

Lecture Shock

Shock has been a prominent, and continuing problem to all physicians, especially surgeons. Since 1956, an extensive study of shock and its mechanisms has been the major research project of the University of Maryland, Department of Surgery. Initially, the project was limited to the animal experimental laboratory. As the studies progressed, two important factors became evident: 1) In order to understand the overall structural patho-physiological and biochemical alterations occurring in the organism, it was necessary to expand the program to include multi-disciplinary support in order to effectively explore basic phenomena occurring at the cellular level; 2) Although animal experimental work was necessary for many baseline and model studies, variance in response of different species indicated the necessity to study shock in man more directly.

The present investigation is characterized by a group effort making fundamental and clinical studies of shock. Particular attention is given to metabolic and biochemical factors. This is emphasized for a number of reasons. Management of clinical shock beyond circulating volume replacement and use of vasopressor agents for circulatory support has been insufficient despite the extensive experimental investigations which have resulted in significant contributions in terms of increased understanding and useful treatments. While the term "shock" implies disaster in the circulatory

element of homeostasis, the picture of physiological and biochemical deficits is much more complex, often obscure, and varies in different types of shock (hemorrhagic, septic, cardiogenic, crush, burn, etc). Hence adequate management of shock concerns early correction of the deficient circulation and the resulting metabolic abnormalities which derive from inadequate tissue perfusion.

Shock is a term long used to describe an entity characterized principally by the inability of an individual to maintain adequate circulation. It is commonly associated with severe injury to the soft tissues, the skeleton, and in thermal burns, the skin. It can also be associated with sepsis, myocardial failure, hemorrhage and other etiological agents. All shock can be easily recognized clinically when hypotension is the principle characteristic. Because of this readily discernable circulatory deficit, and the urgent need to restore the blood pressure to normal, most studies of shock have focused on the circulatory factor, its cause and correction.

In the shock state, however, the biochemical integrity of the cells determines to a large extent whether or not the patient will survive. The shock syndrome is apparently a sum total of many independent and interrelated factors and mechanisms. If the syndrome is to be prevented or treated

adequately, these important phenomena must be identified and sufficiently understood in order to generate therapeutic hypotheses which are amenable to test and evaluation. Considerable information has been gained through extensive animal studies, but comparable clinical studies must be conducted in order to determine man's response to shock. This should also provide a more effective basis on which therapeutic designs can be developed.

Slide → To accomplish the objectives of a study of shock in man, the shock patient must become the core around whom revolves a dynamic research structure. Patient centralization with a peripheral concentration of elaborate facilities is, therefore, required because of the precarious state caused by shock and in the interest of efficiency and economy. The hazardously ill shock patient cannot be moved to investigative areas for study, rather the laboratories in the interest of patient safety must be brought to the patient. A specialized effort of this kind permit an integrated multi-disciplinary probing of important syndrome complexes without disjointed accumulation of information. Cellular physiological and metabolic studies embody a highly organized integrated collaboration of biophysics, physiology and chemistry. The principle of such a functional structure constitutes the basis for a shock-trauma facility.

In 1962, following six years of experimental research, a pilot Clinical Shock Trauma Research Unit was established at the University of Maryland, under the auspices of the Research and Development Command of the Surgeon General, U.S. Army. The major goal of this Unit was to study the many forms of shock in man without interfering with resuscitation. Major objectives of the research are: 1) the elucidation of biochemical and physiological alterations occurring in shock in man, 2) the development of useful therapeutic regimens, and 3) the development of measures to prevent shock.

The necessary operational requirements for developing an effective scientific study included: 1) the establishment of a clinical shock research unit, staffed on a 24-hour basis, which included a special patient ward, specialized research study areas, laboratories, operation room availability and a data processing capability, and 2) the establishment of a more specialized animal research center for concomitant and correlative studies.

slide

These requirements necessitated the assembly of a considerable staff who were willing to accept the challenge of developing an effective research program. A shock team and backup laboratories on a 24-hour basis became mandatory in order to care for and treat the critically ill patient admitted at any hour to the Unit. ~~Much credit must be given to the clinical investigators who have so generously donated their~~

time and effort to the program.

As a multi-disciplinary approach to the problem of shock was conceived, developed, and progressively expanded, changes at the cell and tissue level during perfusion became a principal target in our investigations. Cell function and support mechanisms (ventilation, circulation, neural stimulation, metabolism, etc) are important from several points of view. They are important in terms of their normal and pathological values as functions of time; all of which reflect cellular alterations. In addition, it is important to know more of the mechanisms associated with these biological control systems. In order to describe and formulate our problems concerning these strategic mechanisms in the context of dynamic systems, engineers, mathematicians, and biostatisticians have been added to the research team. The participation by representatives of the latter disciplines has increased the emphasis on more classical methods of analysis.

In pursuing the study protocol, it soon appeared that a number of serious problems existed. First, the studies were of an ambitious nature in a critically ill patient, and, therefore clinical judgment was of prime importance. However, most investigators were surgeons with experience in shock problems and medical research. As a consequence, they are capable of handling these problems and associated therapy. By selecting

only those measurements and studies which in no way hindered treatment or jeopardized the life of the patient, a large volume of data was collected which was heretofore unavailable. Secondly, there was the important matter of making physiologic measurements in patients knowing that a "Steady State" many not exist. This added an additional burden in the process of analysis. Whenever possible the patients served as their own control by returning following recovery for repeat testing. The time period between injury and admission to the Unit varied in each patient. In addition life saving measures were frequently instituted before initial study samples were collected. These situations also added to the problems of data analysis. As these research difficulties in patients were identified, controlled, animal studies were planned and executed. Third, and probably the most important problem was the difficulty in assembling a team of physicians, nurses and biochemists desirous of undertaking a large part of their research time to study and care for shock trauma victims. Fourth, the amount of in-service education necessary to allay the fears and convince the house and staff physicians that the theoretical advantages of controlled therapy and excellent nursing care during such a study would not jeopardize the outcome of the patient but would enhance his chances for recovery. In the beginning the researchers could only make every effort to assure the physician that harm would not result. However, as the program continued to become evident to all that the

laboratory studies performed and the physiological parameters measured resulted in better patient care. These measurements or controls which hertofore were not available, were now assessed and utilized as concrete guidelines for therapy, thus eliminating the necessity of treating the patient empirically.

HEMODYNAMICS OF SHOCK

The concept of shock remains as difficult to define today as it was thirty years ago. What has emerged over the years is appreciation that a knowledge of the pathophysiology of shock is relevant to all seriously ill patients, medical and surgical. Despite Blalock's (1927) observations that the blood pressure was an inadequate guide to the state of the circulation in incipient shock, early authors continued to regard hypotension as the hallmark of shock. With the increasing amount of hemodynamic data which has become available in the last twenty years, opinion has veered to the view that the fundamental body deficit in shock is concerned with the flow of blood through the body and the adequacy of tissue perfusion.

CURRENT ASPECTSHemodynamic

One of the main aims in the management of a shocked patient is to identify accurately the hemodynamic pattern for his particular case and to institute appropriate therapy. Individual patient assessment is essential because

of natural biological variation and the different responses which may accompany the same etiological basis for shock.

It was previously thought that the circulatory disturbance in all cases of shock could be equated with a reduced cardiac output and peripheral vasoconstriction. The classical experiments of Wiggers (1950) in canine hemorrhagic shock and the then existing clinical observations supported this view.

However, by 1965 reports has appeared in the literature describing unusual hemodynamic responses in patients with septicemic shock (Maclean et al., 1965; Hopkins et al., 1965; Wilson, 1965). These patients were characterized by a low "total peripheral resistance," a normal or raised cardiac output, and central venous and arterial pressures which were within the normal range. This high output variety of septicemic shock was also reported in patients with coincidental liver disease. Further studies correlated a number of circulatory patients with various types of shock, their value being largely to suggest the etiology when it was unknown. The converse cannot be automatically assumed when the etiological factor is known, however,

and the only method of establishing an accurate hemodynamic pattern before therapy is from individual cardiovascular measurements.

A satisfactory hemodynamic assessment would include the cardiac output most commonly by dye dilution techniques (Wiggers, 1952) but also by thermal dilution (Branthwaite and Bradley, 1968) or computer analysis of a digital arterial pulse using the cardiac output trend module - the central venous pressure, the intra-arterial pressure and calculated parameters such as the "total peripheral resistance."

Central Venous Pressure

Central venous pressure monitoring has been a focus of discussion in the last decade. The term "Central venous" has been defined as the intravascular space within the right atrium or superior and inferior vena cava extending to the first central venous valve (Latimer, 1971). The central venous pressure is the pressure within this space and is an expression of the rate of venous return to the heart and of myocardial competency (Wilson, 1965; Weil et al., 1965; Landis and Horstenstine, 1950). For practical purposes (in the absence of cardiopulmonary disease) the right atrial pressure changes reflect

similar trends in the left side of the heart (Tristani and Cohn, 1966; Moss et al., 1969; Hanashiro and Weil, 1970).

As with most measurements a single reading is of little value but sequential recordings can be of extreme value in aiding volume replacement. It is insufficiently appreciated that this guide to volume replacement is only reliable with colloid infusions and errors of management (usually "overloading") occur when it is overemphasized during intravenous crystalloid administration. A number of factors require consideration to ensure the validity and usefulness of the information obtained; accurate positioning of the catheter by radiological examination or observation of the characteristic pressure tracing is essential; the catheter must remain fully patent and not kinked; and allowances must be made for superimposed pressure effects from, for example positive pressure ventilation.

The simplicity of the technique is still not fully appreciated. Should peripheral veins be unavailable because of collapse or previous intravenous therapy, the practical skill of subclavian vein catheterization is easily acquired. An awareness of the possible

complications of percutaneous subclavian puncture (Bernard and Stahl, 1971) render them relatively insignificant in what might be a life-saving situation.

Recent observations in some patients suggest that marked discrepancies between the C.V.P. readings and simultaneous pulmonary artery pressure readings (obtained by a Swan-Ganz catheter) exist and that a more accurate assessment of the pulmonary vascular status is obtained by the latter.

FIRST PRIORITIES:

1. Control external hemorrhage (and order blood)
2. Establish airway and provide adequate ventilation.
3. Begin crystalloid infusion and switch as rapidly as possible to colloid infusion.
4. Insert nasogastric tube.
5. Emergency assessment of systems. Look at all parts, front and back, alert specialists.

SECOND PRIORITIES:

1. Emergency investigations (x-rays, etc.) arteriography, peritoneal lavage, etc.

2. Establish catheters, intra-arterial, central venous, and urinary.
3. Draw baseline chemistries - blood gases, etc.
4. Decision for emergency surgery.

THIRD PRIORITIES:

1. Systematic examination
2. Systematic investigations
3. Specialty consultations and notification of the Medical Examiner.
4. Multidiscipline discussion on further management.

The correction of an inadequate circulation has concentrated on providing and maintaining an adequate intravascular volume, cardiac output and tissue perfusion. Evidence of a failing myocardium is an indication for an inotropic agent, usually a cardiac glycoside or isoprenaline or, if refractory to these, perhaps glucagon (Kock et al., 1970), steroids (Carger, 1970) or a glucose-insulin-potassium regime (Laborit, 1963; Majid et al., 1970) is of interest that the previously held view that digitalis was of no benefit unless frank cardiac failure was in evidence is no longer held and a patient's hemodynamic status can often be stabilized by such

therapy before overt failure. Also Thal has provided experimental evidence that digoxin may be the only inotropic agent of value in the presence of sepsis.

The Microcirculation

Interest in the peripheral circulation has moved from the precapillary resistance sphincters to the post-capillary capacitance sphincters. Many of the problems of refractory shock remaining after the correction of volume and myocardial deficits have been attributed to the sustained action of these sphincters. Closely related is the effect of arteriovenous shunting in the peripheral circulations, although the recent demonstration by Wright and his colleagues (1971) that there is no diminution in the rapid clearance of radioactive xenon (^{133}Xe) from the microcirculation of septic shock animals must again question the concept of anatomical shunting.

Vasopressors in Shock

When hypotension was regarded as the main circulatory abnormality in shock, vasopressors (e.g., noradrenaline, metaraminol) were used to maintain the blood pressure if possible. A wider appreciation of Alquist's adrenergic receptor hypothesis and of the pharmacology of

vasomotor drugs, recognition of the detrimental effects such as progressive metabolic acidosis and individual organ failure in persisting peripheral vasoconstriction and the care reports attributing massive intestinal inchemia to vasopressor therapy heralded the end of the indiscriminate use of vasopressors. The natural corollary was to apply vasodilator drugs (e,g,m phentolamine, isoprenaline, steroids and chlorpromazine) to refractory peripheral vasoconstriction and fill up the resultant increase in the intravascular space with volume expanders.

Both Bloch (1966) and Clauss (1968) gave excellent reviews of the rationale behind the use of adrenergic agents. Lillehei and Maclean (1958) reported a prophylactic effect if phenoxybenzamine was given to dogs before endotoxin and this was confirmed by Vick (1964). Abrams (1969) attempted to differentiate the effect of phenoxybenzamine from that of the volume expander which is an essential part of any regime involving peripheral vasodilation. He concluded that the beneficial effects resulted entirely from the plasma volume expansion. A number of additional reports followed; Hermreck (1969) found that phenoxybenzamine had little effect on

the peripheral circulation of infected limbs in experimental animals; Fromm and Wilson (1969) suggested that the drug was of greater therapeutic value after a vasopressor agent had been given; Dell (1970) reported preservation of adequate glomerular filtration after phenoxybenzamine had been given to shocked animals, provided the arterial pressure could be maintained by adequate infusions. The balance of evidence so far available suggests that α -adrenergic blockers can make a useful but limited contribution to the successful management of refractory vasoconstriction in hypovolemic, and in particular, hemorrhagic shock.

Colloids or Crystalloids

The stimulating controversy provoked by the observations of Shires and his colleagues (1964) on extracellular fluid shifts following trauma was largely responsible for the "colloid versus crystalloid" discussions of the last few years. After a period of somewhat irresponsible usage of Ringers lactate as a resuscitatory panacea most clinicians accept that crystalloid solutions have a limited value as very transient volume expanders and promoters of capillary perfusion by hemodilution. It is clear that they are unable

to replace volume loss per se as effectively as colloid solutions. At present the best fluid replacement in shock consists of the closest mimic of the fluid lost. If colloid is indicated some advantage may be obtained by introducing into the fluid regime a "crystalloid hemodilutant." In this context there is evidence (Metcalf, 1970) that hydroxyethyl starch may become the synthetic volume expander of choice.

When the diagnosis of "pulmonary insufficiency following shock": is entertained, largely by a process of exclusion, it appears that continuous positive pressure ventilation may offer an improved prognosis. The primary pulmonary derangement responsible for the syndrome may be the altered pulmonary vascular resistance and the main conflict is in deciding if there is an increased pressure or resistance in the small pulmonary veins (Keller et al., 1967; Sugg et al, 1969) or at the precapillary level (Veith et al, 1967).

Such exciting developments as have been mentioned have provoked world wide interest in the long standing problem of the "shock case". Perhaps the perspective of interest is clarified when we remember that trauma is the main killer of the

young adult population in the developed countries.

However, through the wealth of accumulated research and literature it behoves the clinician to remain convinced that at present the keystone to improved survival rates still remains firmly centered on continuous medical supervision, clinical judgment and prompt but simple therapy.





