CRITICAL CARE

REVIEW

Clinical review: Circulatory shock - an update: a tribute to Professor Max Harry Weil

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Abstract

Circulatory shock is common and associated with high morbidity and mortality. Appropriate shock treatment relies on a good understanding of the pathophysiological mechanisms underlying shock. In this article, we provide an update on the description, classification, and management of shock states built on foundations laid by Dr Max Harry Weil, a key early contributor to this field.

Introduction

Circulatory shock is common and associated with high morbidity and mortality. The word 'shock' is an old term, often attributed to the French surgeon Henri LeDran, although it is interesting that the actual word 'choc' never appeared in the French version of his thesis [1], but only in the English translation [2], in which 'shock' was used to translate the French words 'saisissement', 'commotion', and 'coup' [3]. It was not until 1827 that an English surgeon, George Guthrie, first used the word 'shock' in association with a physiological response to injury [4]. Understanding of the mechanisms underlying shock and the description and classification of shock states came much later and one of the key early contributors to this field was Dr Max Harry Weil, who died last year [5]. In this article, we provide a brief update on circulatory shock, building on the foundations laid by Dr Weil.

Clinical identification of shock states

Shock is best defined as 'acute circulatory failure', as Dr Weil proposed [6], a situation in which the circulation fails to provide cells with sufficient oxygen to be able to perform optimally. Clinically, arterial hypotension is a cardinal sign, but not always present because general vasoconstriction caused by the activated sympathetic nervous system may mask the fall in blood pressure. The usual lower limit for systolic arterial pressure is considered as 90 mmHg, but this is an arbitrary value and may vary from one patient to another - for example, the pressure threshold may be lower in younger than in older individuals.

Weil and colleagues highlighted the importance of blood lactate concentrations in patients with shock many years ago [7,8], and lactate concentrations remain one of the most useful biological tests in this setting. Normal concentrations are around 1 mEq/L (or mmol/L), and a value above 2 mEq/L is considered to reflect the presence of shock (Figure 1). Importantly, in a recent study, mortality was increased even in those who had small increases in lactate concentration to between 1.5 and 2.0 mEq/L [9]. Although generally associated with anaerobic metabolism, raised lactate concentrations may also occur as a result of excessive aerobic glycolysis (for example, during shivering, seizures, hyperventilation) and/or decreased utilization (for example, liver failure, mitochondrial inhibition). Nevertheless, in the context of altered tissue perfusion, the severity of hyperlactatemia is directly related to outcome [10,11]. In addition to single measurements, changes in lactate concentrations over time may have additional predictive value for organ failure and mortality [12].

When assessing the damage an earthquake or fire has caused inside a building, one looks through the windows. Using this analogy, it would be useful to be able to see inside the body to view the damage caused by the shock process. Clearly this is not possible, but the skin, the kidneys and the brain provide us with three types of 'window' through which we can see the effects of the altered tissue perfusion: through the skin 'window', we can see decreased capillary flow, slow refill, cold and clammy skin [13]; through the kidney 'window', we typically see oliguria <0.5 mL/kg/h; and through the brain 'window', we see obtundation/disorientation/confusion that was not present before the shock episode (Figure 2). Unfortunately, we currently have no other 'windows' (for example, it would be nice to visualize the gut and liver, but this is not possible practically; gastric

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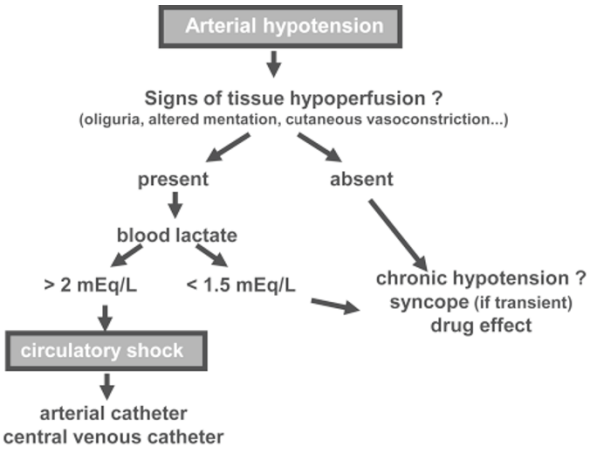

Figure 1. The importance of blood lactate concentrations in determining the presence of shock.

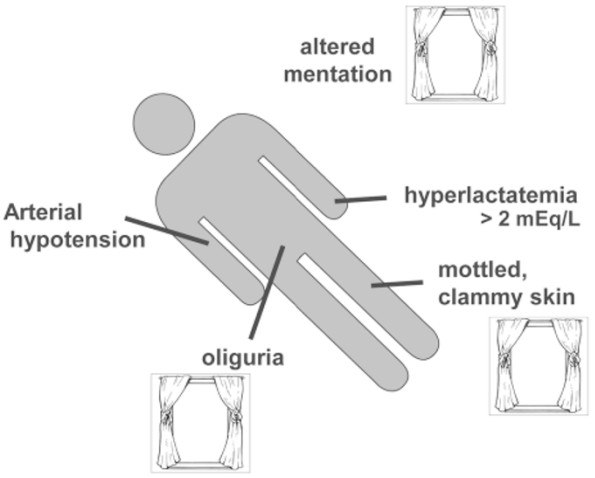

Figure 2. The three 'windows' on shock.

tonometry and dye-clearance were tried but their role was never clearly defined and they are not commercially available). The sublingual microcirculation (see below) may provide us with a new 'window'. This 'window' has been used in several studies [14-18] and has been shown to have high sensitivity for identifying the presence of shock and response to therapy [15]. Although current equipment is not yet suitable for routine clinical use, improvements in the available technology together with supportive clinical trials may make this a valuable window to identify and treat different states of shock.

Figure 3 shows the interaction between arterial pressure, altered tissue perfusion, increased lactate and microvascular alterations.

Classification of shock states

Shubin and Weil [19] defined the pathophysiological states of circulatory shock many years ago, using a classification based on four mechanisms (Table 1, Figure 4). In the first three types, cardiac output is low. In fact, each of the three types is represented by one of the determinants of cardiac output: decreased preload (hypovolemic), altered contractility (cardiogenic), and increased afterload (obstructive). In the fourth type of shock, the distributive defect is the result of the release of many mediators, including cytokines. These mediators can have vasodilating and vasopressor effects, although vasodilating effects predominate in the central circulation. Some of these mediators decrease myocardial contractility, accounting for the myocardial depression associated with sepsis. Despite this myocardial depression, distributive shock in humans is generally associated with an increase in cardiac output. There is also microvascular obstruction because of activated leukocytes and platelets impairing the distribution of blood flow in the periphery. Moreover, because of a defect in the microvasculature, autoregulatory mechanisms are no longer effective in matching oxygen need to oxygen supply and there is an increased shunt of the microcirculation. The resultant increased heterogeneity of microcirculatory perfusion creates areas of no flow in close proximity to areas of flow. Importantly, although the focus of this review is circulatory shock, it must be appreciated that inflammatory mediators and oxidative stress from circulatory shock and reperfusion or due to other factors (for example, sepsis) can also directly cause tissue injury.

Put in very basic terms, something is wrong with the pump (cardiogenic), with the volume (hypovolemic), with the major vessels (high afterload/obstruction) or with the small vessels (distributive/shunting).

Importantly, different types of shock may co-exist. For example, in sepsis there may be a combination of distributive, hypovolemic (sweating, diarrhea, extravasation and so on) and even cardiogenic forms; in anaphylactic shock the same pattern may be present, that is, distributive and hypovolemic (due to severe permeability alterations) with altered myocardial contractility.

Microvascular alterations

Microvascular alterations are common in all shock states. In distributive types of shock we expect these changes, but they can also be observed in cardiogenic shock states [20].

Microcirculatory alterations caused by pathogenic factors and hemodynamic changes are critically involved in the effects of shock on organ function as oxygen transport to the cells becomes compromised due to limitation of convective (flow) and/or diffusive (increased distance between cells and red blood cell-carrying capillaries)

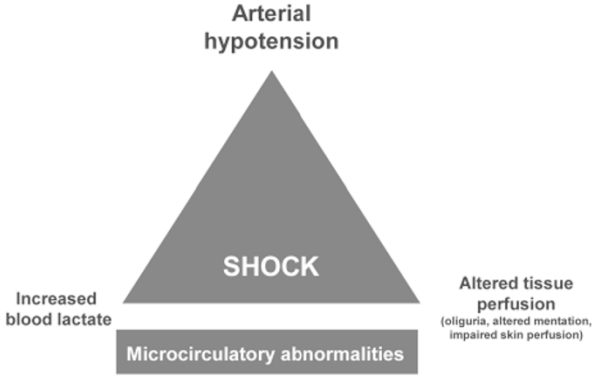

Figure 3. The triangular basis of circulatory shock. The full clinical picture includes the three features of hypotension, altered tissue perfusion and hyperlactatemia, whereas the underlying microcirculatory disturbances are less apparent. However, the systemic presentation is not always complete.

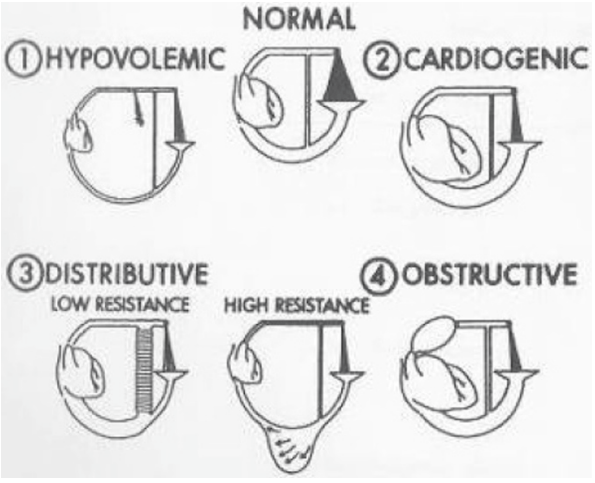

Figure 4. The four types of acute circulatory failure according to Weil and Shubin. Reproduced from [19], with permission.

Table 1. The four pathophysiological types of shock and their principal causes

Pathophysiological type	Cause
Hypovolemic	Hemorrhage, trauma Dehydration
Cardiogenic	Myocardial infarction Cardiomyopathy Valvular disease Severe arrhythmias
Obstructive	Pulmonary embolism Tamponade Aortic dissection
Distributive	Inflammatory response (mediators)

transport of oxygen to the tissues [21]. Cellular alterations of the microcirculation include endothelial dysfunction [22], changes in the hemorheological properties of red blood cells [23], leukocyte activation, coagulopathy and vascular smooth muscle cell alterations causing autoregulatory dysfunction. Endothelial glycocalyx shedding [24], which is highly sensitive to oxidative stress, contributes to the compromise of the endothelial vascular barrier, resulting in tissue edema [25]. From this perspective, the microcirculation could indeed be regarded as a target of shock. Microcirculatory areas with obstructions are shunted, resulting in patchy, heterogeneous hypoxic areas [26]. In addition, cellular changes occur, involving mitochondrial depression [27]. Although this had been clearly identified from animal studies, the true extent to which the above occurred in the clinical setting remained unclear until the late 1990s when the introduction of hand-held video microscopes allowed direct bedside observations of the microcirculation [28]. Heterogeneity of microvascular flow among organs and within the microcirculation, independent of systemic hemodynamic variables, is a characteristic of the microcirculatory alterations seen in human sepsis [16] and capillary obstruction is observed in the presence of normal flow in larger vessels [14,29]. These observations are a direct demonstration of the presence of shunting occurring at the microcirculatory level and give new credence to Dr Weil's appreciation of circulatory shunting as being a key feature of distributive shock [19].

Importantly, studies have demonstrated that persistent sublingual microcirculatory alterations are associated with adverse outcomes in patients with septic shock [29], and that resuscitation therapies, which are effective in the early recruitment of the microcirculation, can improve organ function and outcome in septic shock patients [15,18]. It may, therefore, be that, for early goal-directed therapy to be effective in patients with shock, it must be able to recruit the microcirculation. However, current technology for monitoring the microcirculation is not yet ready for the clinical arena and further clinical trials in different patient groups are needed before the microcirculation can really present itself as a window to monitor and treat shock.

Principles of therapy

Dr Weil introduced the VIP rule (V for ventilate, I for infuse, and P for pump) many years ago [30] for the initial resuscitation of shock, but it is still relevant today.

Ventilation

Adequate oxygenation is of course essential but there is some debate about the use of excessive PaO_2 with suggestions that it may alter the microcirculation,

primarily by inducing vasoconstriction and generating oxygen radicals. After cardiac arrest, in particular, high PaO_2 may be deleterious [31]. The problem in shock is that the widely used, readily available indication of arterial saturation, pulse oximetry, may not be reliable because of the altered skin perfusion that occurs with major vasoconstriction; hence, to avoid the well-known risks associated with hypoxia, we tend to be relatively generous with oxygen administration. Importantly, if there is any question about whether or not a patient needs endotracheal intubation, then this procedure should be performed and not delayed. Non-invasive mechanical ventilation should be used with caution in hemodynamically unstable patients.

Infuse

Fluids should not be withheld based just on the presence of edema, because edema formation may be the result of extravasation of fluids, which decreases blood volume, an effect demonstrated by Dr Weil decades ago [32]. It is also well known that static values of effective filling (pressures or volumes) are a poor predictor of the response to fluids [33,34], so fluids should not be withheld based on these measures. Fluid challenges with pre-set limits can help determine the need for ongoing fluid infusion, as suggested by Dr Weil [35]. Optimal choice of fluid remains debated, although recent studies in patients with severe sepsis suggest that 4% albumin solutions may be of benefit compared to normal saline [36] and hydroxyethyl starch solutions may increase mortality compared to Ringer's acetate [37]. There is some controversy about the use of saline solutions in the presence of severe metabolic acidosis, because of the chloride load.

Pump

Pump effectively refers to the use of vasoactive agents. Vasopressors should be given first to maintain a minimal perfusion pressure, even if there is cardiogenic shock, because dobutamine administration may result in hypotension if there is any degree of hypovolemia. Vasopressors are generally started early, at the same time as fluids, but patients are weaned from vasopressor support as soon as possible. Norepinephrine is preferred over dopamine, as it is associated with lower mortality rates in cardiogenic [38] and in septic [39] shock.

Conclusion

Dr Weil set the basis for much of today's current knowledge of circulatory shock. Therapy for shock should be based on pathophysiological alterations rather than on protocols. Monitoring of shock relies on assessment of arterial pressure, cardiac output, tissue perfusion abnormalities, and blood lactate concentrations. Monitoring of the microcirculation may help, but further study is needed to confirm this.

Abbreviations

PaO_2, partial pressure of oxygen.

Competing interests

The authors declare that they have no competing interests.

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