RES MEDICA
Journal of the Royal Medical Society

Cardiogenic Shock

Andrew G. Leitch
B.Sc.

Abstract

DEFINITION AND PATHOGENESIS

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CLINICAL CRITERIA

The criteria for diagnosis of shock may vary with different authors (hence the anomalous 20% above) but, in general, it is agreed that shock is suggested clinically by the following features: cold, clammy extremities, pallor and cyanosis, rapid, thready pulse, anuria or oliguria, anxiety, restlessness or apathy, and prolonged hypotension. The only objective assessment is of blood pressure and this alone does not define shock. Considerable variation may therefore be expected in diagnosis.

In view of the difficulties in defining the criteria for diagnosis of shock, the individual criteria and the interpretations placed upon them warrant further discussion.

ISSN: 2051-7580 (Online) ISSN: 0482-3206 (Print)
Res Medica is published by the Royal Medical Society, 5/5 Bristo Square, Edinburgh, EH8 9AL

Res Medica, Spring 1969, 6(3): 13-19
doi: 10.2218/resmedica.v6i3.851

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Andrew G. Leitch, B.Sc.

Based on the essay that won the Chest and Heart Association, Scottish Branch, Competition, 1968

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In view of the difficulties in defining the criteria for diagnosis of shock, the individual criteria and the interpretations placed upon them warrant further discussion.

The pallor, coldness, clamminess and oliguria are taken to indicate an increase in activity of the sympathetic nervous system leading to sweating and a reduction in blood flow to the skin and the kidney respectively. Similarly, signs of anxiety, restlessness or apathy are taken to indicate a reduction in cerebral blood flow or cerebral hypoxia. Anxiety or restlessness might be expected in patients who are in pain and apprehensive of their mortal future. Adequate methods for the measurement of arm and cerebral blood flow exist but the measurements do not yet appear to have been made in cardiogenic shock. The tachycardia also reflects the increased activity of the sympatho-adrenal system, the increased rate being due probably to an increase in sympathetic activity to the heart and to the high level of blood catecholamines in shock. The increase in urinary noradrenaline and adrenaline which has been demonstrated after myocardial infarction appears to be related to the clinical severity of the condition. The thready pulse may be taken as an indication of the reduction in stroke volume.

Cyanosis represents an increase in the amount of reduced haemoglobin visible in the sub-papillary venous plexuses and is influenced by the haemoglobin content of the blood. So-called central cyanosis is said to represent an arterial oxygen saturation of less than 90-95% but trained clinical observers are unanimous in their observation only when the oxygen saturation of blood is as low as 75%. The misleading effects of fluorescent lighting are important. Such cyanosis may be due to inadequate pulmonary oxygenation, increased deoxygenation of arterial blood or veno-arterial shunts. All three may be important in cardiogenic shock.

Hypotension is difficult to define in view of the wide range of normal blood pressures in the general population. Indirect measurement of brachial systolic blood pressure with a sphygmomanometer compares favourably with direct intra-arterial recording (at least at normal levels of blood pressure) within certain limitations, e.g., cuff width and length. Whether

the agreement is of the same order in hypotension is not recorded. A systolic blood pressure of less than 100 mm. Hg. or less than 90 mm. Hg. has been taken as indicating shock while others feel that a systolic blood pressure of less than 80 mm. Hg. is a necessary criterion of shock. Others again adhere to 80 mm. Hg. with an "allowance" of 90 or 100 mm. Hg. for previously hypertensive patients. Mutual agreement about the value of blood pressure taken to indicate shock is desirable if therapeutic trials are to be comparable. Hypotension in shock can be taken to indicate that the heart is unable to maintain blood pressure by an adequate output in a situation where the total peripheral resistance is normal or raised. It must be distinguished from the initial hypotension often seen in myocardial infarction which is relieved by analgesics or sedatives and is attributed to pain. Vaso-vagal attacks and excessive doses of morphine, pethidine or sedatives may also be misleading causes of hypotension.

HAEMODYNAMIC CRITERIA

The clinical definition of shock is not entirely satisfactory and since the early classical studies of Coumand attempts have been made to find a haemodynamic expression of shock. Right heart catheterisation is essential in haemodynamic studies if one is to measure cardiac output, central venous pressure and pulmonary artery pressure. It is used for withdrawing samples of "mixed" venous blood for direct Fick or injecting dye for dye diffusion estimations of cardiac output. Cardiac output is traditionally expressed as cardiac index (L/min./m^2) in an attempt to eliminate variations in cardiac output related to body size. The total peripheral resistance can be calculated from the relation

$$\text{Cardiac Index} = \frac{\text{Mean Aortic Pr. - Central Venous Pr.}}{\text{Total Peripheral Resistance}}$$

In animals the haemodynamic consequences of shock have also been studied after coronary embolisation with spores or microspheres, coronary ligation or occlusion.

The outstanding feature of haemodynamic studies has been the uniform demonstration of a fall in cardiac index in cardiogenic shock. It is important to remember that this is an acute fall in cardiac index. In general, the lower the cardiac index, the more severely ill the patient is, although specific instances have recently been described where a very low cardiac index has been present in patients without shock. Hypotension itself is not sufficient to define shock since sympathectomised patients may have adequate tissue perfusion with a slow pulse and a low blood pressure. The effect of fever on the total peripheral resistance may cause a similar phenomenon. Although reduction of cardiac index may be present in non-shocked patients, severe reduction of stroke volume seems to be more "specific" to cardiogenic shock and coupled with the demonstration of an increased cardiopulmonary blood volume indicates failure of the left ventricle as a pump.

Total peripheral resistance in shock has been described as being increased, normal or decreased. Gunnar divides his cases into two groups: one with an increased peripheral resistance which is considered to represent the normal reflex response to a fall in cardiac index and one with a decreased peripheral resistance which is believed to be the result of some vascular reflex from the damaged heart. Patients with a low total peripheral resistance responded to noradrenaline by increasing peripheral resistance which is taken to indicate that the vasoconstrictor mechanism is still functional although reflex vasoconstriction is inhibited by a reflex from the damaged heart. However, in cats the vascular tree can be responsive to noradrenaline in the "shock state" long after it has ceased to respond to sympathetic nerve stimulation.

REFLEX SHOCK?

The heart has many receptors. Stimulation of some of them may lead to hypotension as, for example, in the left ventricular Bezold-Jarisch reflex with veratrine. This may be the mechanism of the bradycardia and hypotension seen in "shocked" dogs which is abolished by vagotomy. Possible receptors for such a reflex have been described. Agress has described another possible reflex in dogs mediated by the dorsal sympathetic roots, but his attempts to identify and block such a reflex in man have not been continued and were presumably unsuccessful. The higher frequency of shock in patients with branch rather than main stem occlusions in the coronary arteries has been given as a possible indication of reflex mechanisms in human cardiogenic shock. However, the significance of a reflex from the injured myocardium remains un-

determined. Dogs with denervated hearts may still be shocked after infarction. Presumably people with transplanted hearts will still be liable to develop shock after myocardial infarction. This and the slow onset of shock do not favour a reflex mechanism.

An acute fall in cardiac index is the basic lesion in cardiogenic shock. Shock is not associated with any particular size or site of infarction. In one study shocked patients had a higher incidence of previous infarction than non-shocked patients whereas the post-mortem hearts examined by Cronin indicated that shock cases had a lower incidence of previous infarction. Cronin suggests that a previous infarct might protect the heart through the development of significant inter-coronary anastomoses. The impairment of cardiac function has been briefly described by MacKenzie et al. In their study measurements of myocardial performance indicated "gross impairment" in cardiogenic shock.

LUNG FUNCTION

MacKenzie's fuller and more important studies in the same paper demonstrated that in shocked patients the PaO_2 was very low (mean 47 mm. Hg.) compared with non-shocked patients (mean 67 mm. Hg.) and that whereas PaO_2 rose to expected levels (mean 391 mm. Hg.) on administration of 87% oxygen to non-shocked patients, in shocked patients with oxygen the PaO_2 still remained remarkably low (mean 119 mm. Hg.). This has since been described by others. A markedly increased alveolar-arterial oxygen tension gradient was also described and has been confirmed by others in cardiogenic shock and in acute myocardial infarction without shock. A significantly increased gradient is present even six to twelve months after infarction. The hypoxaemia is not due to inadequate ventilation since the $PaCO_2$ is normal or even decreased in these cases. The hypoxaemia is due partly to an increased physiological dead space; partly to venous admixture and also in some patients to the presence of a true shunt. The disturbed ventilation-perfusion ratios are probably due, in part, to the fall in cardiac index observed in shock leading to perfusion changes, and, in part, to the increased pulmonary venous pressure accompanying pump failure leading to pulmonary congestion. The rise in left ventricular end-diastolic pressure which is implied in the genesis of pulmonary congestion and oedema in cardiogenic shock has recently been demonstrated. Detailed investigation of the ventilation-perfusion ratio changes in different parts of the lung should be possible with the techniques which have been described, but investigations of this nature have yet to be carried out in cardiogenic shock. They should demonstrate more clearly the nature of the ventilation perfusion imbalance.

The presence of pulmonary congestion in cardiogenic shock probably depends partly on the enthusiasm with which it is sought and partly on the severity of the cases described. For example, Cronin found crepitations absent in most of his 140 cases while Nielson describes frank pulmonary oedema necessitating treatment with digitalis in 30% of his 34 cases. McNicol basing his diagnosis of congestion on the presence of crepitations or rhonchi in the absence of a history of bronchitis found pulmonary congestion in 13 out of 15 shocked patients. Radiological criteria are also valuable. McNicol has demonstrated unequivocally the importance of congestion in the genesis of hypoxaemia after acute myocardial infarction. Two of his shock cases had no clinical evidence of congestion and it is suggested that in these cases the hypoxaemia is due solely to a gross disturbance of perfusion. Indeed, an increased physiological dead space was very evident in these patients. It is in such cases particularly that a regional analysis of ventilation-perfusion ratios would prove interesting.

The true shunt which has been described is thought unlikely to be due to arterio-venous anastomoses "since it disappeared on recovery in two cases". The possibility of arterio-venous anastomoses as a factor in shunt at high altitude has been described in association with an elevated pulmonary arterial pressure but no such relationship between presence of shunt and pulmonary arterial pressure exists after myocardial infarction. It has been suggested that the shunt may be due to "collapse, oedema or blockage of alveoli in some areas of the lung where there is continued circulation." This is more likely.

ACID-BASE BALANCE

The hypoxaemia of cardiogenic shock is associated with a significant acidosis due principally to a rise in the concentration of blood lactate. Kirby and McNicol note that the acidosis found in acute myocardial infarction

is most severe in patients with hypotension (<90 mm. Hg.) plus left ventricular failure (? shocked). The demonstrated rise in lactate/pyruvate ratio is indicative of tissue hypoxia and reflects an increase in the oxidation of $NADH_2$ by the conversion of pyruvate to lactate in the cycle of anaerobic glycolysis. Anaerobic glycolysis is more active in hypoxia because less molecular oxygen is available for the operation of the cytochrome system and aerobic glycolysis.

The increased mortality found with severe acidosis is probably causally related and represents an association between two accompaniments of tissue hypoxia. In man correction of the acidosis leads to an increase in blood pressure in non-shocked patients but this may have been related to the procedure and to the volume infused. The effect of correction in shocked patients is not documented. Other reports associate acidosis with arrhythmias in man, decreased myocardial contractility in dogs, and vasopressor antagonism in dogs. In dogs the combination of acidosis and hypoxaemia is particularly lethal: the survival rate is increased by correction of both.

CORONARY AND OTHER REGIONAL BLOOD FLOWS

The following functional points are also worthy of note. The hypotension of shock will lead to a significant reduction in coronary blood flow since in the human case of infarction (but not the dog and hence partly the dubious relevancy of experimental cardiogenic shock in dogs) the coronary vessels will almost certainly be atherosclerotic, arteriosclerotic or even calcified. This will limit or even eliminate any faculty for vasodilatation in response to hormonal, nervous, metabolic or any other demands. In this situation the coronary flow becomes to a greater or lesser extent dependent on aortic diastolic pressure since most coronary flow occurs during diastole. The existence of coronary autoregulation is still debated but where demonstrated it probably ceases, like cerebral autoregulation, at pressures of 50-80 mm. Hg. The effect of degenerative arterial disease on coronary autoregulation is not known and it should be possible to study this in a suitable animal preparation with and without the complications of myocardial infarction since its effect can only be guessed in man. Arterial disease is found in a wide range of animals including snakes, lizards, tortoises and vultures. Disease can also be produced by altering the diet of rabbits, rats and pigs and this disease closely resembles that found in man. The effect of coronary artery disease on autoregulation of coronary blood flow would be most easily studied in the pig. (For similar reasons the pig would seem to be a more suitable animal than the dog for investigating the efficacy of different forms of therapy in cardiogenic shock). For the moment it is agreed empirically that a pressure of 50-80 mm. Hg. is usually adequate to maintain coronary and cerebral blood flow. Regional flow studies might be interesting here also. In view of the need for a minimum blood pressure difficulties arise in therapy (see later) since attempts to increase the aortic pressure by vasoconstriction to maintain coronary flow will increase the afterload of an already embarrassed heart.

The sympathetic vasoconstriction in shock leads to a reduction in renal blood flow, glomerular filtration rate and urine secretion. If this oliguria (or anuria) is maintained microscopic changes may be visible in the kidney structure. Similarly impairment of liver function has been demonstrated in acute myocardial infarction which is probably related to hepatic vasoconstriction. This may be a factor in the lactic acidaemia.

MICROCIRCULATION

The changes observed in the peripheral circulation in shock have been investigated by many workers. Microscopic examination of the microcirculation in shocked animal preparations has shown great species variation in the behaviour of the microcirculation during shock and it is difficult from the observations which have been made to indicate any consistent microcirculatory defect in shock. However, disturbances of vasomotion and of the flow patterns in exchange vessels have been observed. The role of arterio-venous shunts in the microcirculation remains uncertain.

Coupled with disturbances of flow, pressure and exchange relationships in the microcirculation may be disturbances of the coagulation mechanism which have been observed in shocked patients by the proponents of a hypothetical mechanism for disseminated intravascular coagulation or sludging. This will lead to further disturbance of the exchange and nutritive functions of the microcirculation. If present in cardiogenic shock sludging should be visible in the bulbar conjunctiva.

Mellander using his technique for the indirect study of the microcirculation in cat skeletal muscle has noticed in shock a progressive decline in the precapillary resistance response to sympathetic nerve stimulation while the capacitance response remains. However, unphysiological doses of noradrenaline will retrieve the resistance response when sympathetic nerve stimulation fails. If shock is prolonged the capacitance response to sympathetic nerve stimulation is abolished and intravascular pooling may occur. At the same time disturbances of the relationship between pre- and post-capillary resistances and hence the Starling mechanism will lead to haemoconcentration. Mellander interpreted the refractoriness to sympathetic nerve stimulation as being due to the presence of tissue hypoxia and accumulated "metabolites". The nature of such metabolites remains uncertain but acidosis is probably a factor.

Cat skeletal muscle in haemorrhagic shock is not the human peripheral circulation in cardiogenic shock but comparisons are useful and apparently valid since recent publications allow the following tentative interpretation of peripheral circulatory failure in cardiogenic shock: after infarction cardiac function is severely impaired and although increased sympatho-adrenal activity may be adequate at first to maintain blood pressure it is later inadequate. If the vasoconstriction is severe or prolonged enough it leads to tissue hypoxia and acidosis. Hypoxaemia will exaggerate this phenomenon and total peripheral resistance may fall. Progressively the resistance vessels become refractory to sympathetic nervous stimuli while maintaining some sensitivity to noradrenaline. Ultimately this response also disappears along with the capacitance response. This may lead to acidosis, loss of capillary integrity, haemoconcentration, stagnation, disruption of lysosomes, coagulation of blood and tissue destruction with consequent loss of organ function and death. Prominent among the ultrastructural changes in shock is mitochondrial damage.

The role of the sympatho-adrenal system in this sequence of events is prominent enough to make one wonder what the effect of coronary embolisation or ligation might be in dogs or other animals which had either been sympathectomised or made tolerant of catecholamines. Would the same percentage of sympathectomised or catecholamine-tolerant dogs develop shock as compared with normal animals? If so, would the mortality be altered? Would chemical sympathectomy show the same effect? If the effect was beneficial might it be applicable to human cases as a form of "preventive" treatment for cardiogenic shock? Do people who have been sympathectomised develop cardiogenic shock as often as the rest of the population? If so, do they also have an 80% mortality?

The sequence of events in shock is never seen in its undisturbed entirety since therapy is usually instituted early in the march of events and may modify the picture considerably. However, it obviously fails to alter the picture enough since the mortality remains at 80%. More optimistic figures for mortality are misleading and probably reflect the inclusion in the diagnosis of shock of patients with the brief initial hypotension often seen after myocardial infarction.

THERAPY

The following agents have been, should be or will be, used in the treatment of cardiogenic shock.

INITIAL THERAPY

The supine position in the absence of pulmonary oedema, morphine or pethidine in moderation (hypotensives and respiratory depressants) to relieve pain, bicarbonate for acidosis and standard therapy for arrhythmias may all be required initially.

OXYGEN

In cardiogenic shock, the tissue Po_2 is probably much lower than it should be, and PaO_2 is certainly low. $PaCO_2$ being essentially normal, the administration of 100% oxygen is preferred since the PaO_2 of some patients may be refractory to oxygen therapy.

Hyperbaric oxygen protects against death from arrhythmias in "cardiogenic shock" in dogs and pigs but Cameron has only noticed a "non-statistical suggestion of a reduction in arrhythmias" with such therapy in man.

VASOCONSTRICTORS

Pure vasoconstrictors such as angiotensin have no place in therapy since they increase blood pressure by increasing peripheral resistance at the expense of increasing cardiac overload and decreasing cardiac index.

$\alpha\beta$ drugs such as noradrenaline and metaraminol have been used in classical therapy for years. They:—

1. act in small doses to increase myocardial contractility and cardiac index, and in larger doses to vasoconstrict all regional circulations except the coronary and hence to increase cardiac work and decrease cardiac index.
2. may cause shock.
3. may lead to reversal of the Starling mechanism (which causes net movement of fluid into the circulation in shock) and thus cause haemoconcentration.
4. do not alter the mortality in shocked dogs from the control value in untreated dogs.
5. have not affected the mortality from cardiogenic shock in man which remains at 80%.

The value of these drugs is limited solely to the inotropic effect observed with small doses which is probably useful in a few cases.

α-BLOCKING DRUGS

α-blocking drugs such as phenoxybenzamine or chlorpromazine can be used to provide a low pressure/high flow system which is probably more useful in preventing tissue hypoxia than the high pressure/low flow system achieved with noradrenaline. The logic of α-blocking is that vasoconstriction will be reduced, resistance will fall, capacitance will rise and the reduction in pressure will mean less pressure work for, and a lower oxygen consumption by, the heart. The fall in resistance will lead to increased cardiac emptying and the increased capacitance may be useful in the treatment of pulmonary oedema.

Infusion of fluid—plasma, L.M.W.D., blood —is often combined successfully with this therapy but central venous pressure must be monitored to warn of impending pulmonary oedema. The following facts are known:—

1. Work on "shocked dogs" shows that phenoxybenzamine plus intravenous fluid leads to a very significant increased survival from cardiogenic shock as compared with control or noradrenaline treated animals.
2. In general, survival is improved when the pressure work of the heart is decreased and the volume work is increased — however, the use of intravenous fluids alone, as recommended by Nixon, is not a desirable procedure since the damaged heart is unlikely, in most cases, to operate on the ascending portion of its starting curve in response to distension.
3. α-blocking drugs have been useful in the treatment of low output surgical shock.

LOW MOLECULAR WEIGHT DEXTRAN (L.M.W.D.)

L.M.W.D. decreases blood viscosity, increases circulating blood volume, activates fibrinolysis and is valuable in the treatment of disseminated intravascular coagulation or sludging. In shocked dogs it improves prospects of survival.

HYPOTHERMIA

Reduction of body temperature to 33°C reduces oxygen consumption to ⅔ normal and therefore decreases the demand for oxygen in the tissues. The technique has been used successfully in septic but not in cardiogenic shock. It may be that the enhanced myocardial efficiency is not enough to compensate for the increased risk of arrhythmias.

DIGITALIS

Digitalis should be used in cardiogenic shock where the improved myocardial efficiency which results probably outweighs the increased risk of arrhythmias.

STEROIDS

Massive doses of glucocorticoids (30 mg./kg. prednisolone, 150 mg./kg. hydrocortisone) are in vogue for the treatment of low output surgical shock in man and experimental cardiogenic shock in dogs. Such large doses cause vasodilatation and may help to maintain the integrity of cell membranes and sub-cellular particles such as lysosomes. The use of such large doses in cardiogenic shock is not recorded; smaller doses are ineffective.

ASSISTED CIRCULATION

Most cases of cardiogenic shock are going to die in spite of the administration of oxygen, drugs, etc. Such cases could be helped by some form of assisted circulation. The following are the most likely to be developed.

1. *Counterpulsation* — blood is withdrawn from the femoral artery during systole and pumped back during diastole. The technique is successful in dogs and the minor

surgery required has allowed it to be tried in refractory cases of cardiogenic shock in man. Surgery can be avoided if the vascular tree of the lower limbs is used as the pump and subjected to appropriately phased pressure variations.

2. *Implantable Prosthesis* — the in-series, air-powered, prosthetic auxiliary ventricles of Soroff and Kantrowitz function well but require modification in view of the high frequency of clotting and embolism from the prosthesis.
3. *Artificial Intracorporeal Hearts* — Twenty-six have been reported since 1958 and as yet no animal has survived more than thirty hours with a functioning artificial heart. However, W.H.O. gaily prophesies cardiac factories for the future.
4. *Cardiac Transplantation* — Homograft transplantation is complicated by the difficulties of tissue typing, graft vs. host reaction, catecholamine hypersensitivity, homograft rejection phenomena and its detection and control with immunosuppressive therapy, but is possible. Whether the development of a successful artificial heart will precede the breakthrough in the problems of cardiac transplantation remains to be seen. Meanwhile, there is adequate time to consider the implications of either.

SUMMARY

An attempt has been made to present an up-to-date account of the pathogenesis and therapy of cardiogenic shock and to pursue as far as possible, the relationship between them.

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