Early fluid resuscitation in severe trauma

Tim Harris,[1][2] G O Rhys Thomas,[3][4][2] Karim Brohi[1][2]

[1]Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK

[2]Barts Health NHS Trust, London

[3]16 Air Assault Medical Regiment

[4]Royal London and Queen Victoria, East Grinstead, UK

Correspondence to: T Harris, Department of Emergency Medicine, Royal London Hospital, Whitechapel, London E11BB
tim.harris@bartshealth.nhs.uk

Trauma is a global health problem that affects patients in both rich and poor countries and accounts for 10 000 deaths each day.[1][2] Trauma is the second leading cause of death after HIV/AIDS in the 5-45 year old age group.[w1][w2] Early triage and resuscitation decisions affect outcome in trauma situations.[w3][w4] The two leading causes of mortality in trauma are neurological injury and blood loss.[3][4][w5][w6] There has been considerable improvement in our understanding of trauma resuscitation in the past 20 years, and data from databases and observational trials suggests outcomes are improving.[w7] For patients with severe traumatic injuries (defined as <15 by the injury severity score, an anatomical scoring system), the high volume fluid resuscitation promoted by early advanced trauma life support manuals,[5] followed by definitive surgical care, has given way to a damage control resuscitation (DCR) strategy (box).

This DCR approach has seen a fall in the volume of crystalloid delivered in the emergency department and an associated fall in mortality.[6][w8] In this review, we summarise the evidence guiding the initial period of resuscitation from arrival in the emergency department to transfer to intensive care or operating theatre, focusing on trauma in critically injured adults. This article emphasises newer developments in trauma care. There is debate on whether patients with brain injury should be resuscitated to higher blood pressures, which is briefly discussed later in the text.

How can patients who need DCR be identified?

A DCR strategy applies to patients who present with suspected major haemorrhage. While many definitions exist, the most practical in the acute trauma setting is for estimated blood transfusion volumes of over four units in the initial 2-4 h. Identifying these patients can be a challenge because they are often young with good physiological reserve and may have no physiological evidence of hypovolaemic shock.[7] A number of tools have been developed to identify this group

SOURCES AND SELECTION CRITERIA

We searched Medline, Embase, the Cochrane database, and Google for randomised controlled trials, meta-analyses, and peer reviewed articles, limiting the search to adults. The search was performed once by the lead author (TH) and once by a professional librarian. All articles were shared and supplemented by the author's own libraries. The main search terms used were "trauma," "resuscitation," "fluid," and "goal directed therapy." Ongoing studies were identified from www.clinicaltrials.gov.

KEY COMPONENTS OF DCR

Permissive hypovolaemia (hypotension) (see summary points)

Haemostatic transfusion (resuscitation)—that is, fresh frozen plasma, platelets, or packed red blood cells, and tranexamic acid. Avoidance of crystalloids (normal saline, Hartmann's, Ringer's lactate solutions), colloids (a substance microscopically dispersed evenly throughout another substance; with resuscitation fluids, this term refers to larger molecules dispersed most usually in normal saline, such as gelofusion, haemaccel, or volulyte), and vasopressors

Damage control surgery or angiography to treat the cause of bleeding

Restore organ perfusion and oxygen delivery with definitive resuscitation

of patients; however, physician decision and experience have been found to be just as accurate.[w9][w10][w11][w12][w13] Failure to identify these patients early and to apply DCR is associated with excess mortality.[8]

How can trauma patients in shock be identified?

Shock may be defined as a life threatening condition characterised by inadequate delivery of oxygen to vital organs in relation to their metabolic requirements.[9] A systolic blood pressure of 90 mm Hg is commonly used to define both hypotension and shock; however, oxygen delivery depends on cardiac output rather than blood pressure. Homeostasis with peripheral vasoconstriction acts to preserve blood pressure even as circulating volume is lost. In patients who have had trauma, adequate cardiac output cannot be inferred from blood pressure. Only when blood loss approaches half the circulating volume or occurs rapidly is there a relation between the cardiac output and blood pressure.[10] Patients presenting with hypotension, tachycardia, and obvious blood loss are readily identified as being in a state of haemorrhagic shock. However, many patients will maintain their pulse and blood pressure even after massive blood loss and tissue hypoxia. This condition is termed cryptic shock and is associated with increased mortality.[w14]

The role of basic physiological parameters to estimate the severity of blood loss has been popularised in the advanced trauma life support courses and manuals.[5] These materials describe physiological deterioration with increasing

---

SUMMARY POINTS

Critically injured trauma patients may have normal cardiovascular and respiratory parameters (pulse, blood pressure, respiratory rate), and no single physiological or metabolic factor accurately identifies all patients in this group

Initial resuscitation for severely injured patients is based on a strategy of permissive hypovolaemia (hypotension) (that is, fluid resuscitation delivered to increase blood pressure without reaching normotension, aiming for cerebration in the awake patient, or 70-80 mm Hg in penetrating trauma and 90 mm Hg in blunt trauma) and blood product based resuscitation

This period of hypovolaemia (hypotension) should be kept to a minimum, with rapid transfer to the operating theatre for definitive care

Crystalloid or colloid based resuscitation in severely injured patients is associated with worse outcome

Once haemostasis has been achieved, resuscitation targeted to measures of cardiac output or oxygen delivery or use improves outcome

Tranexamic acid administered intravenously within 3 h of injury improves mortality in patients who are thought to be bleeding

volumes of blood loss, and categorise four stages of shock. But data from a 1989-2007 analysis of the United Kingdom Trauma Audit Research Network database suggest that this model is not reflected in practice. Patients with progressive levels of blood loss to stage 4 haemorrhagic shock (equating to >2 L blood loss) were found to increase their pulse rates from 82 to 95 beats per minute, not to change respiratory rates or Glasgow coma scale, and maintain systolic blood pressures above 120 mm Hg.[11] Although an important part of the initial assessment, physiological derangement alone is neither sensitive nor specific as a tool to identify shock in trauma patients.[7]

There is observational evidence from large datasets in the UK and United States that mortality increases in trauma patients in both blunt and penetrating trauma, while systolic blood pressure falls below 110 mm Hg.[12 w15 w16 w17 w18 w19] A US review of 870 634 sets of trauma records identified that for every 10 mm Hg below 110 mm Hg, mortality increased by 4.8%.[12] Shock index does not improve after risk stratification of trauma patients.[w20]

Metabolic assessment with lactate[w21 w22] and base excess[w23 w24] also predicts blood loss and mortality. Furthermore, these parameters may be increased from exercise around the time of injury (running, fighting) or may be (falsely) low if the hypoxic tissues are not being perfused sufficiently to wash anaerobic products into the circulation (for example, when a tourniquet is applied). For patients in whom central access is obtained, mixed venous oxygen saturation is also a good indicator of blood loss, with levels below 70% suggesting inadequate oxygen delivery.[w25]

Estimated injuries and associated blood loss are an important part of the initial trauma assessment. Clinical examination is augmented by focused ultrasound assessment of the chest, pericardium, and peritoneal cavity (extended focused assessment with sonography in trauma (eFAST), a specific but insensitive test for blood loss); and computed tomography (a sensitive and specific test for blood loss).

What is permissive hypotension (hypovolaemic) resuscitation?

Permissive (hypotension) hypovolaemic resuscitation is used to describe a process that minimises administration of fluid resuscitation until haemorrhage control has been achieved, or is deemed unnecessary on definitive imaging. Resuscitation is the restoration of oxygen delivery and organ perfusion to match requirements. In the 1960s and 1970s, a strategy of high volume crystalloid resuscitation in a ratio of 3 mL per 1 mL of blood loss was promoted, which was

thought to replace intravascular and interstitial losses and reduce the risk of organ failure.[13] However, vigorous fluid resuscitation increases blood pressure, the effect of which increases hydrostatic forces on newly formed clot, dilutes clotting factors and haemoglobin, and reduces body temperature. These effects could promote further bleeding. In permissive hypotension, definitive resuscitation is deferred until haemostasis is obtained. It is now recognised that aggressive crystalloid resuscitation also impairs organ perfusion.[14 w26]

What evidence do we have for hypovolaemic resuscitation?

Considerable animal work has informed our understanding of hypovolaemic resuscitation. In summary, this research found that withholding fluid resuscitation from animals with critical blood loss (about half their circulating volume) was associated with death, whereas animals with less severe blood loss had a lower mortality with no fluid resuscitation.[15]

The table summarises three randomised controlled trials exploring the risks and benefits of hypovolaemic resuscitation.[16 17 w27] These trials provide evidence of a mortality advantage in favour of this resuscitation strategy for truncal penetrating trauma and evidence of no harm in blunt trauma.

The National Institute for Health and Clinical Excellence has recommended that in older children and adults with blunt trauma, no fluid be administered in the prehospital resuscitation phase if a radial pulse can be felt, or for penetrating trauma if a central pulse is palpable.[18] In the absence of this, 250 mL crystalloid fluid boluses are administered and the patient is reassessed until these pulses, as described, return.

Much of the evidence for hypovolaemic resuscitation was developed before the advent of haemostatic resuscitation, as described below. This period of hypovolaemic resuscitation is maintained for as short a period as possible, until the injury complex is defined and any sites of blood loss treated surgically or embolised.

Untreated hypovolaemic shock leads to microvascular hypoperfusion and hypoxia, leading to multiorgan failure.[19] Hypovolaemic resuscitation sacrifices perfusion for coagulation and haemorrhage control. The trauma team carefully balances the resuscitation process to maintain organ perfusion but at lower than normal blood pressure to regulate bleeding. Based on the evidence available, we suggest that fluid resuscitation before haemorrhage control should aim to maintain a systolic blood pressure of 80 mm Hg or a

Randomised trials of permissive hypotension in trauma

Trial	Intervention	Patient group	Setting	Findings	Comments
Pseudo-randomised controlled trial[16]	No fluid resuscitation before surgical intervention in operating theatre *v* crystalloid based resuscitation	Penetrating truncal trauma and systolic blood pressure >90 mm Hg (n=598)	Prehospital and in emergency department	Lower mortality in group with no fluid resuscitation than in group with crystalloid based resuscitation (survival 70% *v* 62%, P=0.04)	Short transport distances, mortality benefit predominantly vascular injuries, young cohort (mean age 31 years), 8% in no fluid group received fluids
Randomised controlled trial[17]	Resuscitation to target systolic blood pressure 100 mm Hg *v* 70 mm Hg	Blunt or penetrating trauma and systolic blood pressure <90 mm Hg in first hour (n=110)	Urban trauma centre resuscitation room	No mortality difference, low mortality of four (7.3%) patients in each group	Low mortality, study underpowered to show mortality difference, observed systolic blood pressures were 114 mm Hg and 100 mm Hg despite targets
Randomised controlled trial: interim analysis[w27]	Intraoperative resuscitation to mean arterial pressure 50 mm Hg *v* 65 mm Hg	Traumatic injuries excluding traumatic brain injury with at least one episode of systolic blood pressure <90 mm Hg (n=90)	Operating theatre	No mortality difference	Observed blood pressures did not differ significantly despite targets; results may not translate to preoperative environment

palpable radial pulse or cerebration by using small volume boluses of 250 mL. This value is arbitrary with little evidence to support it. The 250 mL boluses are able to increase blood pressure, since the circulation is highly constricted with a small volume of distribution. In practice, achieving target blood pressures is challenging. Patients with severe injuries will probably need blood product based resuscitation, as described below.

Fluid resuscitation in traumatic brain injury

This review does not deal in detail with the complexities of resuscitation in brain injury; however, retrospective observational data for patients with traumatic brain injury suggest that any single reduction in mean arterial blood pressure below 90 mm Hg is associated with a doubling in mortality.[w28 w29] Guidelines published by the Brain Trauma Foundation advocate maintaining a systolic blood pressure above 90 mm Hg but do not specifically state whether this is during active haemorrhage.[w30] Currently, there is controversy about whether the guidelines for permissive hypotension should be changed in the presence of head injury because there is no human evidence from prospective studies.

What is the role of blood products in trauma resuscitation?

Severe bleeding in trauma patients can result in disordered blood clotting. Until recently, this effect was thought to be a late phenomenon arising primarily from loss of coagulation factors during haemorrhage and dilution from resuscitation fluids. However, it is now recognised that trauma induced coagulopathy occurs within minutes of injury, and is associated with a fourfold increase in mortality.[20] The process is multifactorial[21] but is partly due to an endogenous coagulopathy that occurs as a result of tissue damage in severe shock.[w31] This understanding has led to changes in the management of trauma haemorrhage.

Haemostatic resuscitation

Haemostatic resuscitation is a combination of strategies targeting trauma induced coagulopathy to reduce bleeding and improve outcomes.[w32 w33]

How do blood products aid in resuscitation?

The main strategy to treat trauma induced coagulopathy is to provide volume replacement that augments coagulation. This replacement has been achieved by the transfusion of fresh frozen plasma, platelets, and packed red blood cells. A retrospective observational study performed on military personnel with similar injuries but differing resuscitation fluid strategies suggested that the use of higher ratios of fresh frozen plasma to packed red blood cells may improve outcomes.[22] Similar results have been seen in other retrospective studies and a few small prospective cohort studies,[23] although the retrospective studies are subject to survival bias.

It is also unclear whether the benefit from these strategies comes from the coagulation factors present in fresh frozen plasma or from reducing the amount of crystalloid and colloid administered. Nevertheless, it seems clear that the usual 1-2 units of plasma previously administered after massive transfusions was insufficient to prevent dilutional coagulopathy. Current consensus is that plasma should be given from the beginning of the resuscitation, alongside transfusions of packed red blood cells, in a ratio of 1 "unit" of plasma for each 1-2 units of packed red blood cells.[24] Very little is known about platelet function in trauma induced coagulopathy or the effectiveness of platelet transfusions.[w34 w35] Although these early strategies of blood product in high doses seem effective, they are based on limited evidence. These regimens also place substantial resource demands on blood banks and are logistically difficult to implement owing to the requirements for rapid thawing and delivery.

Research is also being undertaken to look at alternatives to blood component therapy for the management of trauma induced coagulopathy. Fibrinogen is the central substrate of blood clotting, and levels are low in this patient group.[w36] Some retrospective evidence suggests that patients who receive more fibrinogen replacement (in the form of cryoprecipitate and plasma) have better outcomes in terms of total use of packed red blood cells and mortality.[w37] Fibrinogen is also available as a powdered concentrate and could be a replacement therapy that can be easily administered in trauma induced coagulopathy.[w38 w39]

How do I identify patients with trauma induced coagulopathy?

Standard clotting tests from laboratories such as the prothrombin time do not show any of the key derangements in trauma induced coagulopathy, such as reduced clot strength and fibrinolysis.[25] Furthermore, in a trauma setting, it is impractical to wait for tests that can take up 1 h to process. The point of care versions of these tests (such as the prothrombin time) are prone to be under-read in the presence of low haematocrits. These difficulties have led to a renewed interest in the use of thromboelastography—a point of care assessment of clot generation, strength, and breakdown. This procedure has the potential to provide a rapid assessment of the whole clotting process, but it has not yet been validated in the acute setting.[25] In the absence of a validated diagnostic test at the point of care, management is therefore blind to the status of the coagulation system and relies on clinical judgment and empiric therapy.

What fluids should be used to resuscitate trauma patients who do not need DCR?

Patients who do not need DCR need no immediate resuscitation until definitive imaging has identified the underlying injuries. These patients should be observed carefully for signs of physiological and metabolic deterioration, consequent on disease progression with blood loss, visceral injury, and pericardial or pleural tamponade. Debate continues on the relative merits of colloid or crystalloid based resuscitation strategies, with a recent Cochrane review concluding that there was no evidence that survival was better with one or the other solution.[26]

However, a subgroup analysis of 460 patients with traumatic brain injury (Glasgow coma scale ≤13) from a large randomised controlled trial comparing the safety of albumin in normal saline with normal saline identified a survival advantage in the crystalloid group (33.2% *v* 20.4%, P=0.003).[27]

Hypertonic solutions have been proposed to improve cerebral perfusion and reduce cerebral oedema, and have been advocated for resuscitation of patients with traumatic brain injury.[w40] A meta-analysis of eight randomised trials identified a survival advantage in this group,[w41] but a randomised controlled trial of 229 patients with hypotension and severe traumatic brain injury (Glasgow coma scale <9) who received prehospital resuscitation with hypertonic or normal saline had almost identical survival and neurological function six months after injury.[28] Furthermore, a recent randomised controlled trial of prehospital use of hypertonic solutions was terminated by the data and safety monitoring board after randomisation of 1331 patients, having met prespecified futility criteria. Among patients with severe traumatic brain injury not in hypovolaemic shock, initial resuscitation with either hypertonic saline or hypertonic saline or dextran, compared with normal saline, did not result in improved neurological outcome or survival at six months.[29] Thus, we suggest the use of crystalloid based fluid administration in this cohort of patients who are less severely injured.

Once haemostasis is achieved, what should be done to ensure adequate resuscitation in severe trauma?

Once haemostasis has been achieved with surgical intervention, fracture splintage or angiography, or the requirement for these interventions identified as not necessary, then definitive resuscitation is required. If patients are resuscitated to normal blood pressure and pulse without further parameters being used to evaluate for tissue hypoxia, over half of patients would be inadequately resuscitated, with increased morbidity and mortality.[30 w42] Resuscitation to targets of oxygen delivery or use is termed goal directed therapy, and good quality evidence from randomised trials indicates that this approach should be used in trauma; indeed, the original evidence for this approach came from trauma studies.[w43 w44 w45 w46 w47 31 32]

What other agents should be used in the initial resuscitation period?

Hyperfibrinolysis is common after trauma, owing to associated hypovolaemic shock and tissue injury.[w48] In a recent, large, multinational randomised controlled trial researchers targeted a specific component of trauma induced coagulopathy—hyperfibrinolysis. They showed a reduction in mortality with the use of tranexamic acid, which has antifibrinolytic properties (1 g delivered over 15 min, then 1 g over 4 h, commenced within 3 h of injury).[33]

1 Roberts I, Shakur H, Edwards P, Yates D, Sandercock P. Trauma care research and the war on uncertainty. *BMJ* 2005;331:1094-6.
2 Kauvar DS, Lefering R, Wade CE. Impact of haemorrhage on trauma outcome: an overview of epidemiology, clinical presentations and therapeutic considerations. *J Trauma* 2006;60:S3-11.
3 Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM, et al. The role of secondary brain injury in determining outcome from severe head injury. *J Trauma* 1993;34:216-22.
4 Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. I. Blood pressure and oxygenation. *J Neurotrauma* 2007;24(suppl 1):S7-13.

TIPS FOR NON-SPECIALISTS

Doctors and nurses who care for trauma patients who are severely injured need to be familiar with the principles of resuscitation strategies for damage control, as outlined in this review

A clearly written protocol for massive transfusion facilitates rapid access to and delivery of blood product based resuscitation

Transfer patients with severe traumatic injuries to a dedicated trauma unit

Trauma teams bring together doctors and nurses from a range of disciplines, and scenario based practice is likely to facilitate smooth teamwork

---

QUESTIONS FOR FUTURE RESEARCH

How do we balance the risks of impaired organ perfusion consequent on hypovolaemic resuscitation with clot preservation?

How do we identify and target trauma induced coagulopathy in the acute phase?

What is the most effective combination of blood products for initial trauma resuscitation?

Should patients with traumatic brain injury be subject to different initial resuscitation strategies?

Does therapeutic hypothermia have a role in trauma resuscitation or traumatic brain injury in the acute phase?

5   American College of Surgeons Committee on Trauma. Advanced trauma life support for doctors. American College of Surgeons Committee on Trauma, 1997.

6   Ley EJ, Clond MA, Srour MK, Barnajian M, Mirocha J, Margulies DR, et al. Emergency department crystalloid resuscitation of 1.5 L or more is associated with increased mortality in elderly and nonelderly trauma patients. *J Trauma* 2011;70:398-400.

7   Stanworth SJ, Morris TP, Gaarder C, Goslings JC, Maegele M, Cohen MJ, et al. Reappraising the concept of massive transfusion in trauma. *Crit Care Med* 2010;14:R239.

8   Larson CR, White CE, Spinella PC, Jones JA, Holcomb JB, Blackbourne LH, et al. Association of shock, coagulopathy, and initial vital signs with massive transfusion in combat casualties. *J Trauma* 2010;69:S26-32.

9   Strehlow MC. Early identification of shock in critically ill patients. *Emerg Med Clin N Am* 2010;28:57-66.

10   Wo CJ, Shoemaker WC, Appel PL, Bishop MH, Kram HB, Hardin E. Unreliability of blood pressure and heart rate to evaluate cardiac output in emergency resuscitation and critical illness. *Crit Care Med* 1993;21:218-23.

11   Guly HR, Bouamra O, Spiers M, Dark P, Coats T, Lecky F. Vital signs and estimated blood loss in patients with major trauma: testing the validity of the ATLS classification of hypovolaemic shock. *Resuscitation* 2011;82:556-9.

12   Eastridge BJ, Salinas J, McManus JG, Blackburn L, Bugler EM, Cooke WH, et al. Hypotension begins at 110 mm Hg: redefining 'hypotension' with data. *J Trauma* 2007;63:291-9.

13   Shires GT, Canizaro PC. Fluid resuscitation in the severely injured. *Clin Surg N Am* 1973;53:1341-66.

14   Cotton BA, Guy JS, Morris JA Jr, Abumrad NN. The cellular, metabolic, and systemic consequences of aggressive fluid resuscitation strategies. *Shock* 2006;26:115-21.

15   Mapstone J, Roberts I, Evans P. Fluid resuscitation strategies: a systematic review of animal trials. *J Trauma* 2003;55:571-89.

16   Bicknell WH, Wall MJ, Pepe PE, Martin RR, Ginger VF, Allen MK, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. *N Engl J Med* 1994;331:1105-9.

17   Dutton RP, Mackenzie CF, Scalae TM. Hypotensive resuscitation during active haemorrhage: impact on hospital mortality. *J Trauma* 2002;52:1141-6.

18   National Institute for Health and Clinical Excellence. Pre-hospital initiation of fluid replacement therapy in trauma. Technology appraisal 74. January 2004. www.nice.org.uk/nicemedia/live/11526/32820/32820.pdf.

19   Santry HP, Alam HB. Fluid resuscitation: past, present and the future. *Shock* 2010;33:229-41.

20   Floccard B, Rugeri L, Faure A, Saint Denis M, Boyle EM, Peguet O, et al. Early coagulopathy in trauma patients: an on-scene and hospital admission study. *Injury* 2012;43:26-32.

21   Hess JR, Brohi K, Dutton RP, Hauser CJ, Holcomb JB, Kluger Y, et al. The coagulopathy of trauma: a review of mechanisms. *J Trauma* 2008;65: 748-54.

22   Borgman MA, Spinella PC, Perkins JG, Grathwohl KW, Repine T, Beekley AC, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007;63:805-13.

23   Rajasekhar A, Gowing R, Zarychanski R, Arnold DM, Lim W, Crowther MA, et al. Survival of trauma patients after massive red blood cell transfusion using a high or low red blood cell to plasma transfusion ratio. *Crit Care Med* 2011;39:1507-13.

24   Davenport R, Curry N, Manson J, De'Ath H, Coates A, Rourke C, et al. Hemostatic effects of fresh frozen plasma may be maximal at red cell ratios of 1:2. *J Trauma* 2011;70:90-5.

25   Davenport R, Manson J, De'Ath H, Platton S, Coates A, Allard S, et al. Functional definition and characterization of acute traumatic coagulopathy. *Crit Care Med* 2011;39:2652-8.

26   Perel P, Roberts I. Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* 2011;3:CD000567.

27   SAFE Study Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group; Australian Red Cross Blood Service; George Institute for International Health, Myburgh J, Cooper DJ, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med* 2007;357:874-84.

28   Cooper JD, Myles PS, McDermott FT, Murray LJ, Laidlaw J, Cooper G, et al. Pre-hospital hypertonic saline resuscitation of patients with hypotension and severe traumatic brain injury: a randomized controlled trial. *JAMA* 2004;291:1350-7.

29   Bulger EM, May S. Out-of-hospital hypertonic resuscitation following severe traumatic brain injury: a randomized controlled trial. *JAMA* 2010;304: 1455-64.

30   Claridge JA, Crabtree TD, Pelletier SJ, Butler K, Sawyer RG, Young JS. Persistent occult hypoperfusion is associated with a significant infection rate and mortality in major trauma patients. *J Trauma* 2000;48:8-13.

31   McKinley BA, Valdivia A, Moore FA. Goal-orientated shock resuscitation for major torso trauma: what are we learning? *Curr Opin Critical Care* 2003;9:292-9.

32   Chytra I, Pradl R, Bosman R, Pelnár P, Kasal E, Zidková A. Esophageal Doppler-guided fluid management decreases blood lactate levels in multiple-trauma patients: a randomized controlled trial. *Critical Care* 2007;11:R24.

33   CRASH-2 Collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, 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.

ANSWERS TO ENDGAMES, p 48   For long answers go to the Education channel on bmj.com

Echocardiogram showing evidence of a pericardial effusion (white arrow)

PICTURE QUIZ

Signs of shock and raised jugular venous pressure

1   The chest radiograph shows a globular cardiac silhouette, possibly as a result of fluid surrounding the heart. The echocardiogram shows a large pericardial effusion (figure).

2   Cardiac tamponade. Electrocardiography classically shows diffuse decreased QRS voltages and may display electrical alternans.

3   In view of the slow onset, associated weight loss, and other systemic symptoms, cancer is the most likely diagnosis. In developing countries tuberculosis should also be considered.

4   Beck's triad and Kussmaul's sign were seen in this patient. Pulsus paradoxus could be looked for.

5   Urgent pericardiocentesis under fluoroscopy or echocardiographic guidance should be undertaken. Fluid should be sent for cytology, protein count, and microbiology. The underlying cause of the tamponade will need appropriate management.

CASE REPORT Ear pain and facial palsy

1   Necrotising (malignant) otitis externa.

2   The House-Brackmann grading system.

3   Admission for intravenous antibiotics, aural microsuction, eye care, pain management, and occasionally surgical debridement.

STATISTICAL QUESTION

Hazards and hazard ratios

Statements *a* and *d* are true, whereas *b* and *c* are false.