and when, after 2 months' intensive iron therapy, his red cells numbered more than 5 million per c.mm., the Hb. was still only 12·2 g. per cent.

A rise in B.P. was thus recorded in several patients at a time when maximum Hc. was occurring. On the other hand, it occurred in Case 117, who showed no significant alteration in Hb. levels ; and in Case 106 the maximum reading was recorded when the Hb. was at a level again reached and finally maintained at the end of a week. Case 106 was one in whom excitement was obvious on admission, and throughout her stay in hospital she proved to be of very nervous disposition.

Summary

The great majority of patients investigated in this Group showed blood changes probably indicative of alteration in plasma volume. These alterations were not directly related only to the extent of the burn : degree (depth) and site may have played a part in determining their magnitude. Hc. ceased within the first 24 hours, or continued well into the third day. The evidence obtained from administration of fluid suggests that the rate at which fluid is lost rapidly reaches a maximum in the first 12 hours ; that during the ensuing period—the duration of which is variable—loss occurs less rapidly ; and that, finally, at a variable time, alteration in the balance between loss and return allows haemodilution to occur.

In this Group, low B.P. may be recorded on admission within a few hours of burning, but attention is drawn to the frequency with which high or relatively high values occur, and to the occurrence of these at a time when Hc. is at, or is approaching, its maximum. The blood pressure may, however, be high without any apparent change in Hb. levels.

HAEMOCONCENTRATION—GROUP III. (Burns 16–30 per cent. of body surface.)

Magnitude of Haemoconcentration

Few patients in this Group did not receive transfusion, and only four such cases are described (Fig. 13). The changes in the first 72 hours were remarkably similar in all, and differed little from the more obvious alterations encountered in Group II. These patients not transfused were those who, in the early stages of the investigation, were left to be transfused should need become apparent clinically. The changes therefore are probably the least which may occur in burns in this Group. The changes, in addition, may represent roughly the maximum which may be unassociated with symptoms.

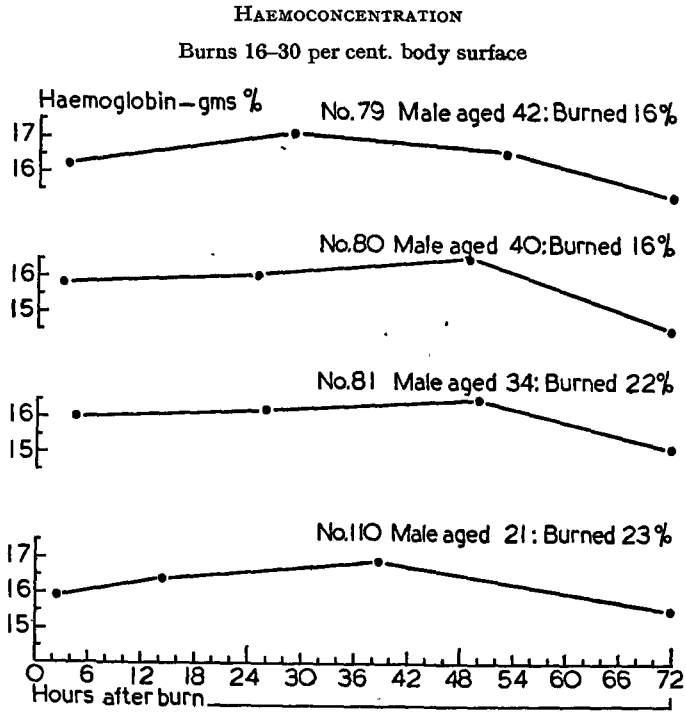

FIG. 13

The majority of the patients received transfusion of serum (Figs. 14–16). In the two young adults least burned (Fig. 14: Cases 8 and 30) abnormally high Hb. levels occurred during the first 6 hours. With commencement of transfusion, no fresh Hc. was recorded, and in the second 12 hours little or no serum was required. A fall of Hc. to relatively normal levels occurred by the end of the third day.

In Case 37, that of a child, a relatively large transfusion was required, but the evidence available does not suggest any diminution in the rate of Hc. during the second 12 hours (Fig. 14).

During the first 7 hours in Case 82 (Fig. 15), the result of serum transfusion at a rate of 4 ml. per minute was to leave the Hb. value little removed from its original level. But between the 18th and 29th hours, transfusion at the rate of

1·6 ml. per minute was associated with haemodilution, in spite of the fact that a rise in the Hb. value followed substitution of saline for serum at the end of this period.

HAEMOCONCENTRATION
Burns 16-30 per cent. body surface

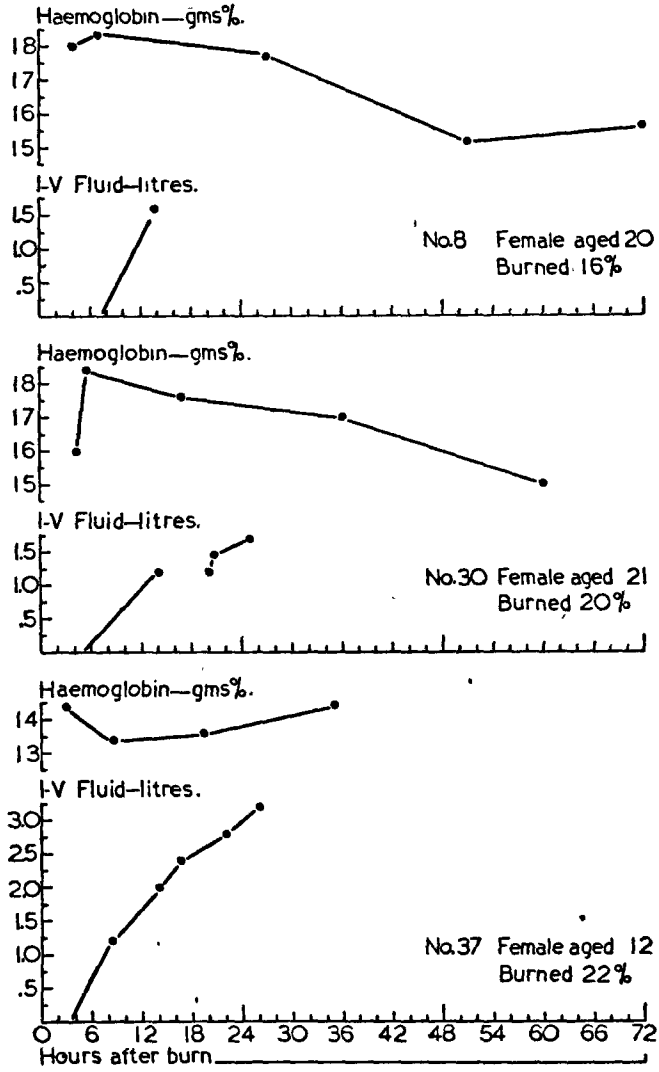

FIG. 14

In Case 83 (Fig. 15), in the first 12 hours, transfusion of serum at a rate of 2·4 ml. per minute maintained Hb. levels practically unaltered, while in the second 12 hours 2·2 ml. per minute caused slight haemodilution. Reduction in the rate of administration to 1 ml. per minute during the following 7 hours was followed by a rise in blood levels for a short period.

Burns 16–30 per cent. body surface

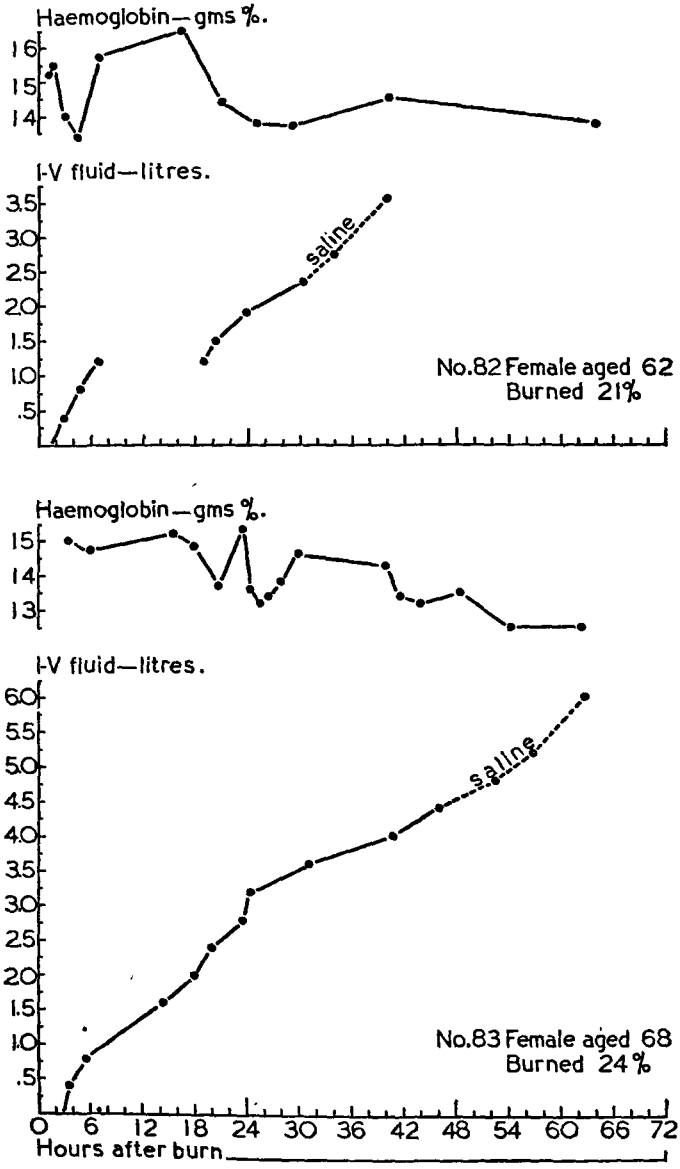

FIG. 15

In Case 32 (Fig. 16), serum transfusion at a rate of 3·2 ml. per minute between 5½ and 17 hours was inadequate, while between 22 and 31 hours, 2·5 ml. per minute caused marked haemodilution.

In Case 33 (Fig. 16), 4·5 ml. per minute from the 2nd to the 12th hour corrected a marked degree of Hc.

HAEMOCONCENTRATION

Burns 16–30 per cent body surface

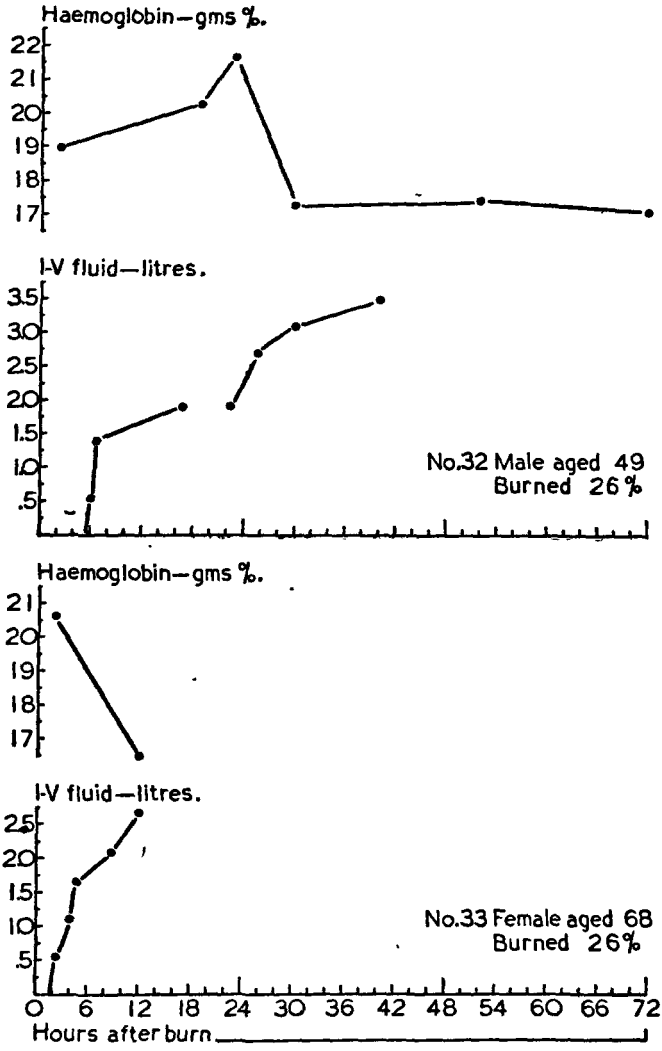

FIG. 16

These findings are summarized in Table XVI :—

TABLE XVI

Patient		*Transfusion*			
		First 12 hours		*Second 12 hours*	
Case No.	*Extent of Burn (per cent of body surface)*	*Rate ml./min*	*Effect on Hb.*	*Rate ml./min.*	*Effect on Hb.*
82	21	4	Level maintained	1·6	Marked fall.
83	24	2·4	Level maintained	2·2	Marked fall.
32	26	2·9	Moderate rise	2·5	Marked fall.
33	26	4·5	Marked fall	—	—

Duration of Haemoconcentration

Though greater Hc. and fluid requirements were noted in this Group, no case showed prolongation of this phase beyond that found in Group II, in which the burns were less extensive.

In Cases 79, 80, 81 and 110 (Fig. 13), none of whom received transfusion, the duration of Hc. varied from about 36 to 60 hours.

In Cases 8 and 30 (Fig. 14), Hc. proceeded for not more than 24–36 hours. In Case 82 the duration of Hc. was about 40 hours ; in Case 83, it was not more than 48 hours, and in Case 32 about 52 hours.

Blood Pressure

Systolic and diastolic blood pressure records in 10 patients in this Group are summarized in Table XVII. An initial high reading was recorded in six.

TABLE XVII

Case No.	Hours after Burning									Remarks
	1–2	3	6	9	12	15	18	21	24	
8		125/80	90/54	Treat	ment	..	118/?			Allowed to develop Hc. (Fig. 14.)
19	90/60	120/70	120/70	120/70		125/70	150/80	130/80		B.P. rose with treatment.
30	120/?	116/86	98/56		100/56			108/56	114/60	Allowed to develop Hc. (Fig. 14.)
32			144/98				102/82		96/80	B.P. fell with progress. Hc. with inadequate treatment. (Fig. 16.)
33	200/100	125/30	165/100	150/100						B.P. fell with haemodilution. (Fig. 16.)
37		110/80	90/60	110/80	104/60	108/70	95/60		100/70	Treated at once. (Fig. 14)
38	165/92 148/86	128/92				110/90		126/90		Same as Case 32.
82	179/94	122/80	120/70			110/70	95/68	115/78	128/76	Treated at once. (Fig. 15.)
83		192/90	188/90	120/75		169/90	160/88	160/84	166/90	Treated at once. (Fig. 15.)
110		150/90								(Fig. 13.)

In Cases 8 and 30, the B.P., normal at first, fell below normal and rose again with transfusion. The normal initial level was associated with Hc. in both.

In Case 19, it is of interest that, with Hc. on admission, a low B.P. was recorded. It rose to normal level with slight haemodilution, and to 150/80 when Hc. again developed due to inadequate treatment.

In Case 32, transfusion was inadequate in the first 24 hours, and the blood pressure fell below normal. The slightly high pressure recorded at 6 hours was associated with Hc.

In Case 38, the high level at ¾ hour fell to normal at 3 hours, when the Hb. was recorded at 18·6 g. per cent.

In Cases 82 and 83, both elderly women, initial hypertension was associated with Hb. levels within normal limits. It is impossible to say whether the levels actually represented Hc. in these patients.

In Case 110, a reading of 150/90 was associated with a Hb. of 15·9 g. per cent.

In these 6 cases, the high B.P. levels were recorded with the highest Hb. levels in 3, where definite Hc. was present in 2, and at a time when Hc. might be expected, in all. A normal B.P. in association with Hc. is shown in 2 cases.

Summary

All patients in Group III showed marked blood changes, but no extension of the progress of Hc. beyond 72 hours is seen. Low B.P. was recorded 1¼ hours after burning in Case 19, but attention is drawn to the occurrence of high and normal B.P.s associated with Hc. in the untreated cases. In some cases, these high or normal levels preceded a fall to subnormal levels, accompanied by a state of shock, for which transfusion had to be given.

HAEMOCONCENTRATION—GROUP IV. (Burns over 30 per cent. of body surface.)

Magnitude of Haemoconcentration

Only 3 patients not transfused are described in this Group. All had very extensive burns. They received only morphine, and all died between 10 and 12 hours after the injury.

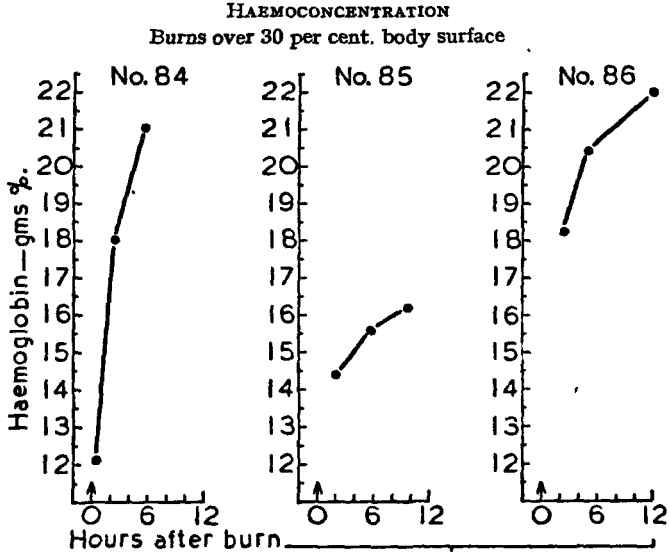

FIG. 17

Case 84 (Fig. 17) indicates how rapidly Hc. may supervene. Assuming a previously normal Hb. level of 12 g. per cent., the findings suggest that approximately 50 per cent. of the plasma volume was lost from the active

circulation in the first 2½ hours, and 70 per cent. 5½ hours after injury. Assuming a previous normal plasma volume of 3 litres, the calculated rate of plasma loss is 12·5 ml. per minute in the first 2½ hours, and 3·3 ml. per minute in the next 3 hours, with an average of 7 ml. per minute during the first 5½ hours. From the other two Cases (85 and 86), no blood records were obtained in the first hour, and, in view of the findings in Case 84, assessment of the degree of Hc. present is not possible. The rate of development of Hc. in the period 2½–5½ hours after injury in Case 85 is less rapid than in Case 84. In Case 86, the curve resembles closely that of Case 84.

Among the cases transfused (Fig. 18) are several which compare very closely with No. 84 in many respects. In Case 46, a child of 10 years, administration

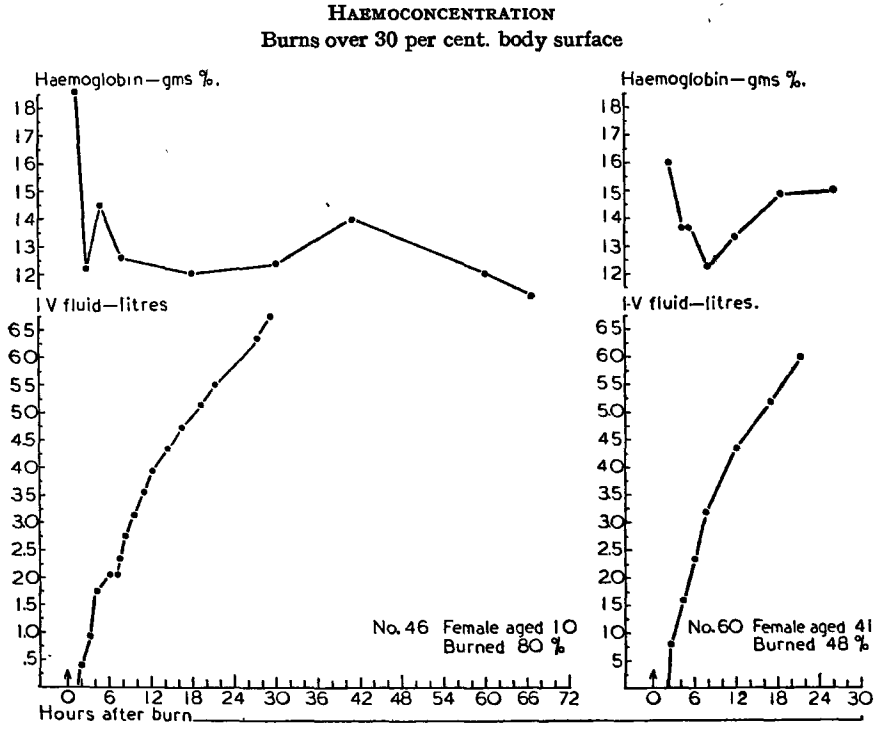

FIG. 18

of serum at a rate of 6·7 ml. per minute produced rapid haemodilution. In Case 60, not quite so extensively burned as No. 84, administration of serum at a rate of 7·3 ml. per minute in the first 12 hours produced only slight haemodilution and, during 12–21 hours, 3·1 ml. per minute was associated with Hc.

Any attempt at calculation from Hb. levels of the amount of Hc., and of the amount of plasma lost during a period of hours, assumes that the plasma : cell ratio is the same throughout the whole circulatory system. This is not so. There is evidence (McIver, 1933), which we can support by only a few figures, that the cell and Hb. content of capillary blood may be higher than that of venous blood. The tendency, therefore, in any assessment of plasma loss based on values obtained from venous blood—as in the Case 84—is towards an understatement rather than an exaggeration of the loss. At least, however,

some idea is obtained from these figures of the rapidity with which the circulating fluid volume may become diminished, and of the extent of reduction which may take place before death in cases of major burns.

Duration of Haemoconcentration

Several patients with extensive burns transfused from an early hour, but not recorded graphically here, serve to confirm the rapid and extreme Hc. which may follow extensive burns. The numbers studied are insufficient to correlate extent of injury with magnitude of change, but in those examined there is no evidence of progress of Hc. beyond 60 hours. In some cases in this group, there was encountered a complication which to a certain extent invalidates any attempt to assess the significance of the Hb. values, namely, the occurrence of haemoglobinaemia and haemoglobinuria. This complication will be discussed when the phase of anaemia is considered.

Blood Pressure

Accurate readings are often difficult or impossible to obtain in cases of widespread and deep burns. In Case 52, however, a youth of 14 burned over 31 per cent. of his body surface, the B.P. at 1 hour after injury was 165/114. A Hb. level, high but still within normal limits, was recorded at this time (16·3 g. per cent.), but, on the evidence already reviewed, this may have indicated Hc. With rising blood values, the B.P. fell to normal. A second case, a child of 9 (No. 49), showed a B.P. of 130/110 9¾ hours after the burn. Both these cases have been described in the preceding report.

Summary

In Group IV the development of Hc. was extremely rapid, and the reduction in blood volume—indicated by the magnitude of the change in Hb. level—was extreme in many extensive cases, considerably more than half the original plasma volume being lost to the circulation within a few hours.

In spite of the extent of the burns—and the rapidity and degree of Hc. liable to occur—hypertension in the early hours after injury is again recorded. Nevertheless, at least in the patients transfused (they were the only ones who survived the shock period) there was no evidence of the progress of Hc. beyond the first 60 hours after injury.

HAEMOCONCENTRATION AND SHOCK—DISCUSSION

It has long been known that Hc. occurs in many forms of shock, both clinical and experimental. In this report, it has been shown that in patients with burns the degree of Hc. is roughly proportional to the extent of the burn. Attention has been drawn to cases showing disproportionate changes, and it is evident that factors other than extent of the injury may sometimes operate. Some indication of these factors may be obtained by consideration of the pathogenesis of the reduction in circulatory blood volume.

Oligaemia and Capillary Permeability

It is generally agreed that diminution of blood volume in burns shock is due to loss from the circulation of almost unaltered plasma. Some of this fluid may be lost from the body as exudate and blister fluid; the amount thus lost varies greatly from patient to patient. A considerable quantity escapes into the tissue spaces. This loss may occur locally at the site of the injury (Underhill *et al.*, 1930; Blalock, 1931); by others (e.g., Moon, 1942), it is believed to occur both locally and generally throughout the capillary bed. It is probable that the extent of the burn will influence greatly the local fluid loss, and that the degree (depth) of burning will have much less effect. Only capillaries damaged to an extent causing increased permeability, but at the same time compatible with active, though perhaps sluggish, circulation through

them, can contribute to progressive reduction in blood volume. The zone of capillary damage satisfying these criteria around a deep burn may be a little larger than a similar zone related to a more superficial injury similar in extent.

Extent and depth of the injury are not the sole governing factors in the production of Hc. (Fig. 10). Since blood volume is largely dependent on the establishment of a balance between the circulating plasma and the extracellular tissue fluid (Best and Taylor, 1939 (*a*)), it is evident that normally the passage of fluid from the capillaries into the tissue spaces is balanced by the return of fluid from the tissues to the blood stream. Reduction in blood volume will be directly related to the amount by which loss exceeds return. If loss is excessive, Hc. may be prevented by a corresponding increase in lymph flow. It is probable, therefore, that factors favouring stagnation of fluid in the tissue spaces will favour the occurrence of Hc. and a reduction of blood volume. Absence of muscle movement, laxity of tissues, and obstruction to the flow of lymph may operate in this way.

Muscular movement has been shown to be a powerful factor in promoting flow of lymph (White, Field and Drinker, 1933), and it is of interest to note that sedation by morphine in cases of extensive burns in our series seemed to hasten death. There is, however, no proof that the sedative increased the rate of Hc., and other factors may be involved.

Laxity of tissues allows the accumulation of greater amounts of fluid before a given tissue pressure is reached, and, therefore, before a balance is established between extra- and intravascular fluid. No conclusive clinical evidence relating these features to the degree of Hc. is at present available, but the use of pressure dressings (Siler and Reid, 1942) and the closed plaster technique (Glenn, Gilbert and Drinker, 1943) in the treatment of burns is based on these considerations.

Obstruction to the flow of lymph may occur directly or indirectly due to burning. Coagulation occurs sooner or later in the plasma distributed through injured tissues (Glenn *et al.*, 1943), and the fibrin slowly produced hinders lymph flow. Experimentally, progressive oedema may be in great part prevented by heparinizing the animal prior to burning. The burn may itself interfere directly with lymph flow, particularly if it is situated on the proximal part of a limb, and especially if the proximal part of the burn is deep. In such a case, the flow of lymph may be much affected and maximum accumulation of fluid and reduction of blood volume may be reached at a relatively early stage. This may be the explanation of unusually great reaction seen during the first week in Case 68 (Fig. 9). In this patient, an area of complete skin loss extended across the entire width of the arm, just above and below the antecubital fossa. Marked oedema of the forearm and hand occurred within 12 hours, at the end of which time the maximum Hb. level was recorded. The oedema had disappeared by the 5th day, and by this time a marked fall in Hb. level had occurred.

These considerations are based on the assumption that at least the greater part of the fluid from the circulation escapes through the damaged capillaries at the site of the burn. Underhill *et al.* (1930) and Blalock (1931) have shown that much loss of fluid occurs locally into the tissues after burns and other injuries. Moon (1942), on the other hand, supports the contention that there is a generalized increase in capillary permeability, though this view has been disputed by many other authors (e.g., Glenn, Muus and Drinker, 1943). Moon cites as evidence the escape of dyes circulating in the plasma at sites remote from the injury during the development of shock; he regards, also, as significant the post-mortem evidence of increase in capillary permeability—capillary engorgement, oedema and petechiae in the lungs and other organs. There is no doubt that extremely congested and oedematous lungs are usually seen in patients dying of shock after burns, and it is well known that petechial

haemorrhages are frequently seen in the viscera, especially under the endocardium. But these findings indicate only the ultimate result of the burn. They are not necessarily evidence of the primary derangement. The great Hc. occurring in the skin capillaries remote from the injury indicates loss of fluid from these vessels, but this may be the result of capillary anoxaemia, which itself is only secondary to oligaemia produced by loss of fluid into and around the injured area. In other words, the general may follow the local increase in capillary permeability. A vicious circle would thereby be established.

This conception is important from another point of view. Fishberg (1940) points out that if fluid exchange between blood and tissues functioned as usual, reduction in blood volume would be followed by resorption of fluid from, and dehydration of, the tissues. He regards the fact that a fall in plasma protein may not occur in such conditions as indicating general abnormality in fluid exchange. Clinically, however, all patients with any but minor burns complain of thirst, which is frequently very severe in those extensively burned. This suggests tissue dehydration. In addition, an initial fall in plasma protein may be recorded simultaneously with rising Hb. values. The evidence is therefore incomplete, and the general increase in capillary permeability may well be a secondary though perhaps an important occurrence, as already suggested.

Oligaemia and Shock

Primary shock was seen rarely during the period of this study, and in those patients in whom it was thought to be present on admission, it was impossible to exclude the presence of some reduction in blood volume. Whether or not some reduction is present, the disturbance in peripheral circulation associated with the fall in B.P. may predispose to general capillary upset and the development of secondary shock.

In all patients with severe burns in whom serial blood readings were recorded, Hc. was found to occur. This change is of significance only in that it reflects the basic upset—a reduction in blood volume. Hc. *per se* cannot be regarded as the significant feature in production of shock (Wood and Blalock, 1941). Serial blood readings are the most satisfactory practical method of assessing changes in blood volume, in spite of the various sources of inaccuracy (Underhill, 1927). This author cites inequality of distribution of red cells as one of these. From the evidence discussed above, it is apparent that venous blood shows less Hc. than capillary blood. In practice, it has been found that blood from either source is satisfactory in the control of administration of fluid.

Rising Hb. levels may be due to the addition of concentrated red cells to the circulation from a reservoir such as the spleen (Barcroft, 1925). Cannon and Izquierdo (1928) have shown that, in cats, excitement may increase the red cell count by as much as 25 per cent. The occasional occurrence of a slight rise in Hb. with a rise in B.P. may be explained on the basis of this mechanism alone. According to the evidence at present available (Brown *et al.*, 1944), the possible " haemoconcentration " so produced in man is of minor degree ; it may explain small changes, but it does not affect the broad principles already discussed.

Symptoms are probably only roughly proportional to the degree of Hc. present. It is difficult to correlate symptoms with blood changes, on account of the absence of precise knowledge of the magnitude of these changes ; but it is probable that only rough correlation exists. This does not imply that oligaemia is not wholly responsible for the symptoms, for similar reduction in blood volume need not affect different vascular systems to the same extent.

In reviewing the magnitude of the blood changes during the first 72 hours, it has been shown that the rate of fluid loss increases rapidly to a maximum in the first 12–18 hours. In no case was it found to progress beyond 72 hours, and in many it was of much shorter duration. If general increase in capillary

permeability be regarded as a secondary phenomenon, early transfusion must be regarded as prophylactic; but, by maintaining the blood volume and so preserving an efficient peripheral circulation, it favours continued loss of fluid from the damaged capillaries at the site of the burn. The amounts of plasma or serum found necessary to maintain blood volume are thus frequently much in excess of the calculated amount lost from the circulation in patients with burns of similar extent who are not transfused. The difference is obvious in the more serious cases, in which amounts of fluid considerably in excess of the normal total plasma volume may be required.

Blood Pressure, Vasoconstriction, and Shock

A low blood pressure is almost invariable in that fully-developed clinical state which is called "shock." In the early stages, however, when other significant changes are occurring, B.P. levels actually higher than normal may be found.

Attention has already been directed to the early occurrence of normal or elevated B.P.s in the various Groups of cases reported above, and to the occurrence of these normal or high levels with demonstrable Hc. From the practical point of view, it is important to assess the value of B.P. readings obtained in the first few hours after injury, in relation to the ultimate fluid requirements of the case.

Of a series of 68 patients in whom an initial B.P. reading was recorded within 3 hours of burning, the great majority showed a B.P. within normal limits. In 20–25 per cent. of the cases, the values were higher than those usually accepted as normal (Fig. 19).

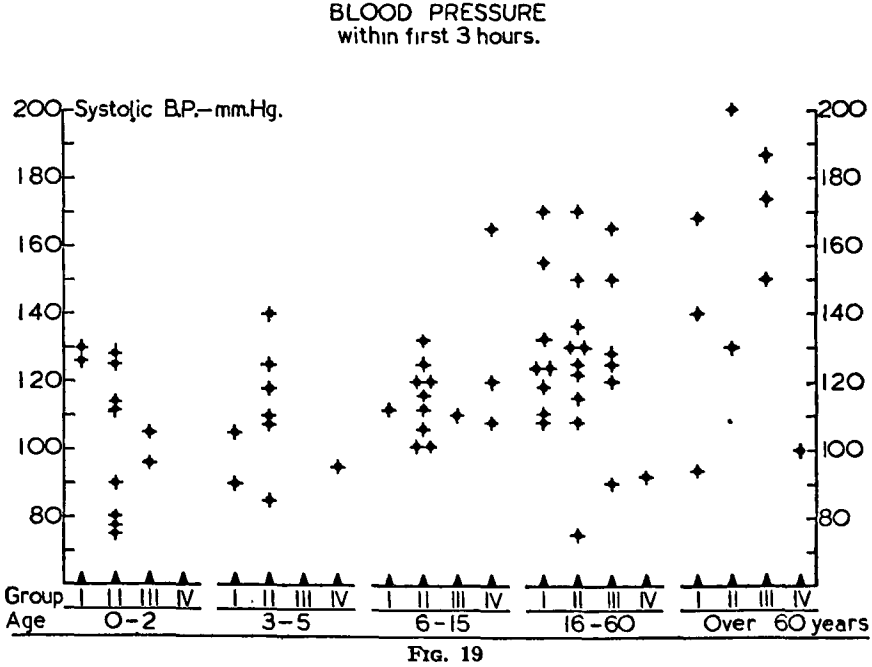

FIG. 19

In some of these patients, the unexpectedly high B.P. levels may not have been related to the injury, and, certainly, among the elderly adults, several cases of essential hypertension were encountered. But in many, even those with a diseased vascular system, subsequent stabilization of B.P. at significantly lower levels has been recorded.

In some, the initial high B.P. was probably due to excitement, a factor difficult to assess. The possible effect of the associated vasoconstrictor activity on the splenic reservoir has already been discussed. In such cases, the rises in Hb. and B.P. may be results of the same process.

The phenomenon of vasoconstriction and a normal B.P. in the presence of a reduced blood volume and symptoms of shock has been noted for many years. Meltzer (1908) recorded the occurrence of all the clinical features of shock in the experimental animal, yet there was little if any reduction in B.P. Mann (1914) pointed out that there is no vasomotor depression or fatigue in shock, and that the peripheral vessels are constricted. This vasoconstriction favours the maintenance of normal B.P. in the presence of a reduced blood volume.

Since Hc., and presumably therefore a reduced blood volume, may be associated with a normal or high B.P., and since (Fig. 19) patients severely burned (Groups III and IV) may share in the high B.P. levels recorded above, it would seem that demonstration of Hc. is a more reliable guide than the B.P. to treatment, because transfusion, to be of maximum benefit, must be given early.

The misleading information which may be given by B.P. is illustrated by Case 52, a youth of 14, burned over 31 per cent. of his body surface. The B.P. one hour after injury was 165/114. It fell to 76/50 at 14 hours, and the patient died with clinical features of severe shock, the need for early transfusion not having been fully appreciated at that stage of the investigation.

In conclusion, it must be emphasized that a fall in blood pressure is a secondary phenomenon and indicates a relatively late stage in the circulatory failure which follows injury.

Peripheral vasoconstriction favours selective distribution of the available blood when the total circulating volume is reduced. This is beneficial in so far as it improves the circulation in the viscera, but ill effects may follow interference with temperature regulation. About 85 per cent. of the total heat loss from the body occurs via the skin (Best and Taylor, 1939(*b*)). This loss is reduced by vasoconstriction, reduction in blood volume, and reduced circulatory rate—all conditions obtaining in the severely burned patient. In burns shock, therefore, heat production may exceed heat loss on this basis alone. An additional factor operating in the same direction is the extensive leathery coagulum found in the severely burned patient, and it would seem that in such cases conditions are very favourable for the development of hyperpyrexia.

In this study, a (mouth) temperature of over 105° F. has been recorded in seven cases, and in two it exceeded 107° F. All but two of the patients had burns involving more than 40 per cent. of the body surface; these two were children with burns, chiefly whole skin loss, involving 10 and 20 per cent. body surface, respectively. In all cases, the hyperpyrexia was recorded between the 10th and the 31st hour after burning. In three cases, shock was inadequately treated, and a cold skin was present for a variable period. In three, Hc. was apparently adequately dealt with from the beginning; the skin appeared flushed and hot. It therefore appears that, though vasoconstriction and skin loss may favour the development of hyperpyrexia, some other factor may also be involved, e.g. reaction to plasma or serum.

It is difficult to justify any special application of warmth to the shocked patient. The skin is cold, but application of warmth to it, if effective in producing active skin circulation, will do so at the expense of tissues more sensitive to ischaemia. In addition, though the vasodilatation so produced restores the function of the skin in temperature regulation, the environment renders the restoration ineffective. If the heat is ineffective in improving skin circulation, it increases the metabolism without increasing the transport of metabolites. Neither result is desirable.

The only treatment which will maintain adequate circulation both in the skin and internal organs, and so prevent the ill effects of ischaemia, is transfusion. The special application of warmth to the skin seems inadvisable, at least until the additional circulatory requirements have been anticipated by this means.

ANAEMIA IN BURNS

It has long been known that anaemia may occur in the burned patient but the nature of the related blood changes, and their pathogenesis, have been little investigated.

The present study includes data on the anaemia (or anaemic trend) after burns of varying severity (Groups I–IV *supra*), together with observations on changes in red cell size, alterations in saline fragility, the reticulocyte count plasma bilirubin, and also haemoglobinaemia and haemoglobinuria.

The Term "Anaemia"

Since the patients' red cell or haemoglobin levels before burning were not known, a condition of "anaemia" has been held to exist wherever serial blood estimations show a significant depression in these values; or when the post-burn level continues strikingly below the normal average.

TIME OF DEVELOPMENT, AND MAGNITUDE OF ANAEMIA

In recording the findings in this section, red cell levels have been indicated by the values obtained for haemoglobin; and, in the accompanying Figures the scale has been reduced by half, compared with that used in the previous section.

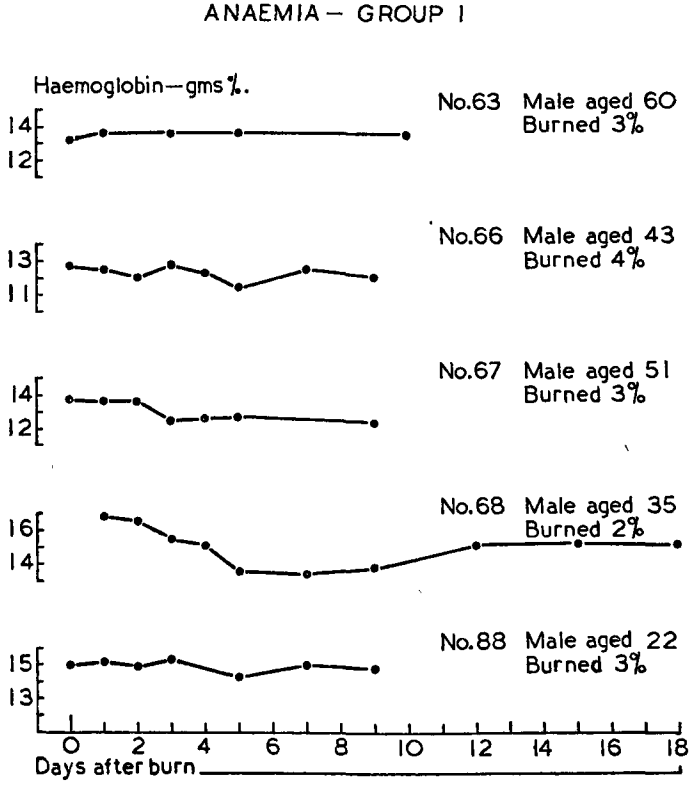

FIG. 20

ANAEMIA—GROUP I. (Burns 0–5 per cent. of the body surface.)

Changes in the Hb. level in 5 patients during the first 9–18 days after burning are recorded in Fig. 20. Only two show a significant variation (Nos. 67 and 68), and in Case 68 the levels recorded between the 5th and the 9th day indicate a temporary phase of anaemia. The others show either no change at all (Case 63), or variations from day to day such as may occur in the normal subject (Brown *et al.*, 1944).

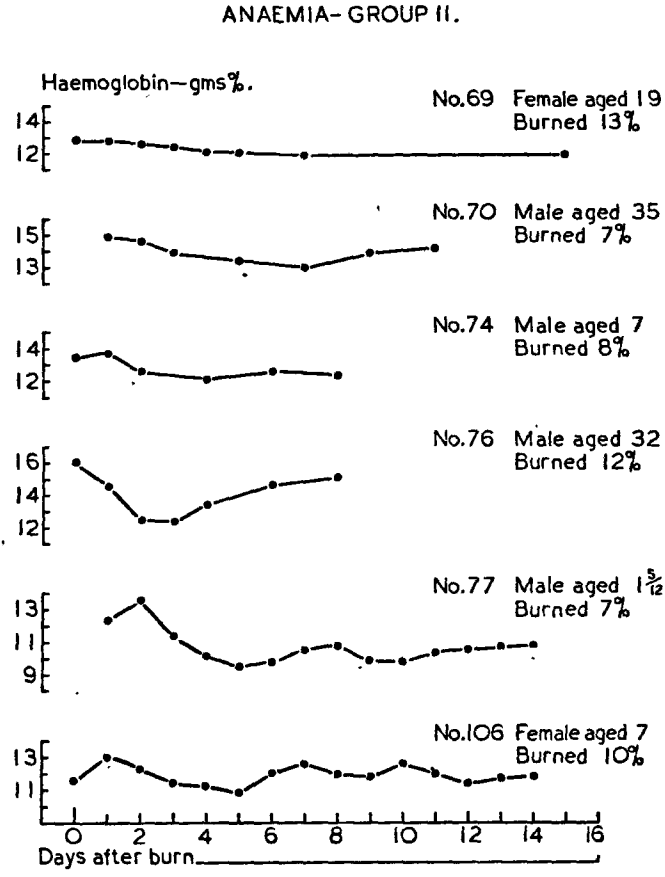

FIG. 21

ANAEMIA—GROUP II. (Burns 6–15 per cent. of the body surface.)

Ten cases are described in this group; of these, 4 received transfusion of serum or plasma. Those not transfused are considered first (Fig. 21).

Cases 69, 74 and 106 show no significant change, in spite of the extent of burning, while Cases 70, 76 and 77 show a definite fall in Hb., with a subsequent rise. (All blood samples from Case 77, and all but the first three from Case 106, were capillary.)

Four cases transfused during the shock period are illustrated in Fig. 22. The shaded area in each indicates the amount of fluid transfused, and the duration of the transfusion. Case 11, in this Group, is shown in Fig. 32 (p. 156). Only two of the four patients recorded in Fig. 22 show an anaemic phase. It is transient. (In Case 21, all blood samples except the first three were capillary.)

In all the cases of Group II, the anaemia, if any, has been temporary and of short duration. The general tendency follows that shown by Case 68 (Group I). The fall in Hb. is maximal by the 3rd to the 7th day (usually the 7th), and levels at which stabilization subsequently occurs are reached by the 7th–15th day.

ANAEMIA–GROUP II.

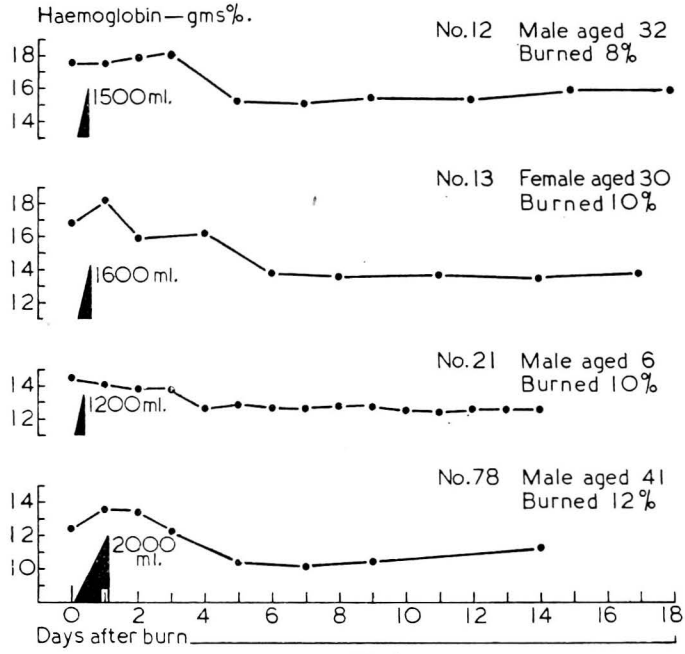

FIG. 22

ANAEMIA-GROUP III.

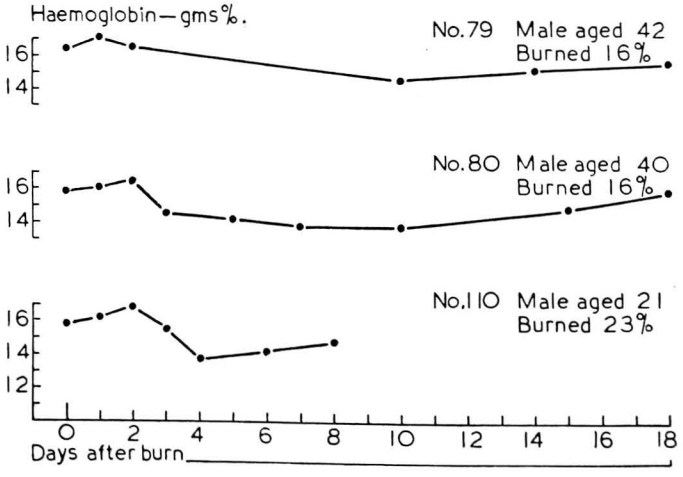

FIG. 23

ANAEMIA—GROUP III. (Burns 16–30 per cent. of the body surface.)

Few patients in this group were not transfused in the shock period, and only three cases are described here (Fig. 23). All show a phase of temporary anaemia. In Case 110 the burns were extensive but superficial. His discharge on the 9th day precluded further observations.

Six cases given serum or plasma during the shock period are described here (Figs. 24 and 25).

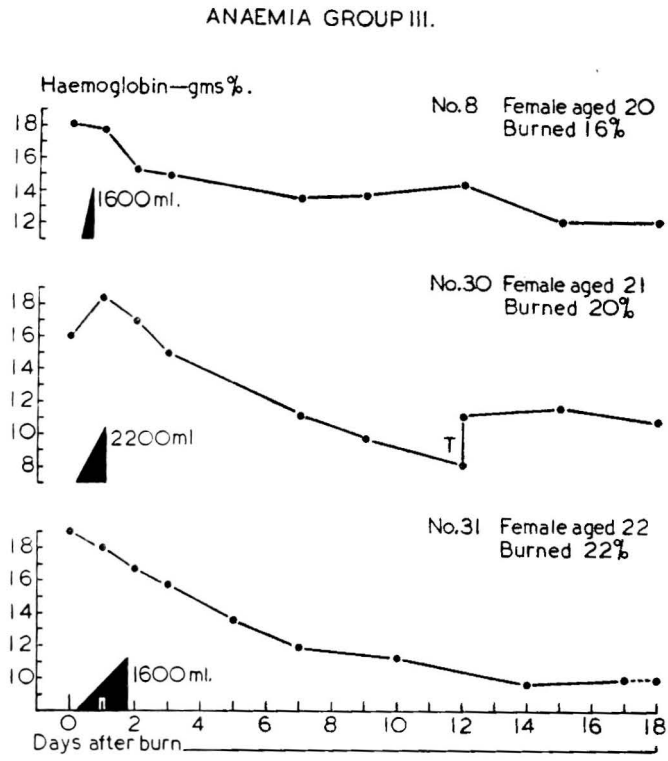

FIG. 24

Case 8 shows an initial fall, maximal by the 7th day and followed by a rise to the 12th day (thus conforming to the type of temporary anaemia previously seen). After the 12th day, a second fall occurred, resulting in anaemia from which recovery was not recorded during the following six weeks. During the first 5 weeks, mild and irregular pyrexia was noted daily. At the end of this period a Hb. level of 10·5 g. per cent. was reached—the lowest recorded. By the end of the 6th week, pyrexia had disappeared, and from then onwards a spontaneous rise in blood values occurred. A Hb. level of 12·9 g. per cent. was reached on the 9th week after burning.

In none of the other Cases (Figs. 24 and 25) was a phase of temporary anaemia recorded. A gradual fall, however, occurred from the 2nd or 3rd day, and by the 10th day abnormally low levels were present.

In Case 30 (Fig. 24), a maximal level is recorded on the 1st day—due to Hc. During the following 11 days, the Hb. concentration dropped from 18·4 to 8·2 g. per cent. At this point, transfusion of whole blood was given. The patient's subsequent course was one of prolonged anaemia, without complete return to normal, during the following four months. During the first month,

her burned surfaces were unhealed and she showed daily pyrexia, varying in degree. Three blood transfusions were given during this period, and no evidence of spontaneous rise in blood values was seen. During the second month,

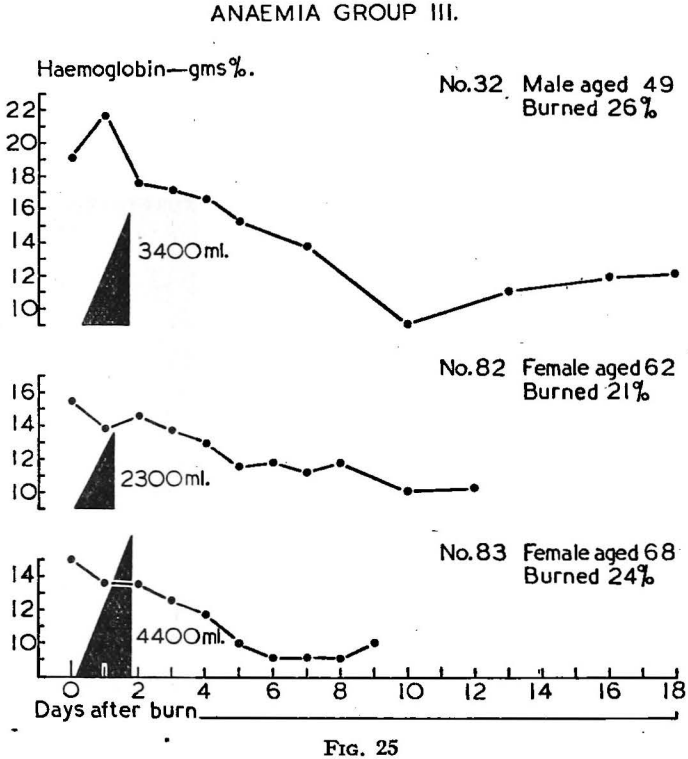

FIG. 25

the mild febrile attacks disappeared, though many areas were still unhealed; and from the beginning of the second month, a slight but sustained spontaneous rise in blood values was recorded. A Hb. level of 11·2 g. per cent. was present eight weeks after burning.

In Case 31 (Fig. 24), a steady fall in Hb. values is recorded during the first 14 days. Little alteration occurred during the third week, but by the end of the fourth week the Hb. level reached 7·7 g. per cent., and a transfusion of whole blood was given. During the second month, further transfusions were necessary to maintain a Hb. level above 10 g. per cent. During the third month, Hb. levels were maintained at about 12 g. per cent. without transfusion, and in the fourth month quite normal levels were reached spontaneously (13·6–14 g. per cent.). During the first two months, the general course was pyrexial, but towards the beginning of the third month the temperature gradually settled. A temporary exacerbation of fever occurred between the 9th and 10th weeks, due to a respiratory complication, but thereafter the course was afebrile.

Case 32 (Fig. 25) shows a rapid drop in blood levels, the lowest Hb. value being recorded on the 10th day. From the 13th day until the 50th day, no significant alteration in Hb. level was recorded (10–11 g. per cent.). By the beginning of the third month, a slight spontaneous rise in Hb. occurred (12 g. per cent.) and this rise was maintained until the beginning of the fourth month, when normal blood values were recorded (Hb. 16 g. per cent.).

During the first seven weeks, the general course of this case was pyrexial a temperature of 100–101° F. being noted daily. Practically no rise in temperature above normal was recorded thereafter.

Cases 82 and 83 (Fig. 25) are similar in many respects. Both elderly women, they sustained burns differing little in extent or severity. Both survived the shock period, to die during the second week; and both developed a significant degree of anaemia. In neither case was any sustained rise of Hb. apparent before death.

Summary

A temporary reduction in Hb. values is recorded in three cases of relatively mild, though fairly extensive, burns. These patients did not receive transfusion during the shock period.

Of the patients more severely burned—and transfused—a phase of temporary anaemia occurred in one; it was followed by a more chronic phase. In all the other cases no temporary phase was seen. Instead, a moderate degree of anaemia developed progressively in the first 14 days, and the low levels were maintained for a month or more. Recovery did not occur spontaneously during the febrile period.

ANAEMIA–GROUP IV.

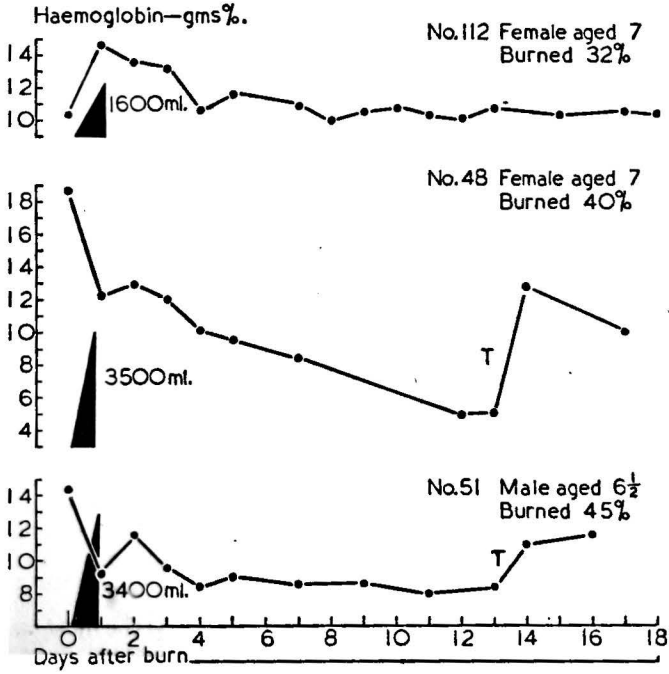

FIG. 26

ANAEMIA—GROUP IV. (Burns over 30 per cent. of the body surface.)

Patients with burns involving more than 30 per cent. of their body surface who were not given plasma or serum transfusions during the shock period did not survive beyond the second day, and the development of anaemia has not been recorded.

Six cases are described to illustrate the blood changes which may follow very severe and extensive burns.

Case 112 (Fig. 26) though burned extensively and moderately severely (32 per cent. whole skin loss), showed remarkably little systemic upset clinically, and remarkably little derangement in blood values. Stabilization of Hb. at a level of 10–11 g. per cent. occurred from the 4th day. (All but the first two blood samples were capillary.)

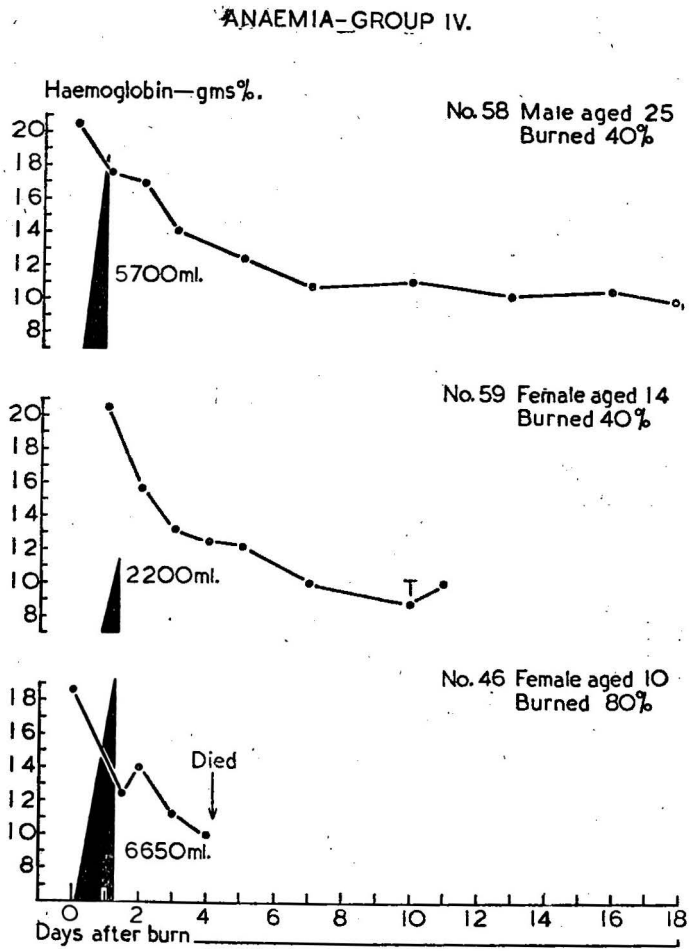

FIG. 27

Case 48, a girl of 7 years, burned 40 per cent., showed the most severe degree of anaemia recorded in any of a series of 33 cases burned over more than 30 per cent. of the body surface. On the 12th day, the Hb. reached a level of 4·8 g. per cent. (R.B.C. 1·57 million per c.mm.). The case is exceptional also, in that death occurred at the end of the third week, due to agranulocytosis. A more detailed statement of the blood findings in this case is made later (p. 161).

Case 51 (Fig. 26) shows the development of anaemia by the 4th day and the maintenance of a Hb. level of about 8·5–8·0 g. per cent. until blood transfusion on the 13th day. This transfusion was followed by little alteration in blood values until about the end of the third week. The gradual development of

anaemia necessitated transfusion again at the end of the first month. At the end of the sixth week, the Hb. level was 9·4 g. per cent., and the child died with hypoproteinaemia and with extensive unhealed burned areas.

Case 58 (Fig. 27) showed a moderate degree of anaemia by the 12th day. A gradual fall in blood values occurred into the fourth week, when blood transfusion was given. The lowest haemoglobin value reached was 9·55 g. per cent. Transfusion raised this level to 12·4 g. per cent., and by the middle of the second month no significant alteration had occurred. By the end of the second month, normal levels were reached spontaneously. In spite of the extensive nature of the burn in this case, a temperature reading above 100° F. was recorded on only three occasions after the 14th day.

Case 59 (Fig. 27) was given blood transfusion on the 10th day. In spite of two more transfusions, the Hb. level two months after burning was 6·9 g. per cent. Seen a year later, with a portion of her burn not yet healed, this patient had a Hb. concentration of 9·3 g. per cent. During her six months' stay in the Burns Unit, this patient was never completely afebrile for more than 24 hours. She was subsequently transferred to an Emergency Medical Services Hospital.

Case 46 (Fig. 27) shows a fall in haemoglobin levels more or less parallel with that recorded in the previous case. Death occurred on the 4th day. This case is discussed in more detail in connection with studies of red cell fragility.

Summary

In this Group, though transfusion was sometimes given, Hb. values below 8 g. per cent. were rarely recorded in the first three weeks. Most of the patients showed a tendency to persistent anaemia lasting a month or more. In Case 58, the anaemia was relatively mild and spontaneous recovery occurred by the end of the second month. Little febrile upset was recorded in this patient. In Case 112 no anaemia is demonstrable. This patient was undoubtedly the least severely burned of all those recorded in this Group.

An extreme degree of anaemia is recorded in one Case (Case 48). It is possible that some factor not operative in the other patients was in part responsible for the apparently disproportionate anaemia, as evidence of other haematological upset also exists. The patient died of agranulocytosis.

Comment

In the patients with small burns (Group I), only one of five showed a definite fall in blood values during the first week. In Group II, at least five of ten cases showed the phase of temporary anaemia. In Group III, all three of the patients with milder burns showed a temporary drop in Hb. These patients were burned superficially though fairly extensively; they were not given saline or plasma in the shock period, and they showed no general clinical upset. In these cases, a closely similar pattern of change is followed by all: the phase of Hc. disappears, and the Hb. level continues to fall usually until the 5th–7th day, after which there is a gradual rise. The level at which stabilization subsequently is shown to occur is reached about the 12th–14th day.

In patients burned over 20 per cent. of the body surface, the temporary phase of anaemia followed by quick recovery has rarely been noted. In Group III there is seen for the first time a progressive fall in red cell values from the shock period until about the 10th–14th day. Thereafter there is a marked tendency for a state of anaemia to persist for a month or more. Spontaneous recovery from this state is usually associated with disappearance of fever, and progressive healing of the raw areas.

Patients in Group IV, with one exception, showed the most severe reaction. Red blood cell levels about 50 per cent. of normal were reached on the 10th–14th day. Thereafter, almost all cases remained more or less anaemic until the burns were well on the way to being healed.

In the more serious cases in Group III, and the great majority of those in Group IV, blood transfusion was required, either at about the 12th day after burning or during the phase of chronic anaemia which followed.

From consideration of these findings, there appear to be three types, or phases, of anaemia which may follow burns :—

(i) A phase of temporary anaemia, which is maximal about the 5th–7th day and which has disappeared by the 10th–14th day.

(ii) A phase of rapidly developing and moderately severe anaemia, less readily reversible and reaching a maximum in 10–14 days.

(iii) A phase of chronic anaemia, the duration corresponding roughly with that of the febrile period, after which gradual and spontaneous recovery occurs.

Associated Findings

Alterations in Mean Corpuscular Volume (M.C.V.)

Only a preliminary report on the findings under this heading is attempted here, and results of further analyses of the changes in cell volume, diameter and thickness will be reported at a later date.

In general, the M.C.V. tends to be relatively high during the first few days after burning, and during this time rapid fluctuations tend to occur. After the first week, changes in cell volume are seen in patients severely burned ; these alterations occur gradually, and the tendency is towards an increase in

TABLE XVIII

	Case No.	*Fig.*	*Serum or Plasma (ml.)*	*Variations in M.C.V.—(c.microns)*
Group I	63	20	—	Initial M.C.V. 99 ; rise to 107–109 on first to fifth day. Subsequent stabilization 96–100 from seventh to twenty-eighth day.
	66	20	—	Initial M.C.V. 98 ; rise to 107 by sixth day ; fall to 87 on 9th day.
	68	20	—	M.C.V. 95, 99, 105, during first 4 days ; stabilization at 95 from twelfth to eighteenth day.
Group II	12	22	1,500	M.C.V. 101, 101, 105 during first day ; stabilization at 87–93 from fifth day.
	13	22	1,600	Fall from 108 to 90 during first three days ; stabilized at 92–98 for month.
Group III	80	23	—	Stable at 96–100 during first two days. Rise to 110 on third day followed by gradual fall and stabilization at 93 on tenth and fifteenth days.
	8	24	1,600	No significant variation at any time ; no reticulocytosis.
	30	24	2,200	Rise from 100 to 110 in thirty-six hours ; thereafter stable at 100 till twelfth day, when blood transfusion was given.
	31	24	1,600	No significant upset till fourth week—reticulocytosis.
	32	25	3,400	M.C.V. maximum at 99 in shock period ; fell to 90 on seventh and tenth days ; rose to 100 later when anaemia developed.
Group IV	48	26	3,500	Initial level 75 ; rose to 98 in twenty-four hours.
	58	27	5,700	For details see Fig. 32 (p. 156).
	59	27	2,200	Gradual rise from 88 at twenty-four hours to 99 on eighth day.
	46	27	6,650	M.C.V. 104–94 in first eighteen hours ; rise to 108 at fifty-four hours and maintained till fourth day (death).

M.C.V. at a period when the patient is anaemic and a degree of reticulocytosis is present. Anaemia has existed, however, without any demonstrated alteration in the average volume of the red cells. A summary of the changes in M.C.V. is given in Table XVIII. Only cases already discussed, and illustrated graphically earlier in this section, are described.

Summary

A rise in M.C.V. tends to occur during the first few days after burning. It is a very variable feature, and the change demonstrated here is only very roughly proportional to the severity of the burn. No constant relation between alteration in M.C.V. and development of anaemia has been shown. The change does not appear to be related to transfusion of serum or plasma.

Variations in Reticulocytes

All degrees of reticulocytosis up to about 12 per cent. have been recorded in the cases already described in this report. A summary of the related findings in some of these cases is given in Table XIX :—

TABLE XIX

Case No.	*Fig.*	*Maximum Reticulocytosis**	*Rise in M.C.V.*	*Notes*
8	24	No rise	No	Anaemia present.
11	32	No rise	No	No anaemia.
12	22	No rise	No	No anaemia.
31	24	5 per cent. on 28th day	Yes	Anaemia present.
32	25	No rise	No	Slight anaemia.
48	26	11 per cent. on 11th day	Yes	Extreme anaemia.
58	27 and 33	6·4 per cent. on 9th day	Yes	Marked anaemia.

* In the cases recorded here, reticulocyte counts were performed on all specimens of blood from which Hb. values were determined (see Figures above), and every third or fourth day subsequently for at least five weeks.

The more marked reticulocyte responses were noted in patients in whom anaemia developed rapidly, and in these the reticulocyte response occurred early (Cases 48 and 58).

Reticulocytosis is not responsible for the rise in M.C.V. found to occur frequently in the first week. No case showed any rise in reticulocytes during this period.

Bilirubin

The variations in plasma bilirubin, and their significance, are discussed by Anderson and Semeonoff (p. 166 below). The inter-relation among the changes in bilirubin, red cell levels, M.C.V., reticulocytes and erythrocyte fragility will be considered when alterations in saline fragility have been dealt with.

Red cell fragility (saline) : Haemoglobinaemia and haemoglobinuria

This section comprises only a preliminary report on the results of serial quantitative estimations of saline fragility in cases of both mild and severe burns. These results are summarized in the accompanying figures (Figs. 28 and 29) as variations in the concentration of sodium chloride in which 50 per cent. haemolysis occurs, that is, as variations in the Median Corpuscular Fragility (M.C.F.). The curves from which the M.C.F. values were obtained by interpolation are, with one exception (Case 46), not shown here.

Variations in Median Corpuscular Fragility (M.C.F.)

In seven patients, fragility tests were made on frequent samples of blood during the shock period, and thereafter at intervals of about three days until the end of the fourth week. The occurrence of death on the fourth day in Case 46, and on the twenty-second day in Case 48, limited the period of investigation in these patients. Only the changes occurring during the first 15 days are illustrated here (Figs. 28 and 29).

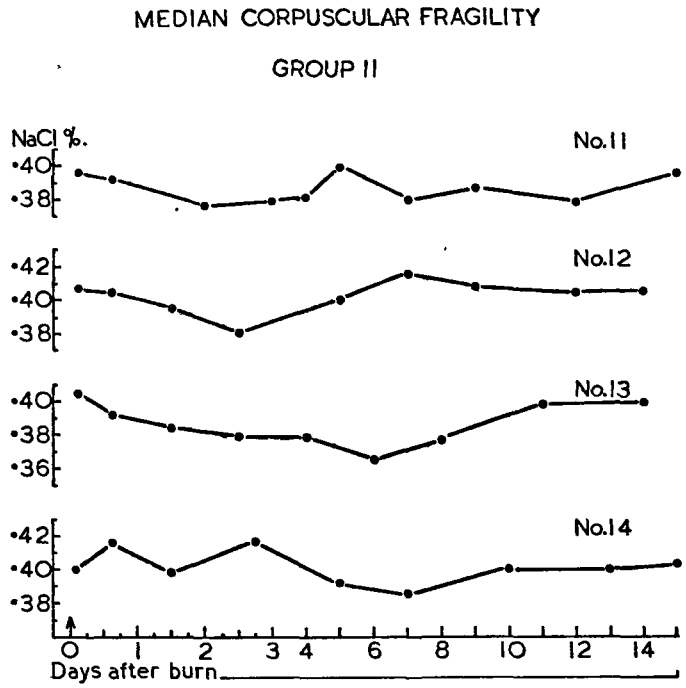

FIG. 28

M.C.F. in normal subjects

In a series of 23 apparently normal adults, comprising hospital staff, medical students and blood donors, the average M.C.F. was 0·408 per cent. NaCl, with a range of from 0·362 to 0·434 per cent. NaCl.

Serial investigations over a 4-day period in three normal adults have given the values indicated in Table XX :—

TABLE XX

Subject	*M.C.F. on 4 consecutive days*				*Range per cent. NaCl*
	1	*2*	*3*	*4*	
1	·431	·435	·435	·432	·004
2	·432	·427	·428	·434	·008
3	·418	·419	·424	·420	·006

M.C.F. in Group II (burns involving 6–15 per cent. of the body surface)

The changes in fragility found in four patients with burns involving 6–10 per cent. of the body surface are shown in Fig. 28. As isolated values, the figures obtained for M.C.F. at any stage in the shock period are within normal limits, but the serial records of every case show a range of variation greater than has yet been found by the same method in normal subjects. It would appear, therefore, that even in cases of minor burns a significant alteration in saline fragility may occur. It may be necessary to review this comparison when more values for normal subjects have been obtained.

If a general tendency to change in the M.C.F. is exhibited after burning, it is towards a reduction during the first 3–4 days. The fall is not sustained, and the subsequent rise may equal or exceed the initial fall.

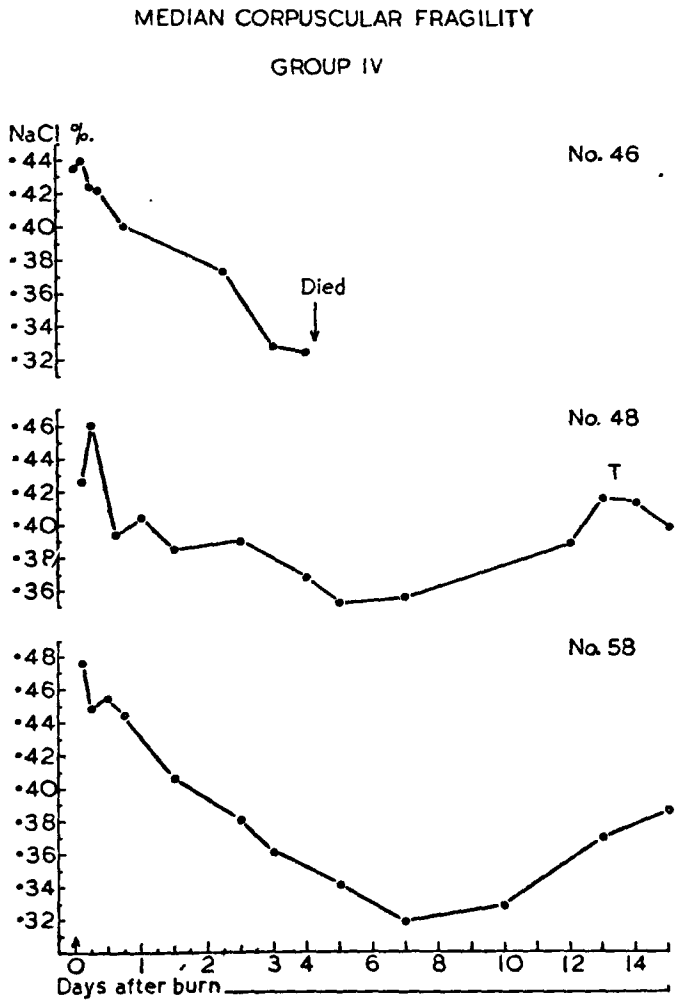

FIG. 29

M.C.F. in Group IV (burns involving over 30 per cent. of the body surface)

In Fig. 29 are shown, drawn to the same scale, the variations in M.C.F. encountered in three patients very severely burned.

In each, the initial values are much above normal. A rapid fall occurs almost at once, and within 36 hours figures within normal limits are recorded in all cases. The reduction in M.C.F. continues more or less regularly until the fifth day (Case 48) and seventh day (Case 58), when the levels are markedly subnormal. The M.C.F. in Case 46 a few hours before death on the fourth day is as low as any recorded in the patients who survived the period reviewed. In the latter, the fall in M.C.F. ceased spontaneously on the fifth and seventh days, respectively, and thereafter a rapid rise towards normal is recorded.

It is of interest at this stage to compare the changes found in Group II (Fig. 28) and in Group IV (Fig. 29). In the former, there is a tendency for a fall to occur during the first 3–7 days and for a rise to follow, previous levels being reached or exceeded by the tenth to fifteenth day. In Group IV, high initial levels are replaced by the lowest recorded levels on the fifth to seventh day, after which a rise occurs. In Cases 48 and 58, during the second and third weeks, levels in the upper limits of normal were reached (not shown on graph).

Thus, burns mild and severe may show the same type of variation in M.C.F., the magnitude of the changes being greater the more severe the burn. In the severe cases, the initial levels are much above normal. In the milder cases, though the initial levels are within normal limits, it is impossible to say whether the values recorded are normal for each patient. As in the case of Hb. levels, it has not been possible to relate the initial levels to the intermediate or final values—even at the end of four weeks, because there is evidence that abnormal variations in fragility may occur for several weeks after the injury.

Fragility in Relation to Haemoglobinaemia and Haemoglobinuria

In estimating saline fragility, it was found impossible in some cases to obtain a haemoglobin-free saline, even in concentrations up to 0·9 per cent. Above a certain salt concentration, the amount of haemolysis persisted unchanged. (The degree of this " residual haemolysis " is expressed below as a percentage of the value for complete haemolysis.) The saline solutions were checked by titration, and fresh stock solutions were prepared ; but the residual haemolysis occurred as before. The bloods in question could not be added even to 0·9 per cent. saline without the occurrence of haemolysis.

Allied to this finding was the observation that, among the routine samples of blood collected through a dry sterile needle into a dry heparinized tube, were a few which showed gross haemolysis. All these specimens were obtained from patients extensively burned. In addition, when specimens of urine could be obtained from these patients during the shock period, they contained blood pigment.

A similar haemoglobinaemia and haemoglobinuria has been reported recently after severe burning, by Cope and Rhinelander (1943) ; and a recent account of alteration in erythrocyte fragility associated with this condition has been given by Shen, Ham and Fleming (1943).

Details of our cases showing haemoglobinaemia are given in Table XXI.

All the patients showing Hb. in the plasma in large amounts were very extensively and severely burned, and all except Case 46 died within 12 hours of the injury. It is possible that other cases had traces of Hb. (less than 0·1 g. per cent.) in the plasma, but no investigation was made into this matter.

TABLE XXI

Case	*Extent of Burn (per cent. of body surface)*	*Hb. g. per cent. Plasma*	*Time (Hours)*	*Haematuria*	*Fragility*	*Notes*
45	75–80	Slight	1¾	1 spec. 8 hrs.	Fig. 30 No. 7	—
46	80	1·54 0·50 0·58 0·38 trace	1½ 3½ 5 8 18	Specimen obtained at 16 hours. None in spec. obtained at 48 hours.	Figs. 29 and 31.	Blister fluid at 3½ hours contained 0·45 g. per cent. Hb.
84	90	Not obvious. 1·2 1·1	½ 2½ 5½	Marked in only sample obtained.	Fig. 30, Nos. 5 and 6.	Capillary sample. Venous sample. Venous sample.
85	70	Not obvious. Rapid lysis in vitro. 0·225	2 5½ 9	Not seen.	Fig. 30, Nos. 1, 2 and 3.	

Case 85 is of special interest, because it was noted that the second sample of blood showed no initial haemolysis but that haemolysis developed rapidly *in vitro*. The haematocrit tube, filled and centrifuged within 5 minutes of withdrawal of blood, showed no obvious Hb. in the plasma, but when sedimentation occurred in the specimen, which had been subject to no undue manipulation, marked Hb. staining of the plasma was found to be present 1½ hours later.

Further Observations on Red Cell Fragility and Residual Haemolysis

Detailed results of the fragility tests performed on samples of blood from patients very extensively burned, and showing residual haemolysis or haemoglobinaemia, are recorded in Fig. 30.

In Case 85 (Fig. 30, Nos. 1–3), at 2, 5½ and 9 hours, an increase in M.C.F. from 0·424 per cent. NaCl to 0·466 per cent. NaCl is seen. In specimens 2 and 3, residual haemolysis of about 5 per cent. occurs in concentrations above 0·50 per cent. and 0·54 per cent. NaCl, respectively. In the sample No. 3, slight haemoglobinaemia was observed (Table XXI).

In Case 115 (Fig. 30, No. 4) the only sample, obtained at 5½ hours, shows a M.C.F. much increased (0·480 per cent. NaCl) and a residual haemolysis of about 5 per cent. The size of the blood sample precluded more than a capillary haematocrit estimation in addition to the fragility test. No gross haemolysis was evident in the fresh specimen, and a single sample of urine showed no haemoglobinuria.

In Case 84 (Fig. 30, Nos. 5-6), the M.C.F. is already above normal at 2½ hours (0·442 per cent. NaCl) and it rises at 5½ hours to a very high level (0·476 per cent. NaCl). On both occasions, 10–15 per cent. haemolysis persists in the higher saline concentrations. On both occasions, haemoglobinaemia was marked (Table XXI).

In Case 45 (Fig. 30, No. 7) only one sample of blood was obtained. It shows a M.C.F. above normal (0·440 per cent. NaCl) and 5 per cent. haemolysis in all saline above 0·54 per cent. Slight haemoglobinaemia was recorded in this sample, and haematuria was marked.

In Case 56, burned 75 per cent., a sample of blood obtained at 1 hour shows a M.C.F. within normal limits (0·408 per cent. NaCl) and no residual haemolysis.

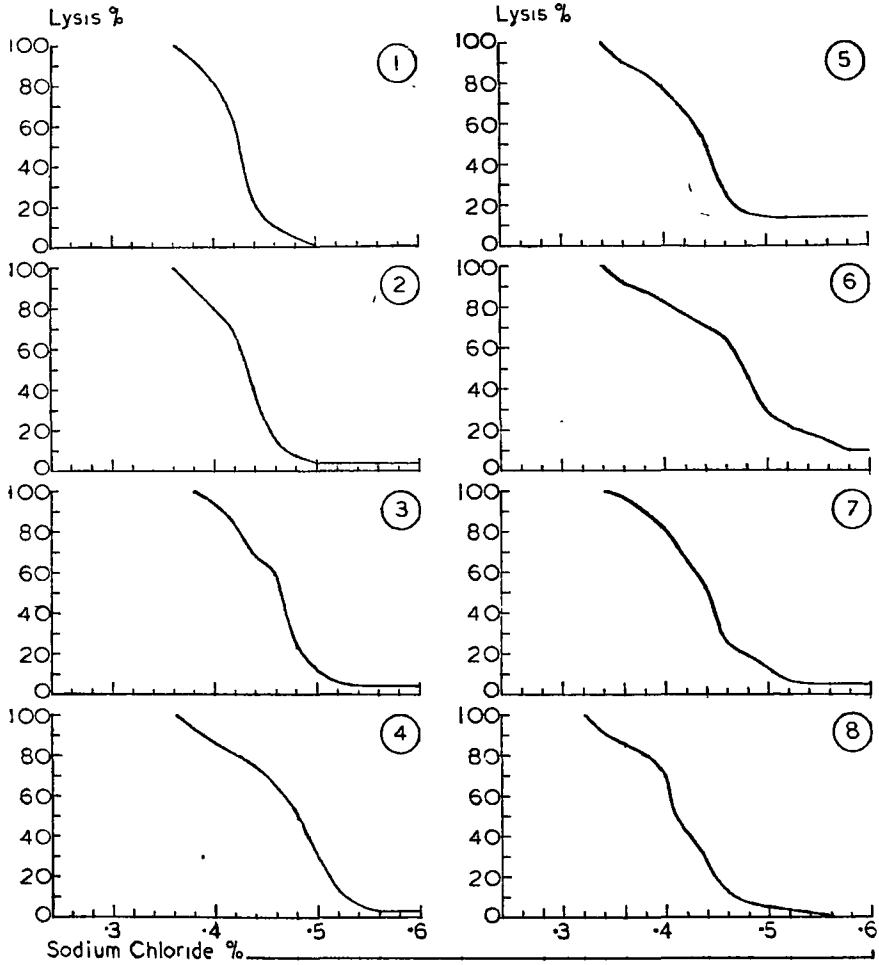

FIG 30

In seeking an explanation of the residual haemolysis, two possibilities have to be considered :—

(*a*) that it was brought about by manipulation of the blood in the microburette, or by this factor in association with (*b*) ;

(*b*) the presence of some degree of haemolysis in the fresh blood.

It seems very unlikely that injury of the cells by manipulation played a part, for the following reasons : The method used in these cases was the same as that employed throughout the entire series, and no residual haemolysis was encountered in any patient with mild burns. No haemolysis was noted after manipulation in the microburette if it were not previously present. As will be seen later, the most careful addition of the blood to the saline from a chemically clean pipette did not alter the results in any way.

It seems equally unlikely that the residual haemolysis noted in the tests was due to the Hb. present in the fresh plasma. In Case 115 (Fig. 30, No. 4), 5 per cent. residual haemolysis occurred, but the fresh specimen showed no gross haemolysis. The maximum plasma Hb. recorded in the whole series is 1·54 g. per cent. (Case 46, Table XXI). Since the whole blood (with a haematocrit of 46 per cent.) was used for the fragility test, the plasma contained only 0·83 g. Hb. per 100 ml. blood, or 4·5 per cent. of the total Hb. present at that time (18·6 g. per cent.). Yet the same sample of blood showed a residual haemolysis amounting to more than 15 per cent. in all strengths of NaCl above 0·52 per cent. The initial haemolysis in this case is not responsible for the residual haemolysis found in the test.

This conclusion is also borne out by the fuller analysis of the readings obtained with the bloods from Case 84 (*see* Table XXI and Fig. 30, Nos. 5–6). The first sample (capillary blood) showed no haemolysis; the second and third (venous blood) showed an equal amount of haemolysis in their plasma, though they differed in their red cell content. It is seen from consideration of the facts related to these two samples of blood (Table XXII) that the plasma haemoglobin cannot account for more than 2·5 per cent. lysis in the fragility tests.

TABLE XXII

Case 84

Blood Spec.	*Hb. g. per cent.*	*Haematocrit.*	*Plasma Hb. per 100 ml. plasma.*	*Plasma Hb. per cent. of total Hb.*	*Residual lysis in Fragility Test.*
2 (Fig. 30, No. 5)	19	60 per cent.	1·2 g.	2·5	15 per cent.
3 (Fig. 30, No. 6)	21·5	70 per cent.	1·1 g.	1·5	10 per cent.

To confirm this conclusion, a known amount of plasma was added to 0·85 per cent. saline as in the fragility test. Figures corresponding exactly with those obtained by calculation were obtained from the blood sample.

In order to make still more certain that manipulation was not responsible for the residual haemolysis, the following experiment was carried out with Specimen No. 3 (Fig. 30, No. 6):—

1·0 ml. blood No. 3 was added to 1·0 ml. 0·9 per cent. saline, using a chemically clean pipette, and the mixture was gently inverted several times.

A control sample undiluted was pipetted in the same way, and inverted for the same period at the same time.

The red cells were then counted:—

Undiluted sample .. .. R.B.C. $5·69 \times 10^6$/c.mm.
Diluted sample (x2) .. R.B.C. $5·22 \times 10^6$/c.mm.
Loss of red cells.. = $0·47 \times 10^6$.
= 8·2 per cent. original number.

About 8 per cent. of the cells had been lysed by the addition of the blood to 0·9 per cent. NaCl. But the estimation of the amount of haemoglobin in the fresh plasma had shown it to be 1·5 per cent. of the total present in the whole blood (Table XXII). It was to be expected, therefore, that on addition to saline the total lysis would be about 9·5 per cent. The figure actually found for residual haemolysis in this sample of blood (Fig. 30, No. 6) was almost exactly the same—viz., 10 per cent.

The fact that the residual haemolysis maintained the same level in all concentrations of saline beyond 0·58 per cent., strongly suggests that the 8 per cent. of cells so represented form a group much more readily destroyed than the remaining 92 per cent., the fragility of which is only slightly increased.

A similar state of affairs may be said to have occurred in the bloods of all the other patients who showed a fragility curve of the type just considered.

Residual Haemolysis, Haemoglobinaemia, and Anaemia in a Patient with Burns Involving 80 per cent. of the Body Surface

It has just been shown that residual haemolysis in the fragility test is due to changes in the red cells which render them unable to withstand dilution of the plasma by 0·9 per cent. NaCl, even in the proportions 1 : 2.

The changes in the fragility curves in Case 46 during the four days of survival after burning are shown in Fig. 31 :—

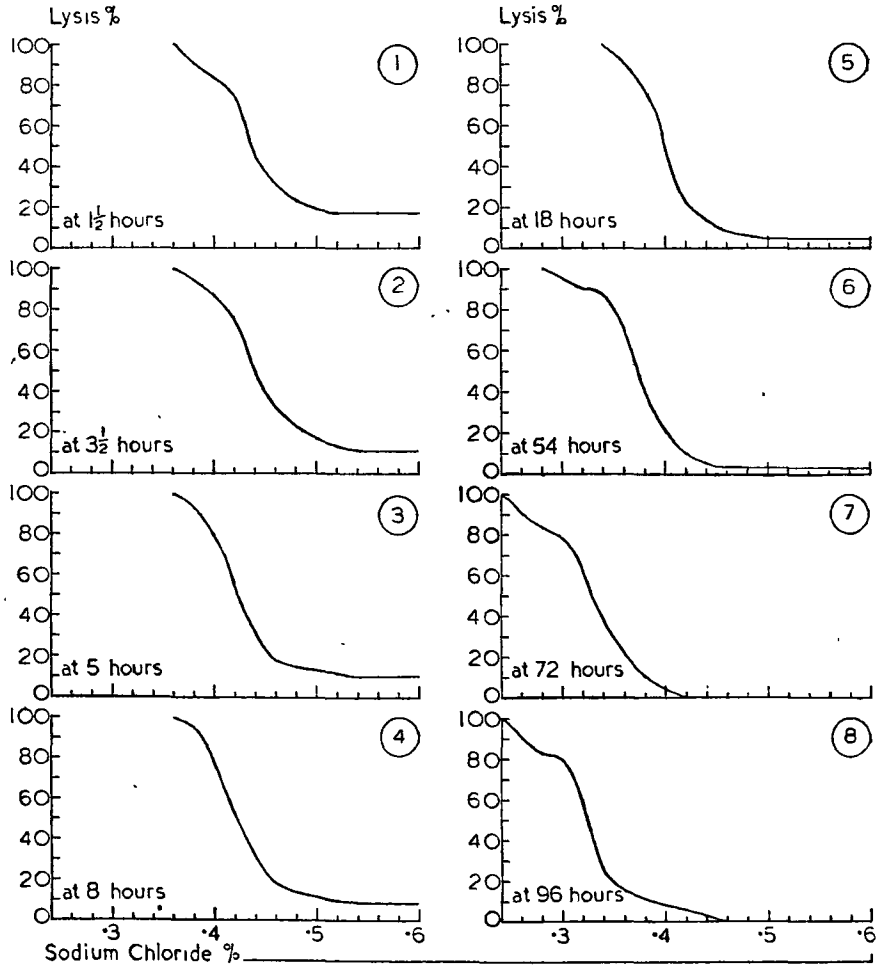

FIG. 31

At 1½ hours (Fig. 31, No. 1), immediately before transfusion was begun, a normal M.C.F. was recorded (0·436), and a residual haemolysis of 15 per cent. was found in all concentrations of NaCl above 0·50 per cent.

A slight rise in M.C.F. occurred at 3½ hours; and, thereafter, as the M.C.F. progressively declined, the amount of residual haemolysis fell until, at 72 hours, when the M.C.F. was 0·328, no residual lysis was evident (Fig. 31, No. 7). The final result on the fourth day shows no residual lysis and a M.C.F. of 0·324.

Reference to Table XXI reveals that haemoglobinaemia was most marked when the residual lysis was at a maximum—early after burning—and that when the residual haemolysis was not found in the fragility test, gross haemoglobinaemia had ceased and Hb. had disappeared from the urine.

During the first 4 days, the Hb. level fell from 18·6 g. per cent. to 10 g. per cent. (Fig. 27), but, owing to major changes in plasma volume which may have occurred during this period, it is impossible to estimate the loss of red cells indicated by this fall. That considerable loss was occurring is certain. The development of haemoglobinaemia amounting to as much as 8 per cent. of the total blood Hb. indicates, to some extent, the degree of haemolysis which had already occurred in the first 1½ hours. It is difficult to say just how much haemolysis is indicated by gradual fall of plasma Hb. to the eighteenth hour; and by the still more gradual disappearance of residual haemolysis in the fragility tests. Even in normal subjects, given not more than 10 g. of stroma-free Hb. intravenously, it takes at least 10 hours for the plasma to be cleared (Ottenberg & Fox, 1938). The failure to clear the plasma of Hb. until the end of 24 hours in Case 46, severely burned, with oliguria, and haemolysis amounting to about 8 per cent. of the circulating red cells at 1½ hours, cannot therefore be taken to indicate continued marked haemolysis throughout the first day. In this case, marked haemolysis occurring during the process of, or very soon after, burning, by itself appears sufficient to explain the persistence of obvious haemoglobinaemia until the eighteenth hour, though the evidence obtained from study of erythrocyte fragility suggests that slight continued haemolysis may have contributed. The gradual disappearance of the residual haemolysis may indicate either that the red cells represented by this part of the curve were recovering their former resistance, or that they were being destroyed. The latter seems the more probable, in view of the degree of increased fragility shown by these cells.

The evidence reviewed suggests, therefore, that marked haemolysis may occur during, or shortly after, the process of burning in cases extensively injured, and that a less rapid process of haemolysis may continue during the following 24 hours at least.

On this basis, it seems possible that, at the time of burning, a certain proportion of red cells exposed to heat are lysed *in situ*; that the residual haemolysis in the fragility tests indicates the proportion of cells which are severely damaged, but survive immediate destruction, to be destroyed more gradually in the next day or two; and that a slight increase in the average fragility of the remaining cells indicates a variable and slight amount of damage sustained by some or all of these cells. Further analysis of the fragility curves may give more information on these points.

Correlation of Findings Associated with Anaemia

It has been shown that the burned patient, roughly in proportion to the severity of his burn, is liable to become anaemic within the first week of injury. A reduction of red cell levels to about 50 per cent. of normal has been the usual finding after severe burns, and patients severely burned have required transfusion on the tenth to twelfth day and later.

The various findings associated with this anaemia have been described individually. In order to correlate these findings, two typical cases, one mildly, the other severely burned, are illustrated (Figs. 32 and 33). Both received serum transfusion in the shock period.

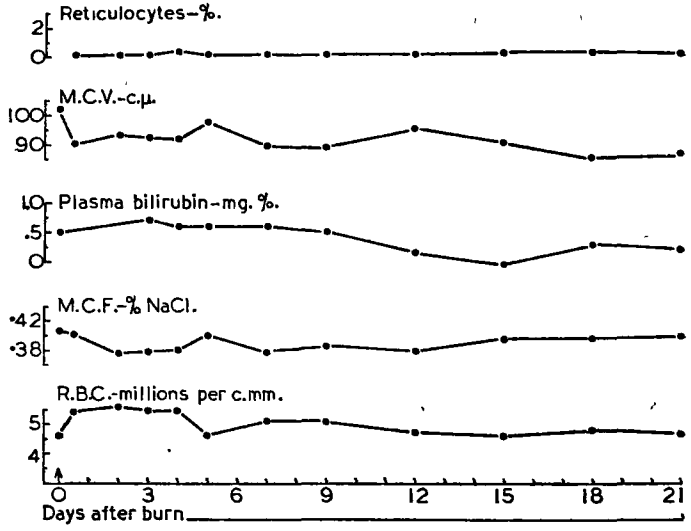

FIG. 32

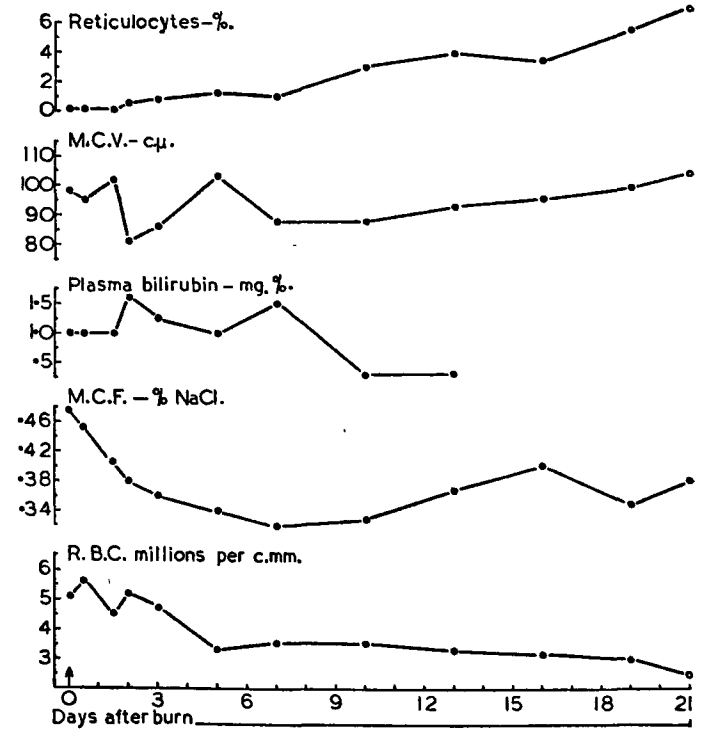

FIG. 33

Case 11 (Fig. 32) suffered a relatively mild burn (6 per cent.) and received 1,000 ml. of serum in the first 24 hours. In this patient, there is no definite evidence of the development of even a mild degree of anaemia, as shown by

red cell, Hb. and haematocrit estimations. The mean corpuscular volume (M.C.V.) is highest at 2 hours ; it fluctuates during the first 12 days, and thereafter significantly lower levels are maintained. The M.C.F. also shows its highest recorded value in the first specimen. A distinct fall occurs till the fourth day, when a rise in M.C.F. takes place. Subsequently, stabilization is evident from about the fifteenth day. The plasma bilirubin is slightly increased during the first 7 days ; thereafter, normal values are recorded. No significant alteration in reticulocytes is observed in the first 21 days after injury.

Case 58 (Fig. 33) suffered a severe burn (40 per cent.) and received 5,600 ml. of serum during the shock period. Marked anaemia is seen to have developed by the end of the first week. The anaemia persists, and by the end of the second week, a reticulocyte response is evident. The M.C.V. varies significantly during the first week, high values being recorded, and relative stabilization occurs thereafter, in the form of a slow steady rise in M.C.V. accompanying the reticulocyte response. The M.C.F. is markedly increased on admission, but by the seventh day a steady and rapid fall has produced values abnormally low. Thereafter, a gradual rise to normal is seen. The plasma bilirubin, already above normal at 3 hours, rises on the second day to 1·7 mg. per cent., a level from which there is little deviation until after the seventh day. A return to normal then occurs.

It is evident that in these two cases the general trend of the variations is very much the same. They differ only in degree. In both cases, the changes are confined almost entirely to the first 7 days following injury. By this time, anaemia is maximal and spontaneous arrest in its progress occurs. Irregularly high values for M.C.V. occur especially in the first few days, and in the second week stabilization tends to occur. Significant changes in fragility occur in the first week. The highest values for M.C.F. are recorded in the first few hours, and the lowest at about the seventh day, after which a rise occurs spontaneously. These changes are accompanied by a rise in plasma bilirubin.

Aetiology of Anaemia in Burns

The anaemia which may follow burns has been shown to vary from a transient change of mild degree to a rapidly progressive and ultimately severe anaemia, requiring several blood transfusions during the first month. In patients extensively and severely burned, a variable degree of anaemia tends to persist for several months.

In seeking the cause of these anaemias, the following possibilities have to be considered :—

1. That the changes are due to haemodilution following the period of Hc. and occurring with the return of fluid from the tissue spaces.
2. That red cells may be irregularly distributed, an excess being stored in the spleen.
3. That actual destruction of red cells occurs.
4. That there is marrow dysfunction, resulting in failure to maintain or produce normal blood levels.

Haemodilution

Since plasma may escape from the circulation into the tissue spaces in sufficient amount to cause demonstrable Hc., it would not be surprising if the return of this fluid into the blood stream were demonstrable as a reduction in Hb. levels. But it is unlikely that return of this fluid would cause apparent anaemia if fluid had not been added to the circulating blood in the meantime, during the period of Hc. The addition of fluid to the bloodstream from tissues remote from the burn has already been discussed, and it is possible that this actually does take place, at least to a minor extent. It seems possible that the return of the fluid from the tissues around the burn, if in sufficient amount,

might then cause excessive haemodilution and apparent anaemia. Attention has been drawn to the factors favouring the accumulation of fluid in the tissues. These factors would be expected to increase the tendency to a phase of haemodilution. Loss of fluid from the surface, and from the body, would have the reverse effect. The occurrence of oedema during the period of Hc., and its disappearance during the development of apparent and temporary anaemia, has been noted.

A final statement on the role of changes in plasma volume in the production of the mild and temporary " anaemia " encountered in cases of Groups I and II might best be made on the basis of direct studies of the volume changes, but, for reasons already given, these studies could not be attempted.

Distribution Changes

Slight variations in Hb. level may be produced by the action of the spleen (Barcroft, 1925; Cannon & Izquierdo, 1928). It seems probable that such variations would be small, and it is unlikely that they could explain the anaemia encountered in patients severely burned. Such a mechanism might contribute to the minor change in Hb. already discussed. Splenic enlargement has not been observed clinically in our burned patients, and at autopsy no significant increase in the size of the spleen has been noted.

Haemolysis

The various changes occurring in the blood, especially after burns involving more than 10–15 per cent. of the body surface, have been compatible with the occurrence of haemolysis, of a degree varying roughly with the severity of the burn.

The early phase of temporary " anaemia " is rarely seen in patients with burns involving more than 15 per cent. of the body surface. Instead, there is a phase of rapidly developing and severe anaemia, reaching a maximum in ten to fourteen days. In the early stages, the size of the red cells (M.C.V.), and the erythrocyte fragility (M.C.F.), tend to increase. Later, with the development of the anaemia, the M.C.F. falls rapidly. The occurrence of haemoglobinaemia and haemoglobinuria has been recorded after very severe burns, and these changes are closely related to the more marked alterations in saline fragility. It would seem that, in all groups, changes of the same type are occurring, and that these changes differ only in degree.

The occurrence of hyperbilirubinaemia and urobilinuria is compatible with, though not necessarily indicative of, a process of haemolysis; and the same may be said of the almost invariable finding of splenic siderosis in cases coming to autopsy after the first week.

Marrow Dysfunction

Failure of red cell production cannot explain the rapid development of anaemia and the early development of a reticulocyte response, and it seems probable that at this stage marrow dysfunction is not a significant factor. But in the later stages, with failure to recover after a month or more and without evidence of progressive blood destruction, defective marrow function may well be responsible for the chronic anaemia which persists until the body temperature has settled and the burned areas are healing satisfactorily. Such an anaemia may well correspond with that encountered in many chronic infections (Vaughan and Saifi, 1939).

There is no evidence that this type of anaemia has been related to the level of plasma proteins, and while depletion of body protein may be a contributory factor, it is not necessarily so (Rytand, 1942).

The Influence of Treatment

Haemolytic anaemia, agranulocytosis and thrombocytopenia have been reported following the use of the sulphonamide drugs, to the actions of which all the patients in this series were exposed. Slight depression of platelet counts

on beginning treatment with sulphathiazole, and increase immediately on its withdrawal, have been noted (Kracke and Townsend, 1943). Changes in erythrocyte fragility have followed the use of sulphanilamide (Antopol, Goldman & Sampson, 1941). Slight increase in reticulocytes has been recorded after moderate doses of sulphanilamide for various diseases (Campbell, 1938); and there is evidence that drugs of this group may cause liver damage (Schattenberg and Harris, 1943).

The demonstration of appreciable absorption of the drug when sulphonamides are applied to burned surfaces (pp. 183–5) suggests at once the possibility that the various haematological abnormalities recorded may have been due, at least in part, to treatment.

In severe burns, haemolytic anaemia is a fairly constant sequel. In fact, it occurs too frequently to be due to sulphonamides alone. No control series untreated with these drugs was, however, available to us, as even the patients treated with penicillin had sulphonamide applied to some area in the first few days at least. It is impossible to assess the part played by these drugs in the production of minor alterations in red cell levels, but it should be noted that many patients showing appreciable blood concentrations of the drugs developed no anaemia and no increase in reticulocytes.

The burn itself must be regarded as responsible for the immediate and great increase in red cell fragility recorded in all the cases of severe injuries. This abnormality was recorded before any treatment, local or general, had been instituted. In addition, a return to normal levels occurred before application of any dressing. By the time, however, that a great decrease in fragility was observed, dressings had been applied in all the cases studied. Since the changes in erythrocyte fragility recorded by Antopol, Goldman & Sampson (1941) were of the nature of increased resistance to hypotonic saline, it is impossible at present to assess the role of chemotherapy in the development of the low levels of M.C.F. recorded here (Fig. 29). It can be said, however, that there was no obvious relationship between the changes in fragility and the blood concentration of the drug.

The role of the sulphonamides in production of changes in the leucocytes is discussed later (p. 162).

The observations of Kracke and Townsend (1943), on the reduction of platelets in relation to treatment with sulphathiazole, are to some extent reflected in the figures obtained during the first 4 weeks in eight cases of burns. No gross abnormality in platelets has been found, even in patients burned very extensively, but a tendency has been observed for the platelet counts to be rather low during the first 2 weeks, and for slightly high counts to appear temporarily at the end of this somewhat variable period. While marked thrombocytopenia has not been seen, Case 45, burned 75–80 per cent. of the body surface, showed a purpuric eruption on the remaining intact skin, within 2 hours of injury. No platelet counts were made on this patient.

Changes in M.C.V. have borne no evident relation to the blood concentrations of sulphanilamide.

Plasma and serum therapy influenced red cell levels during the period of administration, but there is no evidence of any other effect. Temporary haemodilution occurred whether or not these fluids had been given in the shock period. Abnormalities in M.C.V. and M.C.F. were found before the administration of serum or plasma, and in patients not transfused at any stage. Marked haemolysis was observed in cases not transfused.

There is thus no evidence that serum or plasma therapy played any significant part in the production of blood changes, apart from the mechanical effect of haemodilution during the period of their administration.

CHANGES IN THE LEUCOCYTES IN BURNS

The following report is a preliminary account of the changes in the white cells found to occur in a series of 29 cases of burns. For descriptive purposes, the cases are again divided into four Groups. The variations in the total white cell counts during the first 7 days are tabulated below (Table XXIII):—

TABLE XXIII

Total White Cell Count (in thousands per c.mm.)

	Case No.	Hours after Burn*						Days after Burn						
		1	*3*	*6*	*9*	*12*	*18*	*1*	*2*	*3*	*4*	*5*	*6*	*7*
Group I	63							2·6	5·2				4·4	
	64							9·2	11·2	10·4		7·4		
	65	4·8			6·1	9·7			6·8	5·0		3·6		
	66		9·9	8·4	7·0			12·0	11·2	7·1	4·6	8·6		11·2
	67		6·7		3·05			3·1	3·5	6·3	5·9	4·4		
	68								13·0	17·6	14·6	10·0		8·8
Group II	11		11·3			10·0			15·6	8·8	10·0	8·2		9·0
	12		8·4			11·0		8·0		13·6		4·4		11·8
	13		12·6			14·6		19·2		20·8	16·0		18·2	
	14		4·6				12·0		14·6	9·4		12·2		12·4
	16		8·6				9·5	7·0	4·5	4·3	3·1	6·2	11·2	
	21		13·2	13·2	7·9		8·8	18·4	13·0	11·2	4·2	4·0	8·0	10·8
	69			9·2				18·1	11·7	6·0	6·1	4·3	5·4	
	76		9·6				13·0	6·0	12·5		7·0		11·0	
	78		12·3	9·1	6·5	14·6		8·9	6·7	8·6		5·6		
Group III	8		5·0	15·2				14·8	14·0	14·2				10·0
	30		14·4	16·4			19·6		4·5	11·0				11·0
	31		15·4	15·8	21·2			20·8	22·0	17·2		10·6		9·6
	80		19·2					15·4	11·6	9·8		11·6		8·8
	82	7·7	14·0				13·7	18·0	12·3	9·7	12·4	3·1	3·5	6·5
	83						10·4	10·8	25·2	6·7	4·15	3·2	5·6	6·1
	110		13·0			21·6			11·0		10·3		10·2	
Group IV	45	80·0 at 1¾ hours.												
	46	25·4	25·1	19·5	23·8		20·6	12·2	17·6	9·6	8·6			
	48		18·8	14·3			12·8	29·2	21·0	20·0	15·5	12·0		13·0
	54		19·8		28·0			13·0	15·8	16·8				
	58		20·8	32·6		43·6	35·5	29·2		16·8		12·2		19·8
	59							15·5	6·4	6·4	4·2	7·2	12·2	
	85		6·6	15·1										

* Hours only approximately.

Leucocytosis

A rise in the total white cell count after burning was almost a constant finding. In degree, it was roughly proportional to the area burned, and in the more severe cases very high values have been found.

A striking feature of the leucocytosis is the rapidity with which it may appear. It is usually established within the first 3 hours. At this time, there may be a great increase in neutrophil polymorphs (Table XXV), and the Arneth-Cook Index may show a distinct shift to the left (Tables XXIV and XXV).

In all groups, two phases of leucocyte response tend to occur. Typified by Case 21, there is an initial high white cell count within the first two days. A fall then occurs, and normal or low levels may be present on the fourth or fifth day, after which a second leucocytosis frequently occurs—in this case (No. 21) the secondary response reached 18,000 per c.mm. on the eighth day.

In Group IV, one patient showed a very high white count. It preceded an early fatal issue.

Leucopenia

Although leucocytosis occurred in the majority of patients, ten (34·5 per cent.) showed total white cell counts under 4,500 per c.mm. during the first

seven days. In six of these cases, the leucopenia was present on the fifth day, and more detailed study of one of these (Case 16) shows that actual granulocytopenia occurred (Table XXIV).

TABLE XXIV

The White Cells in Case 16—Leucopenia

Time	Total W.B.C.	Total* P	L	M	Arneth-Cook Index—Lobes per cent. 1	2	3	4	5	Notes
3 hours	8,600	8,250	350	0	40	42	12	4	2	8 per cent. vacuolated.
17½ ,,	9,500	8,900	500	100	46	40	12	2	0	0 ,, ,,
21½ ,,	7,000	5,740	1,120	140	48	40	8	4	0	0 ,, ,,
2nd day	4,500	3,440	340	720	56	38	5	1	0	0 ,, ,,
3rd ,,	4,300	—	—	—	—	—	—	—	—	
4th ,,	3,100	1,620	880	600	56	42	2	0	0	6 ,, ,,
5th ,,	6,200	3,600	1,860	740	60	34	6	0	0	8 ,, ,,
6th ,,	11,200	7,500	1,680	2,020	55	35	10	0	0	0 ,, ,,
8th ,,	18,200	14,850	2,800	550	44	43	11	2	0	0 ,, ,,
10th ,,	7,500	6,300	750	450	28	52	17	3	0	0 ,, ,,
12th ,,	4,800	3,900	650	250	33	50	16	1	0	0 ,, ,,

* P = polymorphs; L = lymphocytes; M = monocytes.

It will be seen, also (Table XXIV), that a marked shift to the left in the Arneth-Cook index accompanied the development of the neutropenia, and that vacuolation of the polymorphs, first noted at the third hour, returned with the fall in the polymorphs, and disappeared with the return to normal levels. These changes are of special interest when compared with those shown by Case 48 in the development of agranulocytosis (Table XXV).

Agranulocytosis

In the cases of leucopenia just described, the low white cell levels lasted 1–4 days and were not associated with any clinical upset. In one patient, however, complete agranulocytosis developed, and she died with staphylococcal septicaemia. The changes in the white cells in this case are summarized in Table XXV :—

TABLE XXV

The White Cells in Case 8—Agranulocytosis

Time	Total W.B.C.	Total* P	L	M	Arneth-Cook Index—Lobes per cent. 1	2	3	4	5	Notes
3 hours	18,800	15,700	1,900	1,200	46	42	8	4	0	36 per cent. vacuolated.
6 ,,	14,300	13,500	800	0	63	31	5	1	0	26 ,, ,,
16 ,,	12,800	12,500	300	0	51	38	8	3	0	41 ,, ,,
26 ,,	29,200	27,200	1,700	300	64	30	6	0	0	30 ,, ,,
40 ,,	21,000	16,200	3,000	1,800	52	36	10	2	0	17·5 ,, ,,
65 ,,	20,000	16,600	2,200	1,200	54	36	8	2	0	12 ,, ,,
4 days	15,500	12,600	1,500	1,400	56	33	8	2	1	15 ,, ,,
5 ,,	12,000	9,200	1,900	900	59	30·5	16	4	0·5	10 ,, ,,
7 ,,	13,000	11,100	1,200	700	47	39	12	2	0	5 ,, ,,
12 ,,	14,100	11,600	1,800	700	54	33	10	3	0	2 ,, ,,
13 ,,	8,300	4,500	3,300	500	75	23	2	0	0	30 ,, ,,
14 ,,	5,200	—	—	—	—	—	—	—	—	
17 ,,	2,000	800	1,160	40	80	19	1	0	0	30 ,, ,,
18 ,,	1,060	40	1,000	20	All one lobe.					
19 ,,	0,760	Only one polymorph (basophil) seen.								
20 ,,	0,756	No polymorphs seen.								
21 ,,	0,611	No polymorphs seen.								

* P = polymorphs; L = lymphocytes; M = monocytes.

This patient, a girl aged 7 years, with burns involving 40 per cent. of her body surface, had the burned areas dressed with 10 per cent. sulphanilamide cream 4½ hours after injury. The dressing was renewed on the eighth, eleventh and fourteenth days. From the sixth to the ninth day, a total of 4 g. of sulphapyridine was given by mouth, on account of a respiratory complication. Some improvement followed, though the temperature did not settle completely. A sudden change for the worse occurred on the eighteenth day, when the temperature rose suddenly, with a rigor, to 104·2° F. This level of fever was maintained with little fluctuation until death on the twenty-second day.

A blood transfusion had been given for severe anaemia (Fig. 26) on the thirteenth day. Repeated transfusions, pentnucleotide and liver extract were given from the eighteenth day, without benefit.

Post-mortem examination revealed a slightly enlarged, soft spleen, from which *Staphylococcus aureus* was cultured. Both this organ and the liver showed marked siderosis. The bone marrow was hyperplastic, and the granular series showed a preponderance of myelocytes and premyelocytes with an almost complete absence of more mature forms.

In comparing the changes in the polymorphs seen here with those occurring in Case 16, which showed only leucopenia, it is of interest that again there was a sudden increase in the vacuolated cells with the falling white cell count; and again a marked (and in this case sudden) increase in the shift to the left was noted at that stage in the Arneth-Cook index.

Discussion

It is common knowledge that leucocytosis follows burns, as it does any injury to body tissues. In many of the cases reported here, the initial reaction was so rapid as to suggest a process of rapid mobilization of the leucocyte reserves. In many also, this reaction was followed by a short period during which the levels were normal or little increased, and then by a period of leucocytosis which, beginning on the seventh to eighth day, might continue for a duration depending on the degree of surface infection and on the progress of healing. It would seem that an initial mobilization and redistribution of white cells is followed by increased production.

The occurrence of leucopenia in 34·5 per cent. of the cases examined is of interest, for such a finding has not been previously reported. The similarity between Case 16, with leucopenia, and Case 48, with agranulocytosis, has been noted, and it is possible that the changes are related aetiologically.

Drugs of the sulphonamide series must be regarded as a possible cause of this unusual white cell response. All the patients had a sulphonamide cream applied as a local dressing, and, in some, considerable absorption has been shown to occur (Anderson and Semeonoff, p. 166, below). The frequency of the occurrence of leucopenia is in keeping with the studies of Britton and Howkins (1938) on ambulant patients, and of Bigler, Clifton and Werner (1938) on cases with and without infection. The former authors record the occurrence of leucopenia in 46 per cent. of 50 individuals given 21 g. of sulphonamide in 14 days, while the latter believe that smaller doses over a shorter period cause significant depression of the white cells.

The development of agranulocytosis in Case 48 may have been related to the local application of sulphonamides, though this patient received sulphapyridine orally also. Serial estimations of the concentration of sulphonamides in the blood were not made, but, from the evidence presented elsewhere (Anderson and Semeonoff, p. 166), it is likely that high blood levels followed each renewal of the dressings. Periodic absorption of large amounts of sulphonamide over a considerable period is known to be favourable to the development of this complication.

In considering the possible ill-effects of treatment, it should be noted that, although this fatal complication may have been due to the use of sulphanilamide dressings, it was the only instance of agranulocytosis in a total of over 2,000 burns so treated. The use in lower concentration of drugs less liable to cause agranulocytosis, and less readily absorbed, has been investigated (see p. 185); such precautions should tend to minimise still further the danger of this serious but rare complication.

GENERAL SUMMARY AND CONCLUSIONS

I.—Haemoconcentration

(*a*) A rise in the red cell count, haematocrit and haemoglobin levels, has been recorded after burns involving over 5 per cent. of the body surface. Significant changes may occur in burns even less extensive.

(*b*) Haemoconcentration is roughly proportional to the extent of the burn; and symptoms of shock develop, in association with haemoconcentration, with increasing frequency as the extent of the burn increases. Few patients with burns involving more than 15 per cent. of the body surface fail to develop these symptoms if untreated.

(*c*) Haemoconcentration is regarded as reflecting the significant factor in the production of secondary shock in burns—reduction in blood volume. It can be controlled by transfusion of serum or plasma.

(*d*) Reduction in blood volume probably begins immediately after burning, and as much as 50 per cent. of the total circulating plasma may be lost from the circulation within 2 hours.

(*e*) Loss of fluid from the circulation occurs most rapidly during the first 12 hours; it may continue until the 3rd day; but no patient has been observed, treated or untreated, in whom haemoconcentration progressed beyond the first 72 hours.

II.—Blood Pressure

(*a*) Observations made on 68 cases within 3 hours of burning have shown that in the majority the blood pressure is within normal limits at this stage. It may be above normal.

(*b*) The normal or high blood pressure levels found at this time are unrelated to the nature of the burn, or to the ultimate issue.

(*c*) Normal and high blood pressures have been recorded in association with definite haemoconcentration.

III.—Indications for Transfusion, and its Control in the Shock Period

(*a*) If the effects of oligaemia, haemoconcentration and circulatory stasis are to be avoided, it follows from the above considerations (I*d*) that early transfusion is essential in extensive burns. The greater part of the transfusion will probably be required in the first 12 hours (I*e*), and, as far as blood volume changes are concerned, transfusion will not be necessary beyond the third day.

(*b*) Blood pressure readings obtained within 3 hours of burning are of no value in indicating the need for transfusion; and an isolated haemoglobin or red cell estimation will give no more indication of the requirements than knowledge of the extent of the burn, since the pre-burn levels are not known.

(*c*) Ideal treatment by transfusion comprises the commencement of fluid therapy at an early stage, when little change has occurred, and the maintenance of a circulating blood volume as nearly unchanged as possible.

The initial assessment of the needs of any case must be based on the area involved (I*b*), and the rate and magnitude of transfusion are best controlled by repeated estimations of red cell, haemoglobin or haematocrit levels.

IV.—Anaemia

(*a*) A reduction in red cell levels is a common feature of burns of all degrees. The magnitude of the change is roughly proportional to the burn.

(*b*) Patients with burns involving up to 15 per cent. of the body surface frequently show a mild temporary fall in red cell levels, maximal by the fifth to seventh day, with recovery by the tenth to twelfth day. This change may be due to haemodilution.

(*c*) Burns involving over 15 per cent. of the body surface are frequently followed by a rapidly occurring, moderately severe anaemia, the development of which is associated with a slight and variable increase in red cell size (M.C.V.), increased erythrocyte fragility, and an increase in plasma bilirubin and urobilin excretion. A reticulocyte response follows. This anaemia is haemolytic in origin, damage to a proportion of the red cells occurring at the time of burning. After extensive severe burns with considerable skin loss, a state of anaemia tends to persist until the patient is apyrexial and healing is well advanced. This anaemia is regarded as belonging to the type found in association with chronic infection.

V.—Haemoglobinaemia and Haemoglobinuria

Four cases are described, all with very extensive burns. The condition was associated with a great increase in saline fragility of the red cells.

The condition is regarded as differing only in degree from the less obvious blood destruction occurring in patients less seriously burned.

VI.—Changes in the White Cells

Leucocytosis is almost invariable after burns. It occurs roughly in proportion to the severity of the injury, and may be well marked within 3 hours of burning.

A secondary leucocyte response frequently occurs about the sixth to eighth day, probably due to infection of the raw surfaces.

Leucopenia occurred during the first week in 34·5 per cent. of 29 cases. It may be due to the absorption of sulphonamide compounds used as dressings.

Agranulocytosis occurred in one case: the patient died with staphylococcal septicaemia. The possible relation of this condition to absorption of large amounts of sulphanilamide from dressings is discussed.

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STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART V.—CHEMICAL CHANGES IN THE BURNED PATIENTS

BY

A. B. ANDERSON, Ph.D., M.R.C.S., L.R.C.P.
(Clinical Biochemist, Royal Infirmary, Glasgow)

AND

E. SEMEONOFF, B.Sc.
(Working with a grant from the Medical Research Council)

CONTENTS

INTRODUCTION

The number of investigations reported in the literature of changes in chemical constituents in burned patients is not as large as might be expected, much of the work on the biochemical effects of burning having been done on experimental animals. Without going into a detailed description of the literature, for which the reviews, e.g., those by Harkins (1941) and Rossiter (1943), may be consulted, one may say that there is general agreement that after burns in man a fall in plasma protein and chlorides, and a rise in non-protein nitrogen, may be observed. The evidence regarding other changes tends to be conflicting. In the present study it was considered necessary to investigate patients with burns of all degrees of severity, to determine the importance of any changes observed. The findings of the examination of samples from 70 cases are described. The aim was to obtain serial specimens of blood and complete collection of urine from patients with burns of varying extent. Unfortunately, in many of the more severely burned patients it was not possible to obtain many blood samples, owing to the extent of the burn and the use of available veins for intravenous therapy. Femoral vein puncture

was not performed. In general, serial specimens were not obtained from the smaller children. In view of the frequent blood sampling which was necessary to follow rapid changes in the state of the patient during the shock period, the volume of each sample, and consequently the number of substances which could be estimated in any one patient, was limited. For purposes of comparison, the cases have been arranged in four groups according to the percentage of body surface involved in the burn, namely :—

Group I.—1–5 per cent. of body surface .. 13 cases.
Group II.—6–15 per cent. of body surface .. 28 cases.
Group III.—16–30 per cent. of body surface .. 14 cases.
Group IV.—30 per cent. and over of body surface 15 cases.

This somewhat arbitrary grouping is the same as that used in the haematological study (Part IV, above). Cases are referred to by number, and Appendix I (p. 203) should be consulted for details of the extent of burn, shock treatment, etc. Numbers up to 62 are cases described in the report on " burns shock " (p. 49). The higher numbers are common to this and the haematological report.

METHODS

Urine

The whole 24 hours' urine was collected in bottles, with chloroform, or chloroform and thymol, as a preservative. The volumes were measured in the laboratory. Collection started as soon after admission as practicable. Admission specimens of urine were obtained in nearly all cases and examined by the qualitative tests only.

Qualitative tests for *protein* by the sulphosalicylic acid method, and for *blood* by the guaiac method, were made on each 24-hour specimen.

The *pH* was determined by indicator methods in the Lovibond Comparator.

" *Urea* " was determined by the hypobromite method.

Total nitrogen by microkjeldahl.

Sulphanilamide, both free and total, by the method of Bratton and Marshall (1939).

Urobilin qualitative tests were made by Schlesinger's method on some urines.

Urobilinogen excretion was estimated in a few patients by Watson's (1937) method.

Blood

Samples of approximately 7 ml. were taken by venepuncture, frequently in the first few days, and thereafter at varying intervals for a week to 10 days or longer. It was not possible to adhere to a rigid scheme in all cases.

Potassium oxalate as an anticoagulant produced *in vitro* haemolysis in some samples of blood, and was discarded in favour of heparin. The sample of heparinized blood was often divided, and part used for haematological and part for chemical examination. When serum was required, the blood was drawn into test-tubes of smooth " Pyrex " glass, which gave good separation without haemolysis. Specimens of capillary blood were taken for blood sugar and occasionally for serum protein determinations when venepuncture was impracticable.

Urea was estimated in the whole blood by the urease method of Folin and Wu, using the apparatus described by one of us (Anderson, 1942).

Plasma protein was estimated in the heparinized plasma by the method of Fine (1935). Some estimations of protein were also made on serum by the microkjeldahl method.

Bilirubin was estimated in the plasma or serum by Thannhauser and Andersen's (1921) modification of the Van den Bergh technique, using the Lovibond permanent glass standards.

Blood sugar was measured by the method of Folin and Wu for 0·1 ml. of blood.

Potassium was estimated in the serum by a modification of the method of Kramer and Tisdall (1921).

Sulphanilamide was determined by the method of Bratton and Marshall (1939).

FUNCTION TESTS

Kidney function tests were performed in some patients by van Slyke urea clearance, and *liver function* by Quick's (1936) hippuric acid excretion method: Sodium benzoate was given by mouth, in view of the difficulties of intravenous administration in many burned patients.

RESULTS

In this section, the findings are given with a minimum of comment, as the significance of the results will be dealt with in the discussion.

1.—Alterations in the Urinary Constituents

SPECIFIC GRAVITY

Urines of high specific gravity were excreted for the first few days after the burn. Some examples are given in Table XXVII, from which it will be seen that the specific gravity tended to remain high for the first ten days.

ALBUMINURIA

The 24-hour urines from 45 patients were tested for protein daily for the first week or longer. The results are shown in Table XXVI.

TABLE XXVI

Albuminuria

Group	*Total No.*	*Number Protein Free*	*Traces of Protein only*	*Protein +*
I	11	6	5 (Cases 87, 90, 91, 92, first 2 days).	0
II	15	5	6 (Cases 28, 16, 21, 97, 99, 100, first 2 days).	4 (Cases 69, 78, 98, 105, 2nd and 3rd day).
III	10	3	3 (Cases 37, 34, 110, 1st or 2nd day).	4 (Case 82, 2nd day. Cases 35, 111. Case 83, daily till death on 11th day).
IV	9	0	1 (Case 62, first 2 days).	8 (Cases 51, 54, 84, 115, 1st and 2nd days. Case 60, first 3 days. Case 57, 6th and 7th day. Case 58, 2nd to 5th day. Case 61, 1st to 6th day).
Totals	45	14	15	16

From the table, it will be seen that, with the mild burns in Group I, about half the patients showed a trace of protein in the urine for the first two days. On the other hand, the more severe cases tended to have a definite proteinuria for the first few days, though even here protein was absent throughout in three patients in Group III.

Haematuria

Serial tests for blood were carried out on the urines of 37 of the patients, and positive tests were obtained in one only. This patient was in Group IV, and had very severe burns (Case 60). A number of specimens from other patients not on 24-hour collection, were examined, and blood was found in two cases; Case 84, a 90 per cent. burn, was fatal in 5 hours; Case 54, a 40 per cent. burn, was fatal on the 3rd day. Clinical observations of haematuria were made in two other patients not included in this report; both were children (Cases 45 and 46). Thus haematuria has been observed in five cases in all.

Reaction

The *p*H of the urine was determined in 18 patients, and, apart from a few individual specimens, the reaction was consistently acid, *p*H 5·5–6·6 being the usual range. One exceptional patient (Case 83) passed alkaline urine of *p*H 8·4–9·0 constantly.

Nitrogen Excretion

The daily urea excretion was estimated in 24 patients. It should be pointed out that, as the hypobromite method was used, the figures obtained are for urea + ammonia + a small amount of nitrogen from urates, creatinine, etc., and are all calculated as urea. However, it is thought desirable to refer to the results as "urea". As will be seen from the examples given in Table XXVII, the pattern of nitrogen excretion was similar for all burns. A relative oliguria was present for the first one or two days, and the output of nitrogen was relatively small. On the second or third day, there was a marked increase in the nitrogen excretion in all cases. Amounts of 30–40 g. "urea" were usual at this stage in the male patients. In those with mild burns, the excretion soon fell to more ordinary levels, of 15–20 g. p. diem., while, with the more severe burns in the males, the increased nitrogen excretion continued for some days, the highest figure recorded being 55 g. "urea" on the 6th day in a Group III case (No. 19). The females all showed a much lower level of excretion, which might be partly explained by a lower intake of food. Total nitrogen was not estimated in all these patients, but, as will be seen from the examples, it followed very closely the "urea" excretion, the ratio "urea": total N being constantly close to 2. No nitrogen partition studies were carried out. Nitrogen balance experiments were not attempted, because the nursing and ward facilities were not reliable for accurate metabolic work, and also a method for determining the loss of nitrogen from the raw surface into the dressings, which may be very considerable in some burns, had not been worked out. Balance experiments omitting this source of loss are obviously misleading.

In Case 60, the output fell during the third week, and later to very low levels of 3–4 g. total N for several days. This was associated with a poor intake of food, and with continued loss from the large raw surface of the burnt area; it will be discussed later, in connection with the plasma protein level.

Bile

Positive tests for bile were obtained in the urine of Case 118, from the 9th to the 16th day. This child aged 1½ years was jaundiced, with clay-coloured stools, and had a papulovesicular rash. The jaundice cleared up, and its aetiology is still uncertain. Bile was not found in any other urines.

TABLE XXVII

Urines

24 hours noon—noon	*Volume mls.*	*Sp. Gr.*	*pH.*	*Albumin*	*Blood*	*Urea g. total*	*Total Nitrogen g.*
Case 66, Group I, 4 per cent. burn :—							
1st	670	1,028	6·8	0	0	15·9	8·6
2nd	960	1,028	6·2	0	0	28·8	15·3
3rd	520	1,025	6·2	0	0	14·5	6·7
4th	960	1,018	6·0	0	0	18·7	9·0
5th	1,160	1,018	6·0	0	0	22·4	
6th	910	1,023	6·3	0	0	18·2	
Case 16, Group II, 15 per cent. burn :—							
1st (16½ hours) ..	420	1,020	5·0	tr.	0	6·7	3·7
2nd	550	1,028	5·4	0	0	17·9	8·9
3rd	1,090	1,012	6·6	0	0	15·6	7·3
4th	870	1,012	6·9	0	0	16·6	7·7
5th	930	1,013	7·4	0	0	16·3	
6th	1,180	1,012	7·1	0	0	15·1	
7th	1,260	1,010	7·9	0	0	8·3	6·0
8th	1,350	1,008	6·8			5·7	3·8
9th	850	1,008	7·0	0	0	4·1	2·1
Case 36, Group III, 26 per cent. burn :—							
1st	310	1,036	5·3	tr.	0	9·6	5·0
2nd	490	1,031	5·3	0	0	19·3	10·4
3rd	790	1,029	5·5	0	0	33·6	17·1
4th	770	1,014	6·2	0	0	16·0	8·0
5th	550	1,026	5·6	0	0	18·1	
6th	880	1,025	6·2	0	0	30·7	
7th	820	1,024	6·0	0	0	25·3	
8th	1,000	1,019	5·5	0	0	26·4	
9th	1,000	1,022	6·6	0	0	28·8	
Case 57, Group IV, 47 per cent. burn :—							
1st	690	1,030	5·2	tr.	0	13·9	7·5
2nd	400	1,027	5·3	0	0	11·2	5·9
3rd	840	1,025	6·2	0	0	31·2	15·7
4th	1,400	1,026	6·7	ft. tr.	0	50·4	
5th	1,140	1,025	5·4	tr.	0	36·4	
6th	1,020	1,024	5·4	+	0	31·5	
7th	740	1,026	5·6	+	0	26·3	
8th	830	1,027	5·4	tr.	0	32·5	
9th	830	1,027	5·6	tr.	0	29·0	
10th	800	1,026	5·6	ft. tr.	0	23·9	
11th	640	1,022	6·8	0	0	13·5	
Case 60, Group IV, 45–50 per cent. burn :—							
1st (17 hours) ..	600	1,015	5·4	++	+	6·7	9·4
2nd	900	1,017	8·6	+	0	17·4	10·3
3rd	630	1,020	7·3	+	0	15·5	8·1
4th	500	1,026	6·0	tr.		12·8	6·6
5th and 6th.							
7th	1,000	1,018	6·3	tr.	0	22·5	10·7
8th	980	1,019	6·6	+	0	17·1	8·05
9th	1,110	1,016	6·4	+	0	17·5	7·15
10th	1,380	1,018	6·0	+	0	24·7	9·8
11th	1,570	1,013	6·0	tr.	0	19·9	
12th	1,250	1,014	6·0	tr.	0	17·8	

Urobilin and Urobilinogen

These will be considered below, with the blood bilirubin findings.

2.—Alterations in Blood Constituents

(*a*) Blood Urea

Considerable day-to-day fluctuations may occur in the blood urea after burning, and therefore only cases in which serial determinations on the first 4 or 5 days were obtained are considered here, with the exception that definitely abnormal figures in scattered samples are included. Cases in which a number of scattered normal readings were obtained have to be excluded from consideration, as no conclusions can be drawn from them, in view of the possibility of abnormal blood urea values on the days when specimens were not taken.

All figures above 45 mg. urea per 100 ml. whole blood are considered as abnormal, and these are divided arbitrarily into two groups: 45–75 mg. per cent. and above 75 mg. per cent. The results from 27 cases are summarized in Table XXVIII. The highest figures, and the days on which they were found, are given. It will be seen that some rise in blood urea above 45 mg. per cent. was observed in most cases.

TABLE XXVIII

Blood Urea

Group	*Total No.*	*Urea 45–75 mg. per cent.*	*Urea above 75 mg. per cent.*
I	4	3 Case 88, 1st day, 47 mg. per cent. Case 65, 1st day, 59 mg. per cent. Case 67, 3 hours, 53 mg. per cent.	
II	9	4 Case 71, 2nd day, 57 mg. per cent. Case 78, 4th day, 54 mg. per cent. Case 69, 3rd day, 47 mg. per cent. Case 108, 2nd day, 63 mg. per cent.	
III	8	6 Case 111, 3rd day, 69 mg. per cent. Case 32, 3rd day, 53 mg per cent. Case 19, 4th day, 55 mg. per cent. Case 37, 3rd day, 49 mg. per cent. Case 82, 1st day, 68 mg. per cent. Case 35, 5th day, 74 mg. per cent.	2 Case 41, 2nd day, 166 mg. per cent. Case 83, 2nd day, 86 mg. per cent.
IV	6	3 Case 43, 1st day, 66 mg. per cent. Case 86, 10 hours, 52 mg. per cent. Case 84, 3 hours, 50 mg. per cent.	3 Case 60, 5th day, 79 mg. per cent. Case 52, 2nd day, 86 mg. per cent. Case 54, 3rd day, 132 mg. per cent.
Totals	27	16	5

Even in Group I, specimens taken soon after the burning showed a rise (Case 65—up to 59 mg. 2 hours after burning). In Group II an increase was seen in four cases on the 2nd, 3rd or 4th day. No specimens fell in the over 75 mg. per cent. category in either Group I or Group II.

In Group III, six patients had blood urea measurements in the 45–75 mg. per cent. division. The peak occurred on the 3rd or 4th day, except in Case 82, where the highest figure was found 24 hours after the burn, and fell gradually to normal at the end of the first week. The daily readings for this patient are given in Fig. 34.

Of the two patients in this group who come into the over 75 mg. per cent. division, one (Case 41), a child of 4 with a 28 per cent. burn, had a blood urea of 66 mg. per cent. at 19 hours, of 166 mg. per cent. at 42 hours, and died

at 48 hours. In the other (Case 83), a woman aged 68, the blood urea rose rapidly on the 2nd day to 86 mg. per cent. and fell rapidly to 39 mg. per cent. on the 4th day ; the patient died on the 11th day (see Fig. 34).

The six cases in Group IV were all fatal. The three in the 45–75 mg. per cent. division did not survive the shock period. Of the three patients in the over 75 mg. per cent. division, one (Case 60) survived for 65 days. The other two (Cases 52 and 54) died on the 2nd and 3rd days respectively.

The fluctuations in the blood urea from day to day are illustrated by the four patients charted in Fig. 34. The rise in blood urea may be described as reversible, i.e. returning to normal as seen in Fig. 34, or irreversible as shown in the patients who died in the first two or three days. The significance of this will be discussed later.

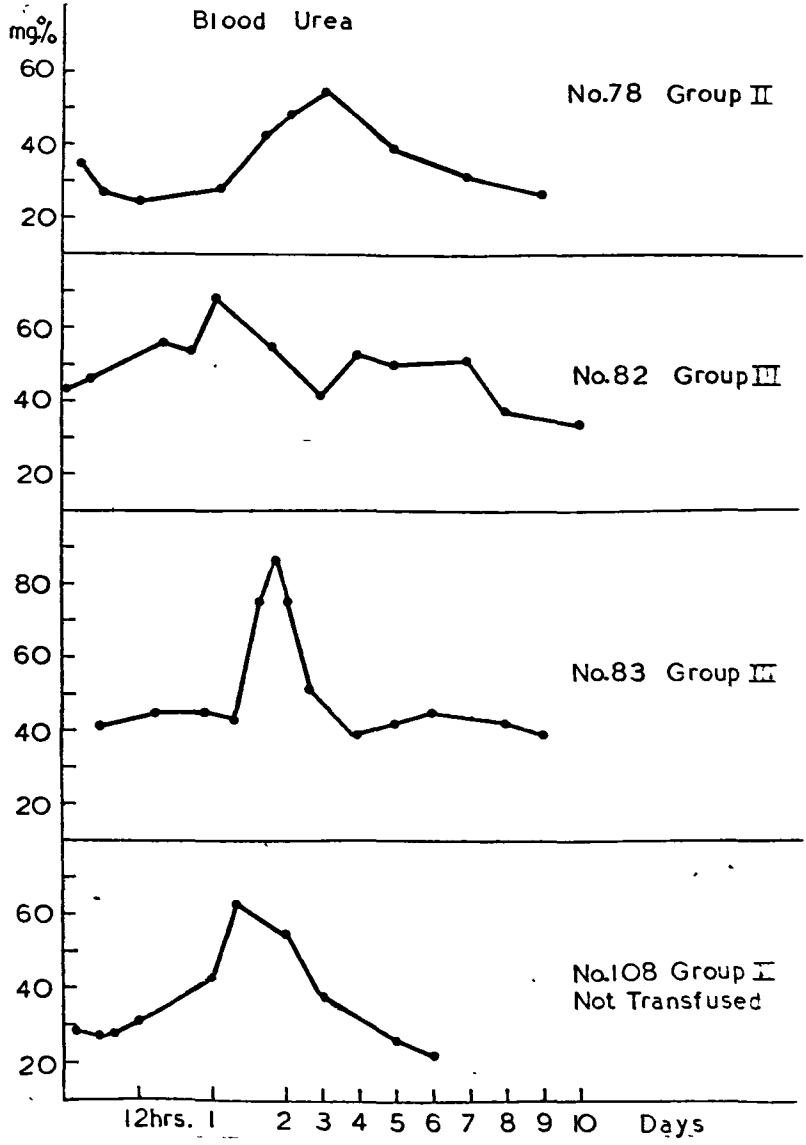

FIG. 34

(*b*) PLASMA PROTEIN

In considering the plasma protein concentration, an obvious important difference between the patients, apart from the severity of the burn, is that between those receiving transfusions of serum or plasma and those not transfused. In Group I none of the patients was transfused. Serial protein estimations were obtained in four, and in three of them practically no fall in protein (no figure below 5·6 g. per cent.) was observed. In the fourth, No. 65, a boy of 16 with a 4 per cent. burn, the protein fell to 5·3 g. per cent. on the fourth day and rose to 6·0 on the 6th day.

In Group II, of 11 patients with satisfactory serial determinations, five were not transfused and are shown in Fig. 35, and seven were transfused, of whom four

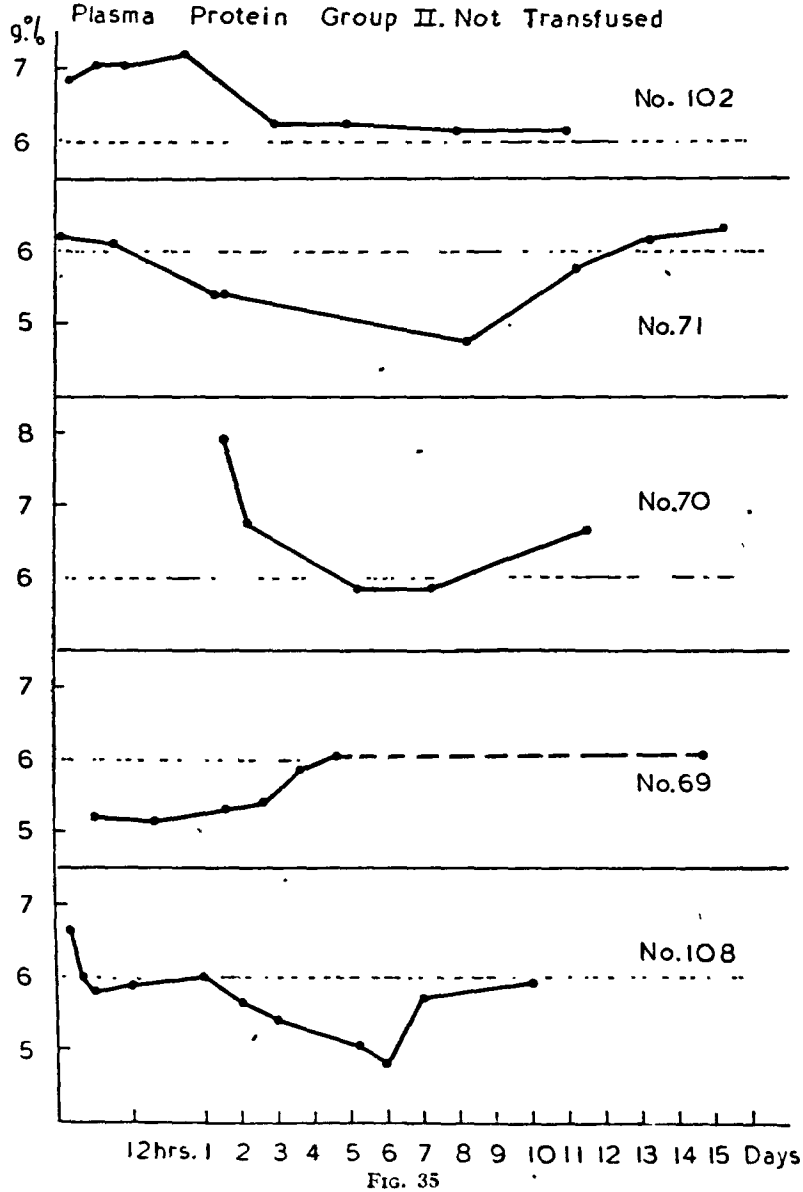

FIG. 35

are charted in Fig. 36. The cases which were not transfused were the milder burns with less shock. As will be seen from Fig. 35, four out of the five showed a fall in protein from above 6 g. per cent. to 6 g. per cent. or below in the first 2 days, and in two of these (Nos. 71 and 108) a further fall to below 5 at the end of a week, with subsequent recovery to 6 g. per cent. The fourth (Case 69) had a low plasma protein to begin with, which rose to normal on the 4th day.

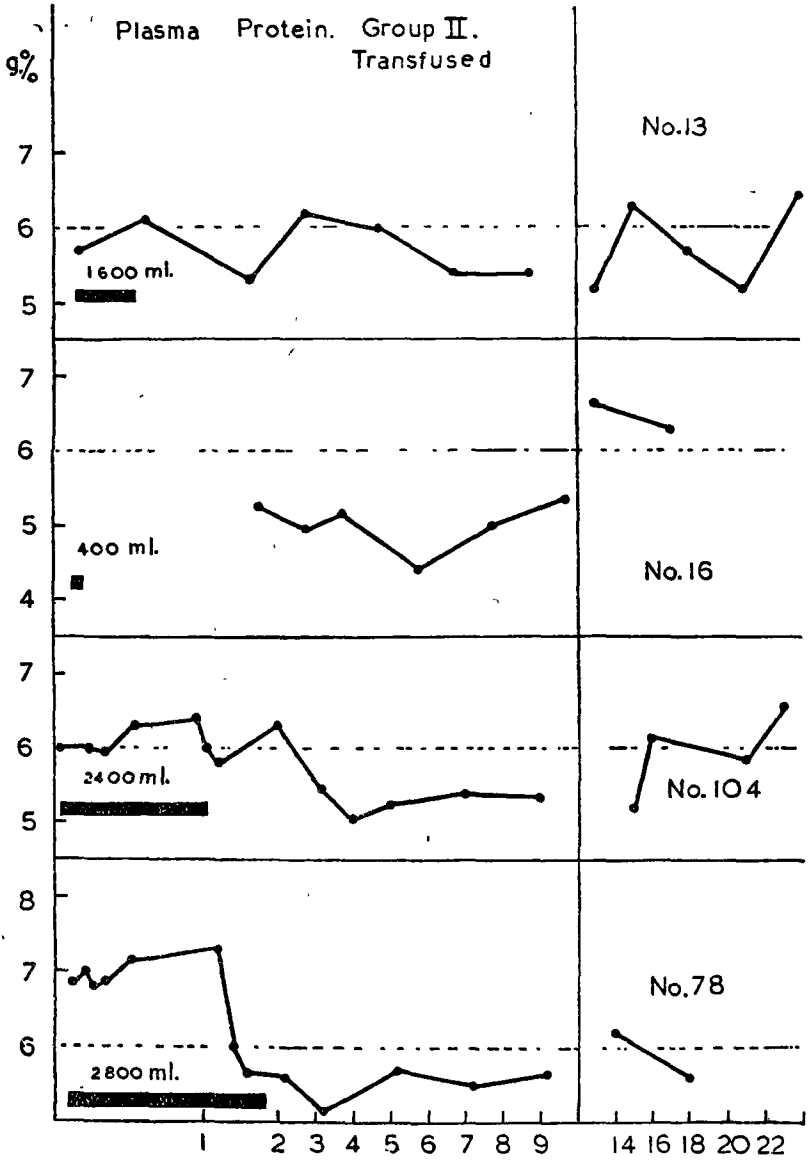

FIG. 36

The transfused patients of Group II (Fig. 36) showed a definite fall in protein on the 2nd or 3rd day, and in No. 78 this fall occurred rapidly on the 2nd day, before the transfusion was stopped. Recovery to normal levels was slower in these patients than in the non-transfused.

All Group III patients received transfusions, and three are charted in Fig. 37. The alterations in plasma protein concentration in these patients are similar to those found in the Group II transfused patients. Of especial interest is Case 83. Transfusion of serum commenced at the 3rd hour, and was discontinued at the 45th hour, when 4,400 ml. of serum had been given. As will be

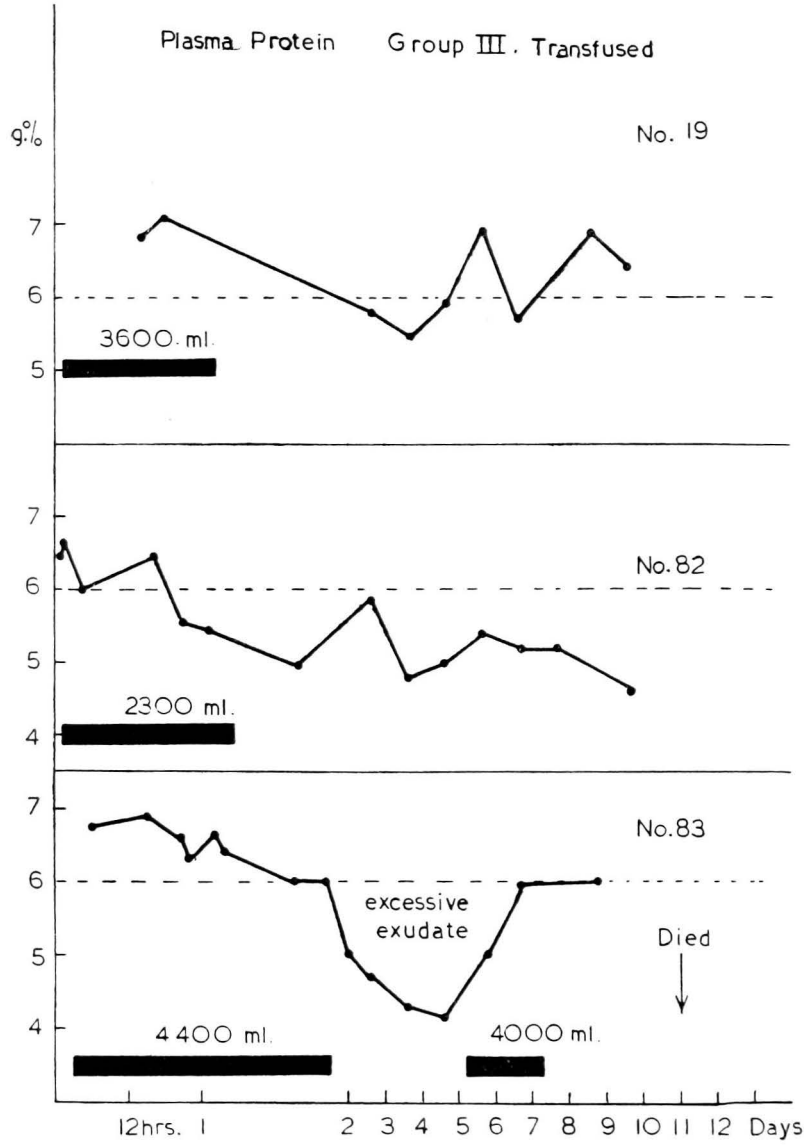

FIG. 37

seen from the chart, a rapid fall in protein concentration occurred about the time transfusion was stopped, and by the fourth day the protein was only 4·3 g. per cent. An excessive exudation of fluid occurred in this patient,

coinciding with the rapid fall in plasma protein. On the 5th day, a further transfusion of serum was started, and 4,000 ml. were given over 2 days. This second transfusion raised the plasma protein level to 6·0 g. per cent. where it remained until the patient died on the 11th day.

In most of the patients of Group IV, insufficient readings were obtained for charting, but from scattered samples it is possible to draw some conclusions. Three patients died in the first 24 hours; in these, no readings were obtained. Two died on the 2nd day, in one of whom (Case 52, a boy of 14) two specimens showed 4·5 and 4·3 g. per cent.; in the other (Case 43, a girl of 6) one specimen at 18 hours showed a protein level of 7·7 g. per cent. One patient died on the 3rd day (Case 54, a man of 40); a specimen at 7 hours had 6·1 g. per cent. of protein, and another at 48 hours 6·95 g. per cent., 12 hours before death.

One patient died on the 4th day (Case 46, a child of 10), and at 18, 30, 42 and 68 hours the plasma protein values were 7·5, 7·0, 6·0 and 6·6 g. per cent., respectively.

Thus, in these severely burned patients, dying in the shock period, no fall in plasma protein was observed, except in Case 52.

Two patients died in the 3rd week. In one (Case 48) there was no very great fall in plasma protein; and in the other, insufficient specimens were obtained.

Three patients survived more than 3 weeks. In Case 57, a man with a 47 per cent. burn who lived for 36 days, the plasma protein on the 3rd, 9th, 18th and 26th days was 5·9, 5·45, 5·0, 5·85 g. per cent. respectively. Case 60, a woman aged 41 with a severe burn of 50 per cent., survived for 65 days. In this patient only a few specimens of venous blood could be obtained, owing to obliteration of the veins, and the later specimens were all of capillary blood. The results are shown in Table XXIX :—

TABLE XXIX

Case No. 60; woman aet. 41, 50 per cent. burn.

Time after burn	*Plasma protein*	*Remarks : I. V. Therapy (D. serum = reconstituted dried serum)*
12 hrs.	7·0 g. per cent.	4,800 ml. D. serum.
18 hrs.	6·9 g. per cent.	800 ml. D. serum.
33 hrs.		Total shock treatment: 7,200 ml. D. serum.
5th day	5·8 g. per cent.	Urine Total N.: 10·7 g.
13th day	3·9 g. per cent.	Oedema present.
21st day		Urine Total N.: 3·0 g.
22nd day		Urine Total N.: 3·1 g.
31st day	4·35 g. per cent.	
32nd day		Urine Total N.: 2·83 g.
37th day	4·48 g. per cent.	800 ml. D. serum 34th day.
47th day	3·81 g. per cent.	
48th day	4·80 g. per cent.	1,200 ml. serum 47th day.
51st day	3·85 g. per cent.	

Difficulty was experienced in getting this patient to eat, and the protein intake was insufficient. The fall in nitrogen output is striking.

The third case was of a boy with a very severe burn, in whom only capillary blood could be obtained. The results are shown in Table XXX :—

TABLE XXX

Case No. 51 ; boy aet. 6½, 46 per cent. burn.

Time after burn	*Serum protein*	*Remarks : I. V. Therapy (D. serum = reconstituted dried serum)*
1st day		Shock treatment : 3,400 ml. D. serum.
14th day	6·6 g. per cent.	260 ml. whole blood.
15th day		400 ml. D. serum.
17th day	6·0 g. per cent.	
30th day		400 ml. whole blood.
31st day		800 ml. D. serum.
34th day	4·28 g. per cent.	
37th day	4·4 g. per cent.	
43rd day		Died.

The boy became slightly jaundiced during the last few days. Extensive liver damage was found post-mortem (see p. 199).

Two patients survived. In the first (Case 58), a man aged 25 with a 40 per cent. burn, the plasma protein on the 6th day was 5·4 g. per cent. ; on the 8th day, it was 6·0 g. per cent. and it remained about the normal level. In the second (Case 62), a boy of 15 with 50 per cent. burn, the protein was 6·5 g. per cent. on the first day, 5·5 g. on the 4th and 7·1 g. on the 7th.

All the protein estimations referred to above were done on 0·2 ml. of plasma or serum, as this was all that was available when other estimations had been carried out. In six patients, where more plasma or serum was available, total nitrogen and albumin and globulin were estimated by the microkjeldahl method. There are not sufficient figures to justify any conclusions, but the reversal of the normal albumin/globulin ratio, which is well recognized to occur in burned patients, was observed.

(*c*) Blood Sugar

Specimens of capillary blood were taken from seven patients for estimation of blood sugar. In some, specimens were taken as soon as possible after the burn, and in the others (patients admitted at night), specimens were taken at noon on the next day or on subsequent days. Results are given in Table XXXI :—

TABLE XXXI

Case No.	*Age*	*Group*	*Time after burn*	*Blood sugar mg. per cent.*	*Remarks*
116	64	I	1¾ hours	186	6 hours after food.
102	35	II	2 hours 3½ hours	154 133	
108	43	II	2 hours	160	
6	29	II	18 hours 2 days 3 days	118 132 125	
47	2	III	15 hours	100	
111	33	III	2 hours	250	
54	40	IV	7 hours 10 hours 1 day 2 days	154 182 154 80	Died 3rd day.

Only one of these patients had undoubted hyperglycaemia. This man (Case 111) had been burned by a mine explosion, and was very distressed when the sample was taken two hours after the burn. It will be seen from the table that the other three patients in whom samples were obtained within 2 hours showed slightly raised blood sugar levels.

(*d*) BILIRUBIN

Serial estimations of plasma or serum bilirubin were made in 23 patients. Four were in Group I, and there was little alteration in the bilirubin from normal levels except in one case (No. 88) where the bilirubin rose to 1·2 mg.

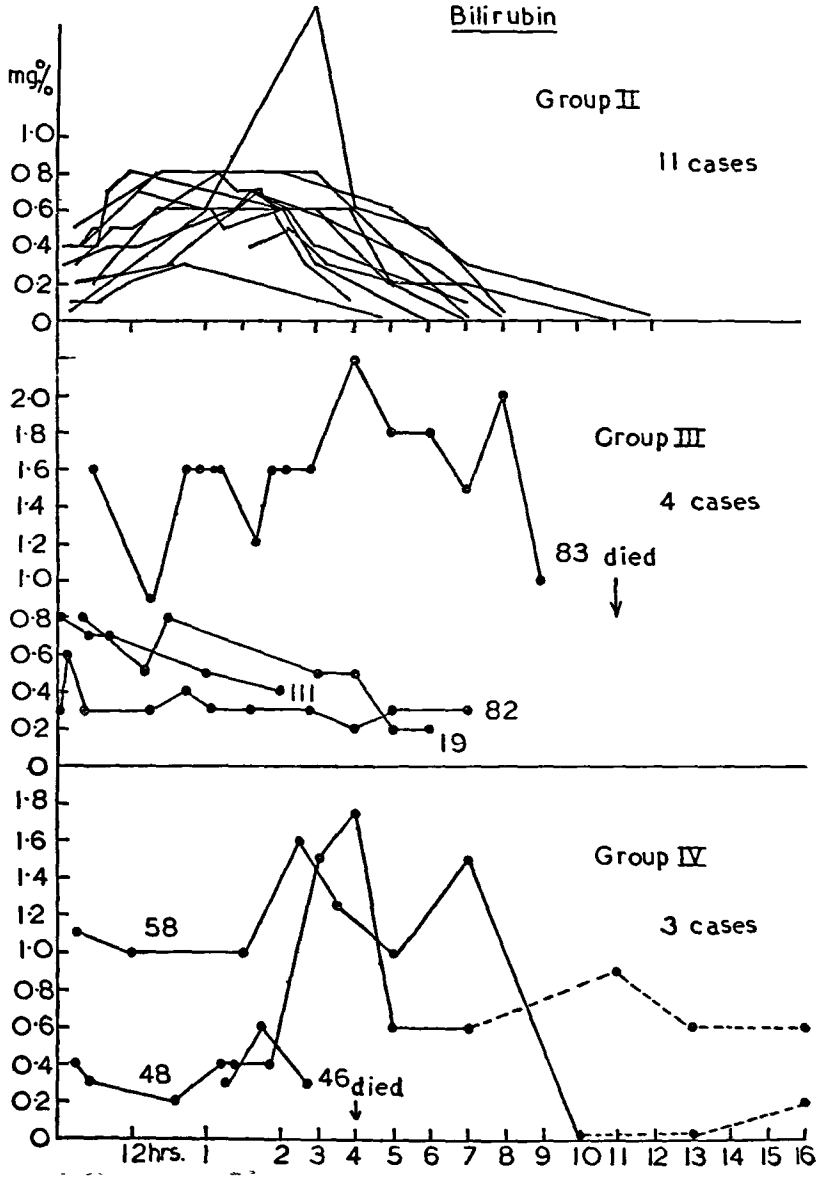

FIG. 38

per cent. on the 3rd day and fell to 0·3 mg. per cent. on the 7th day. This man had a burn of the foot, small in area (1 per cent.) but deep, caused by molten metal running into his boot.

The patients in the other three groups are charted in Fig. 38. It will be seen from the figures that in the 11 cases in Group II the alterations in bilirubin concentration followed the same course. There was a rapid rise up to 0·6 to 0·8 mg. per cent. in the first 24 hours, followed by a more or less rapid fall to normal on the 3rd, 4th or 5th days, and at the end of a week all had reached low levels. There are only two exceptions: one (Case 12) showed a rise to 1·7 mg. per cent. on the 3rd day, which is unexplained; and the other (Case 102) showed hardly any rise in bilirubin at all.

The four patients in Group III gave a more irregular response. One (Case 83) had a constant hyperbilirubinaemia, varying from 1–2 mg. per cent. from six hours to death at 11 days. Two (Cases 19 and 111) showed an early rise to 0·8 mg. immediately after the burn, followed by a steady fall; and the fourth (Case 82) only a transitory rise to 0·6 mg. per cent. in the first three hours, falling immediately to a level of 0·3 mg. per cent.

The three patients in Group IV show an even more variable picture, best indicated by the figure. The bilirubin level did not appear to be associated with the survival of these severely burned subjects. No. 46, who showed little rise in bilirubin, died on the 4th day, while No. 58, who had a constant hyperbilirubinaemia for the first week, survived; No. 48 died at the end of three weeks.

(*e*) (URINE) UROBILIN AND UROBILINOGEN

It was noticed that many of the urines collected were deeply pigmented (e.g. in Cases 57, 36, 78, 82) and, on applying Schlesinger's test for urobilin, strongly positive tests were obtained even after diluting the urine 1 : 10 in some instances. Quantitative estimations of the daily excretion of urobilinogen were carried out on various urines, and serial estimations were obtained in five patients. The results are charted, with the corresponding plasma bilirubin concentrations, in Figs. 39 and 40.

It will be seen from Fig. 39 that in two patients (Cases 110 and 102) the urobilinogen excretion in the urine was 2 mg. or less per diem (in Case No. 110, only the 7th–11th days' excretion was ascertained). This is a normal figure according to Watson (1937), who gives 0–4 mg. a day as the normal range. The figures for plasma bilirubin are correspondingly low in these two cases. By contrast, Case 107 showed a definite rise in output of urobilinogen on the 4th to the 9th day, reaching a peak of 13 mg. on the 6th day. In this patient, the plasma bilirubin showed an early rise to 0·6 mg. per cent., and a fall to 0·2 mg. per cent. on the 5th day.

In Case 104, Fig. 40, the urobilinogen excretion rose from less than 1 mg. on the first two days to 27 mg. on the 4th and 6th days, and, as will be seen from the chart, the plasma bilirubin, which was 0·6–0·7 mg. in the first three days, fell rapidly during the time of the peak excretion of urobilinogen. The excretion of urobilinogen continued to fluctuate at a higher level than normal for three weeks. It must be noted that this patient was six months pregnant.

The fifth patient (No. 108) excreted only the faintest traces of urobilinogen in the urine in the first week. This is explained by the fact that she had a colostomy, which had been made 17 years before and was still working. Therefore, practically none of the intestinal contents passed through the large bowel and there was no reduction of bilirubin to urobilinogen. Her bilirubinaemia followed the usual course of a Group II patient, with a peak of 0·8 mg. at 12 hours after the burn.

(*f*) SERUM POTASSIUM

It was considered that measurements of the serum potassium would be most important in the shock period, in view of the theories that have been advanced concerning the relationship of potassium to shock following injury.

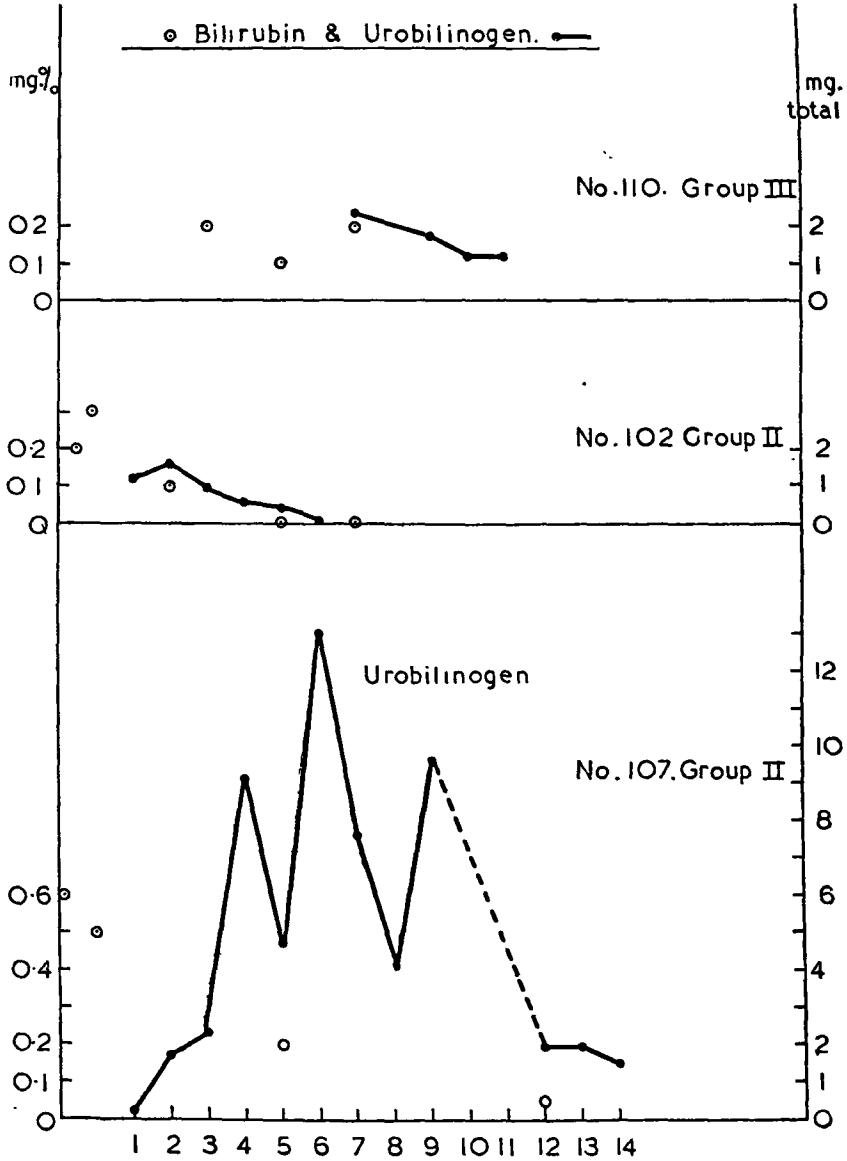

FIG. 39

Figures for serum potassium during the first few days were obtained in eight patients. In only two of these were serial estimations done.

For this estimation, it is essential to obtain serum absolutely free from haemolysis, because of the high potassium content of the erythrocytes. Some of the blood specimens obtained from the more severely burned patients had to be

discarded on account of *in vitro* haemolysis. Unfortunately, heparinized plasma could not be used for this estimation, as the heparin interfered with the precipitation.

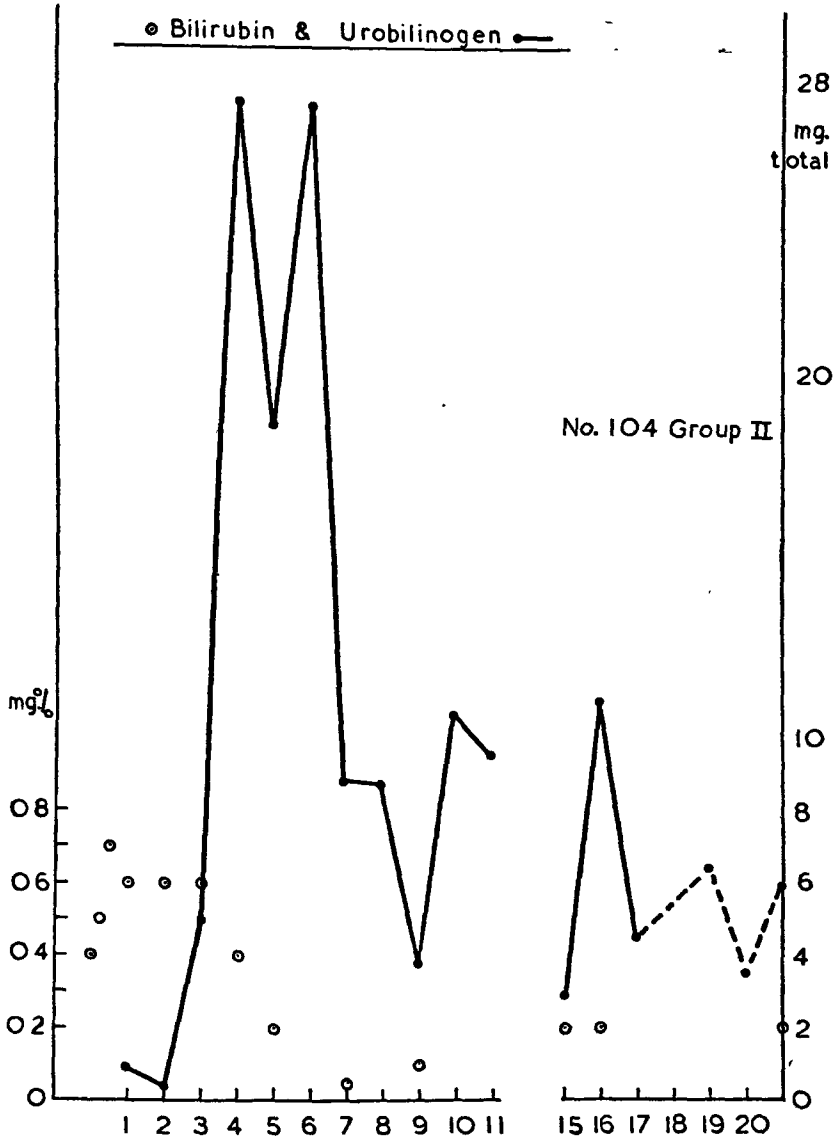

FIG. 40

The results are set out in Table XXXII, from which it will be seen that practically all the figures are within the normal limits of 18–24 mg. per cent. The exception is Case No. 71, which shows 36 mg. per cent. at 13 hours after the burn. The possibility of an odd specimen being slightly haemolysed arises here. It so happens that none of these were fatal cases and, before final conclusions can be drawn, more figures on severe cases would be required.

TABLE XXXII

Serum Potassium

Case No.	*Group*									
88	I	Time	40 min.	16 hrs.	22 hrs.	40 hrs.	3rd day	5th	6th	7th
		K mg. per cent.	21	21·5	24·5	23	22·5	25	23	23
87	I	Time	24 hrs.	48 hrs.						
		K mg. per cent.	19·5	20·5						
92	I	Time	< 6 hrs.							
		K mg. per cent.	23·5							
90	I	Time	3½ hrs.							
		K mg. per cent.	22							
71	II	Time .. .	1 hr.	8 hrs.	13 hrs.	32 hrs.	40 hrs.	4th day		
		K mg. per cent.	22·5	23	36	21·5	27·5	23		
103	II	Time	3 hrs.							
		K mg. per cent.	25							
34	III	Time	24 hrs.	6th day						
		K mg. per cent.	19	26						
62	IV	Time	20 hrs.							
		K mg. per cent.	21·5							

3.—Function Tests

(*a*) Kidney Function

Urea clearance tests were carried out on seven male patients with burns of varying severity, with the results shown in Table XXXIII :—

TABLE XXXIII

Urea Clearance

Case No.	*Group*	*Time after Burn*	*Clearance, per cent. of average normal*	*Urine protein on day of test*
94	I	29 hours	96	Trace
120	I	24 hours	78	0
70	II	54 hours	102	0
98	II	43 hours	90	+
100	II	7th day	74	0
103	II	62 hours	67	0
36	III	4th day	83	0

In these men, all the clearances are within the normal limits, except for Case 103, but even in this patient little loss of renal function is indicated.

(*b*) LIVER FUNCTION

The benzoic acid excretion test was carried out on three patients with small burns only (two in Group I, one in Group II). In these, no loss of function was demonstrated.

4.—Post-Mortem Analysis of Tissue

At the post-mortem examination of patients dying from burns, the brain often appeared oedematous (p. 197). Accordingly, chemical evidence of oedema was sought in three cases by analysing the white matter for water and chloride content, as suggested by Greenfield (1942) in a discussion on cerebral oedema. The method was as follows:—Strips of white matter, as free as possible from grey matter, were rapidly dissected from the fresh brain and weighed in closed vessels. Portions of the order of 2 g. were dried to constant weight in the hot air oven at 100–110° C. and portions of the order of 5 g. were analysed for chloride by the open Carius method.

The results of the analyses of the three brains are given in Table XXXIV. The water content is the same as that found for normal white matter by Stewart-Wallace (1939)—70–75 per cent. The water content of white matter from oedematous brains in his series averaged 82 per cent. The chloride content is higher than that found for normal white matter by Stewart-Wallace, who records 93–154 mg. per cent., but in oedematous brains he found large increases in chloride, to four times normal.

TABLE XXXIV

Water and Chloride Content of White Matter

Case No.	*Survival Time.*	*Per cent. burned*	*White matter*		*Naked eye appearance of brain from post-mortem report*
			Water, per cent.	*Chlorides, as mg. NaCl per cent.*	
115	1 day	66	74·5	200	No gross pathological change.
84	5 hours	90	68·5	188	A suggestion of pressure cone at base. No gross pathological change. Oedema, if present, is slight.
61	16 days	50	71	195	Brain is oedematous and pressure cone noted.

Close (1933) gives 180 mg. per cent. as the average chloride content for white matter. The figures in Table XXXIV do not appear to indicate any oedema of the brain, but only three cases were examined in this regard, and in only two of them did the post-mortem appearances indicate cerebral oedema.

5.—The Absorption and Excretion of Sulphonamides

Estimations of free sulphonamides in the blood were made in 20 patients, and serial estimations of free and total sulphonamide in the urine were made in 24 patients.

The question of absorption of sulphonamide preparations from the raw areas of the burns has already been dealt with to some extent in the report on the control of infection (p. 28). The matter appears to be of sufficient importance to warrant further discussion. Our attention was drawn to the danger of the absorption of sulphanilamide by Case No. 58, already referred to,

where the free sulphanilamide in the blood rose to 30 mg. per 100 ml. on one occasion. The figures for blood and urine sulphanilamide in this man—who had an extensive burn, involving 40 per cent. of the body surface—are shown in Fig. 41. It will be seen from this chart that the blood sulphanilamide rose rapidly to 30 mg. per 100 ml. on the 3rd day after a dressing with C.O./S. 10 per cent.,* then fell rapidly to 4 mg. on the 6th day, when he was dressed with C.O./S. 2 per cent.; it subsequently rose to 8 mg. and continued at 4 mg. during a time when he was dressed partly with sulphacetamide (5 per cent.) and partly with sulphanilamide.

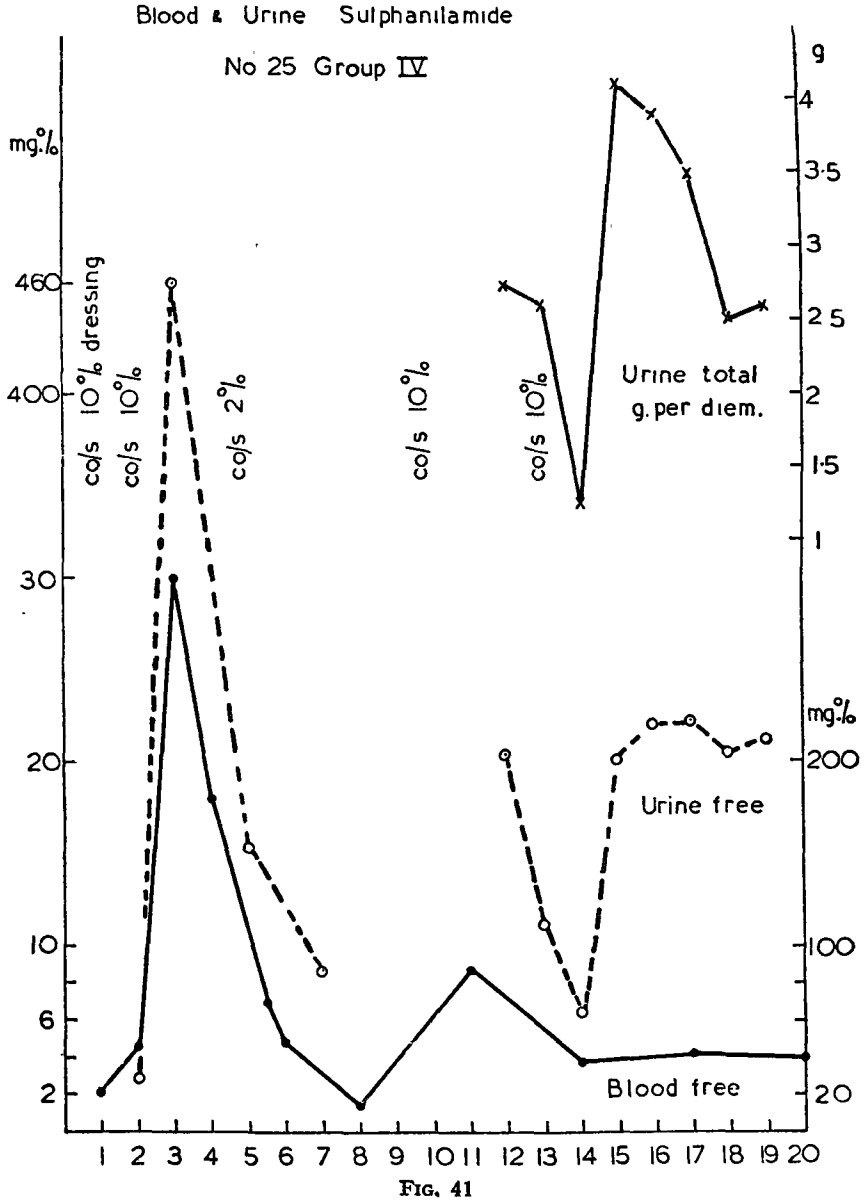

FIG. 41

* C.O./S. 10 per cent. = Cream containing 10 per cent. sulphanilamide in castor oil base.

The urinary concentration of free sulphanilamide followed the blood level, with a peak at 460 mg. per 100 ml. on the 3rd day. In the later period, the total daily excretion varied between 2 and 4 g. It is of interest that, two weeks after the burn, there should have been sufficient absorption from the burned area to give an excretion averaging over 3 g. per day.

As an example of the absorption of sulphanilamide with C.O./S. 3 per cent. dressings, Case No. 19 is charted in Fig. 42. This man, in Group III, with a burn of 19 per cent. of body surface, showed a rapid absorption after the first dressing, with increase in blood level up to 4 mg. per 100 ml. and a total excretion on the 2nd day of 2 g. The blood and urine figures fell rapidly to the region of 1 mg. per cent. and 0·5 g., respectively, by the 6th day. A second dressing of C.O./S. 3 per cent. on the 9th day was followed by a similar rise and fall in absorption and excretion over the following 4 days, during which a total of 6·5 g. was excreted.

By contrast, patients dressed with sulphathiazole showed only a small absorption, as was expected. This is illustrated in Fig. 43, Case 34; the patient had a 20 per cent. burn treated with 3 per cent. sulphathiazole as the plenary dressing. For the first 2 days, nearly one gram of the drug was excreted daily, after which the excretion fell rapidly to low levels.

Other burns dressed with 3 per cent. sulphathiazole showed even less absorption than this.

It is of interest that, even where considerable quantities of sulphanilamide were being excreted and the urine was acid and oliguria present, crystals of sulphanilamide were not seen in the urine.

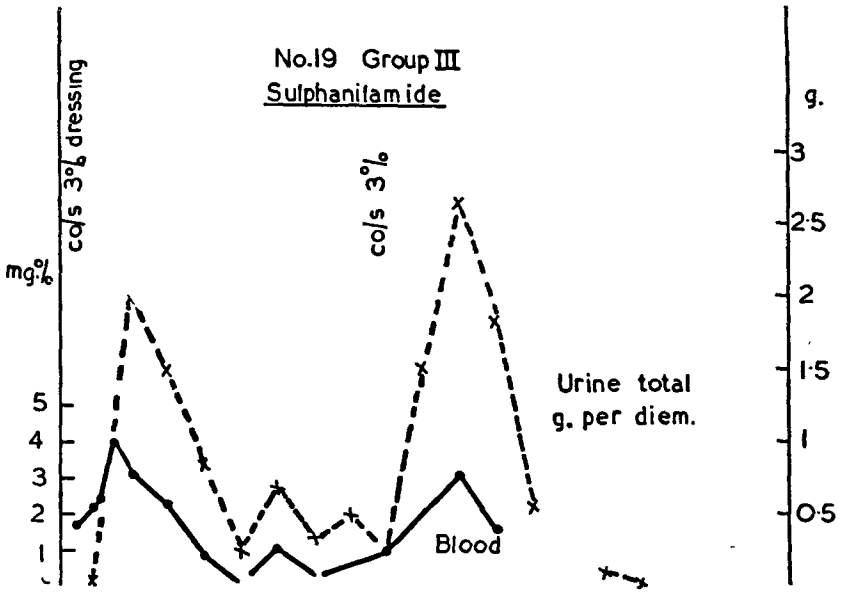

FIG. 42

6.—Correlation in Time of Changes in Blood and Urine

In the description given above of the changes in constituents of blood and urine, each constituent has been considered separately, with the exception of bilirubin and urobilinogen. To complete the picture some correlation between the times at which these changes took place can be made.

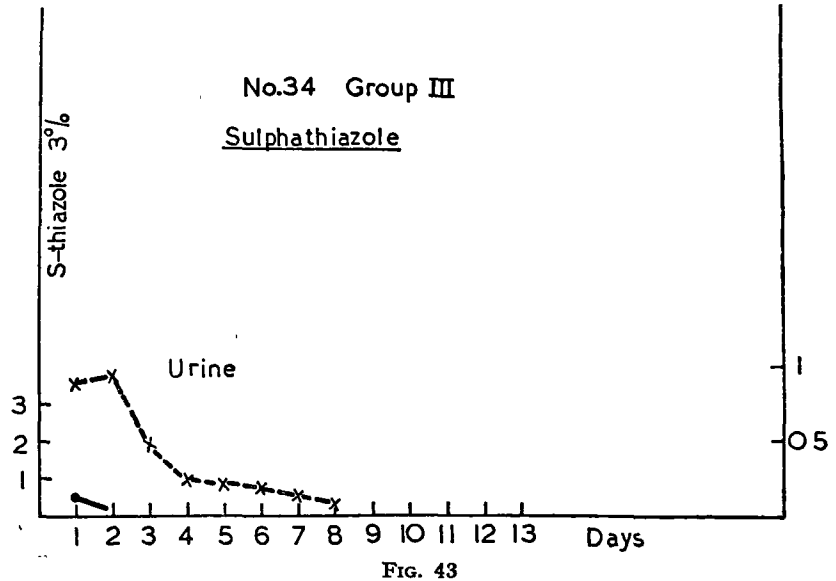

FIG. 43

The results from two men are charted in Fig. 44. One (Case 78), aged 41, with a burn of 12 per cent., was admitted in a state of shock, and 2,000 ml. of serum were given during the first 2 days. There was considerable loss of fluid from the burned surfaces into the dressings. The other (Case 19), aged 51, with a burn of 19 per cent., has been described in the Shock Report, and the following description is quoted from p. 77 above: "One of the few cases in which evidence of primary shock was present on admission—low blood pressure and patient cold, pale and shivering. The burns were dressed with No. 9 Cream . . . and serum transfusions commenced at once (1 hour after burning). Very large amounts were necessary to control the haemoconcentration, considering the extent of the burn. . . . Haemoconcentration continued to occur in this case after the transfusion of serum had been stopped at 26 hours. . . ."

It will be seen from Fig. 44 that the picture was similar in these two cases of burns. There was a considerable fall in plasma protein during the 2nd and 3rd days, accompanied by a rise in blood urea to a peak on the 3rd day. On the 2nd day, there was a large output of nitrogen in the urine, with a peak output on the 6th day in both cases, by which time the blood urea had fallen to normal levels. The changes in blood bilirubin occurred earlier; the peak was in the first 24 hours, and after this there was a gradual fall to normal on the 5th or 6th day.

To summarize the changes generally observed: In the first few hours, there was a rise in bilirubin, with normal plasma protein and normal urea. A transient slight hyperglycaemia was observed in a few cases 2 hours after the burn; at the end of 24 hours, the plasma protein tended to fall and the urea to rise. Urine volume was small, with a small output of nitrogen, for the *first day*, and definite albuminuria was observed with the severe burns. On the *second day*, the bilirubin continued high or started to fall to normal; the plasma protein continued to fall and the urea to rise; the volume of urine increased, and the nitrogen excretion rose to normal or more than normal amount; albuminuria was still present in the more severe cases.

On the *third day*, the bilirubin fell towards normal, with the exception of three cases with continued hyperbilirubinaemia; the blood urea reached a peak or was falling, except in the most severe burns; the plasma protein approached its lowest level, and the urinary excretion of nitrogen was high. Albuminuria was

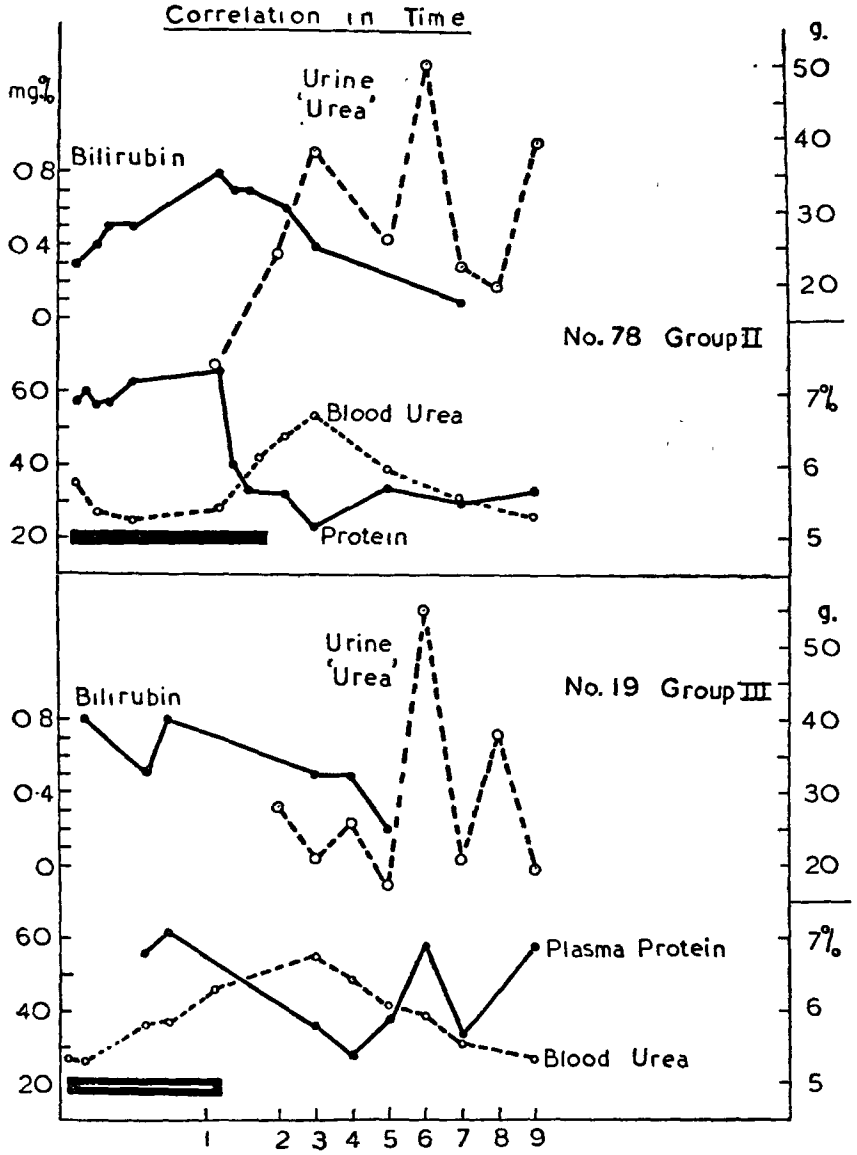

FIG. 44

still present in Group IV burns. On the *fourth day*, the bilirubin was falling, the urea returning to normal, except in the severest burns with uraemia; plasma protein was low, the urinary nitrogen high and the urine free from albumin, with one or two exceptions. In two cases, an increased excretion of urobilinogen in the urine was observed on the fourth day and subsequently. On the *fifth and sixth days*, the bilirubin was normal or approaching normal, with the exception of the three cases with hyperbilirubinaemia; the blood urea was normal, plasma protein continued to be low, the urinary nitrogen was high, reaching a peak of 50 g. " urea " in some males.

In the second week, the more severely burned patients continued to show subnormal values for plasma protein.

DISCUSSION

From the results obtained, some tentative conclusions can be drawn, and it is convenient to discuss the results under the headings—Nitrogen metabolism and kidney function; Bile pigment and liver function; Carbohydrate metabolism; Absorption from the burned surface; Other findings.

Nitrogen Metabolism

There is general agreement that a rise in blood urea and non-protein nitrogen occurs after burns, and our results are in conformity with this. Our observations show that this rise varies from a transient peak with the moderate burns, which may be missed if specimens are not taken frequently, to uraemia in the fatal cases. Patients dying early in the shock period, that is, in the first 24 hours, did not necessarily show a very high blood urea. The uraemia observed in the fatal cases was not extreme in any instance, the highest figure being 166 mg. per cent. There is little evidence of any serious kidney failure. The albuminuria was transient, and large quantities of nitrogenous metabolites were excreted in urines of high specific gravity. Undoubtedly there was failure to excrete much urine or nitrogen in the first 24 hours, but, after this, the kidney appeared to be working satisfactorily and the urea clearance tests did not show any deficiency.

Haematuria or haemoglobinuria was rare, and was seen only occasionally in the most severely burned patients (5 cases in all admissions).

The rise in blood urea would appear to be due to the flooding of the circulation with urea at a greater rate than it can be excreted by kidneys functioning normally. The high specific gravity of the urines points to a shortage of water in the circulation.

While total nitrogen excretion was large in many cases, the figures are not as high as those given by Taylor *et al.* (1943). It was noticeable that nitrogen excretion was much higher in male than in female patients. This may have been partly due to the much smaller intake of food by the female patients, which was commented on by the nursing staff. The increased nitrogen loss may be connected with the fall in 17-ketosteroid excretion reported by several workers, e.g. Cope *et al.* (1943).

The rise in blood urea, and the increased nitrogen loss in the urine, are comparable with the changes found in animals by Clark Peters, and Rossiter (1944). The increased nitrogen loss in the urine is paralleled by that described by Cuthbertson (1930, 1931, 1932) in patients after other forms of injury.

Despite large quantities of serum given intravenously in the shock period, the plasma protein fell to low figures in the first few days. Much of the fall must have been due to actual loss of protein from the burned surface into the dressings. Patients varied considerably in the amount of loss: some were noted as soaking the dressings and the bed quickly; in others, the loss was not so marked. Where exudation was excessive, a very rapid fall in protein was seen (e.g. Case 83, Fig. 37).

In the less severely burned patients the plasma protein rose to normal in the second week, but in those severely burned, who survived the first two weeks, the failure of the plasma protein to regain normal levels, or its continued fall, was one of the main problems. These patients could not ingest sufficient food to enable the protein intake to be kept up to replacement level. This was shown by the decrease in urinary nitrogen, as well as by the fall in plasma protein, which reached oedema levels. This aspect of the burns problem has been stressed by Taylor *et al.* (1943). Intravenous or intra-intestinal therapy with protein digests would appear to be necessary in these cases. It is possible that the low plasma protein in the later stages may be due in part to liver damage.

Bile Pigment and Liver Function

The very early rise in blood bilirubin is a striking feature of all the burns except those in Group I. In some of the severe cases, a hyperbilirubinaemia was present a few hours after the burn. This might be attributed to breakdown of haemoglobin in the burned tissue, a suggestion that has been put forward already by Cope and Rhinelander (1943), or to excessive haemolysis, or to a very early failure of liver function. Judging from the bilirubin levels, any liver damage must have been small, as only four patients had a bilirubin of over 1 mg. per cent., and the highest figure reached was 2·2 mg. per cent. on one occasion. Clinical jaundice was never seen in the first weeks, and was only observed in one case (No. 51) as a terminal event. In this boy, extensive liver damage was found post-mortem (see p. 199).

The increased excretion of urobilinogen found in two cases points to some failure in liver function in these patients, who showed an initial small rise in bilirubin.

The published figures on liver function are not numerous, and in some cases treatment was by tannic acid, which has been shown to produce liver damage. Boyce and McFetridge (1938) report 4 patients tested by Quick's hippuric acid test, all of whom showed some loss of function. Wolff *et al.* (1940) give results of bilirubin, bromsulphalein retention, hippuric acid excretion, and plasma prothrombin in 3 cases of second and third degree burns of 15–25 per cent. of the body surface. One patient, treated with tannic acid, died on the 8th day and the two others were treated with 2 per cent. gentian violet. Bilirubin increased to 2 mg. per cent. in the first 48 hours in two cases, one of which was tannic acid treated. Bromsulphalein retention between the 4th and 15th days was found in each case, and hippuric acid excretion was variable.

Abbott & Holden (1942) give figures for plasma prothrombin in three cases treated with tannic acid; two showed jaundice and had a low prothrombin and, at autopsy, severe liver necrosis. The third had only slight jaundice, no loss of prothrombin, and recovered. The general opinion is that the correlation between the various liver function tests is disappointing.

Carbohydrate Metabolism

From the few readings of blood sugar which we have taken, there is evidence of a very transient rise in blood sugar during the first few hours after burning, but not to the extent which might be expected from the results of animal experiments, e.g., those of Clark and Rossiter (1944). The meagre published figures for blood sugar after burns in man give the same picture as we have found. Davidson (1925), in a study of 25 patients, reported six cases where the blood sugar rose above 160 mg. per cent.; the highest figure he records is 208 mg. per cent. This rise occurred on the first day, and the blood sugar was normal after 24 hours. McIver (1938) examined 16 cases and does not give figures, but says that samples of blood taken on the first day showed in the majority a marked increase, rising as high as 266 mg. per cent. in one case. Lambret *et al.* (1936) reported a rise in three cases, and give figures for one where the blood sugar was 275 mg. per cent. two hours after the burn. Underhill *et al.* (1923) give figures over 160 mg. per cent. in 9 out of 20 patients studied; the highest figure is 216 mg. per cent.

Absorption from the Burned Surface

The absorption of sulphonamides from the surface of even deep burns is of considerable interest, as it gives direct proof that other soluble substances present in or on the burn may be absorbed into the circulation to a very considerable extent. The absorption of sulphonamides from burns has been reported previously; e.g. Gordon and Bowers (1942) found that, after the insufflation of sulphanilamide powder on burns of 22 per cent. of body surface on

three successive days, the blood sulphanilamide concentration rose to a peak of 59 mg. per 100 ml. Zondek *et al.* (1942) reported that a small absorption took place through the intact skin when sulphanilamide was applied in a suitable base, but the blood concentrations were only 1–2 mg. per 100 ml.

EXPOSURE TO SULPHONAMIDE DRUGS

It should be noted that all the patients examined in this investigation were exposed to some concentration of a sulphonamide drug for the first days or weeks after the burn, and the possibility that some of the changes seen were due to the action of the drug cannot be excluded.

SERUM POTASSIUM

As far as the cases examined are concerned, there is no evidence of any significant rise in serum potassium, but in this investigation we have not been able to obtain sufficient figures from the Group IV cases to draw final conclusions. Wilson and Stewart (1939) found the potassium slightly increased in 20 cases, with low serum sodium. Tenery (1941) reports increases in serum potassium with all but the mildest burns, but in no case did the figure reach toxic level. Therefore evidence at present available is against the hypothesis that a rise in serum potassium plays a part in producing burns shock.

In conclusion, we would draw attention to the considerable variations in the responses of individuals burned to the same degree, and to the comparatively small alterations occurring in the chemical constituents even in severe burns.

OUTSTANDING PROBLEMS

(i) CHANGES ASSOCIATED WITH BURNS SHOCK

The opinion that oedema of the brain occurs in burns shock, which is based on the naked eye appearance of brains removed post-mortem (see p. 197), did not receive support from the results of chemical analysis of three such brains, including two with naked-eye evidence of oedema. There is no doubt that capillary permeability is altered locally in burns shock, and a further investigation of the sodium and potassium concentrations in serum and tissues is indicated.

(ii) LIVER DAMAGE

The question whether a partial loss of liver function occurs soon after the burn is still undecided. But the balance of evidence is in favour of some slight loss of function, which may only last a few days even in cases of severe burns. Liver damage may occur later with the unhealed severe burns, and this is a possible factor in maintaining the hypoproteinaemia seen in these patients. The cause of this late damage is not yet known and, apart from the influence of such therapeutic agents as tannic acid, prolonged infection of the large raw absorbing area appears to be the most likely factor.

(iii) MAINTENANCE OF NITROGEN EQUILIBRIUM, AND REGENERATION OF THE PLASMA PROTEINS

The factors which may be responsible for the hypoproteinaemia are (*a*) the continued loss of plasma protein by exudation from the raw surface; (*b*) a metabolic response to injury, with loss of nitrogen in the urine; (*c*) inability of the patient to ingest sufficient protein food to make up for losses (*a*) and (*b*); (*d*) a loss of liver function referred to above; (*e*) infection.

With regard to (*a*), a measure of the actual loss of protein in the exudate would appear to be most desirable. This could be achieved either by an analysis of the dressings, which, according to our preliminary investigations should be possible, or by actual collection of the exudate in some form of envelope dressing.

(*b*) The loss of nitrogen in the urine, while it was large in some of our patients, was not as excessive as that reported by some of the American workers; in fact, in some cases the nitrogen excretion fell to low levels in the late hypoproteinaemia stage. A complete study of nitrogen balance, including the loss by exudation, is required to elucidate this problem.

(*c*) The inadequate intake of protein by mouth can probably be overcome by means of the administration of protein digests intravenously or by intestinal intubation.

(iv) The slow healing and failure of skin grafting, which is such an important problem in the severe burns, has been associated with the plasma protein deficiency. But other factors may be responsible, e.g. avitaminosis. Avitaminosis-C can be excluded, as the patients were given ascorbic acid daily by mouth.

A nutritional lack of members of the vitamin B complex, particularly riboflavin and nicotinic acid, cannot be excluded on theoretical grounds, and, so far as we are aware, a detailed investigation of the vitamin B complex in relation to burned patients has yet to be made.

ACKNOWLEDGMENTS

It is a pleasure to acknowledge our indebtedness to Dr. Leonard Colebrook and our other colleagues on the Burns Unit for much assistance and encouragement.

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STUDIES OF BURNS AND SCALDS

(REPORTS OF THE BURNS UNIT, ROYAL INFIRMARY, GLASGOW, 1942–43)

PART VI.—POST-MORTEM FINDINGS IN THIRTY FATAL CASES OF BURNING

BY

THOMAS GIBSON, M.B., Ch.B., F.R.C.S.E.

(Working with a grant from the Medical Research Council)

CONTENTS

INTRODUCTION

It has been stated (Pack, 1926) that "there are no internal or visceral lesions pathognomonic of burns and scalds" and, while this is probably true, numerous authors have published conflicting reports describing various changes, notably in the liver and in the suprarenals, after burning. Many of the lesions described were probably due either to the local treatment adopted, e.g. central liver necrosis after tannic acid (Wells, Humphrey and Coll, 1940; Erb, Morgan and Farmer, 1943), or to complications of burns, such as infection. The purpose of this paper is to record the post-mortem appearances in a series of cases of burns in which tannic acid was not used, and in which particular attention was paid to the prevention and control of infection. The majority of the findings have been negative, and no particular lesion has been found typical of death from burning. In view of the many different lesions which have been described by other workers, however, these two facts alone are thought to justify publication of our data.

MATERIAL STUDIED

During the period January 1942 to September 1943, permission for autopsy was obtained in 30 patients dying after injury by burning. A complete routine post-mortem examination was performed in each case, and, from most of the bodies, specimens for histological study were removed from liver, kidneys, suprarenals, spleen and thyroid; in some of them, histological specimens were taken also from brain, thymus, heart muscle and skin. Because of the repeatedly negative findings in the other organs, however, kidney and liver alone were studied in a few of the later cases. The autopsies were carried out at a varying time after death, the shortest time being 5 hours and the longest 40 hours. The cadavers had been stored in a refrigerator during the intervening period.

For descriptive purposes, and because of a probable difference in aetiology, it is convenient to divide the deaths into two groups: those which occurred during the "shock period"—which has been arbitrarily regarded as the first 96 hours after burning—and those which occurred after this time. Nineteen deaths occurred during the former period, and 11 between 4 days and 9 weeks after burning.

I.—DEATHS OCCURRING DURING THE "SHOCK PERIOD"

Of the 19 patients in this group, 14 had been treated by transfusions of serum or plasma, while the burns had been dressed with creams containing sulphonamide in proportions of either 3 per cent. or 10 per cent. Most of the remaining 5 patients had received only morphine in doses sufficient to relieve pain. The pathological findings in these sub-groups showed no essential difference, and no purpose would be served in describing them separately. Table XXXIV gives the relevant data for each case; the 5 which received no plasma or serum are given first, as they serve as a partial control over those which follow. The cases are arranged according to the percentage surface area involved in the burn.

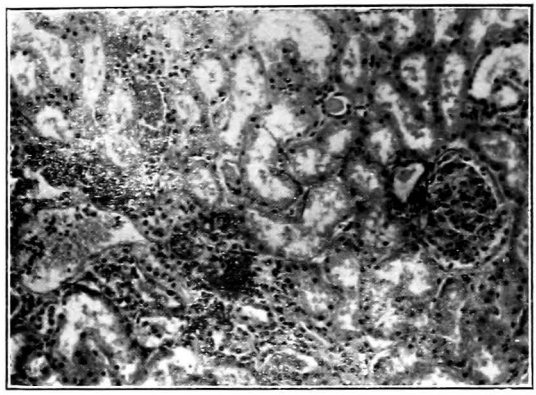
TABLE XXXIV

No.	*Initials*	*Age*	*Area (per cent. of body surface)*	*Survival period (hours)*	*Amount of plasma or serum given (c.c.)*	*Chief pathological findings*	*General notes*
84	C.A.	39	90	5	—	Suggestion of pressure cone in medulla. Collapse in both lungs. Scanty granular casts in kidney.	Just before death, haematocrit reading had risen to 70 per cent.
125	Mrs. M.	59	90	14	—	Congestion and oedema of brain, with excess blood-stained fluid at base. Brown granular casts in kidney.	
115	M.C.	17	66	14	—	Subpleural haemorrhage, ? petechial. Granular casts in kidney. Collapse in both lungs.	
126	Mrs. J.	46	45	26	—	Large pulmonary embolus. Slight oedema and congestion of brain. Marked fatty change in liver.	Patient was conscious until just before death.
127	Mrs. G.	75	25	20	—	Oedema of brain. Fatty change in liver, and casts in kidney.	
46	M.McD.	10	80	90	6,600	Areas of collapse in both lungs. Oedema and congestion of brain. Marked renal changes, with numerous casts.	Blood urea at death = 232 mgm. per cent. Terminal hyperpyrexia.
45	J.M.	6	80	10	1,500	Congestion, oedema and collapse of lungs.	Excessive amounts of fluid given too rapidly intravenously, with clinically acute pulmonary oedema.

TABLE XXXIV—*contd.*

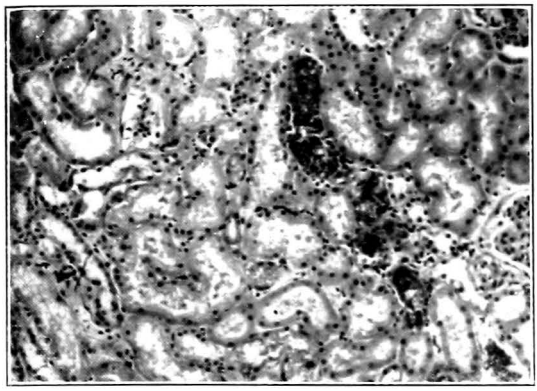
No.	*Initials*	*Age*	*Area (per cent. of body surface)*	*Survival period (hours)*	*Amount of plasma or serum given (c.c.)*	*Chief pathological findings*	*General notes*
56	T. McM.	51	75	22	7,600	Petechial haemorrhages in stomach. Congestion of brain. A few hyaline casts in kidney.	Excessive fluid replacement at late stage.
55	Mrs. C.	50	75	26	3,600	Subarachnoid haemorrhage over occiput. Subpleural haemorrhages. Sub-endocardial haemorrhages, and haemorrhages into renal pelvis.	Burning due to cordite explosion. Inadequate fluid replacement. Hyperpyrexia.
54	W.N.	40	40	39	2,900	Superficial congestion of brain. Petechial haemorrhages in stomach, and under pleura and endocardium.	Inadequate fluid replacement.
52	T.M.	14	31	32	2,300	Slight oedema and congestion of brain. Petechial haemorrhages in stomach, bowel and under endocardium.	Inadequate fluid replacement. Hyperpyrexia.
41	J. McG.	4	30	34	2,650	Pressure cone, congestion and oedema of brain. Petechial haemorrhages in many organs. Fatty change in liver.	Excessive fluid replacement. Terminal hyperpyrexia.
42	B.B.	2	29	11	1,500	Congestion and oedema of brain. Petechial haemorrhage in stomach and endocardium. Small area of collapse in lung.	Inadequate fluid replacement.
33	Mrs. De	68	26	74	2,700	Oedema and congestion of brain. Scanty granular casts in kidney. Marked fatty change in liver.	Inadequate fluid replacement. Terminal hyperpyrexia.
40	J. McF.	2	20	26	800	A few small haemorrhages in thymus.	Inadequate fluid replacement. Mild convulsions.
28	J. McE.	8	14	31	2,350	Marked cerebral oedema. Sub-endocardial haemorrhage.	Excessive fluid replacement. Terminal hyperpyrexia.
27	J. McA.	2	13	11	1,300	Cerebral congestion and oedema. Sub-pleural haemorrhage and petechiae in renal pelvis.	Fluid given too late. Hyperpyrexia.
20	M.W.	6	10	36	1,900	Oedema and congestion of brain. Several infarcts in lung. Petechial haemorrhages in thymus. Haemorrhage in suprarenal.	Excessive fluid replacement. Terminal hyperpyrexia.
10	J.W.	66	6	12	800	Evidence of hypertensive encephalopathy.	Patient died in apoplectic stroke.

FIG. 45



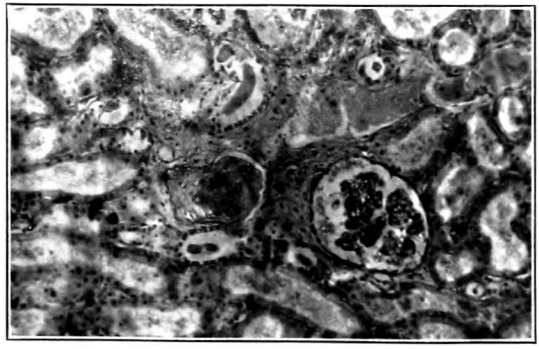
Kidney from Case 46. Note the swelling of the glomerular capsular epithelium, the catarrhal change in the tubules, and the numerous casts of hyaline and granular type. (× 150.)

FIG. 46



Kidney from Case 46. Large ribbon-like granular cast blocking tubule. (× 150.)

FIG. 47



Kidney from Case 46. Note albuminous exudate in the glomerular spaces. Several small hyaline casts are seen, and there is a large laminated pigmented cast (yellow-brown in colour) in the centre of the field. (× 150.)

Pathological Findings

Burned Areas

The degree and extent of burning varied greatly from case to case, and the only constant finding was considerable local oedema of the tissues around the burn. Oedema was not noted in sites other than the burned areas, except in the brain and in the lungs in some cases (see below).

Petechial Haemorrhages

In most of the cases, small punctate haemorrhages were noted in various organs. Histologically, they showed nothing of importance, and no organisms were seen. The mucosa of the stomach and duodenum were the most common sites, and numerous small haemorrhages were usually present. The other sites of such haemorrhages were, in descending order of frequency, sub-pleural, sub-endocardial, in the renal pelvis and in the thymus. Sub-pleural haemorrhages were, as a rule, larger than those elsewhere. In Case 55 a large subarachnoid haemorrhage was present, in addition to petechiae under the visceral pleura and endocardium, but the possibility that this may have been due to trauma to the head cannot be excluded.

Central Nervous System

The most constant finding in all patients dying in the early stages of burns was oedema of the brain, as evidenced by flattening of the convolutions and also by increased fluid in the brain on section. Some cases showed a noticeable excess of cerebro-spinal fluid, after removal of the brain; two had a definite pressure cone through the foramen magnum, while a third showed slight coning. A varying degree of congestion accompanied the oedema: occasionally, it was confined to the surface vessels, but it was more commonly observed in the penetrating branches on section of the brain, particularly in the region of the corona radiata and the basal ganglia. Specimens from basal ganglia, pons and cortex were examined histologically, but the findings were entirely negative.

Kidneys

Kidneys from all these cases were examined histologically. Some showed no pathological change, while others, particularly those from the most extensively burned patients (Cases 84, 115, 46, 45, 56 and 33), presented a varying degree of catarrhal change in the tubular epithelium, especially in the convoluted tubules. Accompanying this, were found a varying number of casts. These were of three main varieties: (*a*) granular and cellular casts, apparently derived from degenerating epithelium; (*b*) hyaline casts; and (*c*) pigmented casts of a brick-red or yellow-brown colour, grossly granular or lamellated in appearance. The casts were most numerous in the convoluted tubules and the ascending limb of Henle's loop. Intact red blood cells were not observed in the glomerular spaces or tubules, but free haemoglobin was present in the plasma and urine of the most extensive cases, and the pigmented casts may have been derived from that source.

These changes were most striking in Case 46, a child aged 10 years, who survived for 4 days with a deeply coagulated burn involving 80 per cent. of the body surface. During life, there was considerable oliguria, and at death the blood urea had risen to 232 mgm. per 100 c.c. The sections of the kidneys showed swelling of the capsular epithelium of the glomeruli, albuminous exudate in the glomerular spaces, considerable catarrhal change in the tubular epithelium (with loss of nuclear staining and partial disintegration of the cells), and numerous casts of all three types mentioned above. The general picture (see Figs. 45–47) bore a close resemblance to that described in patients dying from crushing injuries (Bywaters and Dible, 1942).

The other cases—which survived for a shorter period—showed similar but less obvious changes in the kidneys. The nature of these renal lesions is being more fully investigated, and will be reported later.

Suprarenals

Haemorrhage in the medulla of one suprarenal was noted in Case 20. In view of the suggestion by various workers that upset in the secretions of the suprarenal may be a causative factor in shock, particular attention has been paid to histological examination of this organ, but the findings were almost entirely negative. Various degrees of vacuolation and incipient degeneration of the cortical cells were seen, but were almost certainly due to post-mortem change.

Liver

In view of the work of Wilson *et al.* (1938), and their description of central lobular necrosis in burns and its relationship to death in the shock period, considerable attention has been paid to the liver in this series. No case showed such necrotic changes. Fatty change was, however, noted in five subjects. It was very marked in Cases 126, 127, 41 and 33, and slight in Case 56.

Lungs

Congestion was present in all cases; in some, it was accompanied by a varying degree of oedema, which was apparently related to the amount of intravenous fluid which the patient had received in life. Generally speaking, cases which had no replacement therapy—and those which had had inadequate replacement therapy—showed little or no pulmonary oedema. Oedema was most evident in cases where fluid administration had been excessive, or where replacement therapy had been delayed to a late stage. Six cases showed collapse of the lung: in Cases 84 and 115, the collapse was massive; in Cases 46, 45, 41 and 42, it was confined to small localized patches. One case (No. 20) showed several small haemorrhagic infarcts.

Thyroid

As was to be expected, the histological appearance of the thyroid gland varied considerably. Excluding, however, lesions which had obviously been present for some time before injury, the only relatively constant change was a "nibbled" appearance of the margins of the colloid in the vesicles, and vacuolation of the colloid. This appearance suggested recent and rapid mobilization of the colloid from the vesicles.

Other Organs

The spleen was, as a rule, congested, but no other abnormality was noted. No pathological change was found in the thymus.

Discussion

The most noteworthy feature of this series of autopsies was the absence of any specific lesion gross enough to suggest the proximal cause of death. The mainly negative findings in both suprarenals and liver are specially interesting, since damage to both these organs has been suggested as a cause of fatality. Pathological changes in the suprarenals after burns have been described by Weisskotten (1919), and in recent years adrenal cortical extract has been suggested as a therapeutic measure in burns shock (Wilson *et al.*, 1938; Elkinton, Wolff and Lee, 1940). Except for one case, in which there was a small haemorrhage into one adrenal gland, we have found no evidence of a pathological basis for this line of treatment.

Wilson *et al.* (1938) described central lobular necrosis, with an accompanying eosinophilia, in the livers of burned patients dying during the shock period, and other workers have confirmed these findings (Wells, Humphrey and Coll, 1942). Recent work (Wells *et al.*, 1942; Erb, Morgan and Farmer, 1943; Barnes and Rossiter, 1943; Cameron, Milton & Allen, 1943) has suggested, however, that these lesions were mainly due, not to the burns themselves, but to the absorption of tannic acid applied to the burned surfaces. No patient in the present series was treated with tannic acid, and the absence of any case showing necrotic lesions in the liver lends additional support to the current view. The cause of the fatty change which was noted in five cases is obscure, but the lesion by itself was insufficient to cause death, though it may have been a contributing factor. An interesting point is that, roughly speaking, the occurrence and degree of fatty liver were directly correlated with the length of the survival time. Professor G. R. Cameron points out that fatty liver is frequently evidence of fasting only, and not of toxaemia or anaemia; the degree of fatness of the subject plays a part.

In the kidneys of burned patients, Erb, Morgan and Farmer (1943) noted varying degrees of epithelial degeneration, with hyaline and finely granular casts in the convoluted and collecting tubules—particularly in the latter. In dogs burned experimentally, Keeley, Gibson and Pijoan (1939) noted, at post-mortem, albuminous material within the capsular spaces of the glomeruli, and occasional hyaline and granular casts in the convoluted tubules. Weisskotten (1919) found fibrin thrombi in the glomerular tufts.

In the present series, renal changes were found only in the cases of most extensive burns and cannot be indicted as the cause of death in burns shock, although they may occasionally be a contributory factor. The nature of the change is speculative. The epithelial degeneration suggests some form of "toxic" mechanism, while the pigmented casts—and the general resemblance to the kidney lesions in "crush syndrome"—suggest a relationship to the excretion of haemoglobin derivatives. In extensive deep burns, all the blood circulating through the affected parts is inevitably damaged or destroyed, and the presence of free haemoglobin in the plasma is commonly observed shortly after injury in such patients. At least two of the patients in whom pigmented casts were found post-mortem had had such intense intravascular haemolysis that the blister fluid was notably haemorrhagic, and it seems probable that the pigmented casts themselves were due to excretion of this liberated pigment or its breakdown products.

Riehl (1931) was of the opinion that patients with severe burns died a cerebral death, and he described gross congestion of all the cerebral vessels, with oedema of the brain and increase in the fluid content. In this series also, death appeared to be cerebral in origin, the patients passing through a phase of increasing mental upset to coma and death. The only evidence of damage to the brain, however, was a varying degree of oedema and congestion. (It should be emphasized that the presence of cerebral oedema was usually assessed only by naked-eye evidence of flattening of the convolutions. An attempt was made in three cases to get confirmatory evidence by estimations of the water and chloride content of the white matter, but the figures obtained were not appreciably higher than normal (p. 183). The presence of a pressure cone in at least one of those cases was definite evidence of an increase in intra-cerebral pressure. In addition, in three patients in the terminal stages of burns shock, lumbar puncture was performed and the C.S.F. pressure was found to be considerably increased—between 280 and 320 mm. of saline.)

In a previous paper (Gibson and Brown, p. 49, above), it has been shown that both the onset of cerebral symptoms and death in burns shock may be prevented by adequate fluid replacement. It seems possible, therefore, that

death may be due to anoxia of the vital centres in the brain, and that the cerebral oedema may result from a similar effect on the cerebral capillary walls.

In the other organs, the general picture was one of capiliary congestion, and the factors causing this were probably responsible for the petechial haemorrhages which were noted in various organs. Similar congestion and minute haemorrhages are often found in deaths from traumatic shock, and it seems possible that they are due to anoxia of the capillary endothelium, with loss of capillary tone and rupture at occasional sites. The influence of a hypothetical " toxic factor " cannot, however, be excluded.

II.—DEATHS OCCURRING AFTER THE "SHOCK PERIOD"

There were 11 autopsies in this series. Since the causes of death in the later stages of burns are many and varied, it is not feasible to describe these cases as a homogeneous group. For descriptive purposes, they have been divided as follows :—

(*a*) Deaths due to the existence of an extensive raw area (5 cases).

(*b*) Deaths due to respiratory complications (2 cases).

(*c*) Deaths from other causes (4 cases).

(*a*) *Deaths due directly to the existence of an extensive raw area*

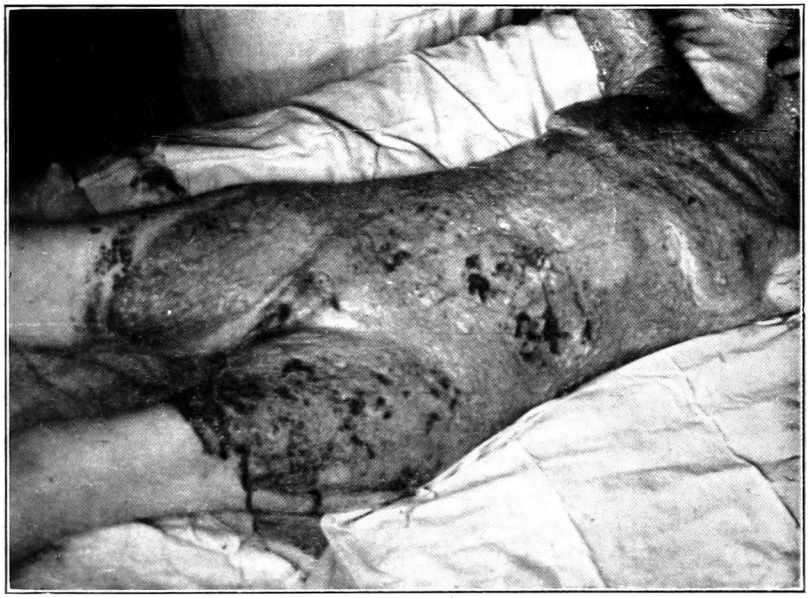
The relevant details of these cases are presented in Table XXXV :—

TABLE XXXV

No.	*Initials*	*Age*	*Extent of burn (per cent. of body surface)*	*Survival period*	*Chief pathological findings*	*General notes*
83	C.M.	68	24	11 days	Extreme congestion of lungs. Heart slightly enlarged. Chronic venous congestion of liver. Small chronic ulcer in first part of duodenum.	
49	E.R.	9	40	31 days	Two chronic ulcers in first part of duodenum. Thrombosis of mesenteric veins. Some basal congestion of lung.	Haematemesis and melaena during life.
51	P.G.	6	45	43 days	Hypostatic congestion of lungs. Splenic culture showed haemolytic streptococci.	
57	R.B.	44	47	37 days	Suppurative broncho-pneumonia. Liver showed scattered areas of necrosis.	
60	Mrs. J.R.	41	50	64 days	Small chronic ulcer in first part of duodenum. Gross fatty change in liver.	Haematemesis during life.

All the patients had been extensively and deeply burned, with the result that, after two or three weeks, when the sloughs had separated, a very large raw surface resulted (Fig. 48). It proved impossible to keep such an area

FIG. 48



Extensive raw surface which resulted in Case 60 five weeks after burning. In addition, the greater part of both arms, and more than half the area of the back, were raw. There was an almost complete lack of granulation tissue.

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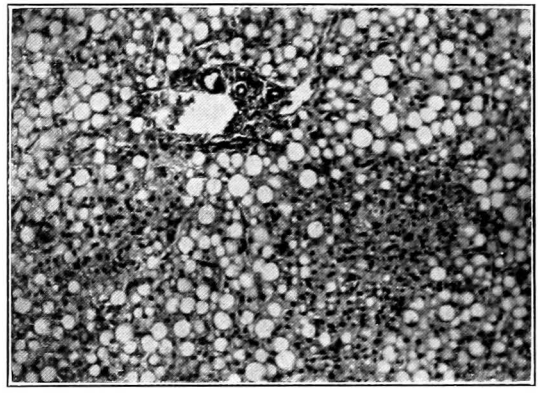
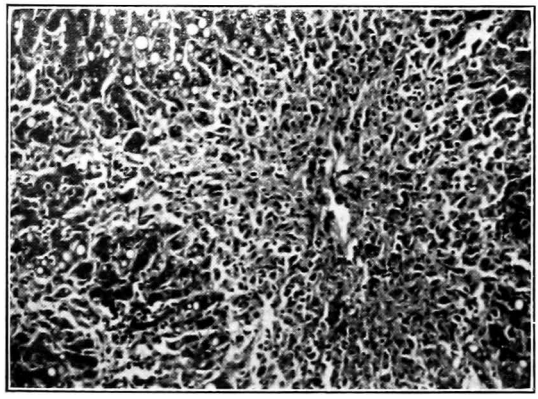
FIG. 49



Liver from Case 60. Massive fatty change involving practically the whole organ. (× 150.)

FIG. 50



Liver from Case 51. Typical area of central lobular necrosis. A slight degree of fatty change coexists. (× 150.)

completely uninfected, and there was constant purulent exudation into the dressings. The temperature remained high, and the plasma protein level fell progressively to 4 gm. per cent. Accompanying the hypoproteinaemia was a progressive degree of anaemia. Transfusions of whole blood and of plasma were administered, but were apparently insufficient to cause much improvement. Recently, Taylor, Levenson, Davidson and Browder (1943) have shown that two factors contribute to the hypoproteinaemia—excessive nitrogen catabolism and a deficient protein-intake. Attempts to supplement the diet by mouth in our cases with casein hydrolysates failed, partly because of the nauseating taste of these preparations. Clinically, death appeared to be due to a combination of infection, hypoproteinaemia and anaemia.

At post-mortem, and for some time before death, two of the patients (Cases 60 and 51) showed some degree of generalized oedema, probably due to the hypoproteinaemia. Little or no granulation tissue had formed on the raw surfaces. Sections of the raw area from Case 60 showed the base to be composed entirely of fat, with some polymorphonuclear infiltration; there were no granulations on the surface, in spite of the fact that more than nine weeks had elapsed since injury.

The majority of the organs showed only generalized pallor (in keeping with the anaemia), and few gross pathological changes were found. The only noteworthy findings were degenerative changes in the liver in three cases, and duodenal ulcers in three cases.

The changes in the liver were variable. Case 60 showed massive fatty change, involving practically the whole organ, with little normal liver tissue remaining (Fig. 49). Case 51 showed large areas of lobular necrosis, central in situation, and some degree of fatty change (Fig. 50). This patient had a haemolytic streptococcal infection of the raw surface, and streptococci were grown in pure culture from the spleen at post-mortem. In Case 57 there were small scattered areas of necrosis throughout the liver, but the appearances were much less marked than in Case 51. As pointed out earlier in this paper, none of the patients in our series had been treated with tannic acid, and the findings in Cases 51 and 57 support the view that, while tannic acid treatment may be the most frequent cause of hepatic necrosis after burns, it is not the only one, especially in cases of long survival.

Three cases showed duodenal ulcer (Nos. 60, 83 and 49). The ulcers were of the chronic or subacute type, but with little surrounding fibrosis, and apparently of fairly recent origin. Two of the patients had suggestive symptoms during life—No. 60, haematemesis; and No. 49, both haematemesis and melaena.

In general, it may be stated that the autopsy findings were in keeping with those resulting from the continued existence of a very extensive raw surface. The hepatic changes were probably due to a toxic effect on the liver from continued sepsis. The occurrence of gastric and duodenal ulcers (Curling's ulcer) after burns is well established, and Harkins (1943) has collected 98 cases; whether the ulcers are to be regarded as due specifically to the burning or to the later infection of the raw surface is difficult to say. Necheles and Olson (1942), in experimental burns in dogs, noted greatly increased gastro-intestinal mobility shortly after the injury, and, clinically, severe vomiting is a frequent occurrence in burns shock (Gibson and Brown, p. 67, above). Haematemesis is also an occasional symptom. It is possible that acute ulcers may form at this period, and later either heal or become chronic. The post-mortem evidence in patients dying during the shock period only partially confirms this suggestion; while congestion and punctate haemorrhages were commonly found, no actual ulceration was observed in either stomach or duodenum.

(*b*) *Deaths due to Respiratory Complications*

In both the cases to be described, death occurred about 96 hours after burning, and they might have been included in the deaths during the shock period. However, as the clinical picture was one of acute respiratory failure rather than of burns shock, it seemed better to describe them separately.

In our experience, the incidence of respiratory complications after burns in young children is high, although this does not seem to be generally recognized. Clinically, the picture is one of acute broncho-pneumonia. Typically, the respiratory rate begins to rise about 24 hours after injury, and this is accompanied by a rise in temperature. Physical examination of the chest shows scattered areas of dullness; the breath sounds become more harsh, and often of bronchial character, and numerous moist adventitious sounds are heard. Three deaths have occurred from this complication, and in two of the patients permission to perform autopsy was obtained. *The lesion found was not broncho-pneumonia but rather a patchy collapse of the lungs*, with some congestion of the bronchial mucosa, this finding being verified histologically. In one case there was no evidence of infection of the lungs, but the other showed microscopic evidence of an early infection.

Collapse of the lungs has already been noted in several of the patients dying in the shock period. No evidence as to its cause was found.

(*c*) *Deaths from Other Causes*

Death in these four patients was due to: agranulocytosis (1 case), miliary tuberculosis (1 case), cerebral softening (1 case), cause unknown (1 case). The details of the cases are as follows:—

Case 48.—Female, aged 7—deep burn involving 40 per cent. of the body surface.

Death occurred on the 22nd day after burning; it was due to agranulocytosis, which had been observed for several days beforehand, and did not respond to either blood transfusion or injections of "Pentnucleotide". This patient had been treated with 10 per cent. sulphanilamide cream locally and, in addition, had received 2 gm. of sulphapyridine by mouth on the third and fourth days; it seems probable that the sulphonamide was the cause of the agranulocytosis. The post-mortem findings confirmed agranulocytosis as the cause of death, and were not otherwise noteworthy.

Case 29.—Male, aged 14 months—burn involving 18 per cent. of the body surface.

Death occurred on the 36th day, following gas and oxygen anaesthesia prior to skin grafting. Post-mortem examination revealed generalized miliary tuberculosis.

Case 61.—Female, aged 37—burn involving 50 per cent. of the body surface.

Death occurred on the 16th day. From the fourth day onwards, the patient had a continuous high temperature, always above 101° F. and rising to above 107° F. on the fourteenth day. All attempts to reduce this temperature failed. Locally, the burns had been infected chiefly with *Proteus* and with staphylococci; on two occasions, haemolytic streptococci were found, but they were rapidly eliminated by penicillin. It seemed unlikely that the temperature was due wholly to infection of the burned area. Post-mortem examination revealed an area of recent softening in the brain; this was situated in the anterior part of the left thalamus, and was about 1 cm. in diameter. There were no other noteworthy findings.

Case 38.—Female, aged 19—burn involving 22 per cent. of the body surface.

Extremely deficient mentally. She received 4½ litres of serum and plasma during the shock period, and showed little evidence of shock. Following this, she gradually became weaker, while the temperature remained high—between 101° and 104° F. Post-mortem examination showed some oedema of the lungs, punctate haemorrhages in the stomach, and a marked trigonitis of the bladder (this latter being attributable to repeated catheterization during life), but no lesion gross enough to suggest the cause of death was found. Splenic culture proved sterile.

SUMMARY

1. The post-mortem findings in 30 fatal cases of burning injuries are described; 19 deaths occurred during the "shock period"; 11 at a later date.

2. In the patients dying within the "shock period", the most noteworthy post-mortem features were:—

(*a*) The absence of central lobular liver necrosis.

(*b*) The absence of damage to the suprarenals (except in one case).

(*c*) The occurrence, in cases of very extensive burns, of catarrhal changes in the renal epithelium, with the presence of various casts, including pigmented types, in the tubules.

(*d*) Oedema and congestion of the brain.

(*e*) The occurrence of punctate haemorrhages in various organs.

3. The deaths after the "shock period" were due to the complications of burns, or to intercurrent disease, rather than specifically to the burns themselves. The causes of death were as follows:—

(*a*) Sepsis, hypoproteinaemia and anaemia, resulting from the presence of a very extensive raw area—5 cases.

(*b*) Respiratory complications—2 cases.

(*c*) Other causes:

Agranulocytosis	1 case
Miliary tuberculosis	1 case
Cerebral softening	1 case
Cause unknown	1 case

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APPENDIX I

SUMMARY OF PATIENTS DISCUSSED IN PARTS III–VI OF THIS MONOGRAPH

(S.B.B. = Superficial blister burn; P.S.L. = Partial skin loss; W.S.L. = Whole thickness skin loss.)

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died? Day of death*
1	4½	F.	8 per cent.; buttock, hand.	4½ per cent. P.S.L. 3½ per cent. S.B.B.	1,600	L.
2	6	F.	7–8 per cent.; head, forearms, abdo., thigh.	Mainly P.S.L.	1,100	L.
3	8	F.	5 per cent.; thigh and leg.	Mainly P.S.L.	1,600	L.
4	2	M.	9 per cent.; arm and shoulder.	4 per cent. S.B.B. 5 per cent. W.S.L.	800	L.
5	5	M.	7 per cent.; axilla and back.	W.S L.	1,000	L.
6	29	M.	12 per cent.; buttocks and thighs.	6 per cent. S.B.B. 6 per cent. P.S.L.	1,000	L.
7	19	F.	15 per cent.; chest and back.	7 per cent. S.B.B. 8 per cent. P.S.L.	800	L.
8	20	F.	16 per cent.; breast, arm, thigh, abdo.	9 per cent. P.S.L. 7 per cent. W.S.L.	1,600	L.
9	31	F.	16 per cent.; abdo., forearm and thigh.	2 per cent. S.B.B. 3 per cent. P.S.L. 11 per cent. W.S.L.	2,700	L.
10	66	M.	6 per cent.; head, neck and shoulder.	Mostly W.S.L.	800	D. 1
11	32	F.	6 per cent.; hands, face.	5 per cent. S.B.B. 1 per cent. W.S.L.	1,000	L.
12	32	M.	8 per cent.; face, palms.	5 per cent. S.B.B. 3 per cent. P.S.L.	1,500	L.
13	30	F.	10 per cent.; face, hands, ankles.	3 per cent. S.B.B. 7 per cent. W.S.L.	1,600	L.
14	27	F.	10 per cent.; back and shoulder.	7 per cent. S.B.B. 3 per cent. W.S.L.	2,500	L.
15	37	M.	10 per cent.; trunk axilla and arm.	7 per cent. S.B.B. 8 per cent. W.S.L.	1,100	L.
16	31	F.	15 per cent.; back and arm.	8 per cent. { S B B. / P.S.L. 7 per cent. W.S.L.	1,200	L.
17	45	M.	15 per cent.; face, neck, shoulder, forearms.	11 per cent { S.B.B. / P.S.L. 4 per cent. W.S.L.	1,400	L.

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died ? Day of death*
18	31	F.	16 per cent.; thighs and buttock.	2 per cent. S.B.B. 14 per cent. W.S.L.	3,000	L.
19	51	M.	19 per cent. ; R. leg.	16 per cent. W.S.L.	3,600	L.
20	6	F.	10 per cent.; trunk and thighs.	6 per cent. P.S.L. 4 per cent. W.S.L.	1,900	D. 3
21	6	M	10 per cent. ; shoulder, chest.	6 per cent. P.S.L. 4 per cent. W.S.L.	1,200	L.
22	9	F.	12 per cent. ; forearm, thighs.	8 per cent. P.S.L. 4 per cent. W.S.L.	1,000	L.
23	2	F.	15 per cent. ; back and buttocks.	8 per cent. S.B.B. 7 per cent. P.S.L.	1,900	L.
24	$\frac{9}{12}$	F.	15–20 per cent. : chest, thighs, R. arm.	15 per cent. P.S.L. approx. 5 per cent. W.S.L.	500	L.
25	5	F.	12 per cent. ; side, buttocks.	6 per cent. S.B.B. 6 per cent. P.S.L. and W.S.L.	1,400	L.
26	$4\frac{1}{2}$	M.	12 per cent.; thigh, buttock, legs.	6 per cent. P.S.L. 6 per cent. W.S.L.	1,600	L.
27	2	M.	13 per cent.; chest, shoulder.	Mostly P.S.L.	1,300	D. 2
28	8	F.	14 per cent.; thighs and legs.	3 per cent. S.B.B. 6 per cent. P.S.L. 5 per cent. W.S.L.	2,350	D. 2
29	$1\frac{2}{12}$	M.	18 per cent ; lumbo-dorsal region.	4 per cent. S.B.B. 4 per cent. P.S.L. 10 per cent. W.S.L.	540	D. 36
30	21	F.	20 per cent. ; buttocks, thighs, arms and back.	Mostly W.S.L.	2,200	L.
31	22	F.	22 per cent. ; R. thorax, axilla, arm.	Mostly W.S.L.	1,600	L.
32	49	M.	26 per cent. ; face, arms and legs.	Mostly P.S L.	3,400	L.
33	68	F.	26 per cent.; neck, trunk, thighs, hands.	10 per cent. P.S.L. 16 per cent. W.S.L.	2,700	D. 3
34	39	M.	20 per cent. ; face, arms, back.	10 per cent. S.B.B. 10 per cent. P.S.L.	3,600	L.
35	68	M.	20 per cent.; chest, arm, forearm.	Mostly W.S.L.	4,400	D. 21
36	37	M.	26 per cent. ; face, hands, arms, trunk.	6 per cent. W.S.L. 20 per cent. P.S.L., S.B B.	2,200	L.

Case No.	Age	Sex	Percentage of body surface burned—and sites	Depth of burning	Total fluid transfused (ml.)	Lived or died? Day of death
37	12	F.	22 per cent.; abdo., thighs, arms.	6 per cent. W.S.L. 16 per cent. S.B.B. and P.S.L.	3,200	L.
38	19	F.	22 per cent.; buttocks, thighs.	5 per cent. S.B.B. 17 per cent. W.S.L.	4,420	D. 8.
39	19	F.	26 per cent.; face, back, hands, legs.	18 per cent. S.B.B. 4 per cent. P.S.L. 4 per cent. W.S.L.	3,540	L.
40	2	M.	20 per cent.; head, hand, shoulder, forearm.	14 per cent. P.S.L. 6 per cent. W.S.L.	800	D. 2.
41	4	F.	28 per cent.; arms, buttocks, thigh.	8 per cent. S.B.B. 10 per cent. P.S.L. 10 per cent. W.S.L.	2,650	D. 3.
42	2 3/12	M.	29 per cent.; trunk, arms, face, neck.	20 per cent. P.S.L. 9 per cent. W.S.L.	1,500	D. 2.
43	6	F.	35 per cent.; trunk, arms, legs.	Mostly W.S.L.	2,250	D. 3.
44	2	F.	40 per cent.; trunk, face, arms, legs.	30 per cent. P.S.L. 10 per cent. W.S.L.	1,900	D. 2.
45	6	M.	75–80 per cent.; trunk, legs, arms.	Mostly W.S.L.	1,500	D. 1.
46	10	F.	80 per cent.; trunk, arms, legs.	Mostly W.S.L.	6,600	D. 4.
47	2	F.	22 per cent.; abdo., thighs, R. arm.	5 per cent. P.S.L. 17 per cent. W.S.L.	1,000	L.
48	7	F.	40 per cent.; trunk, thighs.	5 per cent. P.S.L. 35 per cent. W.S.L.	3,600	D. 22.
49	9	F.	40 per cent.; arm, abdomen, legs.	20 per cent. P.S.L. 20 per cent. W.S.L.	2,200	D. 31.
50	3	M.	44 per cent.; trunk, arms, legs.	24 per cent. P.S.L. 20 per cent. W.S.L.	3,200	L.
51	6½	M.	45 per cent.; trunk, arms, legs.	20 per cent. P.S.L. 25 per cent. W.S.L.	3,400	D. 43.
52	14	M.	31 per cent.; neck, trunk, arms, thighs.	19 per cent. P.S.L. 12 per cent. W.S.L.	2,300	D. 2.
53	68	F.	33 per cent.; back, arms, thighs.	24 per cent. P.S.L. 10 per cent. W.S.L.	2,000	D. 2.
54	40	M.	40 per cent.; trunk, face, arms.	Mostly W.S.L.	2,900	D. 3.
55	50	F.	75 per cent.; face, trunk, limbs.	20 per cent. S.B.B. and P.S.L. 55 per cent. W.S.L.	3,600	D. 2.

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died? Day of death*
56	51	M.	75 per cent.; trunk, arms, legs.	35 per cent. P.S.L. 40 per cent. W.S.L.	7,600	D. 1
57	44	M.	47 per cent.; trunk, arms, legs.	10 per cent. S.B.B. 20 per cent. P.S.L. 17 per cent. W.S.L.	3,600	D. 37
58	25	M.	40 per cent.; neck, trunk, arms, hands, thighs.	Mostly W.S.L.	5,600	L.
59	14	F.	40 per cent.; trunk, buttocks, thighs.	5 per cent. S.B.B. 5 per cent. P.S.L. 30 per cent. W.S.L.	2,200	L.
60	41	F.	45–50 per cent.; trunk, arms, thighs.	Mostly W.S.L.	7,200	D. 64
61	37	F.	50 per cent.; face, trunk, arms, legs.	10 per cent. W.S.L. 40 per cent. P.S.L.	3,600	D. 16
62	14	M.	50 per cent.; head, trunk, arms, legs.	Mostly P.S.L.	6,400	L.
63	60	M.	3 per cent.; R. foot	W.S.L.	—	L.
64	34	M.	1 per cent.; R. wrist	P.S.L.	—	L.
65	16	M.	4 per cent.; head, arms.	S.B.B., P.S.L.	—	L.
66	43	M.	4 per cent.; face, hand.	2½ per cent. S.B.B. 1½ per cent. W.S.L.	—	L.
67	51	M.	3 per cent.; face, neck.	S.B.B.	—	L.
68	35	M.	2 per cent.; R. arm	1 per cent. P.S.L. 1 per cent. W.S.L.	—	L.
69	19	F.	13 per cent.; buttock, legs, arm.	6 per cent. S.B.B. 7 per cent. P.S.L.	—	L.
70	35	M.	7 per cent.; head, forearms.	3 per cent. S.B.B. 4 per cent. P.S.L.	—	L.
71	78	M.	6 per cent.; face, hands.	3 per cent. S.B.B. 3 per cent. P.S.L.	—	L.
72	39	M.	8 per cent.; face, arms.	4 per cent. P.S.L. 4 per cent. S.B.B.	—	L.
73	40	M.	12 per cent.; face, neck, forearms.	6 per cent. S.B.B. 6 per cent. P.S.L.	—	L.
74	7	M.	8 per cent.; face, chest.	4 per cent. S.B.B. 4 per cent. P.S.L.	—	L.
75	1½	F.	14 per cent.; back, buttock.	6 per cent. S.B.B. 6 per cent. P.S.L. 2 per cent. W.S.L.	—	L.

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died ? Day of death*
76	32	M.	12 per cent. ; face, arms, back.	Mostly S.B.B.	—	L.
77	$1\frac{5}{12}$	M.	7 per cent. ; neck, elbow.	P.S.L.	—	L.
78	41	M.	12 per cent.; hands, forearm, leg.	4 per cent. S.B.B. 4 per cent. P.S.L. 4 per cent. W.S.L.	2,000	L.
79	42	M.	16 per cent. ; face, neck, arms.	10 per cent. S.B.B. 6 per cent. P.S.L.	—	L.
80	40	M.	16 per cent. ; face, arms.	8 per cent. S.B.B. 8 per cent. P.S.L.	—	L.
81	34	M.	22 per cent. ; face, trunk, arms.	10 per cent. S.B.B. 12 per cent. P.S.L.	—	L.
82	62	F.	21 per cent.; neck, chest, forearms, thighs, legs.	7 per cent. S.B.B. 7 per cent. P.S.L. 7 per cent. W.S.L.	2,300	D. 41
83	68	F.	24 per cent.; trunk, shoulder, thigh.	4 per cent. S.B.B. 10 per cent. P.S.L. 10 per cent. W.S.L.	4,400	D. 11
84	39	F.	90 per cent. ; all but left flank.	Mostly W.S.L.	—	D. 1
85	78	F.	70 per cent.; trunk, arms, thighs.	20 per cent. P.S.L. 50 per cent. W.S.L.	—	D. 1
86	35	M.	67 per cent.; head, trunk, arms, legs.	Mostly W.S.L.	—	D. 1
87	51	F.	1½ per cent. ; leg	S.B.B. and P.S.L.	—	L.
88	22	M.	3 per cent. ; foot	W.S.L.	—	L.
89	12	M.	4 per cent. ; leg	S.B.B.	—	L.
90	14	M.	4½ per cent. ; face, hands.	S.B.B.	—	L.
91	8	F.	4½ per cent.; shoulder, arm, chest.	1 per cent. S.B.B. 3½ per cent. P.S.L.	—	L.
92	66	M.	4 per cent. ; face, hand.	Mostly S.B.B.	—	L.
93	13	M.	3 per cent. ; face, chest.	1½ per cent. S.B.B. 1½ per cent. P.S.L.	—	L.
94	58	M.	5½ per cent. ; face, neck, hand.	S.B.B.	—	L.
95	9	M.	2 per cent. ; face, hand.	1 per cent. S.B.B. 1 per cent. P.S.L.	—	L.
96	13	M.	8 per cent. ; back	Mostly P.S.L.	—	L.

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died? Day of death*
97	39	M.	7 per cent.; chest	2 per cent. S.B.B. 5 per cent. P.S.L.	—	L.
98	16	M.	13 per cent.; legs	6 per cent. S.B.B. 7 per cent. P.S.L. and W.S.L.	—	L.
99	37	M.	6 per cent.; face, hands, arms.	S.B.B.	—	L.
100	42	M.	8 per cent.; head, arms.	1 per cent. S.B.B. 7 per cent. P.S.L.	—	L.
101	8	M.	9½ per cent.; legs	4 per cent. S.B.B. 5½ per cent. P.S.L.	—	L.
102	35	F.	7 per cent.; abdo., arm, leg.	2 per cent. S.B.B. 3 per cent. P.S.L. 2 per cent. W.S.L.	—	L.
103	59	M.	10 per cent.; back, arm.	5 per cent. S.B.B. 5 per cent. P.S.L.	—	L.
104	25	F.	12 per cent.; buttocks, thighs.	3 per cent. W.S.L. 9 per cent. P.S.L.	2,400	L.
105	33	F.	15 per cent.; chest, arms.	8 per cent. S.B.B. 7 per cent. P.S.L.	2,800	L.
106	7	F.	10 per cent.; back, legs.	6 per cent. S.B.B. and P.S.L. 4 per cent. W.S.L.	—	L.
107	36	F.	6 per cent.; shoulder, arm.	4 per cent. S.B.B. 2 per cent. W.S.L.	—	L.
108	43	F.	14 per cent.; buttocks, thighs.	10 per cent. S.B.B. and P.S.L. 4 per cent. W.S.L.	—	L.
109	16	M.	8 per cent.; legs	Mostly S.B.B.	—	L.
110	21	M.	23 per cent.; arms, neck, chest.	11 per cent. S.B.B. 12 per cent. P.S.L.	—	L.
111	33	M.	29 per cent.; face, neck, arms, back, chest.	26 per cent { S.B.B. P.S.L. 3 per cent. W.S.L.	4,600	L.
112	7	F.	32 per cent.; face, trunk, arms, thighs.	12 per cent. W.S.L. 20 per cent. { S.B.B. P.S.L.	1,600	L.
113–114			These cases have been	omitted from the Reports.		
115	17	F.	66 per cent.; head, trunk, arms, legs.	Mostly W.S.L.	—	D. 2
116	64	F.	3 per cent.; legs	2 per cent. S.B.B. 1 per cent. P.S.L.	—	L.

Case No.	*Age*	*Sex*	*Percentage of body surface burned— and sites*	*Depth of burning*	*Total fluid transfused (ml.)*	*Lived or died? Day of death*
117	2	F.	12 per cent.; back, shoulders.	Mostly S.B.B.	—	L.
118	1 $\frac{6}{12}$	F.	8 per cent.; chest, abdo., arm.	4 per cent. S.B.B. 4 per cent. P.S.L.	—	L.
119	$\frac{6}{12}$	M.	8 per cent.; leg.	6 per cent. S.B.B. 2 per cent. P.S.L.	—	L.
120	25	M.	3 per cent.; face, neck.	S.B.B.	—	L.
121–124		These cases have been omitted from the Reports.				
125	59	F.	90 per cent.; head, trunk, arms, legs.	50 per cent. W.S.L. 40 per cent. { S.B.B. P.S.L.	—	D. 1
126	46	F.	45 per cent.; arms, trunk, thighs.	25 per cent. S.B.B. and P.S.L. 20 per cent. W.S.L.	—	D. 2
127	75	F.	25 per cent.; arms, buttocks, thighs.	15 per cent. W.S.L. 10 per cent. S.B.B. and P.S.L.	—	D. 1

APPENDIX II

Estimation of Area Burned

Throughout this Report, calculation of the areas burned has been based on Berkow's values (*Arch. Surg.*, 1924, **8**, 138), which are shown in the table below, along with the similar values given earlier by Du Bois (*Arch. int. Med.*, 1915, **15**, 868).

	Berkow	*Du Bois*
Head	6 per cent.	6 per cent.
Arms	13½ per cent.	14½ per cent.
Hands	4½ per cent.	4½ per cent.
Trunk	38 per cent.*	35 per cent.
Thighs	19 per cent.	20 per cent.
Legs	12⅔ per cent.	13 per cent.
Feet	6⅓ per cent.	7 per cent.

* (anterior 20, posterior 18 per cent.)

The trunk includes the neck; the lower extremities the buttocks.

Following Berkow, allowance for the different values applying in childhood was made as follows:—

The trunk was reckoned at 40 per cent., the upper extremities at 16 per cent.; for the head, subtract the child's age from 12 and add remainder to the adult value (6 per cent.); for the lower extremities (including the buttocks), subtract the child's age from 12 and subtract the remainder from the adult value (38 per cent.). Thus, for a child of 6, the area of the head will be 6+6=12 per cent.; the area of the lower extremities will be 38—6=32 per cent.

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