Anoxic asphyxia – a cause of industrial fatalities: a review

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Summary

The investigation of commercial diving accidents has indicated that the danger of anoxia, from the inhalation of gases not containing oxygen, is not fully recognized. The problem is more common in a variety of general industrial situations and is an occasional cause of death in anaesthesia. It is a particular hazard with inert gases, which, because they are recognized to be non-toxic, give a false sense of security. The pathological findings consist of pulmonary oedema and petechial haemorrhages, mainly in the brain, lungs and myocardium. Whenever possible, a minimum oxygen content should be included in all gases liable to be respired, but where this is not possible, oxygen analysers and alarms should be provided. Where a general hazard exists, personnel must be warned of the danger.

Introduction

Anoxic asphyxia is still a significant problem in a variety of situations in general industry. Deaths have occurred in welding operations when argon or carbon dioxide are used to shield the weld to exclude oxygen and prevent oxidation of the metals at the high temperatures employed. Argon being much heavier than air is not readily dispersed, and tends to form pockets in confined spaces where the ventilation is poor and layers upwards from the floor. A worker bending down to retrieve a tool may take a breath of nearly pure argon and is then likely to fall down into the zone of high concentration[1]. Nitrogen is often used to 'inert' atmospheres when there is a risk of explosion, as, for example, in oil tankers after the discharge of the cargo. Deaths have resulted from inadvertent entry into the tanks. Liquid nitrogen is used to freeze liquids in pipes, allowing damaged sections to be replaced without the necessity for the pipe to be drained. As the evaporated gas is very cold and denser than air, it also tends to lie in pockets, where again workers risk being overcome by anoxia[2]. Oxygen-deficient atmospheres may be created when the oxygen is removed from air trapped in an enclosed space by oxidative processes, as with corrosion in a caisson or even the hold of a barge loaded with pig iron[3]. Several deaths have also occurred in slurry pits and sewers due to the accumulation of methane.

Anoxic asphyxia has been a significant problem in commercial diving and our investigations have revealed at least 14 deaths world-wide and over 40 episodes of loss of consciousness in the last decade. The mistakes include the incorrect connection of the diver's gas supply to cylinders of pure helium or nitrogen, failure to ensure an adequate oxygen supply when a gas blender has been in use and cross-connection of a pure gas at a higher pressure than the correct mixture. Because there may be no obvious evidence that the wrong gas has been supplied, it has often been difficult to establish the cause of the accident.

In anaesthetic practice, deaths and serious brain damage may result from failure to provide an adequate oxygen content in nitrous oxide. (Shelley FC. Personal communication from the Medical Defence Union, 13 November 1980). For example, when the oxygen bottle on a Boyle's machine empties, pure nitrous oxide may be supplied to the patient as the sole respired gas. As the patient is already anaesthetized, a change in the level of consciousness cannot give warning and the first and only indication of anoxia may be cardiac arrest. Death, or severe brain damage, may also occur if there is a failure to add oxygen to the respired gas when recirculating apparatus is in use[4]. In this case ventilation, because it is assisted, will continue even after cardiac arrest. Hospital gas supply lines have also carried nitrous oxide in place of oxygen and the accidental replacement of oxygen with pure argon has been recorded in an American army hospital[5]. In 1984 an anaesthetic death was reported in the United Kingdom, due to the use of carbon dioxide instead of oxygen, together with nitrous oxide[6]. In Hong Kong in 1990 an unidentified inert gas supplied in an oxygen bottle was responsible for the death of a patient[7].

Pathogenesis

The respiration of a gas without an oxygen content causes loss of consciousness in a matter of seconds, because the respired gas not only fails to provide oxygen, it also removes the oxygen present in the pulmonary arterial blood. Respiring an oxygen-free gas creates a diffusion gradient for the removal of this oxygen by transfer into the alveolar gas. Despite the very rapid fall in arterial oxygen tension, the elimination of carbon dioxide proceeds normally and the respiratory drive is not stimulated appreciably. The loss of consciousness in this form of normocapnic hypoxia would appear to be the primary and immediate effect on neuronal function resulting from failure of energy conversion. The respiratory centre is unable to function and breathing ceases. Where the fall in respired oxygen partial pressure takes place more slowly, it is accompanied by profound fatigue and the victim finds it impossible to take corrective action. Restoring a normal partial pressure of oxygen in the respired gas at this stage is accompanied by an immediate restoration of cerebral clarity and muscular activity. However, the continued oxygen deprivation from the respiration of a gas not

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containing oxygen is rapidly fatal. Cardiac output is maintained for a short time after respiration stops, but then arrests and the circulation fails.

Short periods of severe hypoxia, or prolonged, but less severe hypoxia, may produce cerebral oedema and lead to an elevation of intracranial pressure. Two effects are important in the pathogenesis of this syndrome, vascular dilatation and an increase in vascular permeability. The dilatation appears to be related to local hypoxia affecting the smooth muscle of the vessels. Landis[8] studied the effect of hypoxia on the permeability of the capillary wall in the frog mesentery. Under normal circumstances he found the rate of filtration of liquid through the capillary wall to be directly proportional to the excess of capillary hydrostatic pressure over the osmotic pressure of the plasma proteins. Hypoxia greatly increased the filtration rate and was accompanied by a leakage of plasma proteins. Plasma carbon dioxide accumulation and the consequent pH changes were not shown to be involved. As decerebrate frogs were used, the effect was independent of cerebral mechanisms. He concluded that lack of oxygen alone is capable of producing an increase of permeability in peripheral capillaries, which is sufficient in degree to permit the passage of protein.

Kogure and co-workers[9] have amassed strong evidence that a local parenchymal acidosis produced by anaerobic glycolysis is an active factor in the vasodilation. In the brain, the venules and veins, being thin-walled capacity vessels, dilate widely in hypoxia. The resulting increase in permeability may be so gross as to allow diapedesis of erythrocytes into the perivenular area. The blood-brain barrier is resistant to mild hypoxia, and in the absence of circulation remains impermeable to protein for about three hours after death. However, Olesen[10], also using the frog, has shown that the oxygen tension is critical to the maintenance of small ion permeability. Using microelectrodes to determine the electrical resistance of the pial venular endothelium, he found that 2-5 min of perfusion using pure Ringers solution, giving a pO_2 of 25 mmHg, caused the electrical resistance to drop to about 32% of the control value. Ionic permeability, which is inversely related to the electrical resistance was increased by 50%. In these experiments the vessels were constantly perfused to avoid the accumulation of lactic acid and CO_2, although it has been shown independently that reducing pH in cerebrovascular perfusates to 5.1 does not change blood-brain barrier permeability. Although Olesen felt that the small changes in ionic permeability would not allow the barrier to be permeable to plasma proteins, there is no doubt that a modest increase in the severity of the hypoxia will do so, as evidenced by the diapedesis of erythrocytes seen postmortem in Figure 1.

The escape of plasma proteins into the perivascular zone reduces the osmotic forces retaining liquid in the circulation and focal oedema develops. In continued hypoxaemia the cerebral oedema extends to involve multiple sites. The compression of the microcirculation increases intercapillary distances and extends the zone of the hypoxia. The increased extracellular water content provides a significant barrier to the diffusion of oxygen, because of the poor solubility of oxygen in water creating a vicious circle. If intracranial pressure rises significantly there may be gross interference with cerebral blood flow, and eventually death by

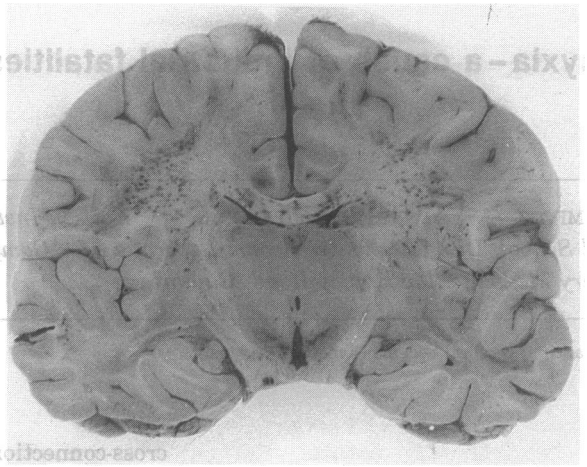

Figure 1. Perivenous white matter haemorrhage in acute anoxic asphyxia

compression of brainstem structures into the foramen magnum[11]. These mechanisms may also be relevant to the cerebral and pulmonary oedema of mountain sickness[12].

Morbid anatomy and histopathology

The necropsy appearances are dependent on the rapidity with which death occurs. When cardiac arrest occurs quickly as a result of the respiration of an anoxic gas, there may be a small number of petechial haemorrhages, mainly in the lungs and in the white matter of the brain (Figure 1). A few haemorrhages may also be present in the skin. The appearances are in marked contrast to the gross haemorrhages and cerebral oedema that characterize asphyxia from respiratory obstruction. Pulmonary oedema is invariably present, which is expected when cardiac action continues after the arrest of respiration. The loss of the integrity of the pulmonary membrane may also be accompanied by some haemorrhage.

Death may be delayed by days or even weeks after a brief period of anoxia and several cases have been detailed by Plum *et al.*[13]. The necropsy appearances were those of a leucoencephalopathy and they commented that pathological studies show the predominant nervous system abnormality to be in the white matter, rather than in neurones. Carbon-monoxide poisoning produces similar changes[14,15]. With this gas, anoxia is due to the exclusion of oxygen from the cytochrome enzyme pathways, rather than the reduction of oxygen transport by haemoglobin[16]. It has been suggested that the white matter is more vulnerable to hypoxia, because of the paucity of cytochrome a3 oxidase. The venous drainage into the Galenic system predisposes to the development of diffuse white matter oedema[17]. Lumsden[15] reported similar atrophy of the white matter as the 'respirator brain', in trauma patients being ventilated where presumably a limited, but severe, hypoxic period had occurred.

Therapy

Different regions of the nervous system show different sensitivity to hypoxia and the patchy damage seen following severe oxygen deficiency is probably due to focal oedema and the no-reflow phenomenon[18], which exerts its effects several hours after the insult[19]. During this time, it is likely that adequate therapy should make a significant difference to recovery.

At the present time, management of acute hypoxia in clinical practice combines the use of oxygen at atmospheric pressure, assisted ventilation, steroids, sedation and hypothermia[20]. In the presence of raised intracranial pressure, a degree of vasoconstriction can be achieved by hyperventilation and hypocapnia. However, as this reduces both cardiac output and cerebral blood flow, it also reduces oxygen delivery. Indeed even oxygen availability at tissue level is reduced, as the haemoglobin dissociation curve is shifted to the left, because of the Bohr effect. Positive end-expiratory pressure (PEEP) has been suggested as a therapy in acute mountain sickness[21], but it increases cerebral venous pressure and may precipitate acute cerebral oedema[22]. Steroids have a beneficial effect on endothelial permeability and evidence of the reduction of focal oedema is available from CT studies[23]. Although limiting the development of oedema, they cannot reduce the extravascular tissue liquid already present and there is therefore a delay in the reduction of intracranial pressure. Hypothermia may be valuable by reducing the metabolic rate and oxygen demand.

After removal from a hypoxic atmosphere, it is obvious that 100% oxygen should be given as soon as possible. In recent years the value of oxygen therapy, first suggested by J S Haldane[24], has been neglected, mainly because of fears of oxygen toxicity and because of problems in the treatment of some patients with respiratory disease. In the correction of severe pulmonary and cerebral oedema at altitude, 100% oxygen may be ineffective, even though at an altitude of 5000 m (17 500 ft) barometric pressure is half the value at sea level and 100% oxygen therefore exerts a pressure of 500 mbars (0.5 ATA). As haemoglobin is fully saturated at this level, attention must be focused on the plasma oxygen concentration, which is increased by a return to the atmospheric pressure of sea level. Ambient pressure can be increased further to good effect by using a hyperbaric chamber. Elevated intracranial pressure has been shown to be reduced by 30% within minutes at 2000 mbar breathing 100% oxygen[25]. This is due to vasoconstriction reducing the volume of the intravascular compartment. Despite the reduction of the cerebral blood flow, tissue oxygen availability, paradoxically, is greatly increased[26]. It is possible that this more vigorous approach may prevent delayed deterioration[13].

Prevention

Whenever possible, gases with sufficient oxygen content to maintain consciousness should be used. In the diving industry this is accepted. Helium supplied offshore now must contain a minimum of 2% oxygen. Although in anaesthetics a mixture of nitrous oxide and oxygen could be supplied premixed to operating theatres and a 50/50 mixture is already available commercially, it must be stored at normal room temperatures, because nitrous oxide liquifies at −5°C. If this occurred, pure oxygen then pure nitrous oxide may be supplied to the patient. An alternative is to provide on-line oxygen monitoring during anaesthesia and this is a legal requirement in many Continental countries. In other situations, for example in industry, where it is necessary to use pure gases, cylinders should carry a warning, and a detailed explanation of the hazard is vital in training.

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