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CASE REPORT

Occurrence of pulsus alternans during anaesthesia of two dogs and one cat and its treatment

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The authors report the occurrence of *pulsus alternans*, a condition characterised by the alternance of pulses of higher and lower amplitude, in two dogs and one cat under general anaesthesia. The presence of an underlying cardiac disease was confirmed in the cat but not in either dog, which – based on history and clinical findings – had presumably normal cardiovascular function before the anaesthetic. Possible mechanisms, including negative inotropy and haemodynamic and Frank-Starling effects, as well as the role of general anaesthesia as the potential triggering factor, are discussed in this report. Ephedrine resulted in the successful treatment of *pulsus alternans*, as demonstrated by the return of normal pulse and synchronisation of heart and pulse rates in the cat and in one dog. In the other dog, pulse pattern and frequency returned to normal once the guidewire for central line placement was withdrawn.

Keywords anaesthesia; cat; dogs; ephedrine; Pulsus alternans

Abbreviations HR, heart rate; PA, pulsus alternans; SAP, systolic arterial pressure

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Pulsus alternans (*PA*) was first described by Traube in 1872 as a succession of pulses of variable amplitude, characterised by the alternance of higher- and lower-peak systolic pressures that occurs in the presence of regular sinus rhythm and independent of respiratory variations.[1] The condition has been widely described in human patients with primary myocardial disease, congenital and acquired aortic stenosis, pulmonary hypertension and embolism, spinal cord injury and after spinal anaesthesia.[2–10]

Unlike in humans, reports of PA in veterinary clinical patients are scarce and involve anaesthetic agents no longer commonly used in practice. The condition has been described in Cocker Spaniel dogs with dilated cardiomyopathy and in one dog anaesthetised with thiamylal and halothane.[11,12]

To the best of the authors' knowledge, PA has never been reported in cats nor in dogs as a complication of general anaesthesia, performed with modern anaesthetic techniques, in the absence of congestive heart failure.

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The authors report the occurrence of this condition during the anaesthetics of two dogs and one cat and its successful treatment with ephedrine in two cases and with the removal of the intravenous jugular guidewire in one case.

Case report

Case 1

A 7-year-old neutered male German Shepherd weighing 43 kg was referred to the Neurology service of the Queen Mother Hospital for Animals of the Royal Veterinary College for investigation of acute-onset ataxia. The dog had a history of previous hemilaminectomy, performed at the intervertebral space T13/L1 6 months earlier.

On presentation, the dog was bright, alert and responsive, and his body condition score was 7/9. On physical examination, heart rate (HR) was 92 beats/min, respiratory rate was 28 breaths/min, femoral pulse was deemed normal and mucous membranes were pink with a capillary refill time of <2 s; rectal body temperature was 38.3°C. Orthopaedic examination revealed bilateral stifle effusion and a restricted range of movement with pain on extension of the left hip. The findings of the neurological exam were ambulatory paraparesis that was worse on the right pelvic limb and mild lumbar pain upon direct palpation. Pre-anaesthetic bloodwork consisted of serum electrolytes, total solids and packed cell volume, which were within the normal ranges for the species. The dog was anaesthetised for magnetic resonance imaging and, depending on the findings, surgery.

After premedication with IV acepromazine (0.01 mg/kg, Acecare; Animalcare, York, UK) and methadone (0.1 mg/kg, Synthadon; Animalcare, York, UK), general anaesthesia was induced with 4 mg/kg propofol (Propofol-® Lipuro; Virbac, Suffolk, UK) titrated to effect and maintained with sevoflurane (end-tidal concentration: 1.1%–2.4%, Sevoflo; Abbott, Maidenhead, UK) in 100% oxygen, delivered via a circle breathing system connected to a 12-mm internal diameter endotracheal tube. A multiparametric module (Datex Ohmeda S/5; GE Healthcare, Amersham, UK), inclusive of electrocardiography, pulse oximetry, oscillometry for blood pressure measurements with the cuff positioned over the radial artery and capnography with expired gas analyser, was used to monitor cardiorespiratory variables during the anaesthetic. Crystalloids (Hartmann's solution; Fresenius Kabi, Runcorn, UK) were infused at a rate of 5 mL/kg/h.

Magnetic resonance imaging demonstrated the presence of progressive right disc extrusion, resulting in marked spinal cord

compression, at the previous T13/L1 hemilaminectomy site. Other findings were right disc extrusion at L6/L7 and static disc protrusion at L7/S1, both resulting in mild compression of the *cauda equina*. Anaesthesia was continued to allow surgical resection and removal of the extruded nucleus pulposus at T13/L1. A ketamine (Ketamidor; Chanelle Medical, Hungerford, UK) infusion (0.01 mg/kg/min) was initiated, with a 0.2 mg/kg IV loading dose, to provide intraoperative analgesia; additionally, methadone (0.2 mg/kg IV) was repeated every 2 h until the end of surgery.

Two hours into the anaesthetic and 10 min after the beginning of surgery, the dog developed PA, as detected by pulse oximetry (see Figure 1) and confirmed by both direct femoral pulse assessment and application of the Doppler probe (Model 811; Parks Medical, NV, USA) over the palmar metacarpal artery, which revealed audible pulse sounds of alternating degrees of intensity. This was in conjunction with transient sinus tachycardia (HR: 138 beats/min, increased from 100 beats/min), which had occurred immediately after surgical incision and was interpreted as an autonomic response to nociception. Pulse rate as detected by pulse oximetry, which counted only one of every two consecutive pulse waves, was 68 pulses/min; systolic arterial pressure (SAP) was 117 mmHg, with mean and diastolic arterial pressures of 95 and 70 mmHg, respectively. Initially, a lidocaine bolus (2 mg/kg IV) was given to reduce the tachycardia, followed by a lidocaine infusion (30 µg/kg/min). This lead to no change, so 30 min later, it was followed by a supplemental methadone dose (0.2 mg/kg IV), with the assumption that an autonomic response to nociception could have triggered both the increase in HR and change in pulse pattern; additionally, IV lidocaine (1.5 mg/kg) was repeated 5 min later to prevent the tachyarrhythmia from worsening. As the pulse pattern remained unchanged, a bolus of ephedrine (0.1 mg/kg, ephedrine hydrochloride; Hameln Pharmaceuticals, Gloucester, UK) was administered IV and resulted, within 5 min, in increased pulse rate, as detected by pulse oximetry, from 55 to 125 and synchronization of pulse and HRs (see Figure 1). This effect lasted for approximately 1 h, after which, in the presence of normal HR ranging from 110 to 115 beats/min, PA reoccurred twice, at 60-min intervals, and was successfully treated with IV ephedrine (0.1 mg/kg) on both occasions. Repeated doses of ephedrine showed some degree of tachyphylaxis, with the increase of HR becoming less prominent after each dose, although pulse rate increased to match HR after each dose. After the surgery, the dog recovered from anaesthesia. Close monitoring of the cardiovascular function in the early recovery period (2 h from tracheal extubation) consisted of continuous electrocardiography, intermittent measurement of blood pressure with oscillometry and frequent assessment of femoral pulse. No abnormalities were detected. The dog's owner declined cardiologic consultation and further diagnostics.

Case 2

A 15.7-year-old neutered female domestic short-hair cat weighing 2.6 kg was referred to the Surgery Service of the Queen Mother Hospital for Animals of the Royal Veterinary College for investigation of a left-sided adrenal mass, identified through abdominal ultrasonography and suspected to be causing hyperaldosteronism (aldosterone plasma level > 5000 pmol/L; reference interval: 160–700 pmol/L), lethargy and weakness. Before referral, the cat had been treated with oral spironolactone (5 mg *q* 12 h, Prilactone tablets 10 mg; Ceva Animal Health, Amersham, UK), oral potassium supplementation (4 mL *q* 12 h, Kaminox liquid; VetPlus, Lancashire, UK) to address hypokalaemia (2.6 mmol/L; reference interval: 3.8–5.5 mmol/L) and intravenous crystalloids (Hartmann's solution) at the rate of 4 mL/kg/h. The latter was discontinued by the primary care clinician after approximately 4 h owing to the development of pulmonary crackles, detected by chest auscultation, that resolved spontaneously without pharmacological treatment.

On admission to the referral hospital, physical examination revealed pale mucous membranes with capillary refill time >2 s, HR of 200 beats/min, respiratory rate of 32 breaths/min and rectal temperature of 37.2°C. Chest auscultation revealed the presence of a grade 3/6 systolic heart murmur; SAP, measured with a Doppler with the probe over the palmar metacarpal artery and the inflatable cuff over the radial artery, was 160 mmHg, and pulse and HRs were the same. Blood biochemistry revealed increased serum creatinine concentration (209 µmol/L; reference interval: 74.5–185.3 µmol/L) and electrolyte values within normal limits; haematology was unremarkable. Ultrasonographic examination of the heart revealed the presence of mild hypertrophic cardiomyopathy, characterised by left ventricular hypertrophy with no signs of atrial enlargement and a mild increase in right ventricular outflow tract velocity (1.84 m/s), compatible with dynamic right ventricular outflow tract obstruction. Computerised tomography confirmed the presence of an 18 mm-diameter left adrenal gland mass, located ventral to the aorta and slightly impinging on the caudal vena cava, with a distinct margin and displaying uniform mild enhancement post-contrast. Except for a marginally enlarged gastric lymph node (diameter 0.7 cm), no signs of thoracic and abdominal metastatic disease were found.

The cat was anaesthetised for surgical mass removal. After premedication with IV methadone (0.2 mg/kg), general anaesthesia was induced with 5 mg/kg of alfaxalone IV (Alfaxan; Jurox Ltd, Crawley, UK). The trachea was intubated with a cuffed 3 mm internal diameter endotracheal tube, connected to an Ayre's T-piece paediatric breathing system to deliver sevoflurane (end-tidal concentration: 0.8%–2%) in 100% oxygen. A fentanyl (Fentadon; Dechra, Shrewsbury, UK) infusion (0.1–0.2 µg/kg/min) was initiated, with a 2 µg/kg IV loading dose, before the beginning of surgery to provide analgesia. Monitoring consisted of continuous electrocardiography, capnography, pulse oximetry, expiratory gases analysis, oesophageal temperature and intermittent SAP measurement with a Doppler probe via palmar metatarsal artery (every 5 min). A variable rate of dopamine (Dopamine; Hameln Pharmaceuticals, Gloucester, UK) infusion (2.5–10 µg/kg/min) was used to support cardiovascular function during anaesthesia. Mechanical ventilation on pressure-controlled mode (set at 10 cmH_2O) was used to maintain normocapnia (end-tidal CO_2: 35–45 mmHg) from the beginning of the anaesthetic; crystalloids (Hartmann's solution) were infused at a variable rate of 2–5 mL/kg/h. It was not possible to tell if there was plethysmographic variability from the pulse trace achieved.

Two hours into the anaesthetic, the cat developed PA, detected by both the pulse oximeter, which showed the alternance of strong and weak pulsations, and the Doppler, which revealed audible pulse sounds of lower intensity on every second beat. This finding was

confirmed by changing the position of the pulse oximetry probe (from the tongue to the auricular pinna and then on the other side of the tongue) and by assessing the femoral pulse. The PA did not resolve after discontinuation of mechanical ventilation. HR was 150 beats/min and had been variable until then (110–180 beats/min). Pulse rate as recorded by the pulse oximeter was 75 pulses/min as only one pulse wave for every two was detected, and SAP was 55 mmHg. Electrocardiography showed a sinus rhythm. A bolus of crystalloids (Hartmann's solution, 5 mL/kg) was administered IV to treat hypotension but failed to improve SAP values. Dopamine infusion was increased incrementally over 20 min from 2.5 to 7.5 µg/kg/min with no appreciable result. As a tentative treatment, 0.1 mg/kg of ephedrine was administered IV and resulted, within 5 min of administration, in increased SAP to 100 mmHg and normal pulse waves synchronous with the heart beats that had also increased from 150 to 180 bpm. The effect of ephedrine lasted 20 min, after which PA and hypotension reoccurred. As a result, ephedrine was readministered at the same dose twice, at 20 min intervals, until the end of the anaesthetic and successfully converted PA. Each dose of ephedrine lead to the conversion of PA and improvement of blood pressure, although some degree of tachyphylaxis was seen, with HR increasing by smaller amounts after each dose.

Recovery from anaesthesia was smooth and uneventful. The cat was transferred to the intensive care unit of the hospital where cardiovascular function was monitored, via electrocardiography and intermittent blood pressure measurement (Doppler), for the first 12 h after extubation of the trachea. PA did not reoccur. Microscopic diagnosis of the mass after removal indicated that it was an adrenocortical adenoma.

Case 3

A 5.4-year-old neutered female Greyhound weighing 21.5 kg was referred to the Surgery Service at the Royal Veterinary College for management of chylothorax after initially presenting to the Emergency Service of the same institution for acute-onset dyspnoea. After intermittent thoracentesis over the initial few days, the dog was treated with rutin (Rutin tablets, Holland and Barrett, Nuneaton, UK) for a week before surgery was planned and was deemed clinically stable at the time of surgery.

Pre-anaesthetic examination revealed pink mucous membranes with a capillary refill time of < 2 s, an HR of 120 beats/min, a respiratory rate of 24 breaths/min and a rectal temperature of 38.3°C. Chest auscultation revealed no cardiac murmur or abnormal pulmonary sounds. Abdominal palpation was unremarkable. Pulses were of good quality and synchronous with the heart. Preoperative packed cell volume, total solids and venous electrolyte concentrations were all unremarkable. The dog was anaesthetised for right lateral intercostal thoracotomy and laparotomy to perform thoracic duct ligation and subtotal pericardiectomy.

The dog was premedicated with methadone (0.2 mg/kg IV) before being anaesthetised with midazolam (0.3 mg/kg IV, Midazolam; Hameln Pharmaceuticals, Gloucester, UK) and propofol (3.9 mg/kg IV). The trachea was intubated with a 10.5 mm internal diameter cuffed endotracheal tube, connected to a circle breathing system to deliver sevoflurane (end-tidal concentration: 1.2–2.2) in 100% oxygen. Monitoring consisted of continuous electrocardiography, capnography, pulse oximetry, expiratory gases analysis and oscillometry for blood pressure monitoring, with the cuff placed over the radial artery.

During surgical preparation, the dog was placed in dorsal recumbency. At this point, a 7.5 Fr, 20 cm catheter was placed into the right jugular vein in a sterile fashion via the Seldinger technique. Before wire placement, HR was 122 beats/min; pulse rhythm, pattern and frequency, as shown by plethysmography, were unremarkable; and SAP was 102 mmHg with mean and diastolic arterial pressures of 75 and 60 mmHg, respectively. As the wire was passed through the IV catheter, the HR read from the electrocardiogram increased to 147 beats/min and showed a pattern of sinus tachycardia, whereas the pulse rate reduced to 75 beats/min. At this time, SAP, mean arterial pressure and diastolic arterial pressure were 78, 69 and 59 mmHg, respectively. The waveform of the plethysmogram also changed to a pattern consistent with PA. Within 1 min, the

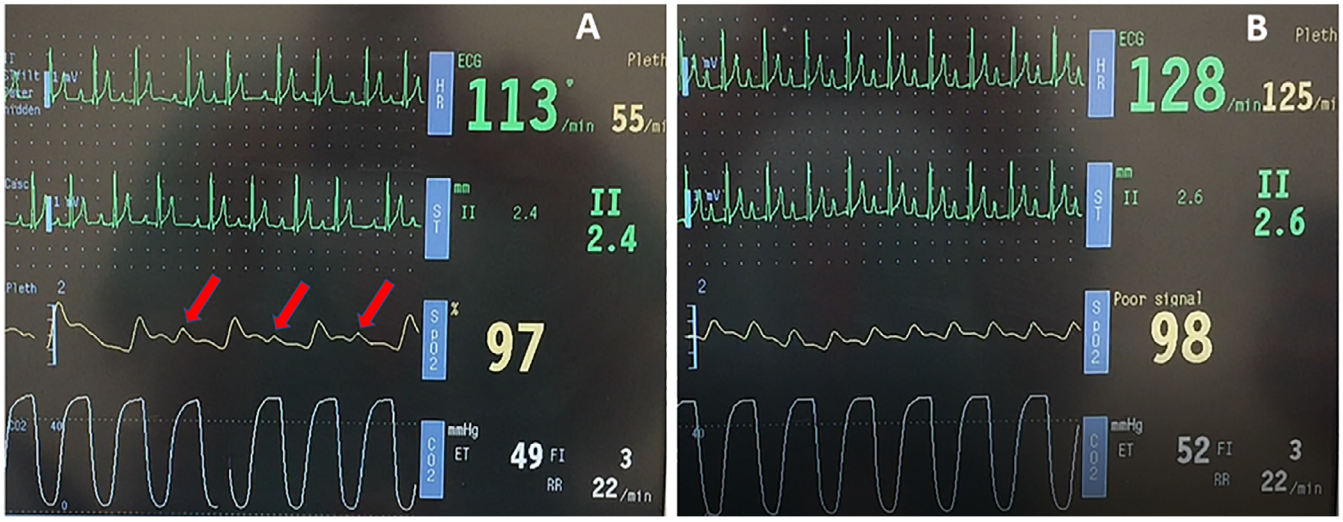

Figure 1. **Pulsus alternance (A) in a dog undergoing spinal surgery under isoflurane anaesthesia, successfully treated with ephedrine administration (B).**

guidewire was withdrawn after passage of the central line. Over the following 10 min, PA resolved as seen on the plethysmogram, and HR reduced to 127 with matching pulse rate; SAP, mean arterial pressure and diastolic arterial pressure measured at this point were 95, 85 and 65 mmHg, respectively. Anaesthetic depth was deemed adequate throughout central line placement and so was not considered to be a cause of tachycardia.

After this event, the rest of the anaesthesia went smoothly with successful thoracic duct ligation and subtotal pericardiectomy. A noradrenaline infusion (0.1–0.3 μg/kg/min) was used for blood pressure support during pericardiectomy due to hypotension during surgical manipulation of the heart. The patient recovered unremarkably after surgery and was discharged from the hospital a few days later.

Discussion

PA may have occurred in the two dogs and cat of this report with different mechanisms.

It is hypothesised that in the dogs, a primary haemodynamic event, namely the sinus tachycardia that occurred in response to surgical nociception in Case 1, and to guidewire placement in Case 3, caused PA.[13] Supraventricular tachycardia has been described to induce PA through a Frank-Starling mechanism, by causing ineffective or reduced ventricular diastolic filling. It is possible that this may lead to an effective filling volume not being reached in every heartbeat. Therefore, an effective volume and pulse is reached in varying intervals, such as every second beat.[14,15] The Frank-Starling mechanism is an intrinsic property of the myocardium, consisting of a relationship between end-diastolic volume, and therefore the degree of stretch of myocardium fibres, and the intensity of the contractile force developed by the heart, which in turn affects both stroke volume and peripheral pulse amplitude.[16] Undetected hypovolaemia could have acted synergistically with tachycardia to evoke a Frank-Starling mechanism in this dog. In support of this hypothesis, experimentally induced decreased venous return to the heart, with resulting relative hypovolemia, produced decreased stroke volume and pulse filling in a canine model.[15] Although, based on history and clinical findings, absolute hypovolemia was not suspected in either dog before anaesthesia, relative hypovolaemia could have occurred during the anaesthetic as a result of volatile agent-driven vasodilation.

Although unlikely, the underlying neurological condition might have acted as a triggering or predisposing factor to PA in Case 1 by causing changes in intravascular volume distribution. Blood volume depletion occurs in some human patients with paraplegia and has been associated with decreased cardiac output and SAP.[17] However, the first dog of this report was paraparetic but not paraplegic. Moreover, the location of the spinal cord compression was too caudal to affect the cardiac sympathetic innervation that, in dogs as in other mammals, arises from the stellate and cervical ganglions, which originate in the first six segments (T1–T6) of the thoracic spinal cord.[18]

Another possible triggering factor in this patient could be the presence of an underlying cardiac condition or, alternatively, of age-related cardiovascular changes. In German Shepherds, aging has been associated with decreased cardiac output and diastolic function.[19] Although the dog had no history of cardiac disease, and both chest auscultation and clinical assessment of cardiovascular parameters were unremarkable, as further diagnostics was declined by the owner, an abnormal cardiovascular function cannot be completely ruled out.

A perturbance of inotropy, as a proposed mechanism for PA in human patients with primary myocardial disease, could have occurred in the cat that had been previously diagnosed with hypertrophic cardiomyopathy.[13] The intrinsic defect in contractility may have resulted from either generalised alteration in contractile force or uneven beat-to-beat recruitment of different cardiac fibres or both.[13] However, in this patient, the increase in HR could have also acted as triggering or contributing factor. Although the HR had been highly variable for the first 2 h of the anaesthetic, when PA occurred in the cat, the HR had been consistently in the higher range (160–180 beats/min) for 20 min and was maintained that high for the remaining duration of anaesthesia, during which PA reoccurred twice.

Another common denominator of the three cases of this report is general anaesthesia, which could have contributed to PA through profound cardiovascular depression, characterised by decreased myocardial contractility and vasodilation. Anaesthetic agents that have been implicated in the occurrence of PA in humans and dogs are thiamylal, pentobarbital, thiopental, cyclopropane and halothane.[12, 20, 21] Usually, general anaesthesia is regarded as a triggering factor for PA in patients with underlying left ventricular dysfunction, although PA was also reported in healthy humans undergoing orthopaedic surgery under halothane anaesthesia.[21] In the dogs and cat of this report, a modern anaesthetic approach was used, and all the agents administered are known to cause considerably less cardiovascular depression than halothane and barbiturates in mammals.[22,23] It is therefore likely that, in these three patients, general anaesthesia acted as a triggering factor rather than as primary determinant of PA. General anaesthesia may have led to cardiovascular depression via multiple mechanisms, including volatile agent-driven vasodilation and reduction in myocardial contractility. Volatile agents have been shown to cause inhibition of the L-type calcium channels, resulting in decreased inotropy and relaxation of the vascular muscle layer.[24]

In Cases 1 and 2, ephedrine successfully caused conversion of PA to normal pulse, as well as synchronisation of pulse and HRs as detected by pulse oximetry and electrocardiography. Ephedrine is a sympathomimetic amine, the effects of which are mediated through the α- and β-adrenergic receptors. Sympathetic activation is elicited by direct interaction with these receptors, as well as by the stimulated release of endogenous catecholamines, including noradrenaline. Besides a direct effect of noradrenaline on β-1 receptors in the myocardium, the stimulation of venous α-1 receptors results in venoconstriction and increased venous return to the heart, whereas activation of arterial α-1 receptors often evokes a baroreceptor reflex, thus decreasing the HR.[25,26] In dogs anaesthetised with isoflurane, ephedrine increased both cardiac index and stroke volume index, which resulted in a transient increase in mean arterial pressure.[27] These combined effects of ephedrine and noradrenaline could have reversed PA through both a positive inotropic effect and a haemodynamic effect – via increased venous return, presumably associated with improved ventricular filling.

Surprisingly, both a fluid bolus and incremental doses of dopamine failed to treat PA in the cat. Fluid therapy was approached conservatively in this patient due to the concern of cardiac overload, and it is

possible that higher volumes could have restored normal pulse. Regarding dopamine, one reason for its inefficacy could be that, despite it producing dual α- and β-adrenergic activation at intermediate (5–10 μg/kg/min) and high dosages (>10 μg/kg/min), respectively, in humans, dopamine-induced venoconstriction is 5–20 times less intense than that of noradrenaline.[28,29] This could have accounted for a less significant augmentation of venous return and diastolic ventricular filling.

In Case 3, the occurrence of PA directly corresponded with the placement of the guidewire through the right jugular vein. It is theorised that the placement of the wire may have both stimulated the right atrium physically, inducing tachycardia, and caused a partial occlusion in the cranial vena cava, reducing venous return to the heart. As the wire was removed, the sinus tachycardia resolved, as did the PA, indicating that tachycardia may have played a significant role. In this case, it is possible that PA was solely a response to wire placement; however, it is also possible that the cardiovascular depression caused by general anaesthesia previously described may have acted as a trigger factor to make this patient more susceptible to PA during wire placement.

Conclusion

PA occurred as a complication of general anaesthesia in two dogs with presumably normal cardiovascular function and in one cat with confirmed mild cardiac disease. Ephedrine administration was successful in treating the condition in two cases, possibly as a result of combined haemodynamic and inotropic positive effects. In the third case, removal of a central line guidewire from the right jugular vein led to the resolution to normal cardiovascular status.

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