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Paroxysmal cough injury, vascular rupture and 'shaken baby syndrome'

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Summary It is widely assumed that subdural and retinal haemorrhage in infants can only result from traumatic rupture of vulnerable blood vessels. An alternative aetiology, that of vascular rupture resulting from excessive intraluminal pressure, is presented in three disease conditions.

(1) Perlman et al., studying premature neonates requiring mechanical ventilation for respiratory distress syndrome, observed ''cough-like'' fluctuations in oesophageal pressure greater than 18 cms H_2O, whose timing matched fluctuations in anterior cerebral artery flow. When 14 out of 24 neonates were paralysed (to prevent abdominal muscle activity) intraventricular haemorrhage developed in all 10 controls but in only one of the paralysed group during paralysis.

(2) New analysis of pressure data extracted from a previous study of prolonged expiratory apnoea showed alveolar collapse induced 100 mmHg intrathoracic cough pressure surges. Superior vena cava pressures up to 50 mmHg were implied, and radial artery systolic pressures over 180 mmHg recorded.

(3) Bordetella pertussis bacteria attach to cilia in the airways, but do not invade the underlying tissue. The irritation causes the powerful coughing paroxysms of whooping cough. Brain haemorrhages and retinal detachment have been observed to result from the high intravascular pressures produced.

The data suggest that any source of intense airway irritation not easily removed (laryngeal infection, inhalation of regurgitated feed, fluff, smoke, etc.) could induce similar bleeding, a paroxysmal cough injury (PCI). Additional objective evidence of inflicted trauma is necessary to distinguish between 'shaken baby syndrome' and PCI.

Introduction

To be effective a cough needs to produce maximum air flow velocity. This is achieved by abdominal muscles contracting suddenly and strongly while airways are temporarily narrowed. Lumb [1], referring to adults, writes ''Transient pressures of up to 40 kPa (300 mmHg) may occur in the thorax, arterial blood and the cerebrospinal fluid during the act of coughing''. The positive pressure produced spreads throughout the thoraco-abdominal cavity (TAC) similarly to that in a tube of toothpaste,

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and is superimposed on all tissues and vasculature within the TAC. This elevation of Superior vena cava (SVC) root pressure will produce a brief reverse flow in all tributary veins that do not have valves, or whose valves cannot withstand the pressure. The resultant flow out of the TAC into the head and limbs will leave veins inside the TAC excessively drained. The cough pressure pulse does not affect transmural pressure of organs enclosed by the TAC, so venous outflow from organs holding reserves (liver, lungs, etc.) will increase to replace that lost to the periphery. The result is increased circulating blood volume and hence raised vascular pressure. Valsalva studies indicate that restoration of normal distribution then takes about 15 s in the normal adult [2,3]. The normal cough is brief so the venous volume increase is small. However if another cough occurs within this period its contribution is added. If a rapid train of coughs occurs within this time, a paroxysm, the resultant pumping action may produce a considerable increase in venous volume, and hence pressure. Evidence from three situations, that this sequence of events can result in nasal, retinal and cerebral haemorrhages is the subject of this paper.

Perlman et al. [4] studied blood flow in the anterior cerebral artery of premature infants requiring mechanical ventilation for respiratory distress syndrome (RDS) at 12 h of age. Intraventricular haemorrhage developed in 21 out of 23 infants with a fluctuating flow pattern, but in only 7 out of 27 with a stable pattern. In a follow-up study [5] of 24 infants with the fluctuating pattern, 10 were given normal ventilator support and 14 additionally underwent muscle paralysis to prevent abdominal muscle expiratory efforts. Intraventricular haemorrhage developed in all the control group but only in 5 of the paralysed group, and of those only one developed haemorrhages during paralysis. They show swings of oesophageal pressure exceeding the range of their recording equipment but at least 18 cm H_2O (13 mmHg) [6]. Changes in blood pressure followed oesophageal events with 0.05—0.25 s latency. They state that the largest fluctuation of blood pressure accompanied ''cough-like'' fluctuations in oesophageal pressure.

Prolonged expiratory apnoea (PEA) [7,8] is associated with the period of newly forming alveoli, principally in the first year of life from about one month of age. It involves very rapidly developing severe hypoxia associated with apnoea, typically for 20—30 s, usually terminating in very powerful inspiratory gasps. (Southall et al. [9] gives a detailed account of the hypothetical mechanisms in the lung and in the brain stem which lead to the development of apnoea.) During apnoea there is usually mild expiratory pressure, but coughs induced by irritant receptors excited by parenchymal distortion superimpose brief powerful expiratory efforts. Some of the chart recordings from our earlier PEA studies contain systemic and pulmonary artery pressure traces. These were extracted and re-analysed for comparison with those in Perlman's neonatal studies.

Methods

Techniques used in the PEA study from which the data for this study were extracted were:

1. Dynamic, beat to beat, estimates of blood oxygen saturation, obtained transcutaneously from a pulse oximeter (Nellcor N100 or N200).
2. Systemic arterial pressure, obtained from a radial artery line.
3. Pulmonary artery pressure, taken from an indwelling Swann Gantz catheter.
4. Diaphragmatic activity, detected by a simple pressure-sensitive capsule stuck to the skin near the chest/abdomen boundary, where diaphragmatic movements exerted a varying pressure on it.

These are described in [7,8].

Results

Fig. 1 shows features associated with a PEA event. Radial artery pressure (b) represents extra-thoracic arterial pressures, limbs head etc. Pulmonary artery pressure (c) is the sum of intravascular pressure and any superimposed intrathoracic pressure, e.g., diaphragmatic inspiratory pressure excursions prior to 0 s. When normal respiration ceased, at 0 s, systemic diastolic pressure (b) started to rise, consistent with blood being pressed out of the lung vascular bed by the expiratory effort associated with apnoea in this condition. This was then restrained by a bradycardic response. Pulmonary artery pressure (c) also rose, regardless of the bradycardia, consistent with increasing pulmonary flow resistance resulting from progressive alveolar collapse, until it went off-scale at about 50 s. Then, at about 63 s a powerful diaphragmatic inspiratory effort was made (d). This seems to have ''unstuck'' many of the collapsed regions, and pulmonary artery pressure rapidly returned to near normal by 70 s. The blood oxygen trace: (a) shows

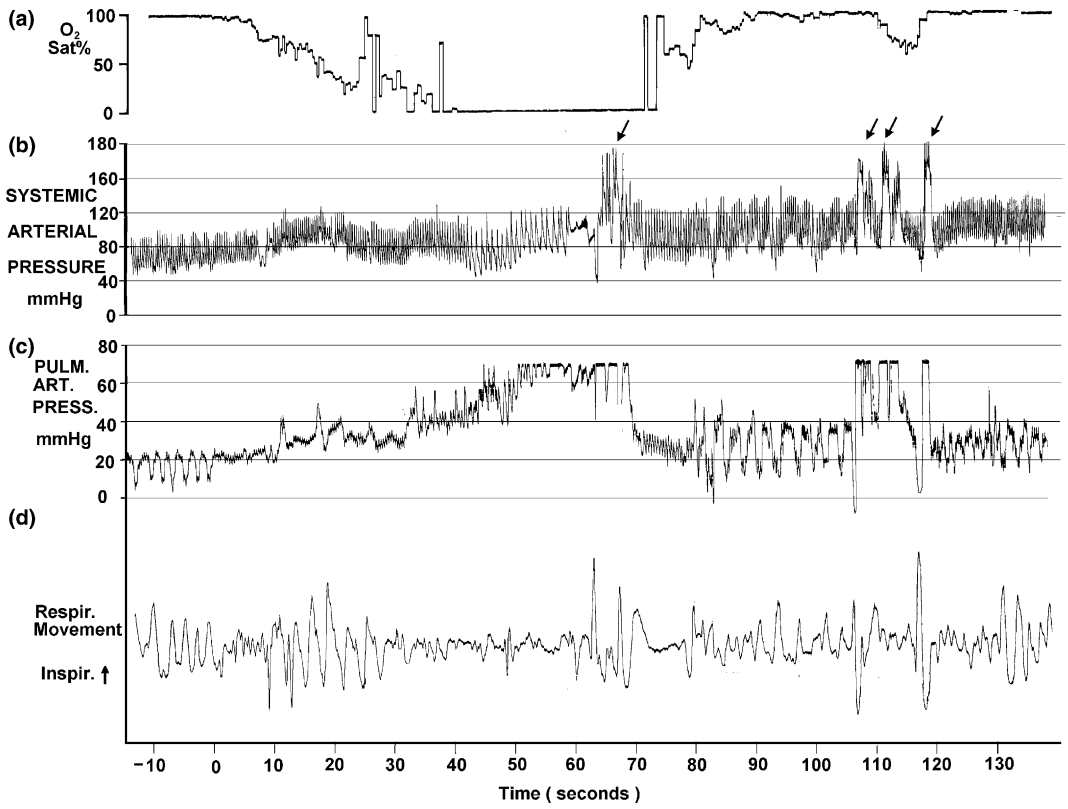

Figure 1 Vascular factors during a PEA event. (a) Transcutaneous blood oxygen, (b) radial artery pressure, (c) pulmonary artery pressure, Diaphragmatic activity (capsule) (d). Girl aged 2.5 years. This child later died, aged 3.6 years, during a similar attack despite ventillation through a tracheostomy, started 20 s after cyanosis [8].

that not all collapsed regions were fully opened and when more normal breathing resumed (80—107 s), it required double the pre-apnoeic inspiratory pressure excursion (c), and pulmonary artery pressure was still raised. Pulmonary C-fibres [10] in the remaining congested areas are believed to be the cause of the coughs (transient positive pressures on both pulmonary and systemic traces, arrows), which interrupted breathing at (107—120) s. This section is shown plotted to a faster time scale in Fig. 2.

Coughs at t1 and t4 are co-ordinated with diaphragmatic activity to produce true coughs (with initial inspiration), those at t2 and t3 are the more primitive purely abdominal expiratory reflexes which are not preceeded by brief inspirations [11] and so do not appear on the capsule trace positioned to detect diaphragmatic effort. These pressure surges add to left ventricular output pressure. At t4 arm artery diastolic pressure rose by over 100 mmHg, during abdominal muscle contraction.

Venous pressures were not directly observed, but the additional pressure can be estimated from the average cough pressure. In the cough sequence (107—120 s), cough pressure was present for 6.5 s out of 12. This would have produced an average increment of roughly 50 mmHg on SVC mean pressure (say 55 mmHg total), driving blood into the head and arm venous beds. The total systolic artery pressure during coughs was about 180 mmHg (b).

Discussion

Pertussis as a ''natural experiment''

Both Perlman's and our studies involved infants in whom some form of surfactant defect was suspected. Whooping cough provides a natural experiment in which, until infection occurs, lungs are normal. The irritation causing the coughing results from the bacterium *Bordetella pertussis* which adheres to ciliated epithelial cells in the respiratory tract, but is not invasive. It disables the cilia, and mucus collects and forms plugs, which can only be removed by forced air flow [12]. Since immunisation was introduced in the 1940s severe cases are rarely seen, but excellent clinical descriptions can

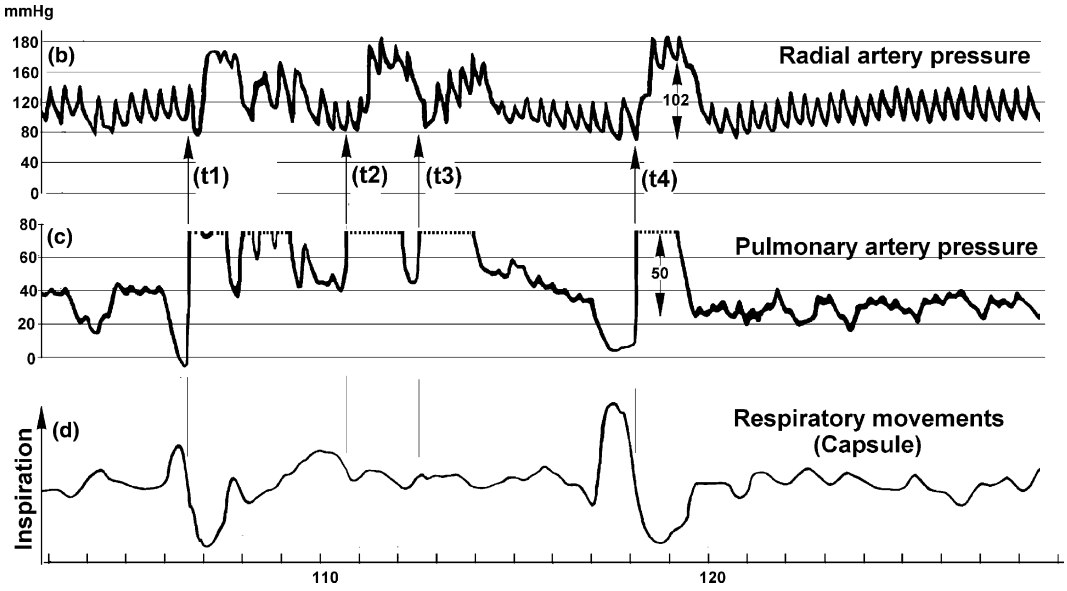

Figure 2 Time expanded version of events from 103 to 129 s. In Fig. 1 the surge pressures in pulmonary and radial arteries appear to be synchronous, but replotting on a faster time scale reveals that pulmonary pressure surge precedes that in the radial artery by about one heart beat The dotted lines across the top of the pulmonary artery pressure trace indicate that pressure above these lines exceeded the range of the recording equipment. Compare [6, Figs 2 and 4].

be found in the literature. Morse et al. [13] described the paroxysms as: ''In a typical paroxysm there is a series of 15—20 short coughs of increasing intensity, and then with a deep inspiration air is drawn into the lungs, making the 'whoop'. A tenacious plug is usually expelled,...Paroxysms...are accompanied by signs of increased venous pressure. The conjunctivae are deeply engorged; there is periorbital edema; and petechial haemorrhages, particularly about the forehead as well as epistaxis are common. During the attack the infant may be cyanotic until the crowing whoop occurs...Central nervous system changes can result from cerebral anoxia or haemorrhages consequent to the elevated venous pressure''. McKendrick and Scott [14] describes complications as occurring solely in the paroxysmal stage as a result of increased pressure in the thorax, abdomen or skull. They appear during or immediately following a severe spasm. Bleeding may occur from any surface or into the brain, but the commonest results of rupture of blood vessels are epistaxis (nasal bleeding), subconjunctival haemorrhage, petechiae in the skin over the neck and upper chest. Haemoptysis, retinal detachment, and bleeding from the ears have all occurred''. He also draws attention to the associated apnoeic aspects: ''Apnoeic attacks are extremely dangerous spasms which are limited to infants under one year, most occurring in those under six months of age... Following a spasm, or succession of spasms, the infant becomes increasingly distressed; he fails to take a deep post-tussic inspiration, becoming ashen grey or deeply cyanosed. He goes limp, loses consciousness, and may be convulsed and die, or, following a few feeble inspiratory efforts, spontaneous respiration may slowly start again and his colour return''.

Mechanics of damage

All three conditions (respiratory distress syndrome, prolonged expiratory apnoea and whooping cough) have in common repetitive high intrathoracic, and hence intracranial venous and capillary pressure, which is independent of the cause of the cough. The same consequences could be anticipated from any other cause (for example, laryngeal infection, milk in the trachea, inhalation of fluff) that leads to extended paroxysms of coughing.

So what are the damage mechanisms and how would they be expected to arise? Our PEA study showed the presence of exceptionally high arterial pressures, and all three disorders evidenced raised venous pressures caused by paroxysmal coughing. Starting with venous pressure hazards, the pulmonary artery pressure traces in Figs. 1 and 2 show superimposed pressure surges greater than 100 mmHg, with a 1:1 mark/space ratio, implying that SVC mean pressures may exceed 50 mmHg. These will be superimposed on all organs within the thorax and abdomen, driving blood out to all venous

beds outside the body cavity. No rupture pressure data has been found for brain capillaries, but West et al. [15], studying pulmonary capillaries in anaesthetised rabbits, found that they ruptured above 40 mmHg. Capillaries deep in the brain will obtain some level of support from their neighbours, but those at the brain surface will not. It would therefore be expected that the brain surface would be the first to show damage, and that some extravased blood would accumulate in fissures, consistent with the ''film of blood'' phenomenon mentioned by Geddes et al. [16] Similarly, retinal and nasal haemorrhages would be expected from the excessive transmural pressures to which their vessels are subjected. The eye and olfactory apparatus are outgrowths of the brain and derive their blood supply from intracranial arteries and veins. The major branch of the ophthalmic artery passes through the cerebrospinal fluid-filled space, emerging in the middle of the optic disc as the central retinal artery [17]. Its ethmoidal branches supply the nasal cavity. Returning venous blood then has to be at a high enough pressure to hold veins open against cerebrospinal fluid pressure So the eye and nasal vessel lumina are subject to any excess intracranial pressure, but their walls are surrounded by virtually atmospheric pressure. Their transmural pressures are actually greater than those of vessels inside the skull which are surrounded by the raised cerebrospinal fluid pressure.

Another important effect suggested by observations in children with whooping cough is the petechial bleeding seen on the neck and ''collar'' region of the upper thorax. These are areas usually draining into the anterior and external jugular veins through short veins. Demonstration of the filling of these veins in response to raised intrathoracic pressure is readily demonstrated by expiration against a closed glottis (Valsalva manoeuvre). These skin areas will reach disruptive pressures sooner than lower areas draining into brachiocephalic and other veins through longer veins. Such petechiae must not be mistaken for inflicted injuries.

Turning now to arterial pressures transients, the brain has a very efficient pressure regulation system in which arterioles also regulate flow to match oxygen delivery to local demand [18] against changes in arterial pressure. They primarily react to local hypoxic metabolites, and take 3—7 s to respond [18]. In hypoxia produced by the coughing, arterioles will be fairly well dilated. For several coughs they will remain dilated, allowing the full arterial pressure to be applied directly to the capillaries. Moreover, there is a limit to the pressure they can withstand, around 200 mmHg in the adult. At excessive pressures arterioles get distended locally, producing a ''string of sausages'' appearance [18]. They then take several hours to recover their normal function, during which time capillaries will be less protected. Systolic pressures of 180 mmHg seen in the figures appear dangerously close to this forced distension limit. In chronic hypertension cerebral vessels are known to be able to withstand much higher pressures than expected [18]. The children in our PEA study were self-selected to some extent, because they had survived frequently enough to have been referred for this condition. Some form of such adaption may have developed enabling them to survive, whereas others may have died at the first attack.

Conclusions

Geddes et al. [16] discussed the fact that subdural haemorrhages similar to those associated with ''shaken baby syndrome'' occur in a number of conditions in which mechanical stress is not a factor. Their study led them to propose a hypothesis which they believed would explain subdural and retinal bleeding in infants in both traumatic and non-traumatic situations: ''...three factors, cerebral venous hypertension and congestion, arterial hypertension and brain swelling, coupled with immaturity and hypoxia-related vascular fragility, provide an alternative physiological scenario for the characteristic subdural bleed of the 'shaken baby syndrome'.'' Though derived from hydromechanical considerations PCI seems to closely match these criteria derived from pathological observations. Venous and arterial hypertension factors match and hypoxia and apnoea are well documented in the case of *Bordetella* triggered coughing paroxysms [12—14]. Additional objective evidence of inflicted trauma is necessary to distinguish between 'shaken baby syndrome' and PCI.

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