

# Fluid Resuscitation In Pre-Hospital Trauma Care: A Consensus View

## Introduction

Evidence based medicine describes clinical practice in which patient care and therapeutic decisions are supported by information gained from a careful consideration of the available worldwide research literature. Ideally, unequivocal clinical conclusions should be drawn based on the results of carefully conducted studies. Unfortunately, even at the beginning of the twenty-first century, in many areas this evidence is patchy or contradictory. Furthermore, a number of the most fundamental questions confronting present day clinicians may never be answered by suitably conducted studies. Initial evidence might suggest, for example, that a particular treatment offers a small survival advantage compared with another, but the number of recruits required to ensure a meaningful trial may render it impractical in terms of logistics and cost. In addition, an increasingly severe ethical framework makes it likely that many definitive clinical studies would not gain ethical approval.

In the meantime, practitioners in all disciplines have to try to base their clinical decisions on whatever sound evidence is available. Most clinicians also find it helpful to trade experiences and ideas. Although such exchanges are strictly speaking anecdotal, they often fill the gaps in our present scientific knowledge, allowing decisions to be made regarding patient care on the basis of shared experience, where firm evidence is inconclusive or absent.

It is with the aim of reconciling clinical experience and current evidence in the Pre-Hospital Trauma setting that the following article has been prepared. Evidence from the scientific literature is cited where possible. The remainder is a consensus reached by experienced trauma personnel from a variety of backgrounds (*Pre-hospital Fluid Resuscitation in Trauma: a consensus meeting. Faculty of Pre-hospital Care, University Hospital Birmingham, 22nd August 2000*). The concept of value being added to raw data through the input of acknowledged authorities is a well-established process in evidence based medicine(1).

It is intended that the issues covered here should continue to be debated and, where guidelines are suggested, it is expected that these will evolve or change as experience and evidence grow together.

## Cannulation

### Issues

Early venous access in trauma patients has traditionally been regarded as of great importance (2, 3). It allows administration

of fluids, where necessary, or other drugs such as anaesthetic, analgesic and resuscitation agents (4). Placement of a venous line is likely to be technically easier in the early stages of shock than when hypovolaemia has progressed and compensatory mechanisms have resulted in peripheral vasoconstriction. As a consequence, paramedics have been encouraged to use such skills in trauma.

While early successful cannulation will save time when the patient arrives in hospital (5), it is also clear that repeated unsuccessful attempts or access with a cannula of insufficient gauge will hinder progress at the same stage.

Recently, interventions made by paramedics before the patient arrives in hospital have come under close scrutiny. In a retrospective study, Demetriades found that outcome was worse in a group of 4856 patients brought to hospital by paramedics than in 926 patients brought in by bystanders, relatives and the police(6). Assuming the results are truly representative, it has been suggested that poor outcomes relate to detrimental effects of pre-hospital advanced life support (ALS) measures. There is other evidence suggesting ALS methods improve survival (7), but the aggressive use of fluid, in particular, has been called into question.

Independent of the use of intravenous fluids, however, transfer time to hospital appears to be an important predictor of outcome(8). Improvements may be possible here. Cannulating ambulance crews appear to spend longer on scene and this extra time does appear to be related to the interventions they perform (9,10,11). If the administration of fluid pre-hospital is open to question, then this apparent delay in transfer in order to obtain circulatory access should also come under scrutiny.

One way to balance the benefits to be gained by obtaining venous access pre-hospital with the risk of lengthening transfer times is to attempt cannulation en route(12). This approach has both training and Health and Safety implications, but has received strong support (13, 14).

The management of entrapped patients is a special situation(15). Here again, the focus should be on keeping the time to hospital as short as possible. The coordinated roles of all the emergency services are critical in keeping delays to a minimum(16). It is likely that efforts to cannulate in these situations will not extend the time of transfer. In addition, there are usually compelling reasons for obtaining a venous line on scene; principally the need for analgesia, but also, on occasion, for resuscitation drugs and fluids.

Consensus Working Group on Pre-hospital fluids representing:  
Faculty of Pre-Hospital Care Royal College of Surgeons of Edinburgh  
Faculty of Accident & Emergency Medicine  
The Armed Forces, Ambulance Services Association, Paramedics, BASICS, London HEMS, Pre-Hospital Care Research

*Consensus View*

Cannulation at an early stage is desirable. However, in most situations, priority should be given to transfer of the patient to a centre where definitive care can be provided. *The on scene time should not be prolonged by attempts to gain a line.* Intravenous access during transit has been employed successfully and should be considered where appropriate expertise and training are available. *A limit of two attempts en route is reasonable.*

*In cases of entrapment, circulatory access should be gained on scene.* This reflects the unique demands of this area of pre-hospital medicine.

## Choice of Fluid for Resuscitation

*Issues*

This area continues to be one in which, despite an increasing body of evidence, no consensus regarding choice of fluid has been reached. Broadly, the choice of options includes:

- no fluid
- crystalloids (isotonic and hypertonic)
- colloids (mainly gelatins and starch solutions)
- oxygen carrying solutions (to include blood and blood substitutes).

The decision is a complex one and includes consideration of the factors listed in Table 1.

Table 1 Factors influencing choice of fluids.

- |   |
|---|
| <ul style="list-style-type: none"> <li>• early haemodynamic effects</li> <li>• effects on haemostasis</li> <li>• pH buffering</li> <li>• oxygen carriage</li> <li>• distribution and capillary endothelial leak</li> <li>• modulation of inflammatory response</li> <li>• safety</li> <li>• method of elimination</li> <li>• practicality and cost</li> </ul> |
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*Early Haemodynamic Effects*

The aim of administering fluids is to restore end-organ perfusion and therefore oxygen delivery. An increase in circulating volume will have a tendency to increase cardiac output and blood pressure. The speed with which a given fluid will produce its effect will largely be determined by its volume of distribution within the body and how quickly it equilibrates. A sudden increase in blood flow may not be beneficial because it has the potential to precipitate rebleeding from sites where physiological mechanisms have brought about cessation of haemorrhage.

*Haemostasis*

In general, administration of fluid has a detrimental effect on haemostasis and a tendency to increase bleeding. To begin

with, primary haemostatic thrombus may be dislodged from a vessel causing rebleeding, as outlined above. Most fluids will cause vasodilatation, at least as a result of reversing hypovolaemia, with similar risks. With the obvious exception of fresh frozen plasma, most will also reduce blood viscosity and dilute clotting factors to the detriment of haemostatic mechanisms. Direct interference with the clotting cascades is seen with some agents, particularly lower molecular weight starches. Finally, hypothermia induced coagulopathy should be avoided, if possible, and the fluids should be warmed.

*pH buffering*

Acidosis results from anaerobic metabolism of energy substrate, producing lactic acid, phosphoric acids and unoxidised amino acids. These can have negative inotropic effects and predispose to arrhythmias. Manipulating pH *per se*, with the use of bicarbonate, for example, is not presently advised since it impairs oxygen delivery to the tissues by its effect on the dissociation of oxygen from haemoglobin. Some fluids, particularly protein-based solutions, have pH buffering properties, which may be beneficial.

*Oxygen carriage*

High flow oxygen is administered routinely to trauma patients. The main thrust of fluid administration is directed towards reversing hypovolaemia. In the early stages, the relative anaemia caused by blood loss is compensated for by the decrease in blood viscosity, which allows improved peripheral oxygen delivery. Anaemia associated with haemorrhage is considered to be secondary in importance to hypovolaemia in the accumulation of oxygen debt. To date, no artificial oxygen carrying solutions have reached widespread use.

*Modulation of the inflammatory response and capillary leak*

Molecular size will determine whether a fluid will remain primarily in the intravascular space or be distributed more widely within the extracellular space. Leakage of relatively large molecules, from the vascular to extravascular space, could exaggerate capillary leakage and even draw fluid out of the intravascular space, where it is primarily required. Both lower molecular weight synthetic colloids and exogenous albumin solutions leave the circulation in this way to a greater or lesser degree(17). Conversely, higher molecular weight colloids, which remain in the intravascular space, exert an oncotic pull which can result in cellular dehydration. Accordingly, these should be administered with adequate amounts of water(18). Evidence suggests that high molecular weight starches may have a

secondary direct down-regulatory action on capillary leak via an action on endothelial surface molecules(19).

#### *Safety*

The fluid of choice must be one that can be administered safely in all patient groups. Some starches and haemoglobin solutions have detrimental effects on renal function. Anaphylaxis has been seen with blood products in particular, but also with gelatins. The communication of viral and prion infections is a risk associated with blood and its derivatives. The possible consequences on a cross-match sample in the later stages of treatment have also caused concern in the use of dextran.

#### *Practicality and cost*

The ideal resuscitation fluid should be cheap, with a long shelf life. It should be easy to store and to warm when required. Except in the rarest of circumstances, pre-hospital administration of blood is almost never achievable.

### **Consensus View**

Modern oxygen carrying compounds and blood substitutes are currently still largely experimental. Blood (together with human albumin solution and fresh frozen plasma) is costly and difficult to store, having a relatively short shelf life. In addition, issues regarding compatibility and disease transmission make blood and its derivatives unlikely candidates as a permanent solution in the pre-hospital situation.

Gelatin based colloid solutions appear to offer few definite benefits over crystalloid(20). In addition, there are theoretical concerns over the distribution of the gelatin molecules in the extracellular space. Not only is there a possibility of pulling fluid from the intravascular space, but in addition, the relatively short half-life of these molecules in the tissues calls into question any supposed advantage over crystalloid. Large molecular weight starches have many of the same problems as a result of a broad spectrum of molecular sizes. The range of molecular weights can be reduced, but methods for achieving this remain costly at present. This field offers the potential for interesting developments in the future.

Isotonic crystalloid solutions are cheap, easy to store and to warm and have an established safety record when they are used appropriately. They produce a relatively gentle rise in cardiac output and are generally distributed evenly throughout the extracellular space. They do not draw water out of the intravascular space. These fluids are neutral in terms of oxygen carriage and inflammatory response. The use of Ringers solution as the fluid of choice in burns is noted. It offers some buffering capacity, but carries a theoretical risk of iatrogenically

increasing lactic acidosis in large doses or in patients with liver failure. Saline in large quantities may produce a hyperchloraemic acidosis. Hypertonic solutions, such as hypertonic saline appear to be beneficial in head injured patients.

*At present, isotonic saline is recommended as the first line fluid in the resuscitation of a hypovolaemic trauma patient.*

### **Quantity of Fluid Used in Resuscitation**

#### *Issues*

The dilemma that faces medical personnel confronted with a hypovolaemic trauma patient is essentially the balance between:

- administering fluid; thereby risking rebleeding and increased blood loss
- and
- withholding fluid; thereby allowing the possibility of immediate or rapid death from hypovolaemia, prior to arrival in hospital.

This quandary is not new. Cannon's 1918 paper(21) makes it clear that he considered administration of fluids before the surgical control of bleeding to be dangerous. The same outlook governed thinking on fluid replacement in the Second World War (22).

There is evidence that in penetrating torso trauma, aggressive use of intravenous fluids is detrimental to outcome(23). In a randomised controlled trial, patients received either no fluid pre-hospital or immediate fluid resuscitation. Reduced mortality and complications were seen if fluid resuscitation was delayed until surgery. Although methodological criticisms have been raised(24), this study remains extremely influential because it is a rare prospective, randomised study in this area. There are also animal studies that raise similar doubts about the effectiveness(25) or safety(26) of early fluid replacement.

The majority of trauma seen in the United Kingdom is blunt trauma. Unfortunately, there is little available data from human studies regarding whether blunt trauma differs significantly from penetrating trauma in its behaviour. In a retrospective case-matched review of severe trauma victims, 217 patients who had on-site fluid replacement fared worse, in terms of mortality, than controls receiving no fluid (27). Increased pre-hospital times and fluid administration were identified as risk factors, requiring further investigation.

Enthusiasm for aggressive fluid resuscitation during the second half of the twentieth century probably had its roots in early animal haemorrhage experiments conducted by Wiggers and other workers in the 1950's and 1960's(28). In his classic model, blood was taken out through a catheter until a set pressure was reached, after which withdrawal ceased.

Administration of fluid following this improved outcome. Traverso employed a similar porcine model (29, 30), but this time a fixed volume was removed. The problem with both studies is that haemorrhage had ceased prior to resuscitation and would not recommence due to its controlled nature. In the trauma patient, there are no such guarantees.

More recently, animal experiments have attempted to replicate the possibility of uncontrolled haemorrhage more closely. There are two main groups of experiments; external haemorrhage models (eg rat tail amputation) and internal haemorrhage models, where a controlled injury to a great vessel or major abdominal artery produces hypovolaemia. Overall, the external haemorrhage models suggest that bleeding and mortality will increase if fluid is administered prior to haemostasis (26, 31-33). Some authors, however, found improved survival in resuscitated rats, though Sindlinger noted increased blood loss (34). Soucy identified anaesthetic agents as an important confounding factor and there are many methodological arguments, which make extrapolation to human trauma difficult (35, 36). Internal haemorrhage experiments on rats and pigs appear to provide clearer evidence that aggressive fluid administration reduces survival(37-40).

Many of the ways in which fluid may worsen bleeding have been outlined already. Bickell discusses these mechanisms in some detail(37). He suggests that a major danger in penetrating large vessel injury is that the improvement in haemodynamics brought about by administration of fluid will cause primary extraluminal thrombus to be dislodged. Using a porcine aortotomy model, he confirmed that aggressive replacement of blood loss with three times the volume of crystalloid increased haemorrhage and decreased survival.

Attention has therefore become focused on resuscitation strategies. Stern and Kowalenko bled pigs rapidly through a femoral catheter then produced an aortotomy using steel wire. Animals haemorrhaged down to a pulse pressure of 5 torr. They were then resuscitated to a systolic pressure of 40, 60 or 80 torr. The most bleeding and the highest mortality were seen in the 80 torr group. The 60 torr group were less acidotic than the 40 torr group. Riddez performed a standardised aortotomy in dogs. There were four resuscitation groups; no fluid, 1:1 volume ratio Ringers, 2:1 Ringers and 3:1 Ringers replacement. Aortic blood flow increased with the amount of fluid used. Blood loss also increased. The highest mortality was seen in the no fluid and the 3:1 groups. The authors felt that the deaths in the less aggressive fluid replacement groups were due to shock and those in the more vigorously resuscitated dogs were due to re-

bleeding. Similar findings in rats were noted by Capone and Kim(33, 41). These findings appear to suggest that the best strategy is not to withhold fluid altogether, but that a moderate replacement policy is likely to be most successful.

Permissive hypotension describes the approach in which the blood pressure is allowed to remain below the normal levels seen in health, with the aim of maintaining vital organ perfusion without exacerbating haemorrhage. A review of hypotensive resuscitation is provided by Hyde(42).

If hypotensive resuscitation is the best paradigm, the problem will be translating its use practically into the field. One prescription will not be suitable for all trauma victims. It is also vital that in the pre-hospital phase of patient care, strategies are straightforward, reflecting the difficulties of treating trauma victims on scene and in transit, without detailed diagnostic information. One method to minimise the risk of excessive fluid administration is to give small boluses of fluid at a time. The number of these could even be limited unless authorisation was sought by means of a call to a control centre. 250ml boluses are easy to administer from 500ml or 1 litre bags.

Protocols can be based around easily available physiological measures. The presence or absence of a radial pulse gives an approximate guide to whether the blood pressure is above or below 80-90 mmHg. Brachial pulse corresponds to about 70-80 mmHg and a central (femoral or carotid) to 60-70 mmHg (43). It is known that a degree of hypotension in trauma can be tolerated and that this tolerance is linked to physiological compensation mechanisms, especially to haemostasis. Differing limits on the degree of hypotension that should be permitted can be found(44, 45). However, it is likely that subgroups tolerate hypotension differently. The head-injured patient may require a higher pressure in order to maintain cerebral perfusion and reduce secondary brain injury(46). Patients with penetrating torso trauma probably require lower pressures.

#### *Consensus View*

*Fluid should not be administered to trauma victims when a radial pulse can be felt. Judicious aliquots of 250 mls should be titrated for other patients. If the radial pulse returns, fluid resuscitation can be suspended for the present and the situation monitored. In penetrating torso trauma the presence of a central pulse should be considered adequate. In children less than 1 year old, the use of a brachial pulse is more practical as it is easier to feel.*

#### **Summary**

Fluid administration for trauma in the pre-hospital environment is a challenging and controversial area. There is not yet any

equivocal answer which can be supported by clear evidence. Nevertheless, a careful reading of what evidence is available does allow some provisional conclusions to be drawn. We believe that the following represent the best possible current expert consensus on pre-hospital fluids in trauma. As future evidence brings clarity to this area, these guidelines can be modified, and further consensus statements will be issued taking into account such information.

When treating trauma victims in the pre-hospital arena:

- Cannulation should take place en route where possible
- Only two attempts at cannulation should be made
- Transfer should not be delayed by attempts to obtain intravenous access
- Entrapped patients require cannulation at the scene
- Normal saline is recommended as a suitable fluid for administration to trauma patients
- Boluses of 250 ml fluid may be titrated against the presence or absence of a radial pulse (caveats; penetrating torso injury, head injury, infants)

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## References

1. Evidence-based Medicine, 1998. **3**: p. 34-35.
2. American College of Surgeons Committee on Trauma, ed. *American College of Surgeons Committee on Trauma: ATLS - Advanced Trauma Life Support for Doctors*. 1997. 31.
3. Pons PT, et al. Prehospital venous access in an urban paramedic system—a prospective on-scene analysis. *J of Trauma-Injury Infection & Critical Care*, 1988. **28(10)**: p. 1460-3.
4. Mahoney P and PJ Haji-Michael, Therapeutics, in *Pre-Hospital Medicine*, I Greaves and KM Porter, Editors. 1999, Arnold. p. 167-177.
5. Wears RL and CN Winton. Load and go versus stay and play: analysis of prehospital fluids therapy by computer simulation. *Ann Emerg Med*, 1990. **19(2)**: p. 163.
6. Demetriades D, et al. Paramedic vs private transportation of trauma patients. Effect on outcome. *Arch of Sur*, 1996. **131(2)**: p. 133-8.
7. Jacobs LM, et al. Prehospital advanced life support: benefits in trauma. *Journal of Trauma-Injury Infection & Critical Care*, 1984. **24(1)**: p. 8-13.
8. Pepe PE, et al. The relationship between total prehospital time and outcome in hypotensive victims of penetrating injuries. *Annals of Emerg Med*, 1987. **16(3)**: p. 293-7.
9. Powar M, et al. Hidden impact of paramedic interventions. *J of A & E Med*, 1996. **13(6)**: p. 383-5.
10. Nicholl J, et al. The costs and benefits of paramedic skills in pre-hospital trauma care. Health Technology Assessment (South Hampton, NY), 1998. **2(17)**: p. i-iv, 1-72.
11. Johnson GS and HR Guly. The effect of pre-hospital administration of intravenous nalbuphine on on-scene times. *J of A & E Med*, 1995. **12(1)**: p. 20-2.
12. Joint Royal Colleges Ambulance Service Liaison Committee, Guidelines for Cannulation.
13. O'Gorman M, P Trabulsky, and D B Pilcher. Zero-time prehospital i.v. *J of Trauma-Injury Infection & Critical Care*, 1989. **29(1)**: p. 84-6.
14. Slovis CM, et al. Success rates for initiation of intravenous therapy en-route by pre-hospital care providers. *Am J Emerg Med*, 1990. **8**: p. 305-7.
15. Scott J. Immobilisation and extrication, in *Pre-Hospital Medicine*, I Greaves and KM Porter, Editors. 1999, Arnold. p. 634-5.
16. Wilmink AB, et al. Vehicle entrapment rescue and pre-hospital trauma care. *Injury*, 1996. **27(1)**: p. 21-5.
17. Sutcliffe A. Crystalloids and colloids for volume replacement. *Trauma*, 1999. **1(2)**: p. 115-123.
18. Gosling P. Albumin: Friend or Foe? *Trauma*, 2000. **2(2)**: p. 125-134.
19. Boldt J, et al. The influence of volume therapy and pentoxifylline infusion on circulating adhesion molecules in trauma patients. *Anaesthesia*, 1996. **51**: p. 529-35.
20. Wilson RF. Blood Replacement, in *Management of Trauma: Pitfalls and Practice*, RF Wilson and AJ Walt, Editors. 1996, Williams and Wilkins. p. 51-69.
21. Cannon W, Fraser J and E Cowell. The Preventative Treatment of Wound Shock. *JAMA*, 1918: p. 618-621.
22. Office of the Surgeon General, *Surgery in World War II*, General Surgery. 1952: US Government Printing Office. 6-17.
23. Bickell WH, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries (see comments). *New Eng J of Med*, 1994. **331(17)**: p. 1105-9.
24. Various authors, Correspondence. Immediate versus delayed fluid resuscitation in patients with trauma. *New Eng J of Med*, 1995. **332(10)**: p. 681-3.
25. Chudnofsky CR, et al. Early versus late fluid resuscitation: lack of effect in porcine hemorrhagic shock. *Ann of Emerg Med*, 1989. **18(2)**: p. 122-6.
26. Krausz MM, et al. Hypertonic saline treatment of uncontrolled hemorrhagic shock at different periods from bleeding. *Arch of Sur*, 1992. **127(1)**: p. 93-6.
27. Sampalis JS, et al. Ineffectiveness of on-site intravenous lines: is prehospital time the culprit? *J of Trauma-Injury Infection & Critical Care*, 1997. **43(4)**: p. 608-15; discussion 615-7.
28. Wiggers CJ. Experimental Hemorrhage Shock, in *Physiology of Shock*. 1950, The Commonwealth Fund, New York. p. 121-143.
29. Traverso LW, WP Lee, and MJ Langford. Fluid resuscitation after an otherwise fatal hemorrhage: I. Crystalloid solutions. *J of Trauma-Injury Infection & Critical Care*, 1986. **26(2)**: p. 168-75.
30. Traverso LW, et al. Fluid resuscitation after an otherwise fatal hemorrhage: II. Colloid solutions. *J of Trauma-Injury Infection & Critical Care*, 1986. **26(2)**: p. 176-82.
31. Krausz, MM, et al. "Scoop and run" or stabilize hemorrhagic shock with normal saline or small-volume hypertonic saline? *J of Trauma-Injury Infection & Critical Care*, 1992. **33(1)**: p. 6-10.
32. Rabinovici R, MM Krausz, and G Feuerstein. Control of bleeding is essential for a successful treatment of hemorrhagic shock with 7.5 per cent sodium chloride solution. *Sur, Gyn & Obs*, 1991. **173(2)**: p. 98-106.
33. Capone A, et al. Uncontrolled hemorrhagic shock outcome model in rats. *Resuscitation*, 1995. **29(2)**: p. 143-52.
34. Sindlinger JF, et al. The effects of isotonic saline volume resuscitation in uncontrolled hemorrhage. *Sur, Gyn & Obs*, 1993. **177(6)**: p. 545-50.
35. Soucy DM, et al. Effects of anaesthesia on a model of uncontrolled hemorrhage in rats. *Crit Care Med*, 1995. **23(9)**: p. 1528-32.
36. Soucy DM, et al. Isotonic saline resuscitation in uncontrolled hemorrhage under various anaesthetic conditions. *Ann of Sur*, 1995. **222(1)**: p. 87-93.

37. Bickell WH, *et al.* The detrimental effects of intravenous crystalloid after aortotomy in swine. *Surgery*, 1991. **110(3)**: p. 529-36.
38. Bickell WH, *et al.* Use of hypertonic saline/dextran versus lactated Ringer's solution as a resuscitation fluid after uncontrolled aortic hemorrhage in anesthetized swine. *Ann of Emerg Med*, 1992. **21(9)**: p. 1077-85.
39. Craig RL and GV Poole. Resuscitation in uncontrolled hemorrhage. *Am Sur*, 1994. **60(1)**: p. 59-62.
40. Stern SA, SC Dronen, and X Wang. Multiple resuscitation regimens in a near-fatal porcine aortic injury hemorrhage model (see comments). *Ac Emerg Med*, 1995. **2(2)**: p. 89-97.
41. Kim SH, *et al.* Hypothermia and minimal fluid resuscitation increase survival after uncontrolled hemorrhagic shock in rats. *J of Trauma-Injury Infection & Critical Care*, 1997. **42(2)**: p. 213-22.
42. Hyde JAJ, SJ Rooney, and TR Graham. *Hypotensive Resuscitation. Trauma*, 1998: p.177-185.
43. Anonymous, Shock, in Trauma Care Manual, I Greaves, KM Porter, and JM Ryan, Editors. 2000, Arnold. p. 71-86.
44. Stern SA, *et al.* Effect of Blood Pressure On Haemorrhage Volume and Survival In Near-Fatal Haemorrhage Model Incorporating A Vascular Injury. *Ann Emerg Med*, 1993. **22**: p. 155-163.
45. Bock BF, *et al.* Pre-Hospital Medical Care of the Injured Patient, in Management of Trauma: Pitfalls and Practice, RF Wilson and AJ Walt, Editors. 1996, Williams and Wilkins. p. 8-9.
46. Miller JD and DP Becker. Secondary Insults to the Injured Brain. *J R Coll Surg Edinb*, 1982. **27**: p. 292-298.