BURNS

PATHOLOGY AND THERAPEUTIC APPLICATIONS

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To

Betty, Michael, Peter and Brian

PREFACE

THE clinical and pathological studies on burns have been closely connected and the mainspring of some of the best investigations on burns pathology has been the improvement of therapy. A book devoted to the pathology and disordered physiology after burning should therefore incorporate the practical applications and therapeutic lessons. No apology is needed for this since the challenge of clinical problems has stimulated many clinico-pathological and experimental investigations which have shown that certain pathological effects can be modified by therapy. These studies have been supplemented by experiments of a more theoretical and academic nature, some of which have later had a practical application. Of course the pathology of burns is not divorced from general pathology, the principles of which are applicable to the disorders which follow burning. For example, the inflammatory reaction and the healing process of the skin are special illustrations of the phenomena of inflammation and repair; and the haemodynamic effects, biochemical and metabolic disorders, electrolyte and water imbalance, renal dysfunction, endocrine changes and other sequelae and complications have parallels in other branches of medicine and surgery. Nevertheless, the pattern of changes in burned patients is unique. Their study has contributed to the understanding of normal body processes and has helped to develop general pathology.

Knowledge of the pathology of burns is widely diffused in the international medical literature, and the present work is an attempt to bring this together within the covers of a book of reasonable size. Considerable knowledge has been gained during the last twenty years and the newer and older facts are presented in this book. The advances in knowledge reflect the general progress of medicine and partly result from technical advances which include methods for measuring plasma and red cell volume, the development of histochemistry, flame photometry and steroid chemistry, the use of radioactive tracers, electrophoresis, chromatography and cardiac catheterization, as well as established histological, biochemical, haematological, bacteriological and other procedures.

This is the first book in English devoted to the pathology of burns although there are a number of excellent monographs on treatment. It is my hope that it adequately fills the gap in medical literature. A wide range of topics is discussed, and whilst the approach is

basically functional, morphology has not been neglected and has been stressed when it is the basis of understanding. The influence of treatment on function and structure is dealt with and I have attempted to interpret the significance of pathological findings and to correlate functional and other changes with clinical effects. The recent advances in knowledge have solved a number of problems, but new problems, at a higher level of understanding, have emerged and these have been posed in the various chapters. I have tried to maintain a critical attitude throughout the book, to accept only the results of experiments and investigations which have been adequately performed and to discard ideas and theories which new facts have undermined or which are not supported by facts. When important differences of opinion have arisen I have presented the different ideas and their factual basis with the intention, if I may borrow a Chinese proverb, of "letting all schools of thought contend", but I have not shirked from giving my own opinions. The results of nearly ten years' experience of burns pathology, including a number of hitherto unpublished studies, have been included in the text.

The book has been planned in two main parts. Chapters 1 to 5 are concerned with the skin, and much of Chapter 8 on mortality and causes of death is an introduction to Chapters 9 to 22 which deal with the various body systems and organs. Chapters 6 and 7 are concerned with infection and its control, whilst Chapters 23 and 24 deal with special kinds of burns. In the reader's interest the clinical and therapeutic lessons are dealt with, as far as possible, under special headings at the ends of chapters. This has not always been possible, and many implications are discussed in the general text. With a few exceptions the illustrations are original. Some have been published before in various medical journals, but most of them have been specially made for this book from material collected and prepared at the Birmingham Accident Hospital.

It is my hope that the book will be of interest to surgeons, pathologists and other doctors concerned with burned patients either regularly or occasionally, that it will be of use to postgraduate students of surgery and pathology, and that the references will help the more specialized reader.

SIMON SEVITT

June 1957

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S. S.

CONTENTS

CHAPTER 1

TRANSFER OF HEAT TO AND THROUGH THE SKIN

AN UNDERSTANDING of the changes which occur in the skin from burns and scalds must take into account the mode, duration and temperature of burning. Upon these depend the temperatures and tissue changes at the skin surface and deeper levels.

TRANSFER TO THE SKIN

Heat may be brought to the skin by convection, radiation or conduction. Transfer by conduction has much greater power to heat the skin and produce burning than heat transfer by other means.

Convection.—Heat is transported by a current of hot gas. The rate of transfer to the skin depends on the temperature of the gas, its velocity, its nature and on the temperature of the skin surface.

Hot air flowing at normal eddy current rate (about 1·6 kilometres per hour) transports only about 0·4 calorie per square centimetre per minute to the skin when its temperature is 100°C and the skin temperature 40°C; whilst air at 400°C transports 4 calories per square centimetre per minute (Henriques and Moritz, 1947). As this heat is absorbed by the skin its surface temperature will rise and the uptake of heat will fall.

Steam at 100°C transports under the same conditions as much as 300 calories per square centimetre per minute because of its high latent heat of condensation. For this reason steam produces much severer burns than hot air.

Blasts of hot air varying from 100° to 500°C were used by Ashe and Roberts (1945), who studied the minimum time of exposure required to produce persistent redness and blister burning in human volunteers. Persistent erythema was caused by air at 100°, 200°, 300°, 400° and 500°C in 4–5 seconds, 1·5 seconds, 0·6, 0·2 and 0·1 second respectively. Air blasts at the same temperatures caused blistering in 7–10 and 2–3 seconds, and 0·7, 0·25 and 0·2 second respectively. The time–temperature curves were exponential but for blister burning there was greater deviation from a simple exponential function.

Radiation.—Heat energy, mainly in the infra-red part of the spectrum, is radiated from a hot source in linear fashion, and when it meets the skin, part is absorbed and part is reflected from the surface. The

rate of uptake of energy by the skin depends on the absolute temperature of the source, its radiation spectrum and effective emissivity of heat, the square of the distance between the source and the skin, the absorptivity and conductivity of skin and on certain constants. The skin is also losing heat by radiation so that the effective rate of uptake is the difference between the rate of heat gain and heat loss.

The main factors which influence burning are source temperature, distance and time of exposure. Prolonged exposure to the sun's rays does not produce burning from heat (sunburn is due to ultra-violet radiation), but given a radiant source the temperature of which is thousands of degrees Centigrade, burning can occur within a fraction of a second if the distance from the source is relatively small.

Conduction.—Heat is conducted from a hot solid or liquid in direct contact with the skin. Burns from hot liquids or *scalds* are essentially the same as those due to hot solids. The temperature of the skin surface rises instantaneously to that of the heat source and is maintained at this temperature during the period of contact when the heat source does not cool during the burning episode, that is when its heat capacity is high or when the period of contact is limited. This explains why burning by immersion in hot water causes more severe burns than for example the spilling of water at the same temperature for the same period on the skin. In the former event the heat source may be considered as having an infinite heat capacity and does not cool during the burning unlike the water which causes the scald by spilling. Similarly burns from the spilling of hot fluids which rapidly evaporate, such as hot alcohol, are less severe than burns from water at the same temperature. Burns by molten metals are deep because of the high temperature of the metal and its latent heat of solidification.

TRANSFER OF HEAT THROUGH THE SKIN

Normally the temperature of the surface of the skin is lower than the temperature of the dermis, but if heat is to be transferred from the heat source through the skin, the temperature of the skin surface must rise above that of the dermis. This can be achieved through heat conduction, convection or radiation from the source. Once the temperature of the skin surface is sufficiently raised heat will flow towards the dermis and raise the temperature of the skin at different levels. The rate of transfer of heat depends on the heat capacity of the skin and on its thermal conductivity, that is on its powers to take up and transport heat. The initial effect is a rapid uptake of heat but after a time the skin becomes heat-saturated; the heat flow then depends on thermal conductivity and skin surface temperature.

This simplified picture is modified by various factors including site variations in the thickness of the epidermis and dermis, various physiological factors such as the cooling effect of the blood flow (which may alter during burning) and on any oedema which may form during the burning episode. A theoretical and experimental study of this complex matter was made by Moritz and Henriques (Henriques and Moritz, 1947; Moritz and Henriques, 1947; Henriques, 1947; Moritz, 1947). They measured the heat capacities and conductivities of pig epidermis, dermis, subcutaneous fat and muscle. The heat capacities are high because of the high water content of tissues—0·86, 0·77, 0·55 and 0·9 calorie per gramme respectively—but the conductivities are low, hence the insulating effect of skin. As a result of experimental and theoretical considerations they developed a general theory of heat flow through the skin. This enabled them to estimate the time–temperature relationship during burning within the epidermis and at the epidermo-dermal junction. They demonstrated the important difference between the mode of transfer of heat by conduction on the one hand and by convection or radiation on the other. For a given source temperature, burning by conduction has at least a thousand times greater power to injure the epidermis than burning by radiation or by convection of relatively immobile air. This is because contact and conduction raises the surface temperature of the skin immediately to that of the source whilst radiation and convection raise the surface temperature relatively slowly.

Temperature gradient.—This is the difference or gradient of temperature between the surface and the deeper layers of the skin. Experimental work on this gradient has been carried out by Mendelssohn and Rossiter (1944), Henriques and Moritz (1947), and by the author using contact burns. A hypodermic needle with a copper-constantan thermocouple in its tip was inserted into the subdermis, a constant-temperature burning iron was applied to the skin surface superficial to the needle point, and the temperature of the subdermis was recorded every few seconds. The application of the burning iron is immediately followed by a rapid increase in the subdermal temperature, the unsteady state, followed by a period of temperature equilibrium, the steady state. Fig. 1 shows a typical result. The subdermal temperature was 36°C and the temperature of the burning iron was 60°C. Application of the burner was followed by a rapid rise in the subdermal temperature (44° at 5 seconds), then a slower rise (46° and 48° at 10 and 20 seconds respectively) until the subdermal temperature finally stabilized at about 50°C. During the unsteady

state the temperature gradient between the surface and the subdermis rapidly diminished as heat was being absorbed and transferred to deeper levels. The temperatures of all the skin layers must have risen and the temperature difference between any particular layer and the surface must have fallen in a fashion similar to that observed between the subdermis and the surface. The final steady state indicates equilibrium between heat gain and heat loss in the subdermis and heat "saturation" of the skin.

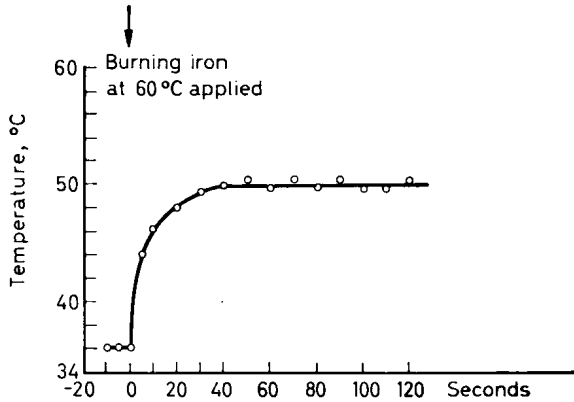

FIG. 1.—Serial temperatures in the subdermis during the application of a burning iron at 60° C on the shaved abdomen of a guinea-pig. A rapid rise of temperature (unsteady state) is followed by a slower rise, and finally a constant temperature of about 50°C is reached (steady state). The unsteady state signifies a rapid uptake of heat to satisfy the thermal capacity of the skin, whilst the steady state indicates equilibrium between heat gain from the burning iron and heat loss from thermal conductivity to the deeper tissues.

Effects of burning at different layers in the skin.—The quality and duration of the vertical gradient of temperature during burning determines the subsequent changes at different levels in the skin. Different combinations of temperature and duration of burning can produce similar pathological changes in the epidermis, such as necrosis, or similar pathological changes in the subepidermal capillary plexus, whilst the deeper changes at different levels in the dermis may be quite different depending on the temperatures reached. For example, Fig. 2 shows in contact burns of the guinea-pig the minimal combinations of temperature and duration of burning which just produce a permeability increase in the dermal vessels (curve PP). This was established by the slight but definite appearance of blue

dye in the burned skin after the introduction of Evans blue into the blood-stream (Sevitt, 1954). The minimal permeability response occurred after burning at 58°C for 5 seconds, 54° for 30 seconds, 52° for 60 seconds, 50° for 3 minutes, and so on. However, the prolonged burns must have heated the dermis to a greater depth than the shorter ones and the changes below the superficial capillary plexus will have differed.

Different vertical gradients of temperature produce different vertical gradients of damage in all the constituents of the dermis.

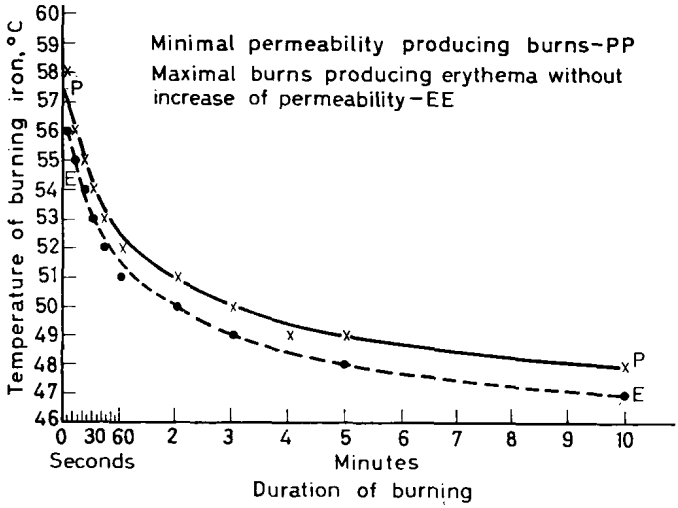

FIG. 2.—The minimal temperatures and periods of application of the burning iron which just produce an increase of permeability in the dermal capillaries of the guinea-pig. Combinations at and above curve PP produce an increase of permeability, but at and below EE erythema is the only visible evidence of burning.

The most severely damaged tissues are the superficial ones, and in the dermis there is a gradient of damage to the hair follicles and sweat ducts and to the capillary network. Thus the depths of dermal epithelial necrosis, increased capillary permeability and capillary stasis are determined by the duration and nature of the vertical gradient of temperature during burning. In other words the depth and nature of the inflammatory reaction in the skin, including probably the protein concentration of the exudate, as well as the manner of healing and the clinical course of the burn are determined by this vertical gradient. This does not mean that they are not influenced by subsequent events including therapy.

Flash burns.—Here the burning temperature is high but the duration of burning is very short (*see* Chapter 23). The temperature of the epidermis or even only its superficial layers may rise considerably whilst there may be only a small temperature rise in the upper dermis and perhaps none in the deeper part. Necrosis in this superficial variety will be confined to the epidermis. However, slight prolongation of the high temperature may permit the dermal temperature to rise considerably and this will result in a deep burn.

Influence of oedema during burning.—With surface burning temperatures between 55° and 60°C the equilibrium temperature at the dermis-fat junction during the steady state tends to remain constant; 50°C in the guinea-pig (Mendelssohn and Rossiter, 1944) and 48°C in the pig (Henriques and Moritz, 1947). Sevitt (1949) found that there is a rapid onset of considerable oedema associated with developing capillary stasis when the dermal temperature rises to or above 48°C in the guinea-pig; the oedema rapidly accumulated and greatly increased the thickness of the dermis. Thus the appearance of relatively cool oedema fluid during the burning process counterbalances the tendency to an increase in the dermal temperature due to the uptake of heat from the external heat source. The result is a constant equilibrium temperature for burns in which dermal oedema rapidly forms. Sometimes the subcutaneous temperature actually falls temporarily after the initial rise and this is due to the rapid accumulation of a larger amount of oedema fluid.

The effect was not seen with lower burning temperatures which did not produce oedema rapidly nor with higher burning temperatures which rapidly coagulated the dermis and the blood vessels.

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CHAPTER 2

CELLULAR HYPERTHERMIA AND THE HISTOLOGY OF BURNED SKIN

THE EFFECTS of heat on skin are important because they may lead to profound systemic changes such as oligaemic shock, anaemia, renal failure and metabolic disorders and also because of the light they have shed on such general biological problems as necrosis, inflammation, healing and infection.

The reactions of skin to heat may be divided into (1) direct tissue damage and (2) an inflammatory reaction (Chapter 3). These effects are related, first because they are manifestations of heat injury to physiologically different cells, and secondly because they are dynamic changes altering with time and influencing one another.

For purposes of discussion the tissue changes will be considered under two main headings, cellular hyperthermia and the histological changes in burned skin.

CELLULAR AND BODY HYPERTHERMIA

All animals, plants, bacteria and viruses are sensitive to heat, but there is considerable variation in the temperatures which they can withstand. Plants generally die at between 40° and 50°C and animals at between 30° and 45°C, but different genera and species in both kingdoms vary greatly. Many bacteria are killed below 60°C within half an hour, others can survive 70°C, and bacterial spores usually require temperatures between 100° and 120°C before they die. Some algae normally live at 53°C, infusoria have been found in springs at over 80°C, and even tadpoles have been observed in the hot springs of Yellowstone Park (quoted by Cameron, 1952). Presumably their ability to withstand these high temperatures has evolved by selection and adaptation. Some lower forms of life like *Paramoecium* can be experimentally adapted to high temperature by gradual exposure.

In warm-blooded animals variations in heat sensitivity among different somatic cells are known but further investigations are needed. Human spermatozoa at 37°C lose their motility and die in 24 hours, and spermatogenesis fails to develop or declines in undescended testicles. The brain is probably next in order of susceptibility; in

In rabbits the lethal cerebral temperature is 42°–43°C (approximately 107°–109°F). Between 46° and 50°C (115° and 122°F) leucocytes are killed (Schultze, 1865) and irreversible changes occur in red cells at about 50°C. In guinea-pigs the permeability of capillary endothelium increases after the dermis reaches a temperature between 41° and 45°C (106°–113°F) and irreversible capillary changes (stasis) occur after it reaches 47°–48°C (116°–118°F) (Chapter 3). The critical temperature of death for epidermal and other cells is discussed later.

Nevertheless the temperature at which cell death occurs depends on the duration of exposure. The time–temperature relationship may well be influenced by other environmental factors, by the age of the cells and by their degree of activity. Basically the effect of hyperthermia depends on the difference between the rate of injury to protoplasm and the rate of recovery and repair.

BODY HYPERTHERMIA

The body's temperature may rise to the injurious level of 42°–43°C either by its failure to lose metabolic heat or by exposure to a high environmental temperature. The effects include (1) a generalized vasodilatation which may cause a relative oligaemia and peripheral circulatory failure, (2) respiratory symptoms, the first of which is polypnoea, caused by reflex stimulation of the respiratory centre; later respiratory failure may occur, and (3) possible central cardiac failure. It is difficult to say which of these produces death. Hartman (1937) drew an analogy between the effects of high temperature and the pathology of anoxia. He found a decreased oxygen content of arterial and venous blood. Some of the older workers thought that death resulted from heat inactivation of intracellular globulins (Halliburton and Mott, 1903). After the experimental exposure of pigs to temperatures found in burning buildings there was often an acute hyperpotassaemia due to release of potassium mainly from damaged red cells, and this was associated with or caused a rapidly fatal central heart failure (Moritz and his colleagues, 1947). Death occurred when the rectal temperature rose to about 42°C (107·6°F) but the blood temperature was higher. Patients dying of heat-stroke show venous congestion, petechiae in the brain and mucous membranes, cloudy swelling and possibly necrosis in the liver, kidneys and myocardium, swelling of the spleen and depletion of adrenocortical lipoid; delayed manifestations include pyknosis and disintegration of cortical neurones (Malamud, Haymaker and Custer, 1946).

HYPERTHERMIA OF EPIDERMAL AND OTHER CELLS

Before discussing the morphological and biochemical effects of heat on cells the interrelationship between time and temperature