Shock—the clinical problem in perspective

G. K. MCGOWAN

Bristol Royal Infirmary

IN THIS introductory talk I propose to offer you a brief critical survey of the history of clinical shock, followed by a review of some of the outstanding problems in this field at the present time. Much of the information for the first part of my talk is derived from an excellent historical review written by Blalock (1934).

Shock is a term which has been applied for many years to a clinical syndrome marked by pallor, sweating, apathy and a feeble pulse. Early authors of the Seventeenth and Eighteenth Centuries usually described this condition in relation to trauma, and because many of their patients were shocked in the absence of external bleeding, e.g. victims of crush injuries, the importance of diminished circulating blood volume was not recognized; indeed some of these patients were treated by venesection. During this period stress was laid on the neurogenic aspect, an attitude which culminated much later in the theories of Crile (1901) who suggested, at the end of the Nineteenth Century, that shock was due to exhaustion of the vasomotor centre as a result of overstimulation via the sensory nerves. Nowadays the neurogenic aspect of traumatic shock is considered to be relatively unimportant, though it certainly plays some part in the circulatory disturbance of such patients and is the main cause of fainting among blood donors.

The importance of a deficiency of blood volume was indicated as early as 1832 when Latta published a dramatic and convincing account of the resuscitation of shocked cholera patients by intravenous infusion of salt solution. The lesson was not learned, and it was only in the early years of this century that Leonard Rogers applied the same principle to the treatment of cholera patients in Calcutta. Even then it took about 20 years for the same principle to be generally applied to other forms of dehydration such as that of intestinal obstruction.

Nevertheless, saline was used to replace blood loss around the end of the Nineteenth Century, but the successful transfusion of blood had to await the discovery of blood groups in 1907, and for many years thereafter the inadequate supply of blood limited its use. In the First World War the studies of wound shock by Bayliss & Cannon (1919) led to

the first plasma substitutes in the form of saline containing gum acacia or gelatin. In the Second World War the supply of blood and plasma was well organized and was widely used in the treatment of casualties. At the same time further studies of shock were made by several investigating teams, notably Grant & Reeves (1951) who wrote a classic report for the Medical Research Council. These studies led to a much greater understanding of the complexity of the factors involved in the circulatory disorders of battle casualties. As a result of further American investigations during the Korean War (Howard, 1954) the surprising magnitude of the volume of blood required by some casualties was revealed.

It is common for the lessons of war to be forgotten in peace time, but in the last 20 years the knowledge gained has been progressively though slowly applied to civilian hospital patients. Fortunately there has been a steady increase in the establishment of intensive care units in which treatment tends to be concentrated in the hands of those with a special knowledge of shock, and this has accelerated progress.

The success with which patients suffering from oligæmic shock are now generally treated has led to a wider awareness of so-called normovolaemic shock which is refractory to transfusion, and among the many workers in this field I would mention in particular MacLean and his colleagues (1967) in Canada and Weil and his associates (Weil & Shubin, 1967) in the United States. It is now recognized that this condition is usually caused by infection, especially by Gram-negative bacteria, but the mechanism is not yet clear. Control of the infection is necessary if the patient is to survive, and to keep the patient alive while this control is being attempted various measures have been employed. However, as the underlying circulatory disorder is not fully understood, these measures are either symptomatic or based upon an unproven theory of the mechanisms involved.

A very popular form of therapy until quite recently was the administration of vasoconstrictor drugs in order to correct the hypotension in these patients. The fact that they were often already vasoconstricted, and that any further constriction of the

arterioles imposed an additional load on the heart while reducing tissue perfusion, was conveniently forgotten in the satisfaction of correcting, in part at least, one of the signs of shock. The use of vasoconstrictors is no longer fashionable, and the pendulum has swung to the other extreme; there is currently a vogue for the use of vasodilator drugs with the object of improving tissue perfusion and reducing the load on the heart. As these drugs dilate the veins as well as the arterioles they cause the central venous pressure to fall, and it is often necessary to compensate for this by administering fluids to maintain the filling of the heart. In many cases of reported benefit from this regimen it is impossible to be sure that the patient had been adequately transfused before the drug was given and that transfusion without the vasodilator would not have produced an equal benefit. Recent work however, notably by MacLean and his colleagues (1967), has produced some good evidence for the value of isoprenaline (isoproterenol), a drug which not only produces vasodilatation but also stimulates the myocardium.

A recurrent theme in the history of shock has been the importance of the adrenal glands. It has been known for 50 years that very large amounts of adrenaline injected into animals can produce shock, and the possibility that clinical shock might be due to the over-production of such hormones thus arose. There is little evidence to support this theory, but it remains possible that, under certain circumstances, vasoconstriction beyond a certain point is harmful. This is the view of the proponents of vasodilator therapy, and if it is argued that vasoconstriction is a compensatory reaction which should not be tampered with, they can reply that such a reaction may be the best for an injured animal who can only survive by a fight or by flight, but is not necessarily ideal for a human who is being cared for in a hospital bed. Those who supported the use of vasoconstrictors, however, were usually obsessed with the importance of the hypotension in shock, and believed that it was due to an inadequate degree of vasoconstriction; this was at first ascribed to exhaustion of the adrenal medulla and later, when the medulla had been shown to remain active, to a failure of noradrenaline action owing to a deficiency of hydrocortisone, the presence of which is probably necessary for noradrenaline to be effective.

The latter theory is one of the many justifications which have been advanced for the treatment of shock with adrenal corticosteroids. The use of these hormones in physiological doses was first advocated on the basis of the similarity between clinical shock and an Addisonian crisis, and it was supposed that the adrenal cortex became exhausted. This view was widely adopted when hydrocortisone became readily available for intravenous injection. However, the

results of such treatment were not impressive, and when assays of plasma hydrocortisone were carried out it became clear that there was in fact no failure of the adrenal cortex except in those patients whose adrenals had been suppressed by previous corticosteroid therapy. The supporters of hydrocortisone therapy have recently shifted their ground; the drug is now advocated in pharmacological doses (five to ten times the physiological dose) on the grounds that it is a vasodilator and that it has some protective action against endotoxins. Even at this dosage the results in clinical shock are in my opinion unimpressive.

This brief review will, I hope, reinforce a sceptical attitude towards claims made for the latest shock treatment. This is necessary because the difficulties of proving the efficacy of new forms of treatment in clinical shock are so great. In the past, claims have been based largely on animal experiments, but in general these have not proved a reliable guide. For instance, two of the most popular methods of producing experimental shock, bleeding into a reservoir to maintain a constant degree of hypotension, and the injection of near-lethal doses of endotoxin, bear little relation to haemorrhage and infection in man. In any case it is known that the responses of animals to procedures causing shock may be very different from those of man. Animal experiments have provided valuable information about shock in animals, but it should never be assumed that such information is applicable to man until it has been tested and proven in man. There is, therefore, no substitute for clinical trial, and this poses many problems. In the long run the criterion of success is survival, but many shocked patients will die in any case because the underlying condition is untreatable. A successful trial on these lines requires a large series of patients where those who receive the treatment can be compared with matched controls. This is difficult to achieve, and if the early stages of the trial appear to show that the treatment is effective it becomes impossible to withhold it from the controls. Hence, it is usual to work without controls and to study the effects of a given treatment in individual patients, and here the difficulty is to decide on some objective measurement of the circulation which will reliably reflect improvement or deterioration in the circulatory state as a whole.

Let me now turn to the problems which face us at the present time.

Firstly, as I have just stated, we need a readily available method of assessment which will truly reflect the circulatory state of the patient and which can be used to measure the effect of treatment. Blood pressure is an unreliable index, for it depends as much on arteriolar tone as on cardiac output, and may be low when the circulation appears to be

satisfactory in other respects. Assessment of the pulse volume is, in my opinion, much superior, and probably reflects the cardiac stroke volume, but the relationship has not been defined and at present the pulse volume can only be assessed subjectively. Measurement of the cardiac output may be the best single criterion of the state of the circulation, but is unlikely to be available in every hospital treating shock. Moreover, as we do not know the distribution of the cardiac output between the body organs, nor the extent to which arterio-venous shunting occurs, nor the effect of illness on the metabolic needs of the tissues, we cannot predict the level of cardiac output which will be adequate for an ill patient. Biochemical estimations have considerable possibilities, and if shock can be regarded as a state of inadequate tissue perfusion, plasma lactate may well be the best index. Mixed venous oxygen content, or arterio-venous oxygen difference, may be valuable as measures of adequacy of the circulation provided that significant arterio-venous shunting does not occur. If the value of such tests is established, as seems likely, it should be possible to devise adequate bedside methods of estimation.

Secondly, we still need to know more about the detection and treatment of oligæmia—and here I include conditions where the blood volume, though not reduced, is inadequate to distend sufficiently a relaxed vascular compartment. Is the central venous pressure (CVP) the best guide, as some of us believe, and, if so, should we transfuse to the upper limit of the normal range or until there is an undue rise of venous pressure for a small additional infusion? Why may methods of internal and external manometry of CVP give different results, and is one clinically less reliable than the other? Under what circumstances can it be shown that reliable estimations of blood volume are of greater clinical value than reliable estimations of central venous pressure?

Thirdly, we need to know far more about the type of shock which occurs in infection. We know that in early or mild cases the typical pattern is of warm hypotension, with a normal or raised cardiac output, so that apart from the hypotension the circulation appears to be more than adequate; and yet the plasma lactate is raised suggesting that tissue perfusion is inadequate. At this stage there is hyperventilation and the blood pH is normal or raised. In late or severe cases the pattern changes to one of cold hypotension with a fall in cardiac output despite an adequate central venous pressure, with a rise of

plasma lactate to much higher levels and with frank metabolic acidosis. There is good reason to believe that the initial circulatory pattern is one of vasodilatation, and it is known that endotoxins produce this effect. The late stage, however, is almost certainly one of myocardial failure, and this is not, so far as I know, a recorded effect of endotoxin in experimental animals, possibly because it is a late effect for which the animal does not survive long enough. There certainly appears to be some toxic effect on the myocardium in man. We know that a similar course of circulatory failure may occur in severe cases of pancreatitis which have been adequately transfused, although they are apparently not infected; is it here due to vasoactive peptides derived from the breakdown of protein by pancreatic trypsin and, if so, do endotoxins produce the same effect by activating protease precursors? With regard to the raised plasma lactate in the presence of a hyperdynamic circulation, is it really an index of a generalized inadequacy of tissue oxygen supplies rather than a failure of the liver to clear lactate from the blood, or an effect of adrenalin secretion? If so, is it due to shunting or is there some block of oxygen utilization? How important are local factors, such as sludging of blood and coagulation disorders?

These are some of the problems of today as I see them. Many of them will be dealt with by the speakers who follow, and I am looking forward with keen interest, as I am sure you all are, to hearing their contributions.

References

- BAYLISS, W.M. & CANNON, W.B. (1919) Wound shock and haemorrhage. *Med. Res. Comm. Spec. Rep.* No. 25.
- BLALOCK, A. (1934) Acute circulatory failure as exemplified by shock and hemorrhage. *Surg. Gynec. Obstet.* **58**, 551.
- CRILE, G.W. (1901) *An Experimental and Clinical Research into Certain Problems Relating to Surgical Operations*. Lippincott, Philadelphia.
- GRANT, R.T. & REEVE, E.B. (1951) Observations on the general effects of injury in man with special reference to wound shock. *Spec. Rep. Ser. med. Res. Counc. (Lond.)*, No. 277.
- HOWARD, J. (1954) Shock and circulatory homeostasis. *3rd Josiah Macy Found. Conf.*
- LATTA, T. (1831) Letter to the Secretary of the Central Board of Health, London, affording a view of the rationale and results of his practice in the treatment of cholera by aqueous and saline injections. *Lancet*, ii, 274.
- MACLEAN, L.D., MULLIGAN, W.G., MACLEAN, A.P.H. & DUFF, J.H. (1967) Patterns of septic shock in man. A detailed study of 56 patients. *Ann. Surg.* **166**, 543.
- WEIL, M.H. & SHUBIN, H. (1967) *Diagnosis and Treatment of Shock*. Williams & Wilkins, Baltimore.