Continuing Medical Education

The Nomenclature, Definition and Distinction of Types of Shock

Thomas Standl, Thorsten Annecke, Ingolf Cascorbi, Axel R. Heller, Anton Sabashnikov, Wolfram Teske

Summary

Background: A severe mismatch between the supply and demand of oxygen is the common feature of all types of shock. We present a newly developed, clinically oriented classification of the various types of shock and their therapeutic implications.

Methods: This review is based on pertinent publications (1990–2018) retrieved by a selective search in PubMed, and on the relevant guidelines and meta-analyses.

Results: There are only four major categories of shock, each of which is mainly related to one of four organ systems. Hypovolemic shock relates to the blood and fluids compartment while distributive shock relates to the vascular system; cardiogenic shock arises from primary cardiac dysfunction; and obstructive shock arises from a blockage of the circulation. Hypovolemic shock is due to intravascular volume loss and is treated by fluid replacement with balanced crystalloids. Distributive shock, on the other hand, is a state of relative hypovolemia resulting from pathological redistribution of the absolute intravascular volume and is treated with a combination of vasoconstrictors and fluid replacement. Cardiogenic shock is due to inadequate function of the heart, which shall be treated, depending on the situation, with drugs, surgery, or other interventional procedures. In obstructive shock, hypoperfusion due to elevated resistance shall be treated with an immediate life-saving intervention.

Conclusion: The new classification is intended to facilitate the goal-driven treatment of shock in both the pre-hospital and the inpatient setting. A uniform treatment strategy should be established for each of the four types of shock.

Cite this as:
Standl T, Annecke T, Cascorbi I, Heller AR, Sabashnikov A, Teske W: The nomenclature, definition and distinction of types of shock. Dtsch Arztebl Int 2018; 115: 757–68. DOI: 10.3238/arztebl.2018.0757

Department of Anesthesiology, Intensive and Palliative Care Medicine, Städtisches Klinikum Solingen gGmbH: Prof. Dr. med. Thomas Standl, MHBA

Department of Anesthesiology and Intensive Care Medicine, University Hospital of Cologne: Prof. Dr. med. Thorsten Annecke, DESA

Institute of Clinical and Experimental Pharmacology at the University Medical Center Schleswig-Holstein, Campus Kiel: Prof. Dr. med. Dr. rer. nat. Ingolf Cascorbi

Surgical Center/Emergency Department, Department of Anesthesiology and Intensive Care, University Hospital Carl Gustav Carus, Technische Universität Dresden: Prof. Dr. med. Axel R. Heller, MBA, DEAA

Department of Cardiothoracic Surgery, Cardiac Center, University Hospital of Cologne: PD Dr. med. Anton Sabashnikov

Department of Orthopedics and Trauma Surgery, Kath. Krankenhaus Hagen gGmbH: PD Dr. med. Wolfram Teske

In the first descriptions of shock the focus was exclusively on traumatic hemorrhagic shock, but later this changed and five different types of shock came to be distinguished (1). Although it is true that all types of shock can lead to the same final stage of multiorgan failure as a result of the imbalance between oxygen demand and supply, the differences in their pathogenesis and pathophysiology make it desirable to change their classification, partly for teaching purposes, but also, especially, because different therapeutic measures are needed for the different types of shock. The new classification makes no claim to be binding, and the therapeutic effects are as a rule limited primarily to restoration of vital functions, in particular cardiovascular function consistent with survival.

For the reasons given above, the new classification comprises just four main categories:

- Hypovolemic shock
- Distributive shock
- Cardiogenic shock
- Obstructive shock.

Of these, hypovolemic shock is divided into four subcategories and distributive shock into three. Obstructive shock has been given a category of its own. Although this nomenclature and classification is schematic and there is some overlapping between the main groups, these four main groups can be basically assigned to four organ systems (*Figure 1*) that, owing to differences in their pathogenesis and pathophysiology, require group-specific—or, in other words, organ-specific—treatment (*Figure 2*):

- Blood and fluids compartment
- Vascular system
- Heart
- Circulatory system.

Because of the difficulty of carrying out prospective randomized studies in shock patients, the recommendations for treatment are based largely on guidelines and registry studies. If available, the

Classification of types of shock

- Hypovolemic shock
- Distributive shock
- Cardiogenic shock
- Obstructive shock

recommendation grade (RG) from the guidelines is given. Where no recommendation grade is available, the recommendation is that of the present authors (*eTable 1*). The effects of the interventions presented on survival and disability-free survival are in some cases not strong.

Learning goals

After reading this article, the reader should:

- Be familiar with the new classification of types of shock
- Understand the different pathogenesis and pathophysiology of the four main categories of shock
- Know the different therapeutic approaches to the various types of shock.

Hypovolemic shock

Hypovolemic shock is a condition of inadequate organ perfusion caused by loss of intravascular volume, usually acute. The result is a drop in cardiac preload to a critical level and reduced macro- and microcirculation, with negative consequences for tissue metabolism and the triggering of an inflammatory reaction.

Hypovolemic shock is divided into four subtypes (2):

- Hemorrhagic shock, resulting from acute hemorrhage without major soft tissue injury
- Traumatic hemorrhagic shock, resulting from acute hemorrhage with soft tissue injury and, in addition, release of immune system activators
- Hypovolemic shock in the narrower sense, resulting from a critical reduction in circulating plasma volume without acute hemorrhage
- Traumatic hypovolemic shock, resulting from a critical reduction in circulating plasma volume without acute hemorrhage, due to soft tissue injury and the release of immune system mediators.

Pathogenesis and pathophysiology

The characteristic feature of both, hemorrhagic and traumatic hemorrhagic shock is bleeding. However, differences exist between the two subcategories in terms of the extent of soft tissue damage. Clinically the most significant cause of hemorrhagic shock is acute bleeding from an isolated injury to a large blood vessel, gastrointestinal bleeding, nontraumatic vascular rupture (e.g., aortic aneurysm), obstetric hemorrhage (e.g., uterine atony), and hemorrhage in the region of the ear, nose, and throat (vascular erosion). The shock is triggered by the critical drop in circulating blood volume; massive loss of red blood cells intensifies the tissue hypoxia.

Traumatic hemorrhagic shock is distinguished from hemorrhagic shock by the additional presence of major soft tissue injury which aggravates the shock. A typical example of this type of shock is polytrauma, most usually caused by road traffic accidents and falls from a great height. Diffuse bleeding, hypothermia (especially ≤ 34 °C), and acidosis lead to life-threatening coagulopathy (3, 4). The soft tissue injury leads to postacute inflammation, further reinforcing this process. At the microcirculatory level, leukocyte–endothelium interactions (5) and destruction of endothelial membrane-bound proteoglycans and glycosaminoglycans cause microvascular dysfunction with capillary leak syndrome. At the intracellular level a metabolic imbalance arises (6) with possible mitochondrial damage (7) and a negative influence on the vasomotor system (8).

Hypovolemic shock in the narrower sense and traumatic hypovolemic shock show significant fluid loss without hemorrhage.

Hypovolemic shock in the narrower sense arises from external or internal fluid loss coupled with inadequate fluid intake. It can be caused by hyperthermia, persistent vomiting and diarrhea (e.g., cholera), or uncompensated renal losses (e.g., diabetes insipidus, hyperosmolar diabetic coma). Sequestration of large quantities of fluid in the abdomen, e.g., in ileus or liver cirrhosis, also leads to a reduction of circulating plasma volume. The pathologically raised hematocrit as well as the increased leukocyte and platelet interactions additionally impair the rheologic properties of the blood and can lead to persistent organ damage even after the patient has been treated for shock ("no-reflow phenomenon").

Typical causes of traumatic hypovolemic shock are large surface burns, chemical burns, and deep skin lesions. The trauma also activates the coagulation cascade and the immune system, potentiating the impairment of the macro- and microcirculation. The inflammatory reaction results in damage to the endothelium, increases capillary leak syndrome, and causes severe coagulopathy (9, 10).

It may be possible to draw some cautious conclusions about the incidence of traumatic hypovolemic and traumatic hemorrhagic shock from the Trauma Registry of the German Trauma Society (*Deutsche Gesellschaft für Unfallchirurgie*). In the 2017 annual report, out of 40 836 patients, 27 147 (66%) had a maximum severity of injury of AIS 3

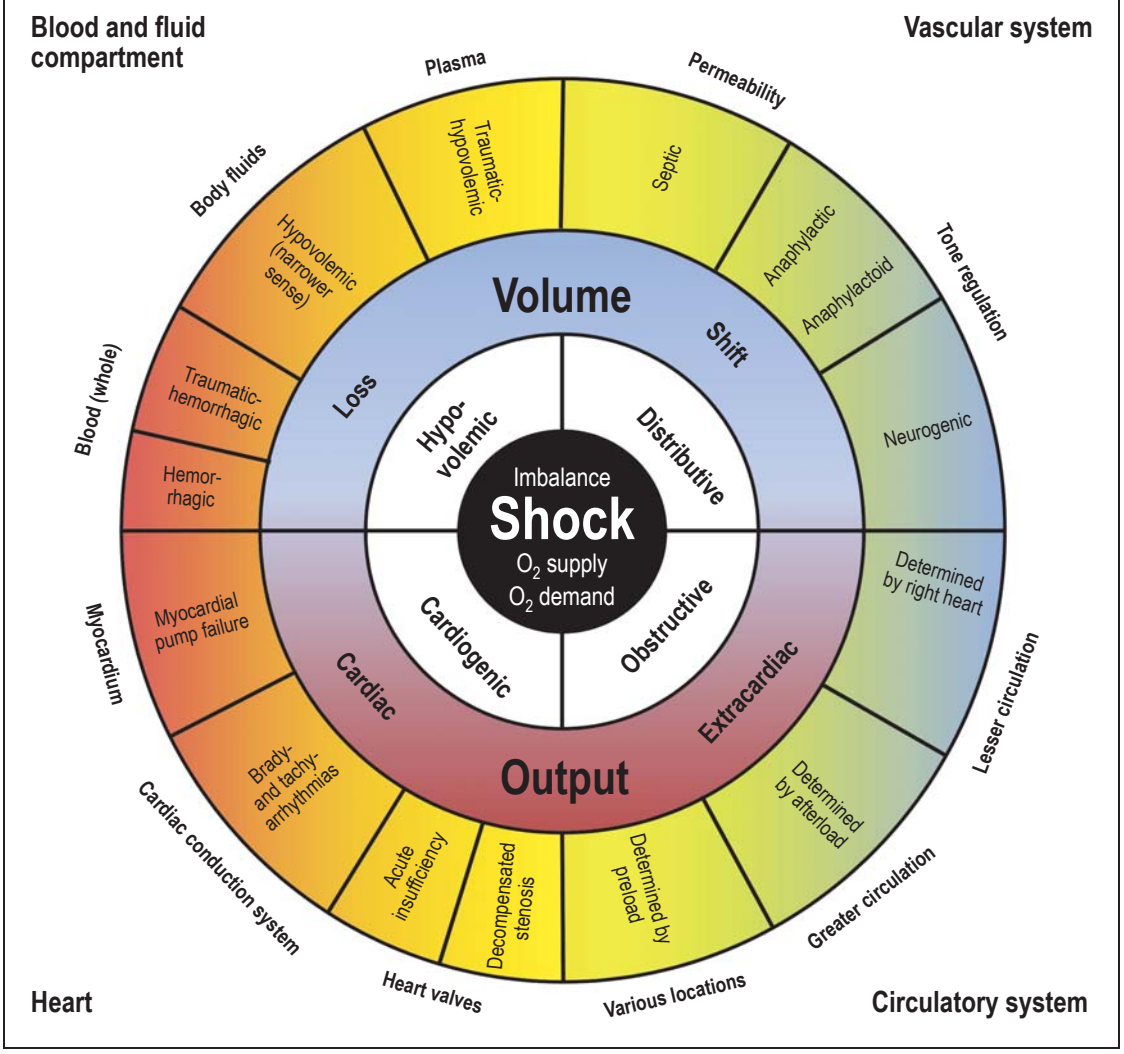
Hypovolemic shock

Hypovolemic shock is a condition of inadequate organ perfusion caused by loss of intravascular volume, usually acute.

Physiology of hypovolemic shock

The result is a drop in cardiac preload to a critical level and reduced macro- and microcirculation, with negative consequences for tissue metabolism and the triggering of an inflammatory reaction.

FIGURE 1



Synoptic view of the four types of shock (inner, white field) with the organ systems primarily associated with them (outer corners), sites and mechanisms of manifestation (outside the circle), and pathogenetic and pathophysiologic features (outer and middle sectors of the circle). To maintain clarity, mixed types of shock are not depicted.

(Abbreviated Injury Score) or more, and 10 639 (26%) had life-threatening injuries (ISS, Injury Severity Score ≥ 11), on the basis of which the number of patients can be calculated to be around 30 000 per year. The incidence of gastrointestinal hemorrhage in Germany is around 100 000 patients per year, of whom roughly 10 000 suffer hypovolemic shock. These figures, together with those for the remaining subtypes of hypovolemic shock, lead to a total of about 50 000 patients per year (*Table 1*).

Treatment

The preclinical and clinical treatment of hypovolemic shock consists of immediate intravascular volume replacement (fluid resuscitation) with balanced crystalloids (recommendation grade: B) using wide-bore

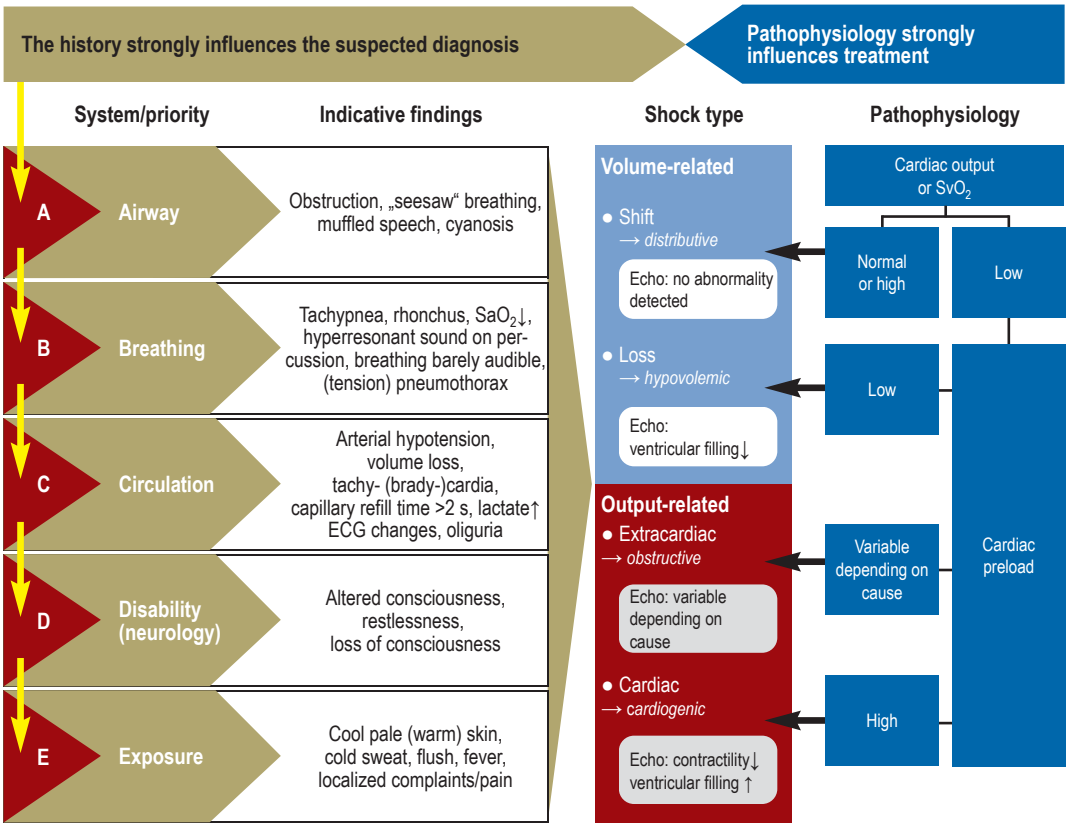
Hypovolemic shock in the narrower sense and traumatic hypovolemic shock

Hypovolemic shock in the narrower sense and traumatic hypovolemic shock show significant fluid loss without hemorrhage.

Causes

Typical causes of traumatic hypovolemic shock are large surface burns, chemical burns, and deep skin lesions.

FIGURE 2



Algorithm for differential diagnosis as the basis for treatment of the different types of shock
SvO_2, central venous oxygen blood saturation

peripheral venous access and, in a patient who is hemorrhaging, rapid bleeding control (*Table 2*). To prevent or alleviate hypoxia, endotracheal intubation with normoventilation usually follows (recommendation grade: A). The extent of blood loss can be roughly estimated using the ATLS (Advanced Trauma Life Support) score (11). Trauma patients with shock should be transferred directly to a trauma center (recommendation grade: B).

Surgical management should be undertaken as soon as possible using the damage control surgery (DCS) approach (12). Persisting hypotension, especially in patients with head trauma, should prompt administration of a vasconstrictor (e.g., norepinephrine) to achieve a systolic arterial pressure (SAP) ≥ 90 mmHg (recommendation grade: B) (13).

In patients with controllable bleeding up to age-specific and comorbidity-specific hemoglobin threshold values, red cell concentrate (RCC) transfusions are given. Those with uncontrolled bleeding, irrespective of the current hemoglobin value, should receive transfusions of RCC, fresh frozen plasma (FFP), and platelet concentrates (PC). Patients with traumatic or peripartum bleeding should also be given 1 to 2 g tranexamic acid at an early stage (recommendation grade: A) (14–16). Multidisciplinary treatment includes early stabilization of coagulation by means of coagulation factors, either as individual factors or as FFP, together with surgical prevention of further blood loss (17).

In patients with gunshot or stab wounds to the body cavities or a ruptured aortic aneurysm, blood pressure shall be stabilized at a permissive hypotension (SAP = 70 to 80 mmHg) by norepinephrine infusion and moderate volume replacement until

Multidiscipinary treatment

Multidisciplinary treatment includes early stabilization of coagulation by means of coagulation factors, either as individual factors or as fresh frozen plasma (FFP), together with surgical prevention of further blood loss.

Distributive shock

Distributive shock is a state of relative hypovolemia resulting from pathological redistribution of the absolute intravascular volume and is the most frequent form of shock.

bleeding control is achieved (recommendation grade: B) (13).

For patients with large burns, the modified Brooke formula can give an indication of the volume replacement required in the first 24 h (18).

Distributive shock

Distributive shock is a state of relative hypovolemia resulting from pathological redistribution of the absolute intravascular volume and is the most frequent form of shock (*Table 1*). The cause is either a loss of regulation of vascular tone, with volume being shifted within the vascular system, and/or disordered permeability of the vascular system with shifting of intravascular volume into the interstitium. The three subtypes are septic, anaphylactic/anaphylactoid, and neurogenic shock.

TABLE 1

Relative incidences of the various types of shock

Type of shock	Relative incidence (authors' own calculations)	Relative incidence (representative published figures [25])
Hypovolemic	27%	16%
Distributive	59%	66%
	Made up of: septic 55%, anaphylactic and neurogenic 4%	Made up of: septic 62%, anaphylactic and neurogenic 4%
Cardiogenic	13%	16%
Obstructive	1%	2%

Septic shock

Sepsis is defined according to the current Sepsis-3 criteria as a dysregulated response by the body to an infection resulting in life-threatening organ dysfunctions. These are characterized and quantified by an increase in SOFA (Sequential Organ Failure Assessment) score by ≥ 2 points (*eTable 2*) (19). In the emergency care setting, the "Quick SOFA" (qSOFA) score can be used for screening, requiring only a preliminary examination of state of consciousness, respiration rate, and blood pressure. If there are pathological alterations of these parameters (obtunded consciousness, respiration rate ≥ 22/min, systolic blood pressure ≤ 90 mmHg), and if infection is suspected, the presence of sepsis may be assumed (20).

A lactate value above 2 mmol/L and persistent hypotension requiring the administration of vasopressors to keep mean arterial blood pressure (MAP) above 65 mmHg define septic shock (21). Hypovolemia as the sole cause of circulatory failure must be ruled out, for example by echocardiography (19, 21).

Pathogenesis and pathophysiology

Patients over the age of 65 years with immunosuppression or underlying malignant disease are disproportionately affected. In some patients the inflammatory response is small or nonexistent (19, 22, 23). In Germany about 280 000 patients annually are affected by sepsis; the incidence is rising every year by about 5.7%, and between 2007 and 2013 the mortality fell from 27.0% to 24.3% (20). About 35% of these patients suffer from septic shock, representing a total of about 100 000 patients per year (*Table 1*).

The core of the pathophysiology is the endothelial dysfunction, which leads to dysregulation of vascular tone resulting in vasodilation, impaired distribution, and volume shifting in the macro- and microcirculation, and to a rise in vascular permeability (capillary leak syndrome) (22–25). Frequently, biventricular impaired myocardial function is also present in the form of septic cardiomyopathy (26), which contributes to patient mortality (26, 27). Septic shock is a mixed form of a variety of pathologies (hypovolemia, vasodilation, impaired cardiac function, and mitochondrial dysfunction) and is usually associated with complex coagulopathies (22–25).

Treatment

Apart from an increased level of alertness and rapid diagnosis, septic shock requires treatment to support the circulation by the infusion of balanced crystalloid solutions (recommendation grade: A), administration of vasopressors (norepinephrine, vasopressin if needed), in some cases also inotropic drugs (e.g., dobutamine), and organ replacement therapy (recommendation grade: B) (*Table 2*). Advanced invasive monitoring is indicated to allow tailored therapy for the impaired hemodynamics. Echocardiography has a central part to play here (22, 24, 28). In all sepsis patients, as soon as samples have been obtained for microbiological study, calculated broad-spectrum antibiotic therapy and (if possible) source control (causal treatment) should be started as soon as possible (recommendation grade: A) (29). Noninfectious disease involving extensive mediator activation (e.g., acute pancreatitis) may lead to a clinical presentation similar to that of septic shock. This

Septic shock

Sepsis is defined according to the current Sepsis-3 criteria as a dysregulated response by the body to an infection resulting in life-threatening organ dysfunctions.

Prevalence

In Germany about 280 000 patients are affected by sepsis every year; the incidence is rising every year by about 5.7%, and between 2007 and 2013 the mortality fell from 27.0% to 24.3%. About 35% of these patients suffer from septic shock.

TABLE 2

Typical drugs for treatment of the various types of shock

Drug	Indication	Main effect	Important adverse effects	Dosage
Blood and coagulation products				
Red cell concentrates (RCC)	Hemorrhagic shock, traumatic hemorrhagic shock, all other types of shock in patients with signs of anemic hypoxia	Replace lost red blood cells, increase blood oxygen concentration, increase blood coagulability	Hyperkalemia (check length of storage of RCC), acute transfusion reaction, sensitization in case of non-identical subgroup infection (cytomegaly, HIV, hepatitis A, B, C, E)	According to effect, need, and transfusion trigger in the individual case, 1 RCC raises Hb value by approx. 1 g/dL. In patients with massive hemorrhage: RCC:FFP:PC = 4:4:1
Fresh frozen plasma (FFP)	Hemorrhagic shock, traumatic hemorrhagic shock, all other types of shock in patients with acquired coagulopathy and bleeding	Replaces coagulation factors and volume	Anaphylaxis, acute transfusion reaction, sensitization in case of non-identical subgroup infection, volume overload, TRALI, infection (cytomegaly, HIV, hepatitis A, B, C, E)	Initially 20 mL/kg, then according to effect and individual need. 1 mL/kg raises the coagulation factor(s) concerned by approx. 1%.. In patients with massive hemorrhage: RCC:FFP:PC = 4:4:1
Coagulation factors (fibrinogen, PPSB = F II, VII, IX and X)	Hemorrhagic shock, traumatic hemorrhagic shock, all other types of shock in patients with acquired coagulopathy and bleeding	Selectively replace individual factors after loss/use of vitamin K inhibitor and NOAC-induced hemorrhage	Risk of thromboembolism, contraindication: HIT2	1 IU/kg causes the relevant factor to rise by approx. 0.5–1%
Platelet concentrates (PC)	Trauma and hemorrhage-induced coagulopathy with thrombocytopenia	Replaces platelets	Acute transfusion reaction, sensitization in case of non-identical subgroup infection, anaphylaxis	1 apheresis PC raises the platelet count by approx. 20 G/dL. In patients with massive hemorrhage: RCC:FFP:PC = 4:4:1
Tranexamic acid	Hemorrhagic shock, traumatic hemorrhagic shock, peripartum hemorrhage	Inhibits plasmin activation, reduces hyperfibrinolysis	Diarrhea, vomiting, nausea, allergic dermatitis; administration later than 3 h after trauma may be harmful	Early (<3 h) in patients with hemorrhage, especially when peripartum or due to trauma: 1–2 g i. v.
Solutions for infusion				
Isotonic balanced full electrolyte solutions	All types of shock, when cardiac preload is concomitantly reduced due to intravascular volume depletion or obstruction	Replaces fluids lost due to electrolyte imbalance or volume shift, increases stroke volume by raising cardiac preload	Volume overload, pulmonary edema, peripheral edema	Initially 10–20 mL/kg i. v. repeatedly according to effect and volume response
Vasoconstrictors, positive inotropic agents, and vasodilators				
Epinephrine[*1,*2]	All types of shock, when use of other catecholamines fails to achieve adequate vasoconstriction and increased inotropy: cardiopulmonary resuscitation, anaphylactic shock	α1-Receptor-mediated vasoconstriction β1-Receptor-mediated positive inotropia β2-Receptor-mediated bronchodilation	Myocardial ischemia, stress cardiomyopathy, tachyarythmias, oliguria/anuria	0.3–0.6 mg i.m. (autoinjector in anaphylaxis cases), continuously according to effect and need: 0.05 to 1.0 (up to a maximum of 5.0) µg/kg per min i. v. Bolus doses: 5–10 µg i. v.; with CPR: 1 mg i. v. every 3–5 min
Dobutamine[*2]	Cardiogenic shock, all types of shock with insufficient ventricular pump function	Predominantly β1-receptor-mediated positive inotropic effect	Rise in heart rate ≥ 30/min, rise in BP ≥ 50 mmHg, headache, cardiac arrhythmias, possible drop in BP due to β2-receptor-mediated vasodilation	Continuously according to effect and need: 2.5 to 5 (up to a maximum of 10) µg/kg per min i. v.
Norepinephrine[*2]	All types of shock with reduced peripheral resistance	Predominantly α1-receptor-mediated vasoconstriction, (low) positive inotropic effects	Peripheral ischemia, rise in BP, reflex bradycardia, cardiac arrhythmias	Continuously according to effect and need: 0.1–1.0 µg/kg per min i. v. Bolus administration: 5–10 µg i. v.
Milrinone[*2]	Cardiogenic shock	PDE-3 inhibitor: positive inotropic and vasodilatory effect	Drop in BP due to vasodilation, ventricular ectopic beats and tachycardia, ventricular fibrillation, headache	Continuously according to effect and need: 0.375–0.75 µg/kg per min i. v.
Levosimendan[*2]	Cardiogenic shock	Calcium sensitizer	Drop in BP due to vasodilation, ventricular tachycardia, headache, extrasystoles, atrial fibrillation, heart failure, myocardial ischemia, dizziness, gastrointestinal disorders	Single use only: 0.05–0.2 µg/kg per min/24 h i. v.
Vasopressin[*3]	Shock states, especially septic shock, when norepinephrine alone does not achieve the required vasoconstriction and lost volume has been replaced	V_1-mediated (catecholamine-independent) vasoconstriction	Ischemia, reduced cardiac output, bradycardia, tachyarrhythmia, hyponatremia, ischemia	Continuously according to effect and need: 0.01 up to max. 0.03 U/min i. v.

Drug	Indication	Main effect	Important adverse effects	Dosage
Cafedrine hydrochloride 200 mg Theodrenaline-hydrochloride 10 mg[*4]	Neurogenic shock	β1-Receptor-mediated inotropy and α1-receptor-mediated vasoconstriction Rise in BP with peripheral resistance unchanged and moderately reduced heart rate	Palpitations, symptoms of angina pectoris, cardiac arrhythmias	¼–1 ampoule (2 mL) usually diluted with NaCL 0.9% to a total of 10 mL i. v. Maximum: 3 ampoules/24 h
Glyceryl trinitrate[*2]	Cardiogenic shock	Vasodilation to reduce preload in particular	Development of tolerance	Continuously according to effect and need: 0.3–4 µg/kg per min i. v.
Sodium nitroprusside[*2]	Cardiogenic shock	Vasodilation to reduce afterload	Risk of cyanide toxicity	Initially: 0.1 µg/kg per min i. v., then: double the dose every 3–5 min up to 10 µg/kg per min i. v.
Anti-inflammatory and antiallergic drugs				
Dimetindene maleate[*1]	Anaphylaxis/ anaphylactic shock	Blocks H_1-receptor-mediated action of histamine	Drowsiness, fatigue, dizziness, nausea, dry mouth	4–8 mg over 30 s/24 h i. v.
Methylprednisolone[*1]	Anaphylaxis/ anaphylactic shock	Synthetic glucocorticoid, potent anti-inflammatory effect	Glucocorticoid-associated adverse effects only when given long-term	0.5–1 g/24 h i. v.
Hydrocortisone[*5, *6]	Septic shock with persistent instability after fluid and vasopressor therapy Adrenal insufficiency	Endogenous glucocorticoid, substituted in patients with reduced or no cortisol production	See Methylprednisolone	Initially: 100 mg over 10 min then: 200–500 mg/24 h i. v.
Fludrocortisone[*7]	Neurogenic shock Septic shock?	Mineralocorticoid	If given long-term: edema, hypertension, hypokalemia	0.1–0.2 mg/24 h p. o.

Sources of dosage recommendations:
[*1] Guideline for acute therapy and management of anaphylaxis. S2 guideline (31), [*2] German–Austrian S3 guideline "Infarction-related cardiogenic shock—diagnosis, monitoring, and therapy" (37), [*3] drug information for Empressin® February 2015, [*4] drug information for Akrinor® September 2016, [*5] Angus and van der Poll 2013 (24), [*6] drug information for Hydrocortison® March 2018, [*7] drug information for Astonin-H® June 2014.
DIC, disseminated intravascular coagulation; RCC, red cell concentrates; FFP, fresh frozen plasma; HIT2, heparin-induced thrombocytopenia type 2; i. m., intramuscular; i. v., intravenous; PC, platelet concentrates; TRALI, transfusion-related acute lung injury; PPSB, prothrombin, proconvertin, Stuart factor, and antihemophilic B factor; CPR, cardiopulmonary resuscitation; BP, blood pressure; PDE-3, phosphodiesterase 3

is due to activation of the same mediator cascade by noninfectious molecular signals of soft tissue damage (22).

The pathophysiology and pathogenesis of toxic shock syndrome (TSS) are related to those of septic shock. TSS is characterized by fever, severe hypotension, and skin rash as the main symptoms. It is usually triggered by toxins from certain staphylococci. The incidence is 0.5 / 100 000, and mortality is between 2% and 11%. Treatment is the same as that recommended for septic shock.

Anaphylactic and anaphylactoid shock

Anaphylactic shock is characterized by massive histamine-mediated vasodilation and maldistribution with a shift of fluid from the intravascular to the extravascular space.

Pathogenesis and pathophysiology

Anaphylaxis is an acute systemic reaction usually mediated by IgE-dependent hypersensitivity reactions. The central role is played by mast cells and the histamine they release. In Germany, the incidence of anaphylactic reactions is 50 per 100 000 / year; they are the reason for about 1% of emergency admissions. Lifetime prevalence is reported at 0.5% to 2% and mortality at 2% to 20%. On a conservative assumption that 10% of these patients suffer shock, this results in a total of 8000 shock patients a year. The most frequent trigger in children is food products (58%), whereas in adults it is insect venom (55%, of which 70% are wasp stings and 20% bee stings), followed by drugs (21%, two-thirds of these being diclofenac, acetylsalicylic acid, and antibiotics, and 1% being ACE inhibitors or

Anaphylactic and anaphylactoid shock

Anaphylactic shock is characterized by massive histamine-mediated vasodilation and maldistribution with a shift of fluid from the intravascular to the extravascular space.

Clinical presentation of anaphylactic shock

The clinical presentation varies greatly from one individual to another according to the dose and site of entry of the antigen and the degree of sensitization. Initially, skin manifestations, abdominal symptoms, or respiratory symptoms may be prominent.

beta-blockers). Intensifying factors include physical effort, stress, and acute infection.

Anaphylactoid shock is caused by physical, chemical, or osmotic hypersensitivity reactions that are IgE-independent. Mediators are released from mast cells and basophilic granulocytes independently of any antigen–antibody reaction or presensitization. Typical triggers are X-ray contrast media.

The clinical presentation varies greatly from one individual to another according to the dose and site of entry of the antigen and the degree of sensitization. Initially, skin manifestations, abdominal symptoms, or respiratory symptoms may be prominent. Anaphylactic reactions may resolve spontaneously or may progress despite appropriate therapy. In anaphylaxis with fatal outcome, thromboembolic events are seen as often as arrhythmias and ventricular dysfunction (30).

Treatment

Patients with severe anaphylactic reactions require constant monitoring, as late reactions including arrhythmias, myocardial ischemia, and respiratory failure may manifest as late as 12 hours after the initial event. In terms of drug treatment, for anaphylactic shock especially the administration of epinephrine (plus norepinephrine, if necessary) and forced fluid replacement are required (31). In patients with bronchospasm, β-sympathomimetics and, as second-line treatment, glucocorticoids are indicated (as they are in patients with delayed progressive symptoms) (31). Histamine antagonists suppress the histaminergic effects (*Table 2*). Treatment for anaphylactoid shock is the same as for anaphylactic shock.

Neurogenic shock

Neurogenic shock is a state of imbalance between sympathetic and parasympathetic regulation of cardiac action and vascular smooth muscle. The dominant signs are profound vasodilation with relative hypovolemia while blood volume remains unchanged, at least initially.

Pathogenesis and pathophysiology

The pathomechanisms of neurogenic shock can be divided into three groups (*eFigure*):

- Direct injury to the centers for circulatory regulation due to compression (brainstem trauma), ischemia (e.g., basilar artery thrombosis), or the influence of drugs
- Altered afferents to the circulatory center in the medulla oblongata due to fear, stress, or pain or dysregulated vagal reflexes
- Interruption of the descending connection from the bulbar regulatory centers to the spinal cord, especially in patients who have sustained trauma above the middle of the thoracic spine (paraplegia).

At 15% to 20%, spinal cord injuries are the most common cause of neurogenic shock (32), followed by surgical intervention in the lumbar region (33). Neurogenic shock can occur due to cerebral ischemia, subarachnoid hemorrhage, meningitis, or, more rarely, during or after epileptic seizures, rapid onset of Guillain–Barré syndrome, pandysautonomia, or cerebral herniation. Occasionally, neurogenic shock can be triggered by stress or severe pain, or even after a karate kick.

Neurogenic shock is characterized by the sudden drop of SAP to <100 mmHg and heart rate to <60/min with obtunded consciousness (rapid onset in bulbar injury) and, in patients with high spinal cord injury, loss of spinal reflexes (34). The capacity of the splanchnic venous system and skeletal musculature rises while systemic venous pressure drops markedly. Mortality is around 20%.

Treatment

The critical element in treating neurogenic shock is the treatment of the cause. In addition to rapid fluid replacement, norepinephrine is given at increasing dosages until peripheral vascular resistance rises (*Table 1*). To restore vascular tone, direct- or indirect-acting sympathomimetics can also be given (35). Mineralocorticoids to increase plasma volume are also a therapeutic option.

Cardiogenic shock

Cardiogenic shock is primarily a disorder of cardiac function in the form of a critical reduction of the heart's pumping capacity, caused by systolic or diastolic dysfunction leading to a reduced ejection fraction or impaired ventricular filling. It is defined by SAP <90 mmHg or mean arterial blood pressure of 30 mmHg below the baseline value and cardiac index (CI) <1.8 L/min/m^2 without pharmacologic or mechanical support or <2.0 L/min/m^2 with support (36). According to the German–Austrian S3 guideline, cardiac index determination is not required for a clinical diagnosis of cardiogenic shock (37). In addition to these hemodynamic and clinical criteria, evidence of cardiac dysfunction is required, together with the exclusion of other types of shock (differential diagnosis).

Neurogenic shock

Neurogenic shock is a state of imbalance between sympathetic and parasympathetic regulation of cardiac action and vascular smooth muscle. The dominant signs are profound vasodilation with relative hypovolemia while blood volume remains unchanged, at least initially.

Cardiogenic shock

Cardiogenic shock is primarily a disorder of cardiac function in the form of a critical reduction of the heart's pumping capacity, caused by systolic or diastolic dysfunction leading to a reduced ejection fraction or impaired ventricular filling.

Pathogenesis and pathophysiology

The cardiac dysfunction may be due to myocardial, rhythmologic, or mechanical causes (*Figure 1*). With the myogenic form, reduction of pump function due to acute coronary syndrome (ACS) is the preeminent cause. Other causes include various cardiomyopathies, myocarditis, pharmacotoxicity, and blunt trauma to the heart. Mechanical causes include advanced acute and chronic valvular disease and mechanical complications after myocardial infarction or caused by intracavitary structures impeding flow (thrombi or tumors). Tachycardia and bradycardia may also result in the clinical picture of cardiogenic shock. Based on an average of 280 000 myocardial infarctions in Germany and an 8% incidence of cardiogenic shock among these cases, it can be estimated that 23 000 patients suffer cardiogenic shock every year (*Table 1*). The main symptoms of cardiogenic shock are agitation, disturbed consciousness, cool extremities, and oliguria. Death in patients in cardiogenic shock is usually caused by hemodynamic instability, multiorgan failure, and systemic inflammation.

To maintain adequate cardiac output and hence sufficient organ perfusion, systemic counter-regulation mechanisms such as the sympathetic nervous system and neurohumoral, renal, and local vasoregulation are activated.

Treatment

Echocardiography and invasive monitoring are the pillars of diagnosis. The primary goal of treatment is removing the cardiac causes of the shock. This includes the earliest possible coronary reperfusion in ACS by means of percutaneous coronary intervention (PCI) with the insertion of stents (bare metal stent, BMS; drug-eluting stent, DES) (recommendation grade: A), surgical or other interventional treatment of mechanical causes and structural heart disease, and surgical or interventional ablation, and pacemaker therapy (36, 38). In addition to this, symptomatic treatment is undertaken with the aim of improving end organ perfusion, microcirculation, and cellular oxygen utilization. This includes not just catecholamines such as dobutamine (recommendation grade: B), norepinephrine (recommendation grade: B), and epinephrine (recommendation grade: 0), vasodilators (recommendation grade: 0), calcium sensitizers (recommendation grade: 0), PDE_3 inhibitors (recommendation grade: 0), antiarrhythmic drugs, and more (*Table 2*), but also mechanical circulatory support such as intra-aortic balloon counterpulsation (recommendation grade: B), surgical and percutaneous interventional implantable ventricular support systems, and extracorporeal membrane oxygenation (ECMO) (37, 38).

Obstructive shock

Obstructive shock is a condition caused by the obstruction of the great vessels or the heart itself. Although the symptoms resemble those of cardiogenic shock, obstructive shock needs to be clearly distinguished from the latter because it is treated quite differently (39).

Pathogenesis and pathophysiology

Disorders involving impaired diastolic filling and reduced cardiac preload include vena cava compression syndrome, tension pneumothorax, pericardial tamponade, and high-PEEP ventilation. A pulmonary artery embolism or mediastinal space-occupying mass increases right-ventricular afterload, while at the same time left ventricular preload is reduced by obstructions in the pulmonary flow. The same mechanisms occur with an intracardial mass. Obstruction of the aortic flow can be distinguished from this, as it leads to a rise in left ventricular afterload (e.g., Leriche syndrome [aortoiliac occlusive disease], aortic dissection, and high-grade aortic valve stenosis). After trauma, especially, combined shock forms are seen, e.g., with tension pneumothorax and hemorrhage. No figures exist for the incidence of obstructive shock, but it is likely to be the rarest form of shock.

The pathophysiology of obstructive shock can be classified according to the location of the obstruction in the vascular system in relation to the heart (*Figure 1*). Mechanical intra- or extravascular or luminal factors reduce blood flow in the great vessels or cardiac outflow with a critical drop in cardiac output and global oxygen supply. The result is a state of shock with tissue hypoxia in all organ systems. Common to all these obstructive states is the often rapid, massive drop in cardiac output and blood pressure.

The symptoms of obstructive shock are nonspecific and the condition is characterized by the compensatory autonomic response in the form of tachycardia, tachypnea, oliguria, and altered consciousness. Hypotension may be quite modest initially and this can lead to underestimation of the clinical situation (39). For the differential diagnosis, careful clinical examination is essential (auscultation, percussion, ultrasonography including echocardiography), but it must be accurate and prompt, because of the speed with which the state of shock progresses. Obstruction of intrathoracic blood flow can lead to cervical venous congestion or

Main symptoms of cardiogenic shock

The main symptoms of cardiogenic shock are agitation, disturbed consciousness, cool extremities, and oliguria. Death in patients in cardiogenic shock is usually caused by hemodynamic instability, multiorgan failure, and systemic inflammation.

Obstructive shock

Obstructive shock is a condition caused by the obstruction of the great vessels or the heart itself. Although the symptoms resemble those of cardiogenic shock, obstructive shock needs to be clearly distinguished from the latter because it is treated quite differently.

to atypical peripheral pulses. Tension pneumothorax may be associated with subcutaneous emphysema and deviation of the trachea visible in the neck, while aortic dissection or Leriche syndrome may cause pain in the chest or abdomen. The "4 H's and 4 T's" rule of reversible causes of cardiocirculatory arrest (40) involve three obstructive causes: pericardial tamponade, tension pneumothorax, and thromboembolism.

Treatment

Obstructive shock needs immediate causal treatment. Simple measures may suffice, such as changing the position of a patient with caval compression syndrome or adjusting the ventilation of the patient where the level of PEEP is too high. According to the underlying cause of the obstruction, a pulmonary embolism is treated with thrombolysis; tension pneumothorax or pericardial tamponade are relieved immediately by thoracic or pericardial drainage (recommendation grade: A); and Leriche syndrome is treated by surgical embolectomy.

Conflict of interest statement

Professor Annecke has received third-party funding or equipment for research projects or for carrying out clinical studies from CytoSorbents, Pulsion/Maquet, Corpuls, Köhler Chemie, Aerogen, and Medtronic.

Professor Standl has received lecture fees and reimbursement of conference fees and travel expenses from B. Braun, MSD, Pajunk, Grünenthal, and Fresenius.

The other authors declare that no conflict of interest exists.

Manuscript received on 28 September 2017, revised version accepted on 27 August 2018.

Translated from the original German by Kersti Wagstaff, MA.

References

1. Adams HA, Baumann G, Gänsslen A, et al.: Die Definitionen der Schockformen. Intensivmed 2001; 38: 541–53.
2. Adams HA, Baumann G, Cascorbi I, et al.: Interdisziplinäre Behandlungspfade: Hypovolämischer Schock. Eine Empfehlung der IAG Schock der DIVI. Monographie Deutscher Ärzteverlag, Köln, 2010.
3. Gänsslen A, Adams HA, Baumann G, et al.: Hämostase im Schock. Teil 4: Spezielle pathophysiologische Aspekte. Anästh Intensivmed 2016; 57: 58–67.
4. Mutschler M, Nienaber U, Brockamp T, et al.: Renaissance of base deficit for the initial assessment of trauma patients: a base deficit based classification for hypovolemic shock developed on data from 16,305 patients derived from the Trauma Register DGU. Crit Care 2013, 17: R42.
5. Deitch E, Condon M, Feketeova E, et al.: Trauma-hemorrhagic shock induces a CD36-dependent RBC endothelial-adhesive phenotype. Crit Care Med 2014; 42: e200–10.
6. Slaughter A, Nunns G, Alessandro A, et al.: The metabolopathy of tissue injury, hemorrhagic shock and resuscitation in a rat model. Shock 2018; 49: 580–90.
7. Karamercan M, Weiss S, Villarroel J, et al.: Can peripheral blood mononuclear cells be used as a proxy for mitochondrial dysfunction in vital organs during hemorrhagic shock and resuscitation? Shock 2013; 40: 476–84.
8. Song R, Bian H, Wang X, Huang X, Zhao K: Mitochondrial injury underlies hyporeactivity of arterial smooth muscle in severe shock. Am J Hypertension 2011; 24: 45–51.
9. Sherren PB, Hussey J, Martin R, Kundishora T, Parker M and Emerson B: Acute burn induced coagulopathy. Burns 2013; 39: 1157–61.
10. Mitra B, Wasiak J, Cameron PA, O'Reilly G, Dobson H and Cleland H: Early coagulopathy of major burns. Injury 2013; 44: 40–3.
11. Lawton LD, Roncal S, Leonard E, et al.: The utility of advanced trauma life support (ATLS) clinical shock grading in assessment of trauma. Emerg Med J 2014; 31: 384–9.
12. Khan S, Davenport R, Raza I, et al.: Damage control resuscitation using blood component therapy in standard doses has a limited effect on coagulopathy during trauma hemorrhage. Intensive Care Med 2015; 41: 239–47.
13. S3-Leitlinie Polytrauma/Schwerverletzten-Behandlung, AWMF Register-Nr. 012/019, Stand 7/2016.
14. Shakur H, Roberts I, Bautista R, Caballero J, et al.: Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010; 376: 23–32.
15. Roberts I, Shakur H, Afolabi A, et al.: The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet 2011; 377: 1096–101.
16. Shakur H, Roberts I, Fawole B, et al.: Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post- partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet 2017; 389: 2105–16.
17. Rossaint R, Bouillon B, Vladimir Cerny V, et al.: The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition. Critical Care 2016; 20: 100.
18. Aoki K, Yoshino A, Yoh K, et al.: A comparison of Ringer's lactate and acetate solutions and resuscitative effects on splanchnic dysoxia in patients with extensive burns. Burns 2010; 36: 1080–5.
19. Singer M, Deutschmann CS, Seymour CW, et al.: The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315: 801–10.
20. Fleischmann C, Thomas-Rueddel DO, Hartmann M, et al.: Hospital incidence and mortality rates of sepsis. Dtsch Arztebl Int 2016; 113: 159–66.
21. Shankar-Hari M, Phillips GS, Levy ML, et al.: Developing a new definition and assessing new clinical criteria for septic shock. JAMA 2016; 315: 775–87.
22. Gotts EJ, Matthay MA: Sepsis: pathophysiology and clinical management. BMJ 2016; 353: i1585.
23. Delano MJ, Ward PA: The immune system`s role in sepsis progression, resolution, and long term outcome. Immunological Reviews 2016; 274: 330–53.
24. Angus DC, van der Poll T: Severe sepsis and septic shock. N Engl J Med 2013; 369: 840–51.
25. Vincent JL, De Backer D: Circulatory Shock. N Engl J Med 2013; 369: 1726–34.
26. Antonucci A, Fiaccadori E, Donadello K, et al.: Myocardial depression in sepsis: From pathogenesis to clinical manifestations and treatment. J Crit Care 2014; 29: 500–11.
27. Werdan K, Oelke A, Hettwer S, et al.: Septic cardiomyopathy: hemodynamic quantification, occurence, and prognostic implications. Clin Res Cardiol 2013; 100: 661–68.
28. Cecconi M, De Backer D, Antonelli M, et al.: Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med 2014; 40: 1795–1815.
29. Rhodes A, Evans LE, Alhazzani W, et al.: Surviving Sepsis Campain: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 2017; 43: 302–77.

Pathophysiology of obstructive shock

The pathophysiology of obstructive shock can be classified according to the location of the obstruction in the vascular system in relation to the heart.

Treatment of obstructive shock

Obstructive shock needs immediate causal treatment. Simple measures may suffice, such as changing the position of a patient with caval compression syndrome or adjusting the ventilation of the patient when the level of PEEP is too high.

30. Triggiani M, Montagni M, Parente R, Ridolo E: Anaphylaxis and cardiovascular diseases: a dangerous liaison. Curr Opin Allergy Clin Immunol 2014;14: 309–15.
31. Ring J, Beyer K, Biedermann T, et al.: Guideline for acute therapy und management of anaphylaxis. S2 guideline. Allergo J Int 2014; 23: 96–112.
32. Pastrana EA, Saavedra FM, Murray G, et al.: Acute adrenal insufficiency in cervical spinal cord injury. World Neurosurg 2012; 77: 561–3.
33. Matsumoto T, Okuda S, Haku T, et al.: Neurogenic shock immediately following posterior lumbar interbody fusion. Global Spine J 2015; 5: e13–e6.
34. Summers RL, Baker SD, Sterling SA, et al.: Characterization of the spectrum of hemodynamic profiles in trauma patients with neurogenic shock. J Critical Care 2013; 28: 531.e1–531.e5.
35. Wood GC, Boucher AB, Johnson JL, et al.: Effectiveness of pseudoephedrine as adjunctive therapy for neurogenic shock after acute spinal cord injury: a case series. Pharmacotherapy 2014; 34: 89–93.
36. Furer A, Wessler J, Burkhoff D: Hemodynamics of cardiogenic shock. Interv Cardiol Clin 2017; 6: 359–71.
37. Werdan K, Russ M, Buerke M et al.: Deutsch-österreichische S3-Leitlinie Infarktbedingter kardiogener Schock – Diagnose, Monitoring und Therapie. Kardiologe 2011; 5: 166–224.
38. Nuding S, Werdan K, Prondzinsky R: Optimal course of treatment in acute cardiogenic shock complicating myocardial infarction. Expert Rev Cardiovasc Ther 2018; 16: 99–112.
39. Pich H, Heller AR: Obstruktiver Schock. Anaesthesist 2015; 64: 403–19.
40. Soar J, Nolan JP, Bottiger BW, et al.: European Resuscitation Council Guidelines for Resuscitation 2015: Section 3. Adult advanced life support. Resuscitation 2015; 95: 100–47.

Corresponding author:
Prof. Dr. med. Thomas Standl, MHBA
Klinik für Anästhesie, Operative Intensiv- und Palliativmedizin
Städtisches Klinikum Solingen gGmbH
Gotenstr. 1,
42653 Solingen, Germany
standl@klinikumsolingen.de

► **Supplementary material**
eTables, eFigure:
www.aerzteblatt-international.de/18m0757

Further information on CME

- Participation in the CME certification program is possible only over the Internet: **cme.aerzteblatt.de**. This unit can be accessed until 3 February 2019. Submissions by letter, e-mail or fax cannot be considered.
- The following CME units can still be accessed for credit:
  – "The neurophysiology and treatment of motion sickness" (issue 41/2018) until 6 January 2019
  – "The diagnosis and treatment of anxiety disorders" (issue 37/2018) until 9 December 2018
  – "Arterial Hypertension" (issue 33–34) until 11 November 2018
- This article has been certified by the North Rhine Academy for Continuing Medical Education. Participants in the CME program can manage their CME points with their "uniform CME number" (einheitliche Fortbildungsnummer, EFN). The EFN must be stated during registration on **www.aerzteblatt.de** ("Mein DÄ") or else entered in "Meine Daten," and the participant must agree to communication of the results. The 15-digit EFN is found on the CME card (8027XXXXXXXXXX).

CME credit for this unit can be obtained via cme.aerzteblatt.de until 3 February 2019
Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1
What is the cause of hypovolemic shock?
a) Increased vasoregulation with volume shift
b) Inadequate organ perfusion caused by loss of intravascular volume, usually acute
c) Cardiac output and myocardial pump failure
d) Right heart–related circulatory failure due to obstruction
e) Decompensated valve stenosis

Question 2
What is a typical feature of hemorrhagic shock?
a) Acute hemorrhage
b) Pallor of the lower extremities
c) Raised body temperature
d) Microvascular dysfunction
e) Bradycardia

Question 3
Which of the following is often accompanied by traumatic hemorrhagic shock?
a) Persistent diarrhea
b) Acute cholera
c) Diabetic coma
d) Polytrauma sustained in a road traffic accident
e) Cirrhosis of the liver

Question 4
Which of the following is a typical cause of traumatic hypovolemic shock?
a) Gastrointestinal bleeding
b) Ruptured aneurysm
c) Hypothermia due to cold exposure
d) Myocardial infarction
e) Large surface burns

Question 5
Roughly how many people (including subgroups) develop hypovolemic shock every year in Germany?
a) 5000
b) 15 000
c) 25 000
d) 35 000
e) 50 000

Question 6
In patients with large surface burns, which of the following can provide an indication of the fluid replacement needed in the first 24 hours?
a) Fick's law of diffusion
b) Beer–Lambert law
c) Modified Brooke formula
d) HOMA Index
e) PROCAM Score

Question 7
What is the definition of sepsis according to the current Sepsis-3 criteria?
a) Dysregulated response by the body to an infection resulting in life-threatening organ dysfunctions
b) Inadequate organ perfusion caused by loss of intravascular volume
c) Primarily a disorder of cardiac function in the form of a critical reduction of the heart's pumping capacity
d) Obstruction of the great vessels or the heart
e) State of imbalance between sympathetic and parasympathetic regulation

Question 8
Which of the following is a main symptom of toxic shock syndrome?
a) Hypertension
b) Tremor
c) Cardiac arrhythmias
d) Nonreactive pupils
e) Skin rash

Question 9
Which of the following patient groups has a disproportionately high incidence of septic shock?
a) Patients over the age of 65 who are immunosuppressed or have underlying malignant disease
b) Children up to the age of 10 with neuroblastoma
c) Adolescents up to the age of 20 who are dialysis-dependent
d) Pregnant women with HELPP syndrome
e) Men up to the age of 60 undergoing radiation therapy for prostate cancer

Question 10
What is the most common trigger of anaphylactic shock in adults?
a) Food products
b) Medical drugs
c) Insect venom
d) Physical effort
e) Acute infection

► **Participation is possible only via the Internet: cme.aerzteblatt.de**

Supplementary material to:

The Nomenclature, Definition and Distinction of Types of Shock

by Thomas Standl, Thorsten Annecke, Ingolf Cascorbi, Axel R. Heller, Anton Sabashnikov, and Wolfram Teske

Dtsch Arztebl Int 2018; 115: 757–68. DOI: 10.3238/arztebl.2018.0757

eTABLE 1

Definition of recommendation grades

Recommendation grade	Description	In words	Symbol
A	Strong recommendation	Should/should not	↑↑
B	Recommendation	Should/should not (weaker)	↑
0	No recommendation	May be considered/ rejected	↔

Source: www.awmf.org/leitlinien/awmf-regelwerk/ll-entwicklung/awmf-regelwerk-03-leitlinienentwicklung/ll-entwicklung-graduierung-der-empfehlungen.html

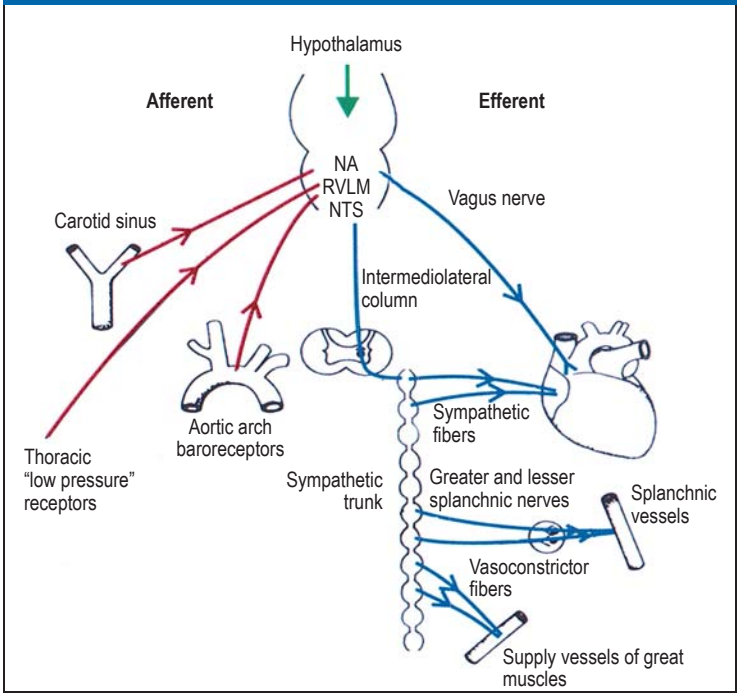
eTABLE 2

SOFA (Sequential Organ Failure Assessment) score as a basis for defining sepsis according to the ESCIM (European Society for Intensive Care Medicine) consensus

			Points			
Organ	Parameter		1	2	3	4
Lung	PaO_2/FiO_2	mmHg	<400	<300	<200 with respir. support	<100 with respir. support
Kidney	Creatinine or urinary output	mg/dL mL/day	1.2–1.9 –	2.0–3.4 –	3.5–4.9 <500	≥ 5.0 <200
Liver	Bilirubin	mg/dL	1.2–1.9	2.0–5.9	6.0–11.9	≥ 12.0
Cardio-vascular system	Blood pressure and catecholamines	mmHg	Mean arterial pressure <70	Catechol. **low***	Catechol. **moderate***	Catechol. **high***
Blood	Platelets	$1000/mm^3$	<150	<100	<50	<20
CNS	Glasgow Coma Scale		14–13	12–10	9–6	<6

*Catecholamine dose low = dopamine ≤ 5 or dobutamine (each dose) for at least 1 hour
moderate = dopamine >5 or epinephrine/norepinephrine ≤ 0.1 µg/kg per min
high = dopamine >15 or epinephrine/norepinephrine >0.1 µg/kg per min

eFIGURE



Pathomechanism of neurogenic shock: Connections in the autonomic system for heart rate and blood pressure regulation. NA, nucleus ambiguus; RVLM, rostral ventrolateral nucleus in the medulla; NTS, nucleus tractus solitarii