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Smoke inhalation injury

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Key points

- Maintain a high suspicion of smoke inhalation in a flame injury.
- Initial resuscitation priorities are administration of 100% oxygen and early intubation with an uncut tracheal tube if airway at risk.
- Utilize lung-protective ventilation strategies and consider early bronchoscopic washout.
- Administer careful fluid therapy to avoid over/under-resuscitation.
- Remember to consider cyanide poisoning as early use of antidote improves outcome.

Definition

Smoke inhalation injury can be defined as damage caused by breathing in harmful gases, vapours, and particulate matter contained in smoke. It can manifest as a thermal injury, chemical injury, and as systemic toxicity, or any combination of these.

Epidemiology

Most burns managed in hospitals are from scalds (54%) and contact burns (23%). Patients with thermal injury from fires and explosions, who are more likely to have smoke inhalation injury, represent only 16% of the total.[1] The pathophysiological sequelae of breathing in smoke are life-threatening and multi-systemic.

Smoke inhalation is present in 2–30% of all flame burns presentations and in higher proportions if facial burns are present.[2] It has a high mortality associated with it and is the most common cause of death at the scene of a fire. The presence of a smoke inhalation injury, alongside patient age and percentage of body surface area burned, is a major determinant of mortality. Inhalation injury increases the risk of death from a burn injury 3.6-fold.[3] Smoke inhalation injury leads to respiratory complications in 73% and acute respiratory distress syndrome (ARDS) in 20%.[4]

Burns are an injury process of vulnerable populations. Age is an important predictor, with older (>64 yr) and younger (<10 yr) victims being more likely to die as a result of a fire, and also representing a disproportionate per cent of those injured by a fire. People with a physical or cognitive disability have a higher mortality rate than matched controls, as do those under the influence of alcohol or other drugs. Risk factors are low socio-economic groups, substandard housing, winter season, and lack of smoke detectors.

The numbers of fire victims have been steadily decreasing, with 388 fire-related deaths in England between 2010 and 2011.[5] Burns treatment, and its associated mortality, has improved greatly with advances in burn and intensive care. However, the mortality rates from smoke inhalation have not improved by the same extent.[6] This is in part due to the complexity of the insult, particularly if pneumonia and sepsis are complications.

Components of smoke

Smoke is a product of combustion, and is a colloid formed of airborne solids, liquid particles, and gases that are mixed with entrained air. The composition of smoke is unique to each fire and depends on the materials present, the availability of oxygen, and the nature of the combustion.

Fires with high temperature and high availability of oxygen produce small amounts of smoke, mainly composed of carbon (soot), the carbon being the visible part of smoke. High temperatures also produce nitrogen oxides. Combustion with limited availability of oxygen will produce a greater number of different chemical components. Incomplete combustion of carbon produces carbon monoxide and of nitrogen-containing materials produces hydrogen cyanide and ammonia.

Up to 150 toxic compounds have been identified. Some common compounds found in smoke are carbon dioxide, carbon monoxide, hydrogen cyanide, aldehydes, and ammonia.

Pathophysiology

There are three mechanisms of smoke-induced injury; they may co-exist within one patient or occur in isolation.[7]

(i) Heat
(ii) Particulate matter deposition and respiratory irritants
(iii) Asphyxiation and systemic toxicity

Heat

Proximal burns of the nasal and oropharyngeal mucosa are common. The body effectively transfers the heat to the upper airway, so thermal burns below the vocal cords are rare. However, smoke containing superheated steam can cause pulmonary damage, but usually this insult also causes glottic swelling and is rapidly fatal. Injury to the upper airways manifests as erythema, ulceration, and oedema. Symptoms of dyspnoea, hoarse voice, and stridor may not be apparent till the swelling is sufficient enough to obstruct the airways.[8] This can progress rapidly, as oedema continues to develop over the first 24–36 h post-injury.

Particulate matter and respiratory irritants

The main cause of pulmonary damage is by inhalation of particulate matter, mainly carbonaceous particles containing toxic chemicals (soot). The particles cause mechanical obstruction, increasing airway resistance and reducing compliance, thus increasing the work of breathing.

The chemical irritants dispersed on the soot vary depending on the materials combusted but frequently include aldehydes from wood and paper, nitrogen oxides from fabric, and halogen acids and sulphur dioxide from rubber. Water-soluble compounds (such as hydrogen chloride) produce profound acidic or alkaline damage to airway mucosa at proximal locations within of the respiratory system. Fat-soluble compounds (such as phosgene) penetrate into the airway mucosa and cause severe delayed damage distal airway tissues, up to 48 h later.

This leads to a cascade of inflammatory mediators and activation of leucocytes which aggregate and release further mediators, producing oxygen free radicals. These combine with cellular DNA to cause damage and subsequent ATP depletion and cell necrosis.

The formation of nitric oxide, a potent vasodilator, from induced nitric oxide synthase in respiratory tissues, leads to increased bronchial blood flow, decreased hypoxic pulmonary vasoconstriction in poorly ventilated areas of lung, and results in V/Q mismatch and hypoxia.

It is the aggregation of these effects that produces the tissue injury and increased pulmonary vascular permeability, leading to decreased diffusion, oedema, and V/Q mismatch. Neutrophil infiltration and fibrinogen activation by inflammatory mediators cause airway cast formation. These casts obstruct the airway and worsen the V/Q mismatch.

Systemic toxicity

Tissue hypoxia can be caused by many mechanisms. Combustion utilizes oxygen, which if not replenished while in a closed space, can cause inspired oxygen concentrations as low as 10–13%.

Products of incomplete combustion can also cause hypoxia. The main toxic compound in fire deaths is carbon monoxide (CO), estimated at leading to 80% of deaths by fire gases.[9] CO intoxication causes tissue hypoxia in three ways. First, it binds with haemoglobin with about 250 times the affinity of oxygen, therefore, preventing oxygen binding. Secondly, it also leads to a shift in the oxygen dissociation curve to the left impeding delivery. Thirdly, it competitively inhibits binding of oxygen with cytochrome oxidase, a key mitochondrial enzyme, significantly impairing cellular utilization of oxygen.

Hydrogen cyanide is a colourless gas with a bitter almond odour which only 40% of the population are able to detect. Smoke inhalation is one of the most common causes of cyanide poisoning and there is increasing international recognition of its importance. The presence of cyanide within modern fires has been demonstrated with various studies, although the exact incidence is difficult to quantify because of the unique nature of each fire and the difficultly of blood testing of cyanide.[6,10,11] It is 20 times more toxic than CO in terms of comparing the Acute Emergency Guideline Levels for the presence of gas in parts per million.[12]

Hydrogen cyanide combines with the ferric ion in cytochrome a3 oxidase in mitochondria with high affinity, and so impairs cellular respiration by structurally changing the enzyme. Thus, anaerobic metabolism ensues, and leads to high lactate levels, and decreased oxygen consumption.

The presence of CO and cyanide has a synergistic effect of asphyxia.

Diagnosis of smoke inhalation injury

History

A careful history should be taken looking for risk factors for smoke inhalation injury. These include:

- Burn/fire in an enclosed space.
- Loss of consciousness at the scene, possibly due to:
  - drugs,
  - alcohol,
  - head injury,
  - hypoxia,
  - carbon monoxide/hydrogen cyanide poisoning.
- Fatalities in the same incident increase the risk of significant injury.

Significant smoke inhalation does not occur outdoors as the smoke is rapidly dissipated in air.

Signs and symptoms

The patient should be examined for the following:

- voice changes, hoarseness, stridor (these are particularly worrying symptoms),
- cough,
- burns to the face, lips, tongue, mouth, pharynx, or nasal mucosa,
- soot in the sputum, nose, and mouth,
- respiratory distress,
- decreased level of consciousness or confusion, agitation,
- clinical hypoxaemia; $S\,p_{O_2}$ <94% in air,
- increased carboxyhaemoglobin (COHb) levels.

Management of smoke inhalation injury

Basic measures

At the scene, measures include evaluating patients and administering 100% oxygen, inquiring about the type of fire and extent of exposure, performing a quick body examination for airway and accompanying injuries including trauma.

Basic monitoring and i.v. access should be established. If there are burns, first aid should be given by stopping the burning process (extinguish flames, remove smoldering clothes) and cooling the burn. Care should be taken to avoid hypothermia.

Primary survey

The primary survey can occur with concurrent management of the airway in a team setting. It should include assessment for upper airway burns while maintaining cervical spine alignment if the history is suggestive of trauma.

Immediate intubation is indicated in patients with the following features:

- impending or actual airway obstruction,
- reduced level of consciousness,
- cardiac arrest,
- hypoventilation.

Intubation should be considered for patients requiring transfer if there is a risk of deterioration en route. Guidance can be sought from the accepting burn centre.

The initial assessment may be reassuring; however, as oedema develops, it can make subsequent intubation difficult, so a low threshold for intubation is sensible (especially in children in whom Poiseuille's law is important). There is a spectrum of patients that do not have a clear indication for intubation, so detailed examination, monitoring, and periodic reassessment become essential. Not all patients who have smoke inhalation require tracheal intubation.

In unclear cases, it may be useful to assess patients with nasal fibreoptic endoscopy after nasal decongestants and local anaesthetic spray. A safe environment, where interventions can be swiftly escalated, must be used.

A retrospective study of 41 patients with smoke inhalation referred to ENT services found that soot in the oral cavity, facial, and body burns were physical findings positively correlated with intubation.[13] Findings at fibreoptic laryngoscopy of oedema of the true and false cords were highly predictive for intubation.

In view of the potential airway emergency, and possible full stomach, it is important to have high levels of preparedness of appropriate skilled staff, equipment, and good communication of initial and rescue airway plans, as highlighted in general airway emergencies in NAP4.[14] Efficient placement should be a high priority; numerous attempts will exacerbate any trauma and oedema and can cause airway loss. Mask ventilation may be also difficult in patients with facial or neck burns.

Techniques to consider include rapid sequence, inhalation induction, or awake fibreoptic intubation. The choice will depend on patient factors, including a pre-existing possible difficult airway, the urgency of intervention, skills, and equipment available. Oedematous, friable mucosa from intraoral burns may bleed, making intubation difficult and secretions from intraoral burn exudate increase the risk of laryngospasm and may further impede the view. Anticipate laryngeal oedema, prepare smaller diameter tracheal tubes, and prepare for the possibility of progression to surgical airway. Patients with significant smoke inhalation and hypoxia may be disorientated and uncooperative with awake techniques.

If the plan is to intubate, ideally a low-pressure cuff tracheal tube should be used and left uncut, as the facial swelling can engulf the tube and dislodge it.

In major burns, there is a risk of hypovolaemia, so fluids and vasopressors should be immediately available. Some clinicians consider ketamine as a good induction agent for this reason.

If rapid sequence intubation is the selected technique by an experienced clinician in airway management, it is acceptable to use succinylcholine in the immediate setting, the risk of hyperkalaemia occurring after 24 h. Cuff pressures should be measured and adjusted. The cuff ties should be regularly checked and bed head elevated to reduce swelling.

Patients with burns >20% and smoke inhalation injury meet the national criteria for referral to a Burns Centre.

Respiratory support

A severe chest burn may require escharotomy. This should be considered if there are restricted chest movements with a full thickness circumferential chest burn. This may present as decreasing tidal volumes requiring higher inspiratory ventilator pressures. Of note, especially in children, a deep burn to the anterior chest and abdomen may compromise respiratory function in the absence of a circumferential burn.

Intubated patients should undergo fibreoptic bronchoscopy to diagnose and grade inhalation injury. The severity does correlate with long-term prognosis, although the best predictor is the $Pa_{O_2}/F_{I_{O_2}}$ ratio. Moreover, the evidence suggests improved outcomes with bronchoscopy and early clearance of particulate matter and washout.[15]

Lung-protective ventilatory strategies limiting tidal volumes to 6 ml kg^{-1} predicted body weight, the application of PEEP, and permissive hypercapnia have been adopted from the ARDS population. There is limited evidence in victims of smoke inhalation that these techniques limit atelectasis and barotrauma,[16–18] but it is a common sense strategy to avoid ventilator-induced lung injury in these at-risk patients

A regimen of aerosolized heparin alternating with a solution of 20% acetylcysteine was studied on paediatric and adult populations with inhalation injury diagnosed on bronchoscopy. Acetylcysteine is a mucolytic agent, and hence should diminish airway cast formation. Heparin is a potent activator of antithrombin III, and so leads to thrombin inactivation and also decreases airway casts. One retrospective case–control study found a significantly decreased mortality, occurrence of atelectasis, and need for re-intubation in the treatment group (class III evidence).[19] In a small single-centre study in adults,[20] it was found the nebulized therapy attenuated lung injury and progression of ARDS compared with historical controls. There are reports of experience using nebulized heparin in Burn Centres in the USA, UK, and Singapore, but there are no large trials to support widespread adoption.

An example of an inhalation protocol

The doses of heparin and acetylcysteine below are suitable for adults and children. Heparin and acetylcysteine should be alternated, so patients receive treatment every 2 h.

- Nebulized heparin 5000 IU diluted with 3 ml 0.9% saline 4 hourly for 5 days.
- Nebulized 20% acetylcysteine solution, 3 ml every 4 h. This may be irritant to the airway and should be discontinued if

Table 1 Parkland formula

Parkland formula for burn resuscitation	
Volume	4 ml×% burn×person's weight in kg
Fluid	Compound sodium lactate (Hartmann's solution)
Timing	Half of this total volume should be administered over the first 8 h, with the remainder given over the following 16 h. It is important to note that this time frame is calculated from the time at which the burn is sustained, and not the time at which fluid resuscitation is begun
When	Given to burns >10% in children and 15% in adults
Maintenance	Children <30 kg should receive maintenance fluids in addition—discuss with accepting burn service

new bronchospasm develops or existing bronchospasm worsens.
- Nebulized salbutamol 2–4 hourly.
- Chest physiotherapy and regular respiratory toilet are essential.

There is no place for prophylactic antibiotics. Patients with inhalation injury do have increased risk for secondary bacterial infection, most commonly *Staphylococcus aureus* and *Pseudomonas aeruginosa*. However, the use of prophylactic antibiotics promotes the emergence of resistant organisms.

Steroids are not recommended in the treatment of inhalation injury but may have a role in preventing post-extubation stridor caused by laryngeal oedema, although there have been no specific studies in burn patients.

Ventilator care bundle

Patients with smoke inhalation injury are at high risk for ventilator-associated pneumonia and standard preventive measures should be instituted where possible.

Cardiovascular support

Adequate support, initially by fluids then pharmacological means as appropriate, should be utilized to minimize tissue hypoxia. There are no data on therapeutic hypothermia for pre-hospital arrest in this patient group.

The Parkland formula (Table 1) is the most frequently used burn resuscitation formula applied to guide initial fluid management. Formulas should not be followed blindly, but fluid infusions should be adjusted to clinical response. Smoke inhalation patients have higher fluid requirements for the same size burn, which may be up to 40% greater. This should be balanced against the attendant risks of pulmonary oedema and worsening capillary leak. Use cardiac monitoring early if available. Avoid large fluid volumes aiming to either correct any base deficit or target urine output in excess of 0.5 ml kg^{-1} h^{-1}.

Investigations

Laboratory studies

Full blood count
Urea and electrolytes
Arterial blood gas
Lactate levels
Carboxyhaemoglobin (COHb) level
Arteriovenous oxygen difference (a reduced level implies inability to utilize oxygen).

Bronchoscopy

Gold standard diagnosis is by bronchoscopy, reported to be 86% accurate. Bronchoscopic findings consistent with inhalation injury include carbonaceous debris and mucosal pallor, ulceration, or erythema. Pulmonary toilet with washout may lessen the injury. Washout fluid can be sent for microscopy and culture. There is no conclusive evidence on the timing and benefit of serial bronchoscopy, although one retrospective study did suggest a slight improvement.[15]

Radiology

Chest X-ray may be normal, although may later show signs of diffuse atelectasis, pulmonary oedema, or bronchopneumonia.

Carbon monoxide poisoning

Assuming carbon monoxide (CO) poisoning in all fire victims is prudent. Standard pulse oximetry will not distinguish COHb from deoxygenated or oxygenated haemoglobin and so overestimates oxygen saturations. Low COHb levels in the emergency department do not exclude significant CO exposure, as timely application of high flow oxygen at the scene will cause rapid washout.

Features of severe poisoning:

- Any new objective acute neurological signs, for example, increased muscle tone, up-going plantars
- Coma
- ECG indication of ischaemia
- Clinically significant acidosis
- Initial COHb levels >30%.

Treatment

Administer high-flow oxygen via a non-rebreathing mask, unless intubated then ventilate the lungs with F_{IO_2} 1.0. Intensive care unit (ICU) admission including mechanical ventilation is likely to be required in cases of severe poisoning. The UK National Poisons Information Service (NPIS) does not currently recommend hyperbaric oxygen therapy in the context of smoke inhalation injury.

Hydrogen cyanide poisoning

There is a risk of exposure to cyanide after smoke inhalation, particularly from fires involving synthetic materials (e.g. furnishings, plastics, vinyl). Such patients are often hypoxic and exposed to carbon monoxide making the diagnosis of cyanide toxicity more complicated.

Cyanide (CN) levels are not readily available (currently, only UK laboratory measuring cyanide levels is in Cardiff), so treatment should not wait for levels. The following suggest cyanide poisoning:

- lactate >7 mmol $litre^{-1}$,
- elevated anion gap acidosis,
- reduced arteriovenous oxygen gradient.

Severe toxicity features:

- Headache, confusion, convulsions, loss of consciousness, fixed unreactive pupils.
- Arrhythmias, myocardial ischaemia and cardiovascular collapse.

Treatment

Immediate management should include high-flow oxygen and supportive ICU care. NPIS can provide advice on the use of specific antidotes. If metabolic acidosis persists despite correction of hypoxia and adequate fluid resuscitation, consider correction with i.v. sodium bicarbonate. Rapid correction is particularly important if there is prolongation of the QRS or QT intervals.

Antidotes

Consider treating burns patients with a good history of smoke inhalation injury who have arterial blood lactate concentration >10 mmol litre^{-1} (indicative of moderate-to-severe poisoning) in the absence of significant burns and after correction of hypotension; a history of loss of consciousness; cardiovascular instability; or cardiac arrest.

If the patient has significant burns and smoke inhalation, clinical judgement must be used to assess the adequacy of resuscitation before attributing elevated lactate to cyanide poisoning. Cardiac output monitoring should be considered. Remember antidotes have side-effects. There are no data available on the length of time that antidotes are effective for after cyanide exposure.

Hydroxocobalamin (Cyanokit®)

Hydroxocobalamin is probably the safest antidote for patients with concomitant smoke inhalation and burns. It works by binding to HCN to form non-toxic cyanocobalamin, which is then excreted by the kidneys. In France, this has been used in the prehospital setting for the last 10 years. It should be given as early as possible after smoke exposure where cyanide toxicity is suspected and given immediately if in cardiac arrest.

Adult dose: 5 g over 15 min, may be repeated×1, given over 15 min–2 h.

Paediatric dose: 70 mg kg^{-1} over 15 min (not exceeding 5 g); may be repeated once to max 140 mg kg^{-1}, given over 15 min–2 h, maximum dose 10 g.

Like all cyanide antidotes, hydroxocobalamin has side-effects, but these are usually not problematic. The most noticeable is the reddish brown skin, mucous membranes (up to 15 days), and urine discoloration (can last up to 35 days). This discoloration can affect colorimetric laboratory blood tests and can trigger false 'blood in line' alarms on haemofiltration machines. It can cause false elevation COHb level on co-oximetry (~5% increase) and transient hypertension which may be beneficial in hypotensive patients. Anaphylaxis reactions are rare.

Other antidotes

- Amyl and sodium nitrites induce methaemoglobin, which combines with cyanide. This will further limit oxygen delivery, so should be avoided in smoke inhalation injury, especially if COHb >10%. Also can cause severe hypotension from vasodilation.
- Dicobalt edetate is toxic and potentially fatal in the absence of cyanide poisoning due to cobalt toxicity. Use only if poisoning is confirmed and is severe.
- Sodium thiosulphate enhances the conversion of cyanide to thiocyanate, which is renally excreted (delayed effect and is used with other antidotes with faster action). Co-administration with hydroxocobalamin may be beneficial.

Conclusion

Smoke inhalation injury is a serious injury with a high associated mortality and morbidity. Early recognition and prompt management are critical. Treatment is predominantly supportive and avoiding iatrogenic complications. There are some recognized treatments for the pulmonary injury and the systemic toxicity, and the subject is being researched for new potential options to modulate the inflammatory response and limit cast formation. In view of the complexity of the injury and the dynamics of the pathophysiology, it is likely that treatment modalities will be multi-targeted.

Declaration of interest

None declared.

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