Vasopressin in Cardiac Arrest and Vasodilatory Shock: A Forgotten Drug for New Indications

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Abstract

Vasopressin is a potent endogenous vasoconstrictor that increases blood pressure and systemic vascular resistance. The administration of exogenous vasopressin during closed and open cardiopulmonary resuscitation in humans was shown to be more effective than optimal doses of epinephrine in several clinical studies. We summarize here the recent experimental and clinical data on the use of vasopressin in cardiopulmonary resuscitation and septic shock. As the use of vasopressin in human resuscitation is now in its early stages, it is expected that accumulated future experience will shed more light regarding the risk-benefit aspects of its use.

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Intravenous epinephrine is the recommended vasopressor drug in the current guidelines for management of cardiac arrest and cardiopulmonary resuscitation. Its beneficial effects are attributed to its strong α-adrenergic receptor-stimulating properties, causing an augmentation of myocardial and cerebral blood flow during CPR enabling rapid defibrillation and preservation of neuronal viability respectively. However, epinephrine use in CPR is associated with some undesirable side effects related to its potent β-stimulating effects. The severe tachycardia and ventricular arrhythmias caused by epinephrine increase myocardial oxygen consumption and contribute to post-resuscitation myocardial dysfunction. Indeed, several clinical studies of cardiac arrest patients suggest that epinephrine may have no benefit over placebo in terms of hospital discharge rates and survival [1]. The use of high dose protocols for the administration of epinephrine, which were associated with higher rates of return of spontaneous circulation, did not contribute to better neurologic recovery or patient survival to hospital discharge [2]. As current methods of CPR and advanced cardiac life support continue to yield poor results, continuous efforts are being invested to find alternative pharmacologic therapies.

Vasopressin is a potent endogenous vasoconstrictor that increases blood pressure and systemic vascular resistance. Similar to epinephrine, it causes selective peripheral vasoconstriction, but with a reduced amount of myocardial oxygen demand. Initial interest in the possible value of vasopressin arose after the observation that endogenous vasopressin levels were markedly higher during cardiac arrest than in normal physiologic conditions. Moreover, higher levels of endogenous vasopressin, measured in patients undergoing CPR, were associated with greater rate of return of spontaneous circulation and chances of survival as opposed to serum levels of epinephrine, which were found to be inversely correlated with patient survival [3]. These observations founded the basis for the experimental [4–7] and later clinical research [8–10] on the possible role of vasopressin in CPR.

CPR = cardiopulmonary resuscitation

Vasopressin physiology and mechanism of action

Vasopressin, a 39 amino acid glycopeptide, is the principal antidiuretic hormone that is essential for preservation of homeostasis and survival. Vasopressin is synthesized in the posterior hypothalamus and is released to the circulation as a result of two main stimuli: increased serum osmolarity and hypotension. Other known stimuli to vasopressin release include pain, nausea, hypoxia, hypercarbia, drugs (i.e., opioids), certain types of malignant tumors, and mechanical ventilation. Several analogues of vasopressin exist (arginine – ADH, lysine – present in swine, oxytocin – induces uterine contraction, ornithin – used for the treatment of varices, and DDAVP – increases factor VIII activity). They differ in chemical structure and physiologic (antidiuretic/vasopressor) activities. In this review we chose to concentrate on arginine vasopressin which is the endogenous analogue (a-antidiuretic/vasopressor activity of 1/1) used in critical care (400 units of arginine vasopressin = 1 mg).

The cellular effects of vasopressin are mediated by interactions of the hormone with two principal types of receptors, V_1 and V_2. V_1 receptors are mainly found in gastrointestinal and vascular smooth muscle, but also in the bladder, myometrium, kidneys and many central nervous system structures. V_2 receptors are predominantly located in principal cells of the renal collecting duct system.

The principal physiologic stimulus for vasopressin secretion is an increase in plasma osmolarity, as sensed by exquisitely sensitive osmoreceptors located in the brain and peripheral vasculature. By binding to the V_2 receptors, an increase in water absorption in the collecting ducts is initiated, resulting in greater water conservation.

The second physiologic stimuli for vasopressin release are hypotension and hypovolemia, as sensed by stretch receptors in the left atrium, aortic arch and the carotid sinus. These non-osmotic stimuli can trigger massive release of vasopressin, which acts as a non-adrenergic peripheral vasoconstrictor by directly stimulating smooth muscle V_1 receptors. Vasopressin-related vasoconstrictive effect may be especially useful when the duration of cardiac arrest is prolonged because the adrenergic pressor response in severe acidosis is blunted, while in the face of severe acidosis vasopressin still has a considerable vasoconstrictive effect [11]. Essential to vasoconstriction is an increase in the concentration of calcium in the cytosol of smooth muscle cells. The biochemical basis for vasopressin-related pressor effect is thought to be via its ability to inactivate K_{ATP} channels in vascular smooth muscle cells [11]. These potassium channels play a key role in determining the membrane potential of vascular smooth muscle cells and thus, vasoreactivity. Opening of these channels (i.e., as a result of acidosis or hypoxia) allows an efflux of potassium, causing hyperpolarization and prevention of calcium to enter the cells. This leads to smooth muscle relaxation and vasodilation. By contrast, inactivation of the K_{ATP} channels leads to depolarization, opening of the voltage-gated calcium channels and increase in the cytosolic calcium concentration, which induces vasoconstriction [11]. Another recently discovered mechanism for vasopressin-induced vasoconstriction is its ability to blunt the accelerated synthesis of nitric oxide following lipopolysaccharide and interleukin-1 stimulation in sepsis [12]. This halts the nitric oxide-mediated vasodilation seen in septic states [11]. Clinically, the vasoconstrictor effects of vasopressin in CPR is mostly peripheral, causing shunting blood flow from organs like skin, skeletal muscle, intestine and fat, while sparing perfusion to vital organs such as heart, kidneys and brain by causing relatively less vasoconstriction in their vascular beds. Furthermore, vasopressin may vasodilate cerebral vasculature [13]. This beneficial effect provided by vasopressin even at low and suboptimal perfusion pressures generated during CPR increases the chances of neuronal viability preservation until full restoration of the circulation. The relative selective vasoconstrictive effects of vasopressin are also used clinically in the therapy for specific clinical conditions requiring vasoconstriction, such as bleeding esophageal varices and abdominal angiography. Another common indication for the use of vasopressin is in the treatment of central diabetes insipidus.

Experimental use of vasopressin

More than 13 animal studies, using models of both closed and open chest CPR, were designed to compare the effects of vasopressin with those of epinephrine during cardiac arrest. Using radiolabeled microspheres, coronary and cerebral blood flows were determined in a closed chest pig model of short and prolonged duration ventricular fibrillation given either vasopressin or epinephrine [4]. Results showed that the use of intravenous 0.8 U/kg vasopressin caused higher coronary and cerebral blood flow as compared to the administration of high dose epinephrine (200 g/kg). Moreover, in an open chest pig model of cardiac arrest, the vasopressin effect lasted longer, and significantly more animals treated with vasopressin could be resuscitated [5]. In another porcine model of short duration ventricular fibrillation, the use of vasopressin achieved a significantly higher cerebral oxygen delivery [6] and ventricular fibrillation median frequency [7] compared with high dose epinephrine. These results contributed to the improved chances of return of spontaneous circulation following the arrest [6,7]. The higher perfusion of vital organs (i.e., brain and heart) during the arrest using vasopressin was explained by its unique ability to shunt blood flow preferentially to the heart and the brain away from non-vital organs, perhaps secondary to nitric oxide release and its related vasodilation [14]. Common to all these studies is the fact that the vasopressin beneficial effect on cardiac physiology is achieved with only minor increase in myocardial oxygen consumption compared to that observed with epinephrine. Indeed, the lack of the β-stimulating effects of vasopressin that can be deleterious, such as aggravation of ischemic damage to the myocardium, is a clear advantage of vasopressin.

Given the longer duration of action of vasopressin compared with epinephrine, post-resuscitation systemic vasoconstriction and myocardial depression may be a concern, as long-term survival after cardiac arrest depends on adequate systemic perfusion. However, it was found that after the administration of vasopressin overall cardiovascular function was not irreversibly impaired [15]. In one study there was a transient decrease in cephalic mesenteric blood flow during and after CPR with vasopressin, but neither renal blood flow nor renal function was impaired [16,17].

The use of repeated doses of vasopressin as compared to epinephrine in a pig model of prolonged cardiac arrest and CPR was evaluated by Wenzel et al. [18]. The vasopressin-treated group exhibited an improvement of coronary perfusion pressure and 60 minute survival compared to the epinephrine group. In another study [19], a single dose of vasopressin was compared with repeated boluses of epinephrine in pigs subjected to 18 minutes of ventricular fibrillation. No difference was observed between the two groups in 24 hour neurologic outcome or in success rate of restoration of spontaneous circulation. However, in a model of prolonged cardiac arrest followed by CPR, repeated boluses of vasopressin ensured full neurologic recovery and improved long-term survival, as compared with epinephrine or placebo [20].

Given the different mechanism of action of vasopressin and epinephrine, few studies tested the combined effect of vasopressin and epinephrine during CPR. Mulligan et al. [21] found that treatment with both agents during cardiac arrest resulted in a more rapid rise in coronary perfusion pressure and an elevated coronary perfusion pressure as compared to using each drug alone. They concluded that these synergistic effects may be of benefit during CPR. Wenzel and co-workers [22] evaluated whether a combination therapy (vasopressin and epinephrine) is superior to vasopressin alone after prolonged cardiac arrest. They found a decrease in cerebral blood flow with combination treatment compared with vasopressin alone, but similar levels of left ventricular myocardial blood flow were reached with the two treatment regimens. In contrast to the previously described experimental studies using a model of adult CPR, Voelckel et al. [23] compared both treatments to either drug alone in a pediatric pig model of asphyxia-induced

cardiac arrest. Their findings suggested that in the pediatric setting of CPR the use of epinephrine might be of certain value compared to vasopressin, as reflected by the higher myocardial blood flow and rate of return of spontaneous circulation achieved using epinephrine alone as compared with vasopressin or their combination.

In special resuscitation circumstances (hypothermia, epidural anesthesia, hypovolemic shock) the use of vasopressin as compared to epinephrine resulted in a better outcome [24,25]. Other advantages of vasopressin include equal vasopressive effectiveness even when the regular intravenous injection is replaced by other routes, as was shown in animal models by Efrati et al. [26] for the intratracheal route and Wenzel et al. [27] for the intraosseous administration.

Thus far, no study has been published regarding the safety or risk-benefit analysis of the use of vasopressin in humans. Its use can cause diverse deleterious effects. Persistent bradycardia and ventricular arrhythmias were described following the use of vasopressin and were attributed to a vagal response to the vasopressin-induced hypertension and to increased vascular resistance [28]. Other described side effects associated with vasopressin administration include prolonged and profound increase in systemic vascular resistance and hypertension resulting in increased afterload, heart failure and depression of myocardial function after CPR [15]. Impaired perfusion to collateral-dependent myocardium and exacerbation of regional ischemia can also be a deleterious side effect of vasopressin [29]. Due to its antidiuretic effect, vasopressin can cause severe hyponatremia when used continuously, as in the treatment of variceal hemorrhage. Nevertheless, none of the above-mentioned possible side effects were described in recently published randomized control trials of vasopressin in human resuscitation [10,30]. In addition, in a study in children, the use of vasopressin for the treatment of vasodilatory shock did not cause episodes of peripheral vasoconstriction or cyanosis requiring that it be discontinued [31]. As the use of vasopressin in human resuscitation is now in its early stages, it is expected that accumulated future experience will shed more light regarding the risk-benefit aspects of its use.

Vasopressin use in clinical investigation

Although laboratory data hint to the potential of vasopressin as an alternative vasopressor during CPR, clinical data on its use in CPR are still not conclusive and are based on the use of vasopressin in CPR after standard advanced life support measures have failed. In most of the existing clinical studies, patients were given large doses of epinephrine prior to vasopressin administration, making it difficult to isolate the effect of vasopressin on the return of spontaneous circulation. For example, in a series of case reports, eight patients were given intravenous 40 units of vasopressin during cardiac arrest after 40 minutes of unsuccessful CPR, including epinephrine treatment. All patients exhibited restoration of spontaneous circulation [8]. Three patients were discharged from the hospital with little or no neurologic deficit. The authors' explanations for the superiority of vasopressin over epinephrine were that unlike epinephrine, vasopressin preserves its potent vasopressor effects even in conditions of hypoxia and acidosis, its effects last longer and it does not increase myocardial oxygen consumption or lactate production [8].

In another study [9], the hemodynamic effects of vasopressin and epinephrine were compared in prehospital cardiac arrest patients who had had prolonged unsuccessful resuscitation for 40 minutes. Ten patients were given intravenous 1 U/kg of vasopressin, resulting in an increase of 28 mmHg in coronary perfusion pressure in four patients but no return of spontaneous circulation.

On the basis of these observations Lindner and colleagues [10] coordinated a small (n=40) prospective randomized study among patients with out-of-hospital ventricular fibrillation resistant to direct current shock. Comparing vasopressin versus epinephrine as first-line therapy, they found that a higher proportion of those treated with 40 units vasopressin survived for 24 hours compared with those given 1 mg epinephrine, but the hospital discharge rate was comparable. Neurologic outcomes during hospital discharge were similar [10]. Stiell et al. [30] recently published data on a prospective, randomized clinical trial of 200 in-hospital patients treated with vasopressin or epinephrine during in-hospital cardiac arrest. The results failed to detect any survival or neurologic outcome benefits with the use of vasopressin compared to epinephrine. They concluded that routine use of vasopressin should be avoided for in-hospital cardiac arrest patients, even as an alternative to epinephrine. The discrepancies in the results of Lindner et al. [10] as opposed to those of Stiell et al. [30] can be explained by the different case-mix (acute cardiac ischemia in the pre-hospital setting versus critical illness and multiorgan involvement in the in-hospital setting) and time to CPR initiation.

Vasopressin use in vasodilatory shock

Refractory hypotension and progressive acidosis not responding to fluids and catecholamine infusion are the causes of early mortality from severe sepsis. Plasma levels of vasopressin in patients with septic shock were found inappropriately low compared to patients in cardiogenic shock [11], and increased sensitivity to the pressor effect of vasopressin was noted among advanced septic shock patients [32]. These observations support vasopressin as an emerging rational therapy for septic shock.

Low flow states caused by hypovolemia or septic shock are associated with a biphasic response in serum vasopressin levels. Early increased release of vasopressin from the neurohypophysis leads to high levels of serum vasopressin. This contributes to the stabilization of arterial pressure and organ perfusion in the initial phase of the shock. However, in the later phase of the shock, vasopressin secretion is deduced from an incompletely understood mechanism that probably involves depletion of neurohypophyseal stores after exhaustive release of vasopressin in the early phase of shock [33]. Clinically, low serum vasopressin levels were found during vasodilatory shock, indicating endogenous vasopressin deficiency [32]. In view of the known clinical outcome of severe vasodilatory shock, which remains poor, and given the experimental and clinical hints as to the relative deficiency of vasopressin in progressive shock states, vasopressin can be considered as a plausible alternative for hemodynamic support especially in sepsis with severe refractory shock. Indeed, reports from clinical trials

demonstrated an improvement in systemic hemodynamics of patients with vasodilatory shock in response to an infusion of exogenous vasopressin, leading to prompt increase in blood pressure and urine output while sparing conventional catecholamines. It appears that vasopressin possesses both direct and indirect effects on the arterial vascular system. While the direct effect is mediated by V_1 receptor activation, vasopressin can also increase the responsiveness of the systemic circulation to catecholamines [13]. These properties support the usefulness of vasopressin in the management of sepsis-induced refractory hypotension. Positive results were reported in a retrospective clinical study of 50 adult patients in severe septic shock [34]. In this study, the use of vasopressin, as a rescue therapy, markedly increased mean arterial blood pressure and urine output while decreasing catecholamine requirements. However, mortality was high (85%) and did not decrease following vasopressin administration. The augmented urine output observed with the use of vasopressin can be explained by vasopressin-induced renal efferent arteriolar vasoconstriction that increases renal perfusion pressure [34]. Another non-randomized small study, which described the early experience of vasopressin treatment in 11 moribund critically ill children suffering from vasodilatory shock after cardiac surgery, demonstrated a beneficial hemodynamic response to vasopressin treatment with 8 of 11 children surviving to hospital discharge [31]. The authors' conclusion was that the use of vasopressin is a viable treatment option for pediatric patients in refractory vasodilatory shock. The doses used for supporting blood pressure in septic states started from a continuous intravenous infusion of 0.01–0.04 U/min [32,34,35]. This range of vasopressin dosage leads to elevation of blood pressure. Doses > 0.04 U/min led to a substantial vasopressor effect but also undesirable vasoconstriction of the splanchnic and coronary vasculature, as well as to a hypercoagulation state [34]. The excessive peripheral vasoconstriction can lead to a reduction of cardiac output, especially in patients sensitive to changes in left ventricular afterload [34].

Current guidelines and future prospective

The use of vasopressin in an intravenous dose of 40 U as an alternative pressor to epinephrine for the treatment of adult shock-refractory ventricular fibrillation (Class IIb) and cardiac arrest (Class intermediate) is currently recommended by the American Heart Association and the International Committee on Resuscitation [36]. In the cardiac arrest scenario, vasopressin can be used as an alternative for epinephrine, particularly when repeated administration of epinephrine is unsuccessful. The classification (Class IIb) for the use of vasopressin requires fair-to-good evidence by the majority of experts classifying it as an optional therapeutic alternative. In the special clinical condition of refractory vasodilatory shock, a treatment trial with vasopressin seems to be a logical choice. In this scenario recommended dosage starts from low dose infusion of 0.01–0.04 U/min aiming for hemodynamic stabilization [34].

Several distinguished papers raising concerns about the use of vasopressin should be noted: Stiell et al. [30], in a randomized controlled trial comparing survival for patients who had cardiac arrest in hospital, failed to detect any survival advantage for vasopressin over epinephrine. The American Heart Association recommendations did not take into account the results of Stiell's study which were published in 2001, and have opened an ongoing debate. Vasopressin is not yet recommended by the U.S. Food and Drug Administration as the vasopressor of choice for the treatment of cardiac arrest or vasodilatory shock. In addition, due to insufficient evidence from prospective trials in humans, these recommendations were also not adopted by the European Resuscitation Council, which did not include vasopressin in its recently updated guidelines [37]. Furthermore, accurate data about optimal dosages, administration interval and the effectiveness of vasopressin on rhythms other than refractory ventricular fibrillation are lacking. In addition, no definite recommendation can be made for the use of vasopressin in the pediatric population as no definitive data have been published on its use in pediatric cardiac arrest or vasodilatory shock. In conclusion, vasopressin is recommended as an alternative first-line vasopressor in adults with ventricular fibrillation and out-of-hospital cardiac arrest. However, this recommendation is based on the results of a small-randomized clinical study and two case series [38]. Thus, in the era of "evidenced-based medicine" there are only limited data to support the use of vasopressin on a regular basis. Results of future large randomized double-blind studies are urgently needed before widespread use of vasopressin can be recommended.

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References

1. Brown CG, Martin DR, Pepe PE, et al. A comparison of standard-dose and high-dose epinephrine in cardiac arrest outside the hospital. The Multicenter High-Dose Epinephrine Study Group. *N Engl J Med* 1992;327:1051–5.
2. Woodhouse SP, Cox S, Boyd P, Case C, Weber M. High dose and standard dose adrenaline do not alter survival, compared with placebo, in cardiac arrest. *Resuscitation* 1995;30:243–9.
3. Lindner KH, Strohmenger HU, Ensinger H, Hetzel WD, Ahnefeld FW, Georgieff M. Stress hormone response during and after cardiopulmonary resuscitation. *Anesthesiology* 1992;77:662–8.
4. Lindner KH, Prengel AW, Pfenninger EG, et al. Vasopressin improves vital organ blood flow during closed-chest cardiopulmonary resuscitation in pigs. *Circulation* 1995 91:215–21.
5. Wenzel V, Lindner KH, Prengel AW, et al. Vasopressin improves vital organ blood flow after prolonged cardiac arrest with postcountershock pulseless electrical activity in pigs. *Crit Care Med* 1999;27:486–92.
6. Prengel AW, Lindner KH, Keller A. Cerebral oxygenation during cardiopulmonary resuscitation with epinephrine and vasopressin in pigs. *Stroke* 1996;27:1241–8.
7. Strohmenger HU, Lindner KH, Keller A, Lindner IM, Pfenninger E, Bothner U. Effects of graded doses of vasopressin on median fibrillation frequency in a porcine model of cardiopulmonary resuscitation: results of a prospective, randomized, controlled trial. *Crit Care Med* 1996;24:1360–5.
8. Lindner KH, Prengel AW, Brinkmann A, Strohmenger HU, Lindner IM, Lurie KG. Vasopressin administration in refractory cardiac arrest. *Ann Intern Med* 1996;124:1061–4.

9. Morris DC, Dereczyk BE, Grzybowski M, et al. Vasopressin can increase coronary perfusion pressure during human cardiopulmonary resuscitation. *Acad Emerg Med* 1997;4:878–83.
10. Lindner KH, Dirks B, Strohmenger HU, Prengel AW, Lindner IM, Lurie KG. Randomised comparison of epinephrine and vasopressin in patients with out-of-hospital ventricular fibrillation. *Lancet* 1997;349:535–7.
11. Landry DW, Oliver JA. The pathogenesis of vasodilatory shock. *N Engl J Med* 2001;345:588–95.
12. Umino T, Kusano E, Muto S, et al. AVP inhibits LPS-and IL-1beta-stimulated NO and CGMP via V1 receptor in cultured rat mesangial cells. *Am J Physiol* 1999;276:433–41.
13. Oyama H, Suzuki Y, Satoh S. Role of nitric oxide in the cerebral vasodilatory responses to vasopressin and oxytocin in dogs. *J Cereb Blood Flow Metab* 1993;13:285–90.
14. Evora PR, Pearson PJ, Schaff HV. Arginine vasopressin induces endothelium-dependent vasodilatation of the pulmonary artery. V1-receptor-mediated production of nitric oxide. *Chest* 1993;103:1241–5.
15. Prengel AW, Lindner KH, Keller A, Lurie KG. Cardiovascular function during the postresuscitation phase after cardiac arrest in pigs: a comparison of epinephrine versus vasopressin. *Crit Care Med* 1996;24:2014–19.
16. Prengel AW, Lindner KH, Wenzel V, Tugtekin I, Anhaupl T. Splanchnic and renal blood flow after cardiopulmonary resuscitation with epinephrine and vasopressin in pigs. *Resuscitation* 1998;38:19–24.
17. Voelckel WG, Lindner KH, Wenzel V, et al. Effects of vasopressin and epinephrine on splanchnic blood flow and renal function during and after cardiopulmonary resuscitation in pigs. *Crit Care Med* 2000;28:1083–8.
18. Wenzel V, Lindner KH, Krismer AC, Miller EA, Voelckel WG, Lingnau W. Repeated administration of vasopressin, but not epinephrine, maintains coronary perfusion pressure after early and late administration during prolonged cardiopulmonary resuscitation in pigs. *Circulation* 1999;99:1379–84.
19. Babar SI, Berg RA, Hilwig RW, Kern KB, Ewy GA. Vasopressin versus epinephrine during cardiopulmonary resuscitation: a randomized swine outcome study. *Resuscitation* 1999;41:185–92.
20. Wenzel V, Lindner KH, Krismer AC, et al. Survival with full neurologic recovery and no cerebral pathology after prolonged cardiopulmonary resuscitation with vasopressin in pigs. *J Am Coll Cardiol* 2000;35:527–33.
21. Mulligan KA, McKnite SH, Lindner KH, Lindstrom PJ, Detloff B, Lurie KG. Synergistic effects of vasopressin plus epinephrine during cardiopulmonary resuscitation. *Resuscitation* 1997;35:265–71.
22. Wenzel V, Lindner KH, Augenstein S, Prengel AW, Strohmenger HU. Vasopressin combined with epinephrine decreases cerebral perfusion compared with vasopressin alone during cardiopulmonary resuscitation in pigs. *Stroke* 1998;29:1467–68.
23. Voelckel WG, Lurie KG, McKnite S, et al. Comparison of epinephrine and vasopressin in a pediatric porcine model of asphyxial cardiac arrest. *Crit Care Med* 2000;28:3777–83.
24. Krismer AC, Lindner KH, Kornberger R, et al. Cardiopulmonary resuscitation during severe hypothermia in pigs: does epinephrine or vasopressin increase coronary perfusion pressure? *Anesth Analg* 2000;90:69–73.
25. Krismer AC, Hogan QH, Wenzel V. Cardiac arrest during epidural anesthesia: a comparison between epinephrine and vasopressin in a porcine CPR model [Abstract]. *Circulation* 1999;100(Suppl):I–313.
26. Efrati O, Barak A, Ben Abraham R, et al. Hemodynamic effects of tracheal administration of vasopressin in dogs. *Resuscitation* 2001;50:227–32.
27. Wenzel V, Lindner KH, Augenstein S, et al. Intraosseous vasopressin improves coronary perfusion pressure rapidly during cardiopulmonary resuscitation in pigs. *Crit Care Med* 1999;27:1565–9.
28. Eden E, Teirstein A, Wiener I. Ventricular arrhythmia induced by vasopressin: torsade de pointes related to vasopressin-induced bradycardia. *Mt Sinai J Med* 1983;50:49–51.
29. Foreman BW, Dai XZ, Bache RJ. Vasoconstriction of canine coronary collateral vessels with vasopressin limits blood flow to collateral-dependent myocardium during exercise. *Circ Res* 1991;69:657–64.
30. Stiell IG, Hebert PC, Wells GA, et al. Vasopressin versus epinephrine for inhospital cardiac arrest: a randomised controlled trial. *Lancet* 2001;358:105–9.
31. Rozenzweig EB, Starc TJ, Chen JM, et al. Intravenous arginine-vasopressin in children with vasodilatory shock after cardiac surgery. *Circulation* 1999;100:II182–6.
32. Argenziano M, Chen JM, Choudrhi AF, et al. Management of vasodilatory shock after cardiac surgery: identification of predisposing factors and use of a novel pressor agent. *J Thoracardiovasc Surg* 1998;116:973–80.
33. Landry DW, Levin HR, Gallant EM, et al. Vasopressin deficiency contributes to the vasodilatation of septic shock. *Circulation* 1997;95:1122–5.
34. Holmes CL, Walley KR, Chittock DR, Lehman T, Russell JA. The effects of vasopressin on hemodynamics and renal function in severe septic shock: a case series. *Int Clin Med* 2001;27:1416–21.
35. Argenziano M, Choudhri AF, Oz MC, Rose EA, Smith CR, Landry DW. A prospective randomized trial of arginine vasopressin in the treatment of vasodilatory shock after left ventricular assist device placement. *Circulation* 1997;96(Suppl):II286–90.
36. Anonymous. International consensus on science. American Heart Association: Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2000;102(Suppl):II–I134.
37. European Resuscitation Council Guidelines 2000 for Adult Advanced Life Support. A Statement from the Advanced Life Support Working Group and approved by the Executive Committee of the European Resuscitation Council. *Resuscitation* 2001;48:211–21.
38. Padosch SA, Martin E, Bottiger BW. Vasopressin and epinephrine for cardiac arrest. *Lancet* 2001:358:2082 (Discussion p. 2081).

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Capsule

HIV and needles

A controversial study, led by David Gisselquist, an independent anthropologist from Hershey, PA, USA, suggests that the AIDS pandemic in Africa is caused mainly by reuse of dirty needles in healthcare. This claim disputes the long-held wisdom that sexual transmission is the driving force behind 90% of HIV/AIDS cases.

After analyzing data from the past 20 years, Gisselquist's group estimated that only 25–33% of HIV/AIDS cases resulted from sexual transmission.

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