

Vasopressin for hemorrhagic shock management



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Hemorrhagic shock



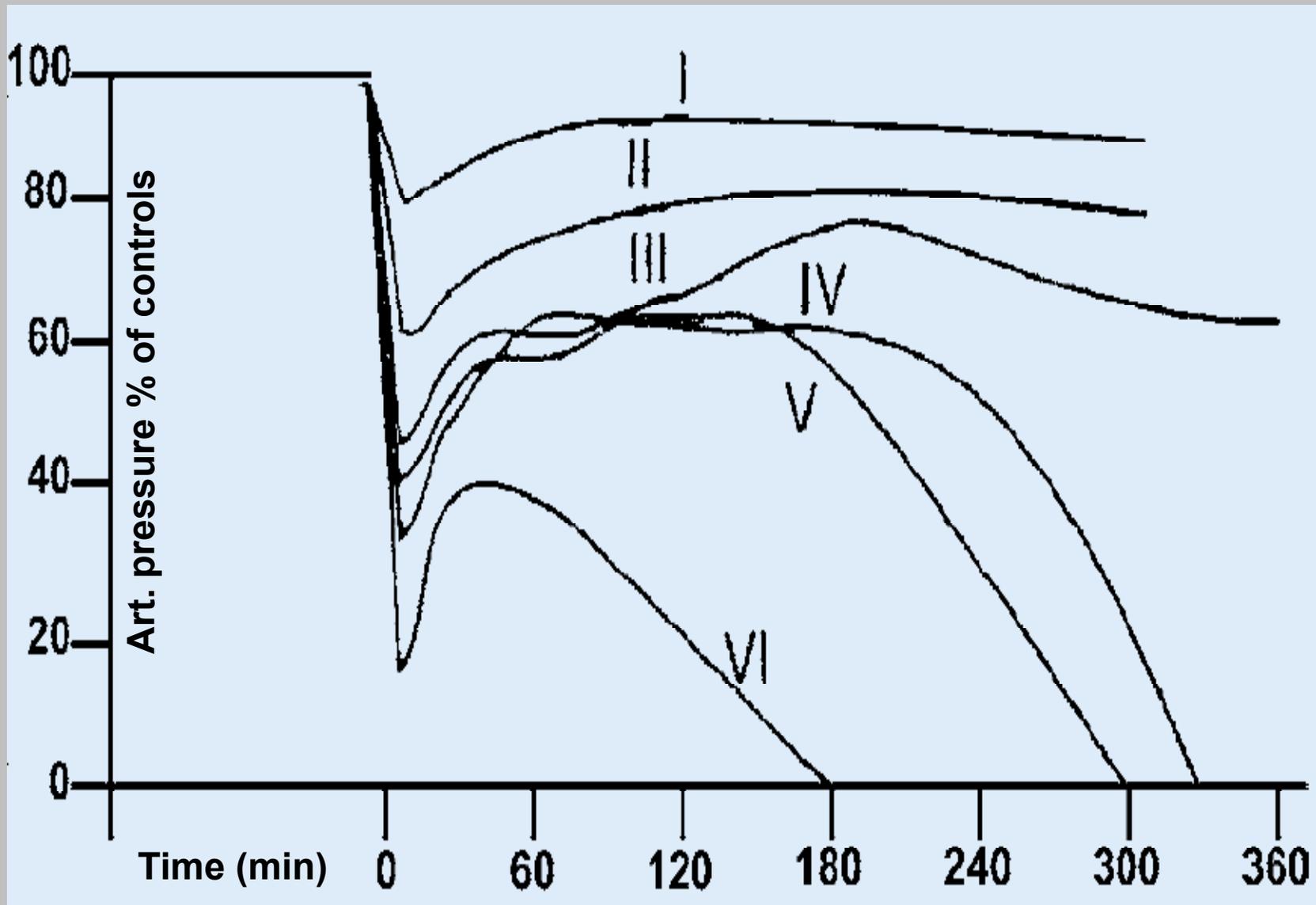
Degree and duration of hypotension affect outcome



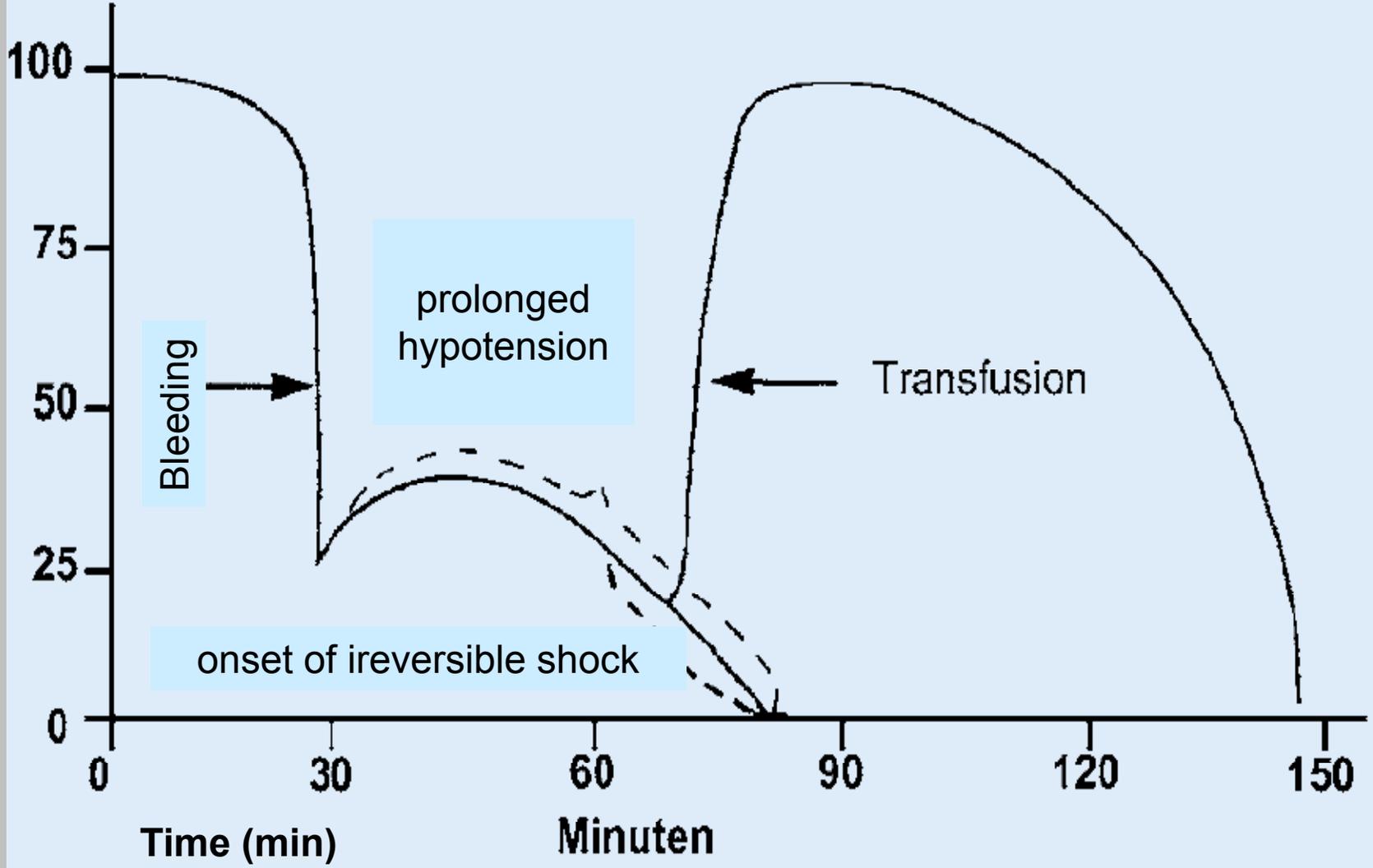
Current concepts of shock management have major flaws

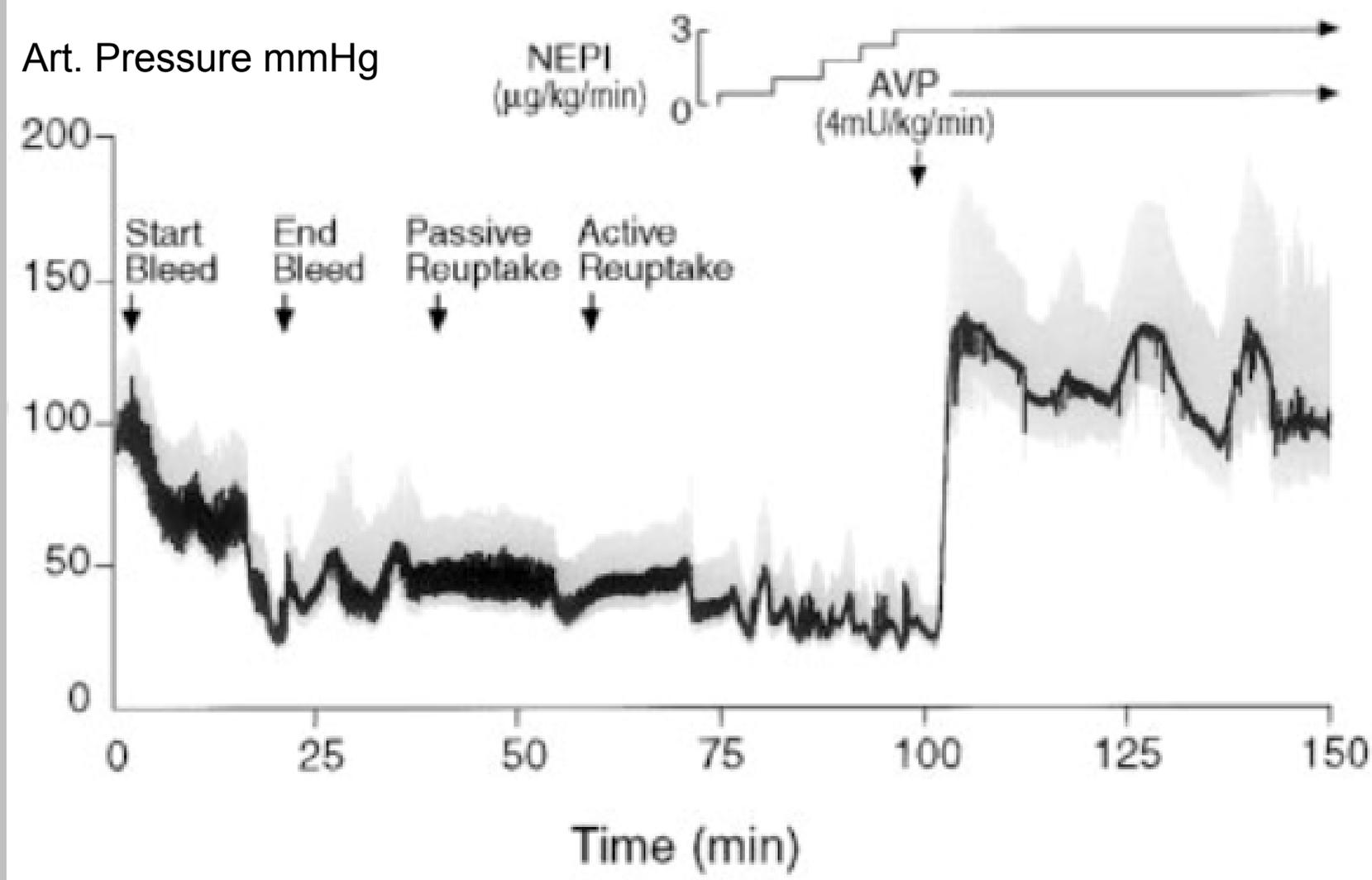


The potential value of vasopressin in shock management

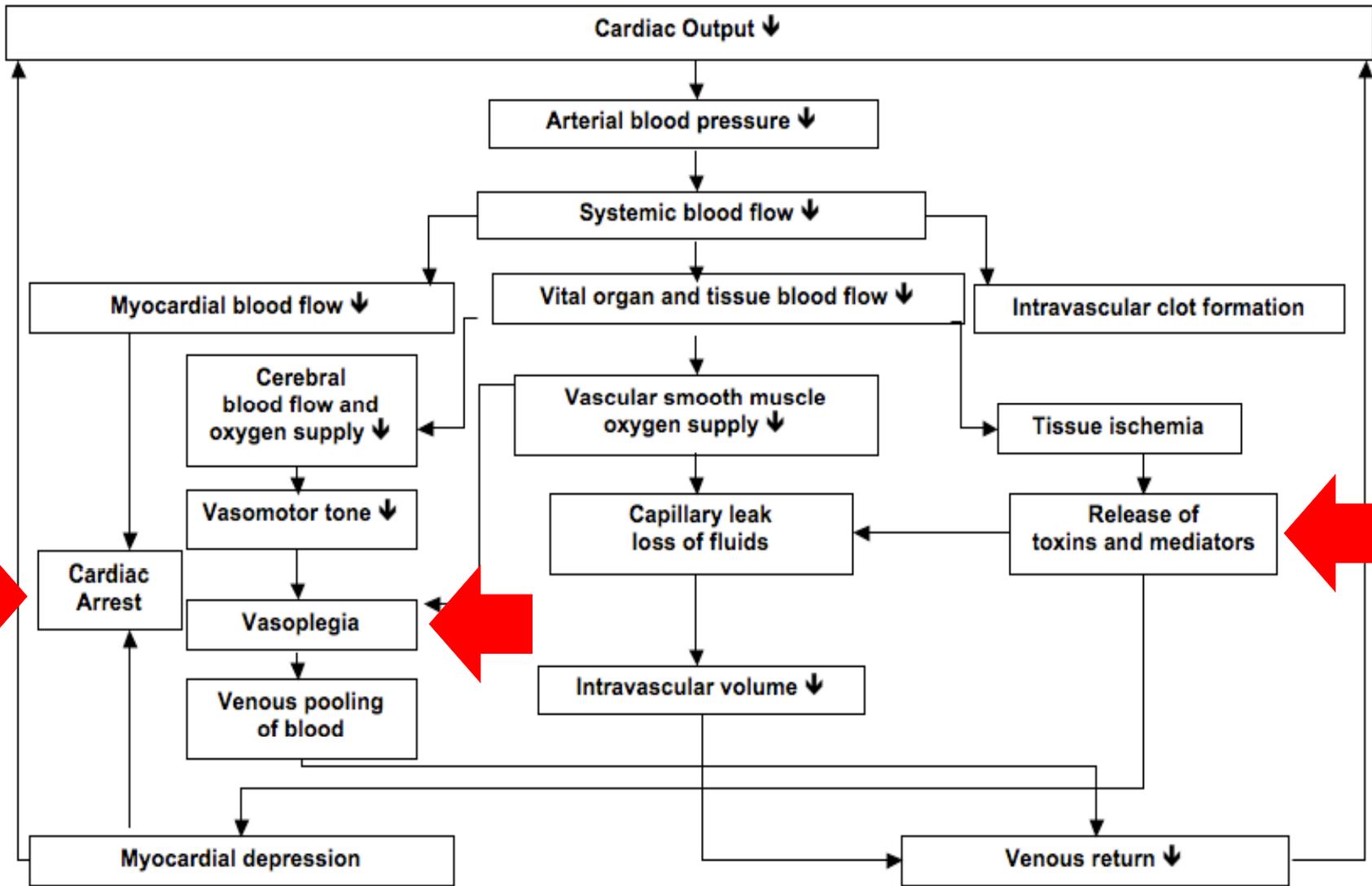


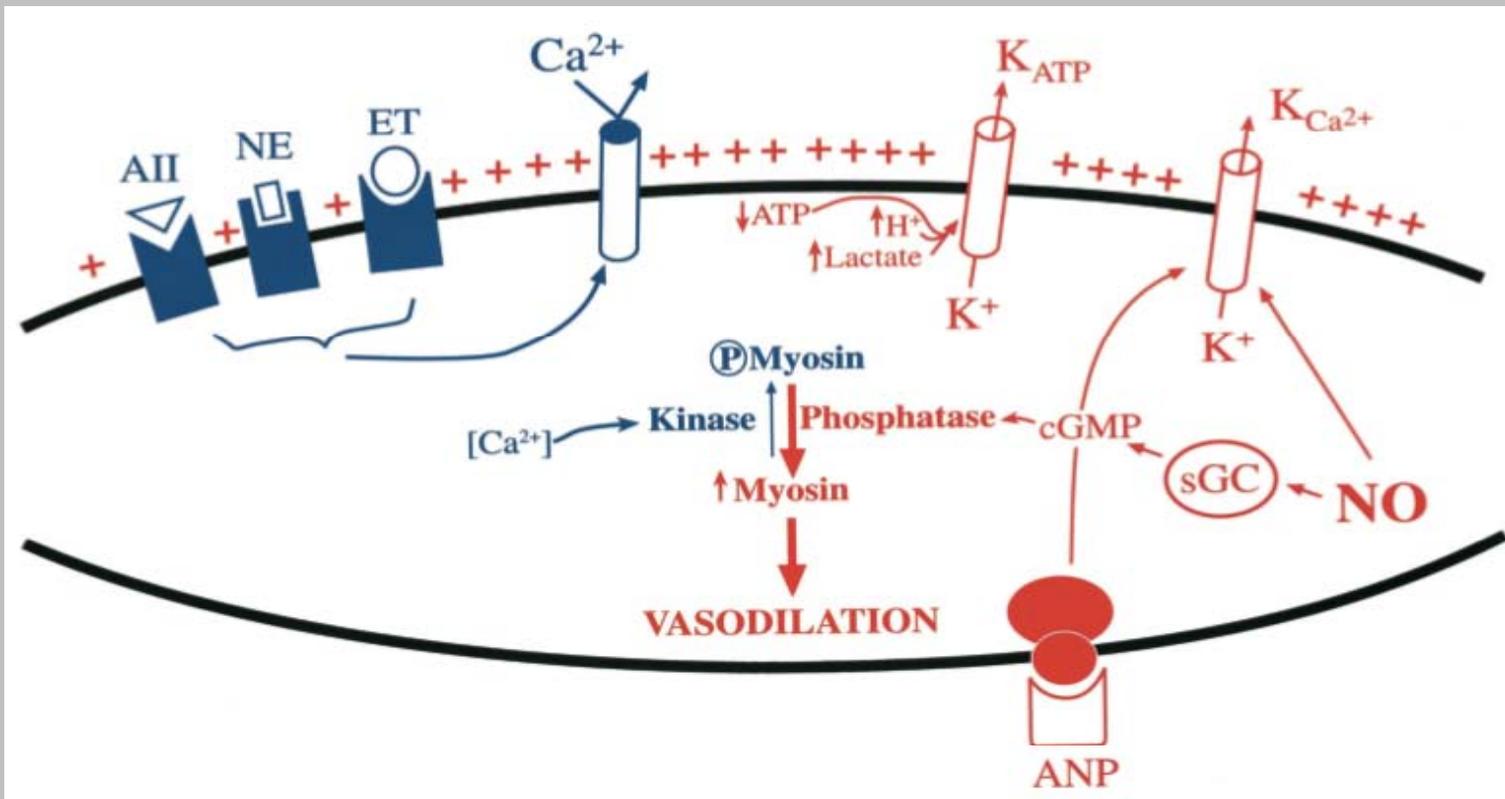
Cardiac output % of controls





Morales D. *Circulation* 1999;100:226-9

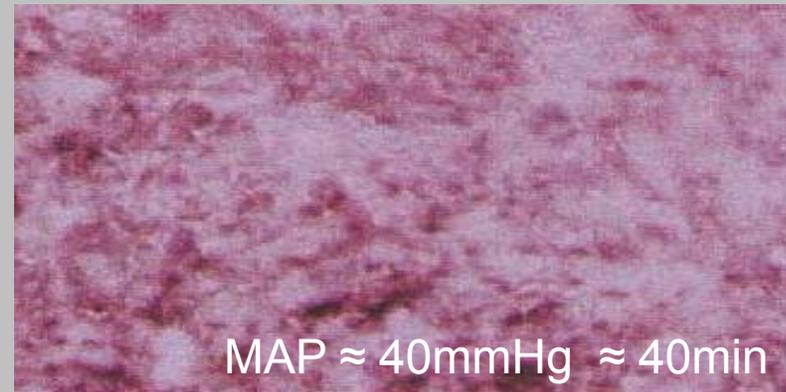
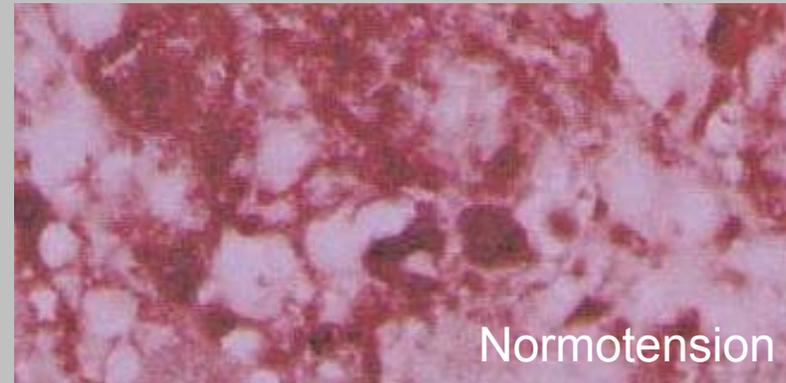
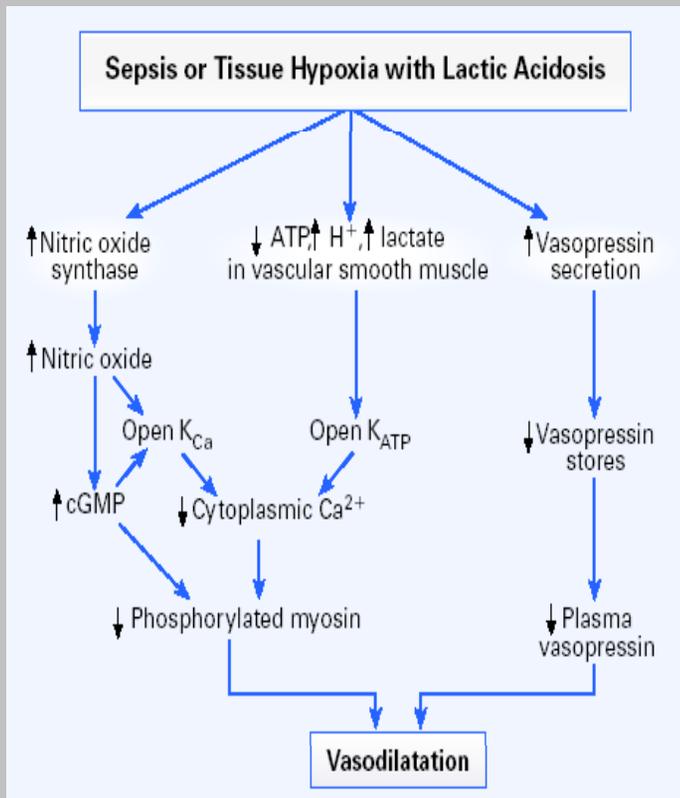




Robin JK. *J Trauma* 2003;54:149-54

Decompensated shock:

NO, ANP, H and Lactate \uparrow , K_{ATP} and $K_{Ca^{2+}}$ channels open
 Hyperpolarisation \rightarrow Ca influx blocked
 Vasoconstrictive hormones ineffective



Landry DW, *N Engl J Med* 2001;345:588

Vasopressin response in multiple trauma patients:
 Significant increase 50x (n=87 major trauma patients)
Integral part of the neuroendocrine response

Westermann I. *Shock* 2007;54:644



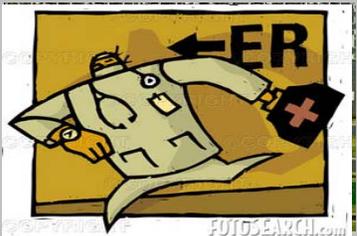
Hemorrhagic shock



Degree and duration of hypotension affect outcome



Current concepts of shock management have major flaws



The potential value of vasopressin in shock management

Timing and volume of fluid administration for patients with bleeding (Review)

Kwan I, Bunn F, Roberts I, on behalf of the WHO Pre-Hospital Trauma Care Steering Committee

No evidence from trials to support or not to support the use of early or larger volume intravenous fluid in uncontrolled bleeding.

About one third of injury deaths are due to shock from blood loss. Preventing shock in people with uncontrolled bleeding is, therefore, very important and is generally done by giving fluids intravenously. The aim is to maintain blood pressure and reduce tissue damage.

The review of trials found that there is uncertainty about the best time to give fluid and what volume of fluid should be given. While increasing fluids will maintain blood pressure, it may also worsen bleeding by diluting clotting factors in the blood. More research is needed.

- No evidence for fluids in uncontrolled bleeding
- Uncertainty what should be given
- Risk of increased bleeding

Clinical effectiveness and cost-effectiveness of prehospital intravenous fluids in trauma patients



Conclusions

This review found no evidence to suggest that prehospital IV fluid resuscitation is beneficial.

There is some evidence that it may be harmful and that patients do comparatively well when fluids are withheld



Based on 4 RCTs



Combat Casualty Care

Assess for shock
mental state / pulse
500 cc Hextent – repeat once

Butler FK. *Mil Med* 2007;127



Civilian Guidelines

Target systolic BP 80-100mmHg
Crystalloids initially
Colloids may be added

Spahn D. *Crit Care* 2007;11



Why do we fail?

Why do people die of shock

- ability of compensation
- onset of decompensation



What can be done?

Mainstems of shock therapy

- repair the problem in time
- interfere with endocrine response



Hemorrhagic shock



Degree and duration of hypotension affect outcome

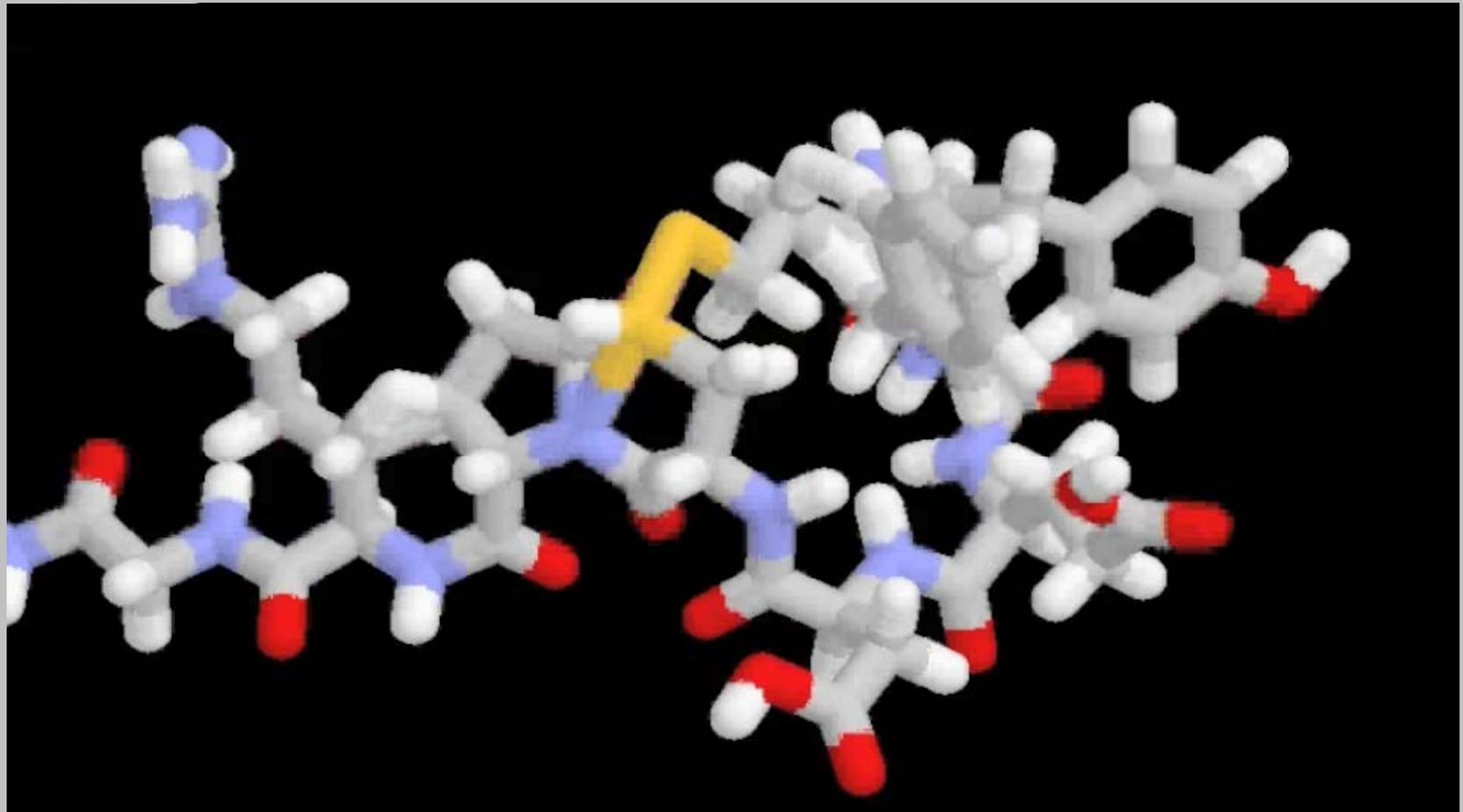


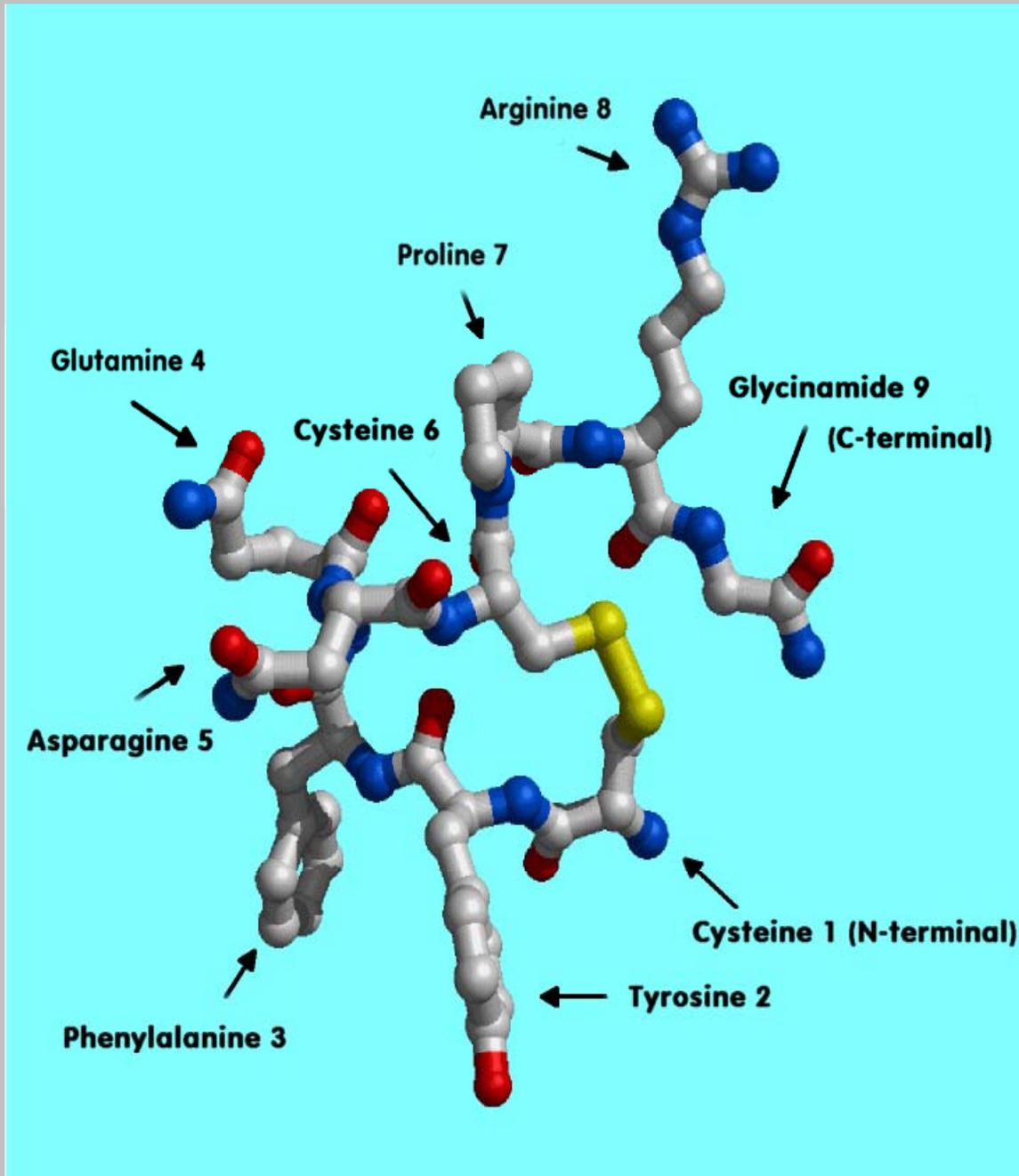
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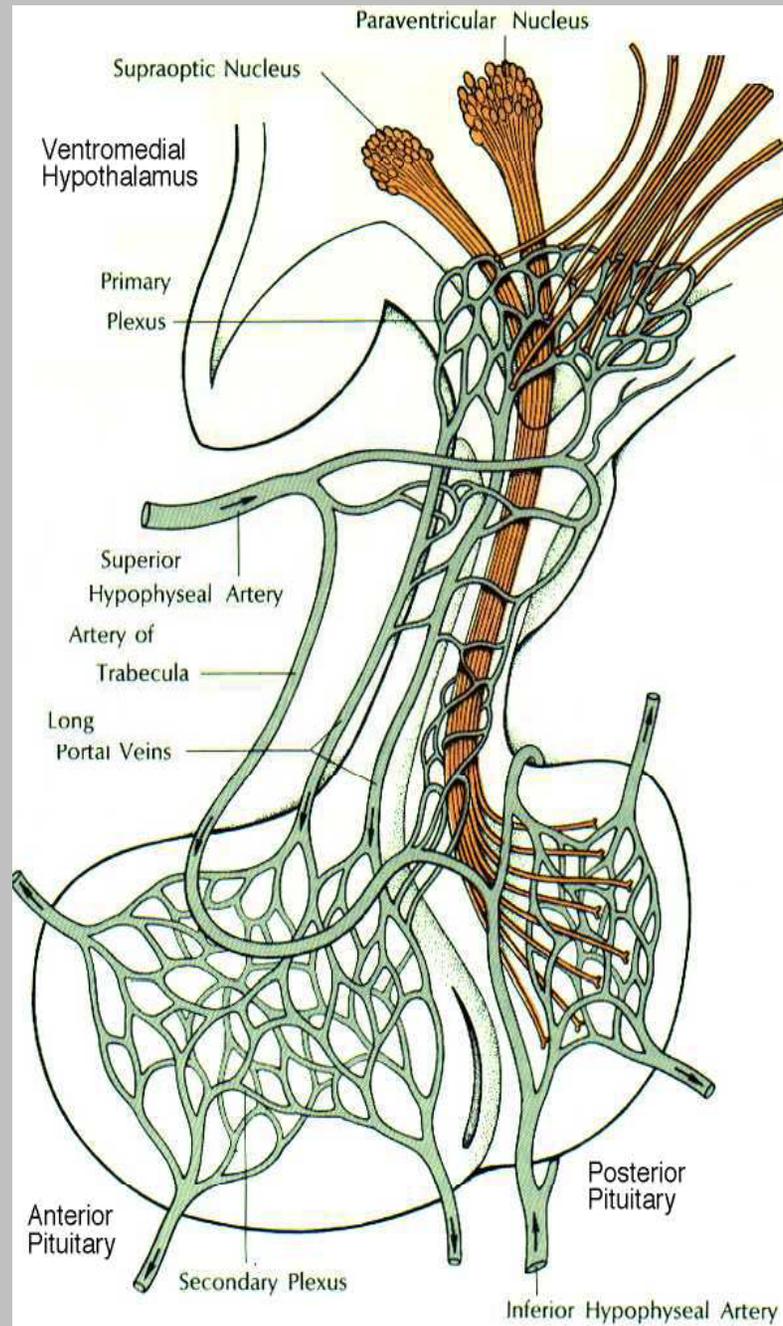
The potential value of vasopressin in shock management

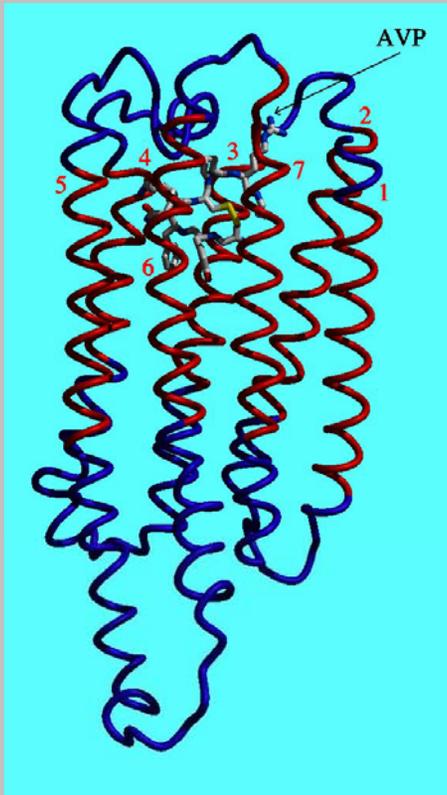
Arginine Vasopressin





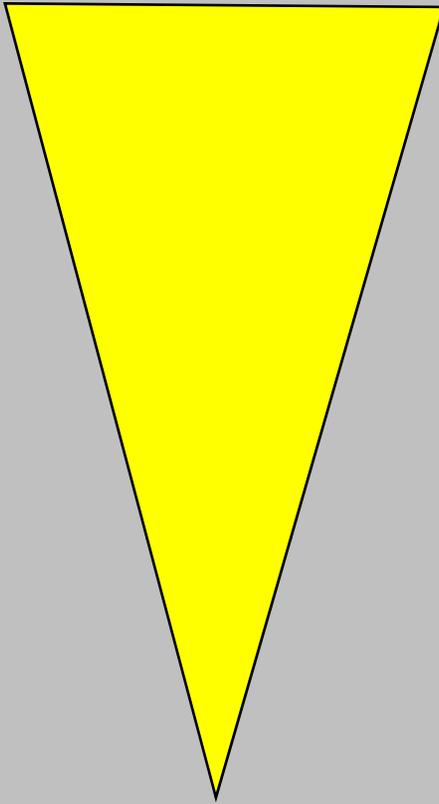
Physiology





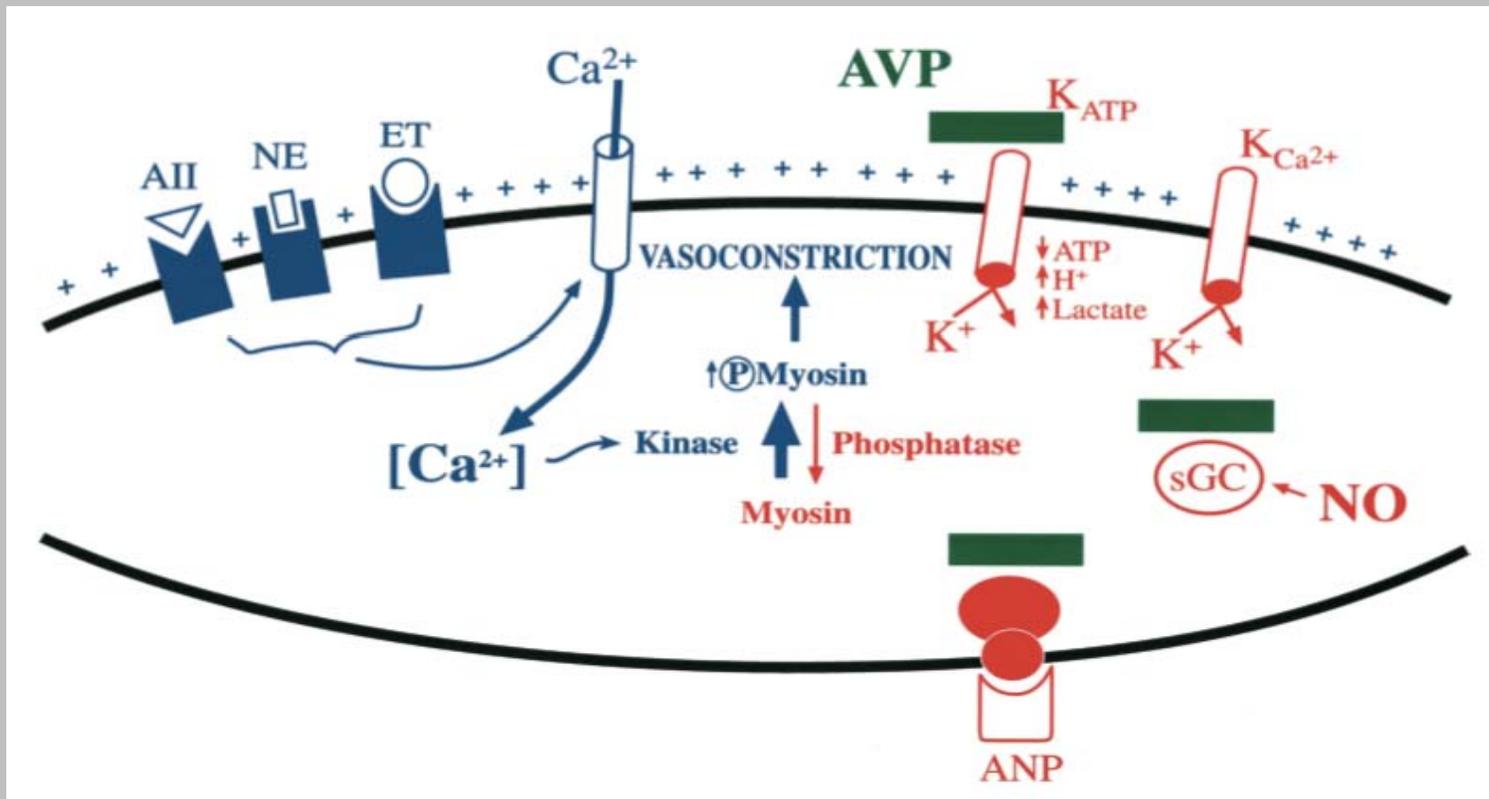
- V_{1a} Receptor
 - Phosphatidylinositol hydrolysis
 - intracellular Ca^{2+} mobilization
 - vasoconstrictive effects
- V_2 Receptor
 - epithelial cells of collecting tubes
 - cyclic AMP production
 - absorption of free water

*Early phase of shock – little or no effect – high plasma level
AVP depletion – hypersensitive pressure response
AVP potentiates conventional vasopressor drugs in shock*



- V_1 Receptor density & sensitivity
 - Skin
 - Muscles
 - Coronary arteries
 - Mesenteric arteries
 - Iliacal vessels
 - Kidney
 - Cerebral vessels

*Distribution pattern – more blood above the diaphragma
In hypovolemic shock – net benefit – venous harvesting*



Robin JK. *J Trauma* 2003;54:149-54

AVP in decompensated shock:

- Block K_{ATP} and K_{Ca²⁺} channels
- Inhibits NO and ANP effects
- Opens voltage gated Ca channels



Miami FL: Chest & Brain Trauma

J Trauma 2005, *Anesthes.* 2004, *CCM* 2006

South Korea: Exsanguination

J Vet Med Sci 2006, 2007

Innsbruck, Austria: Liver Trauma

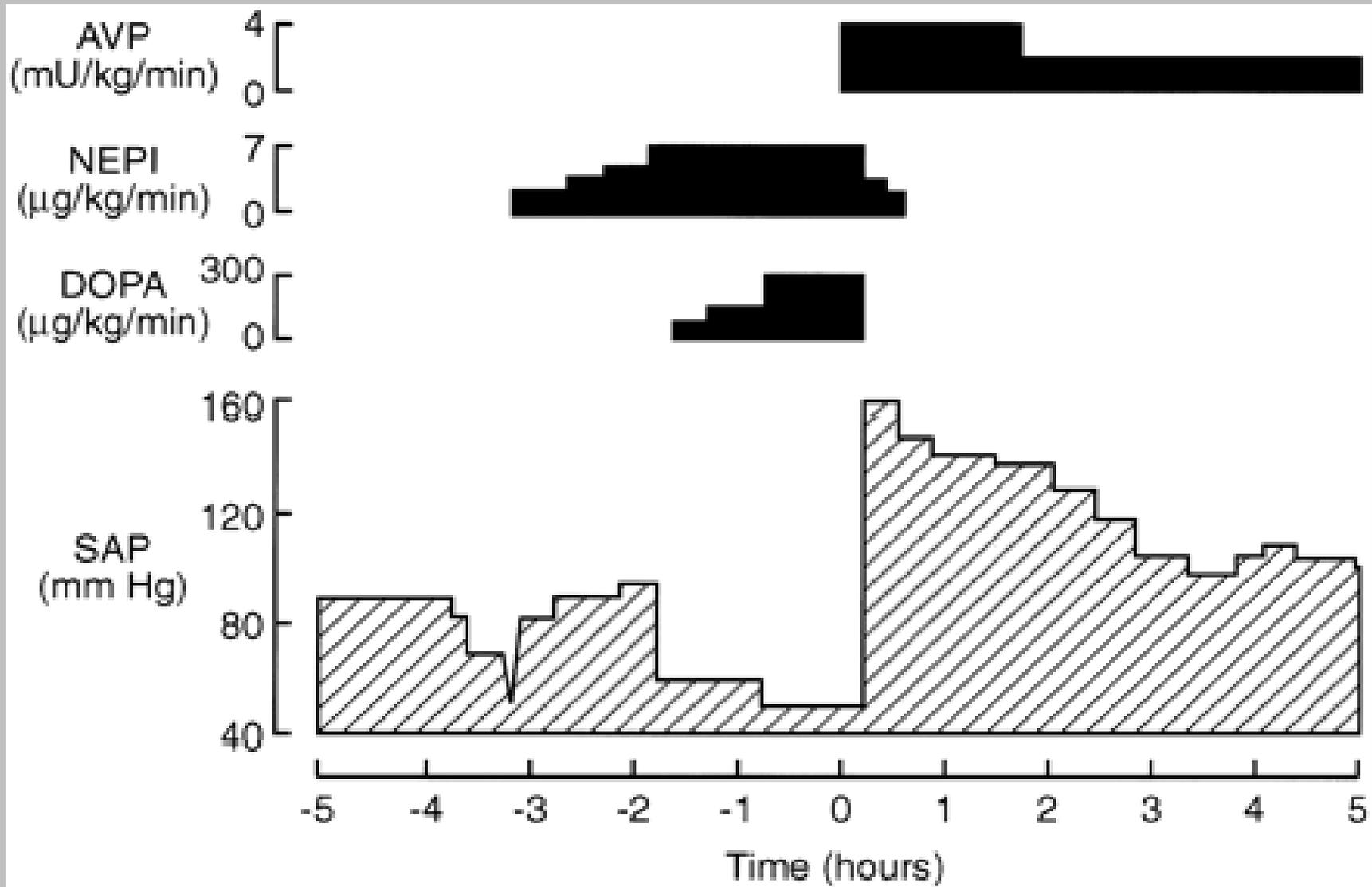
Anesthes. 2003/7, *CCM* 2003, *An Analg* 2004

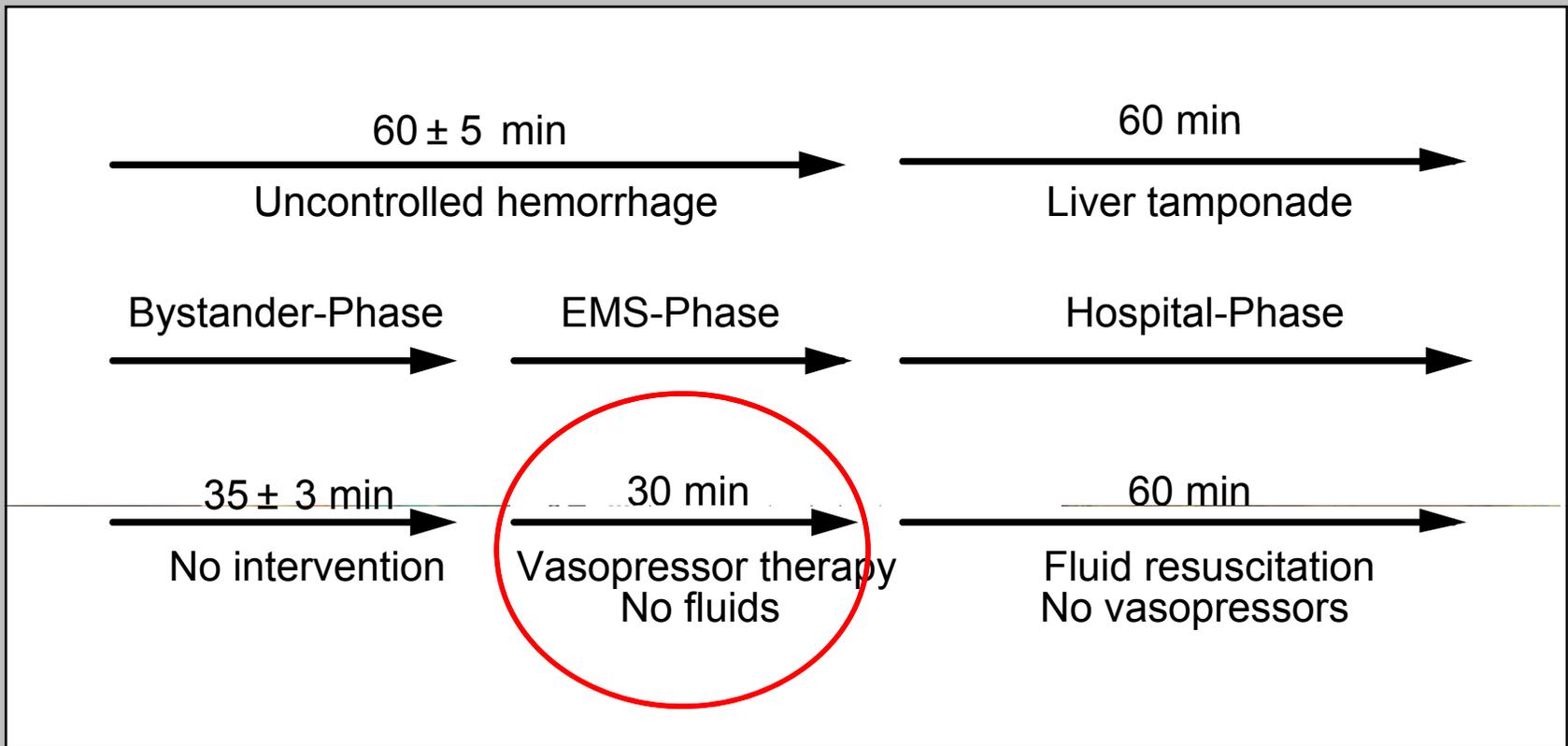
Kiel, Germany: Liver & Brain Trauma

Resuscitation 2007/9

An exact science is dominated by the idea of approximation.

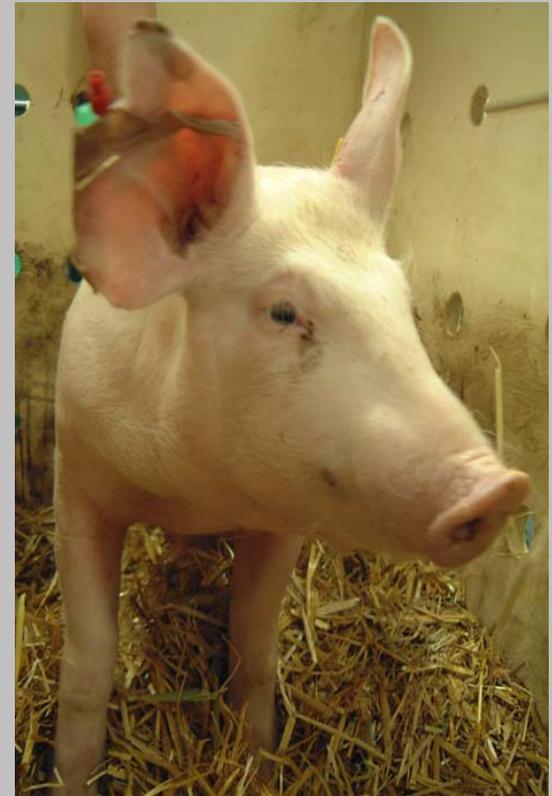
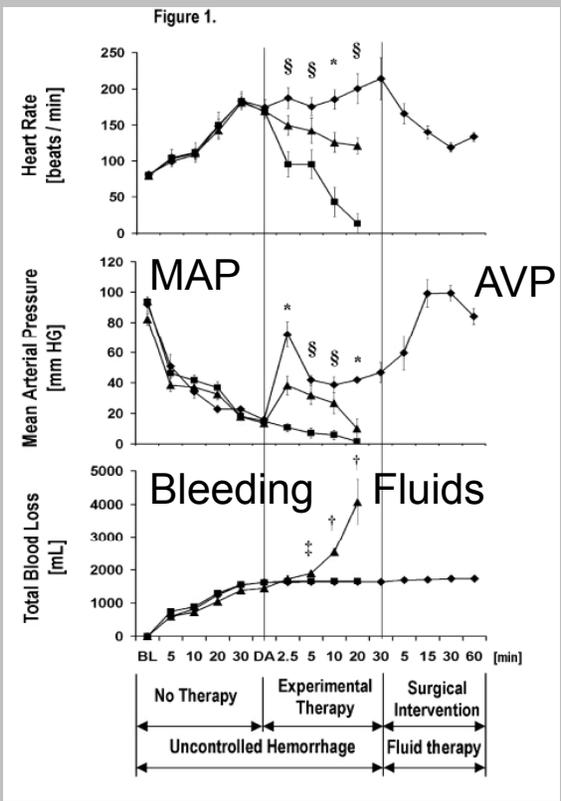
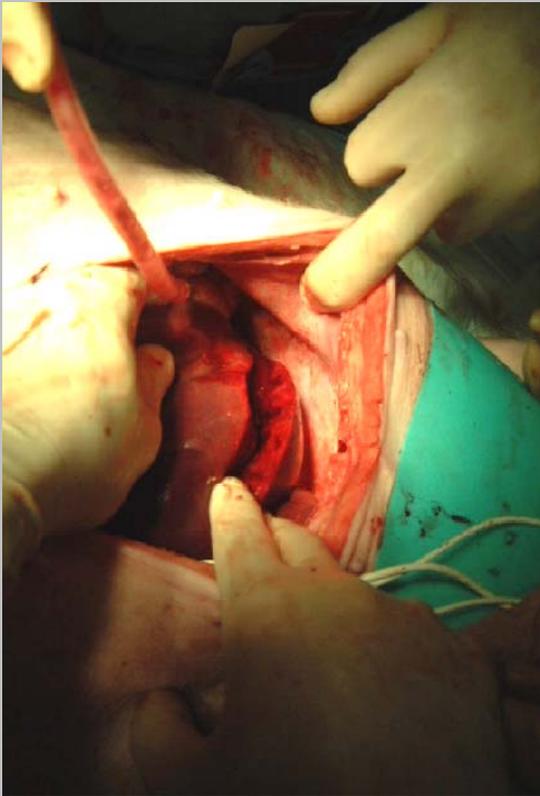
Bertrand Russell





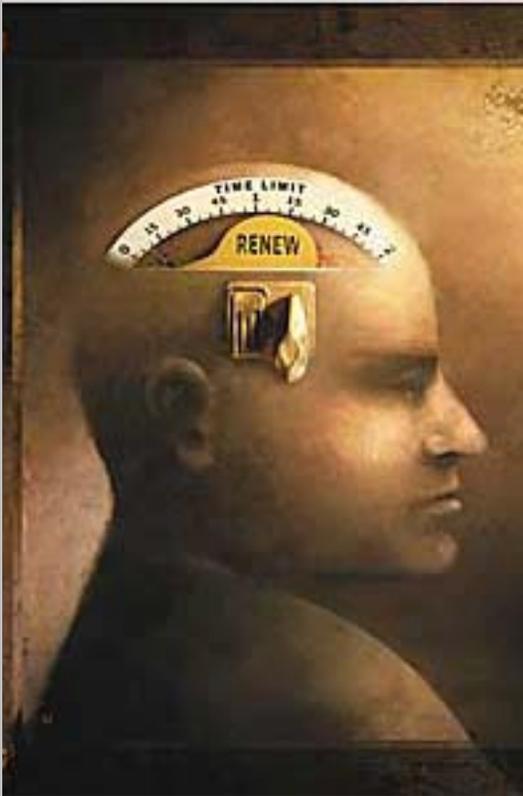
How to simulate uncontrolled hemorrhage?

Penetrating liver trauma with live threatening hypotension



Survival & outcome:

AVP vs. placebo vs. fluids in uncontrolled hemorrhagic shock
 Full recovery after surgery - no signs of gut ischemia



India: Major abdominal surgery

Sharma RM, *Anesth Analg* 2005;101:833-4

Germany: Multiple Trauma

Schummer W, *Anaesthesist* 2005;54:707-708

Japan: Liver Surgery

Tsuneyoshi I, *J Anesth* 2005;19:170-173

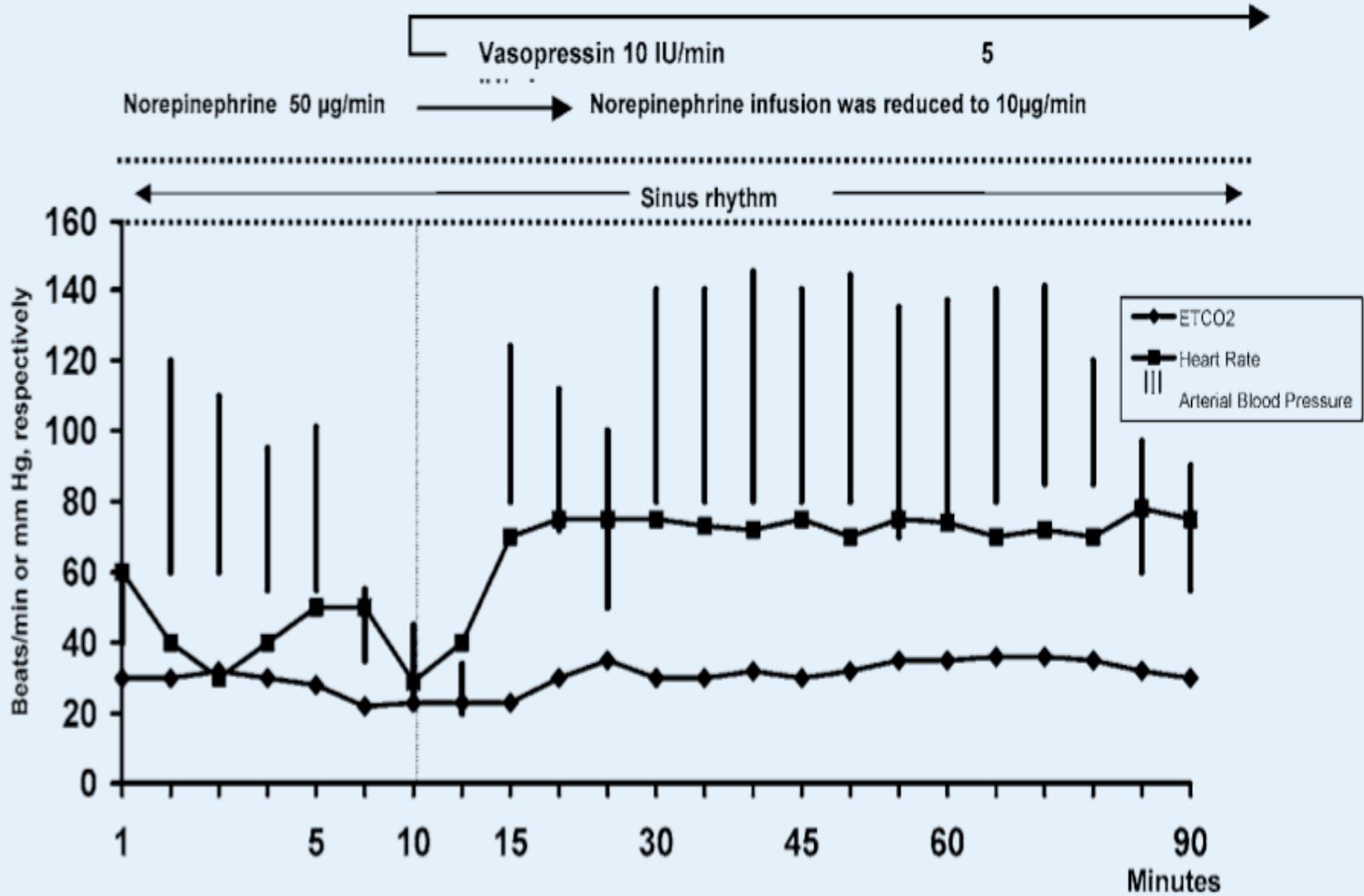
Austria: Blunt Trauma / Trauma CPR

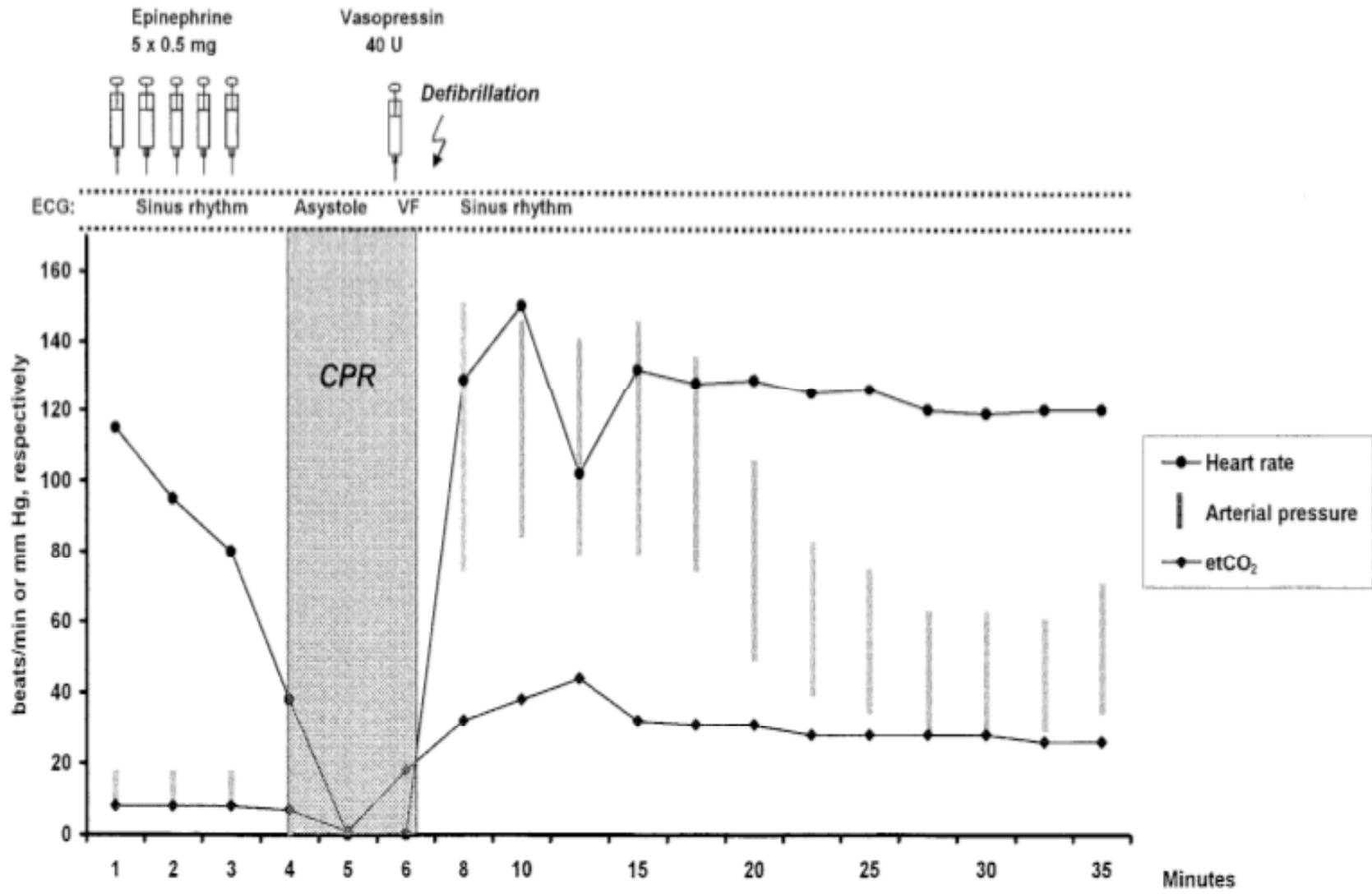
Krismer A, *Anaesthesist* 2005;54:220-4

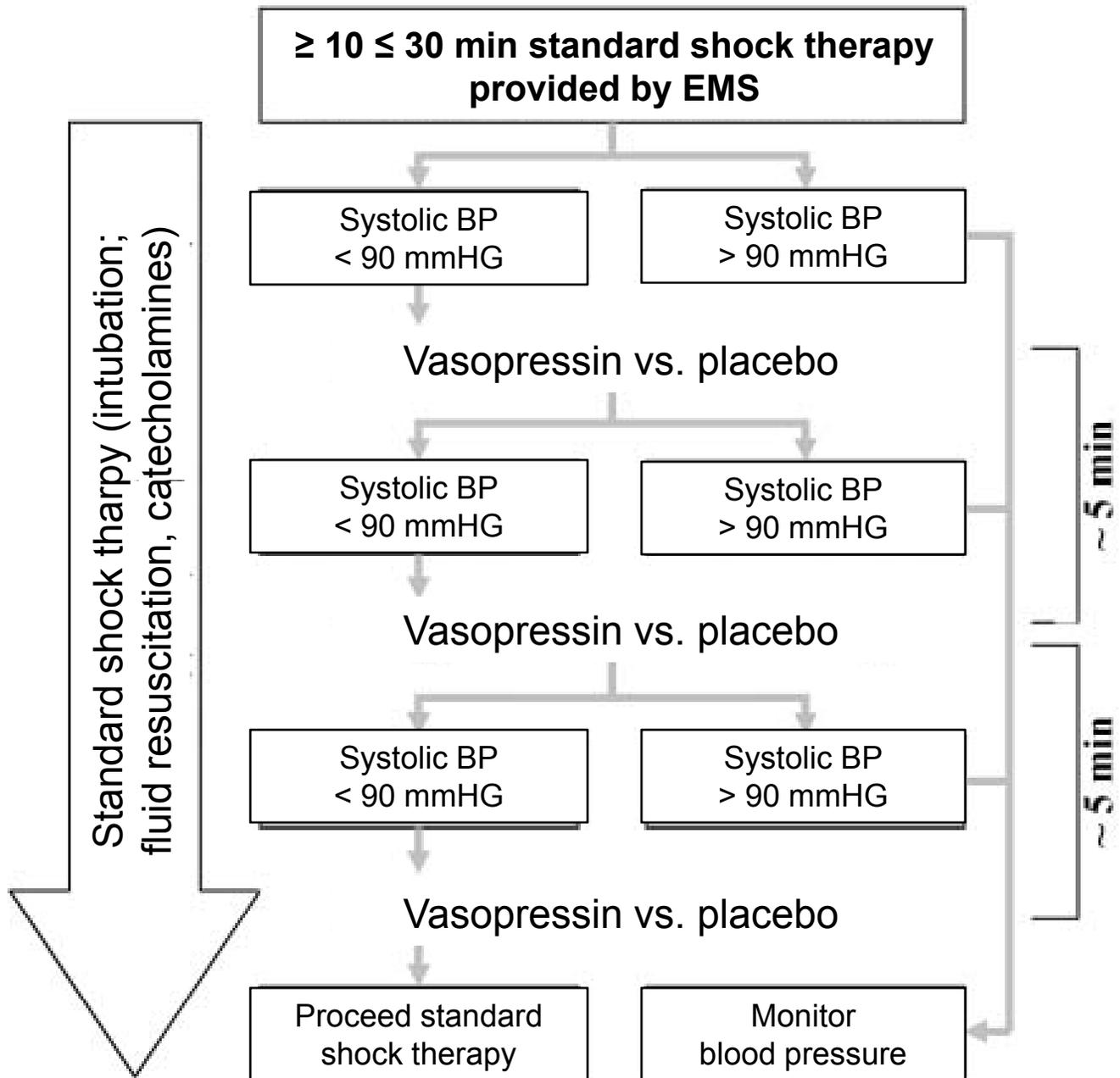
Haas T, *J Trauma* 2004;57:177-9

*It is common sense to take a method and try it.
If it fails, admit it frankly and try another.
May above all, try something!*

Franklin D Roosevelt









AVP is most promising in hemorrhagic shock management

Dosage is still experimental

Consider:

10 U (0.1-0.2 U/kg) bolus dose i.v.

Higher doses are possible

Fluids first?!

*All who drink of this remedy will recover,
except those whom it does not help who will die.
Therefore it is obvious that it fails only in incurable diseases.*

Galen

