Lung injury following hydrocarbon inhalation in aircrew†

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This paper is outlines current knowledge and personal experience gained in managing a significant number of aircraft cabin and flight deck crew and some passengers and aircraft engineers, both nationally and internationally, who have presented with respiratory and other complaints, which have occurred after exposure to toxic fumes on board an aircraft cabin over a twelve year period.

1. INTRODUCTION

In considering this problem it is important to understand that the inhalation of foreign material is a common everyday occurrence in all settings. Inhalation of environmental substances assumes particular importance in the workplace, where toxic fumes and dusts may be present and, following inhalation, cause lung injury or, in some cases, generalized illness. Despite improvements in occupational hygiene, occupational lung disease continues to be an important problem in Western society and elsewhere. For example, recent years have seen a marked reduction in the incidence of mineral dust diseases (pneumoconioses), such as silicosis and asbestosis, but others, such as occupational asthma, continue to pose a significant problem. Whilst there have been significant advances in the protection of the workforce against known risks, it is certain that there are many that are yet to be recognized and it is clear that some are known but not acknowledged. The reasons for this are unclear but include lack of proper knowledge, awareness and training. In some cases, known risks are wilfully ignored or alternative viewpoints or theories promulgated to explain the observations and/or illness, apparently for the purpose of evading responsibility.

The respiratory tract achieves importance in the occupational health setting because it is exposed to potentially contaminated environmental air. Approximately 14 000 litres of air are inspired during the course of a forty-hour working week. This figure is significantly increased as physical activity increases. For example, during moderately heavy exercise ventilation may exceed 100 litre/minute.

Thus, the potential for airborne substances to cause injury to the respiratory tract is important in this setting. Inhaled substances vary in their potential to cause lung disease. Some have a characteristic odour or rapidly cause significant airway irritation and are quickly recognized. Other substances that are not so easily detected may continue to be inhaled, often for prolonged periods, without being recognized (e.g., carbon monoxide). It is, therefore, incumbent on those individuals and organizations involved to appreciate that early recognition of hazards and risks to health are of paramount importance, that prevention is better than cure, and that lung injury may be irreversible.

2. ANATOMICAL CONSIDERATIONS

Occupational lung diseases may involve any part of the respiratory system. In order to better understand the factors involved in the genesis of lung injury and disease secondary to inhaled fumes, aerosols and particulates, it is important to briefly review the anatomical and physiological features of the respiratory tract. This is particularly important as the lung has significant regional differences in terms of physiology and function. The respiratory system can usefully be considered as having four compartments as follows:

- the nasopharyngeal compartment—from the nostrils through the nasal passages and throat to the larynx and vocal cords;
- the tracheobronchial compartment—from the vocal cords to the main airway (trachea), the right and left main bronchi, the progressively smaller airway subdivisions, down to the respiratory bronchioles (internal diameter less than 0.5 μm);
- the pulmonary/parenchymal compartment—from the respiratory bronchioles to the alveoli or air sacs;
- the pleural space—the space between the external lining of the lungs and the internal lining of the chest wall.

The alveoli present an enormous surface area to the inspired air and act as the interface between the blood and the outside air. They have a rich blood supply, which ensures a direct and unique link between the body and

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the external environment. In the alveoli, air is separated from the pulmonary capillaries by an extremely thin alveolar-capillary membrane. Its miniscule thickness (0.4–2 μm) ensures a rapid exchange of oxygen and carbon dioxide between the blood stream and atmosphere. Whilst the lung is particularly well suited for the uptake of gases, it is also prone to the development of disease or injury as a result of deposition of inspired particulates and absorption of volatile compounds. Substances inhaled as solid or liquid aerosols, gases and vapours all vary in their potential to cause lung disease and may cause irritation or actual physical injury.

Materials that can inflict direct injury on lung tissue can lead to respiratory malfunction. This can cause a spectrum of pathological changes including death. Thus, the importance of inhalation as a route of exposure to noxious substances in the workplace cannot be overemphasized. It is not possible, within the limits of this paper, to discuss more than briefly the effects of inhaled foreign materials on the lung and the mechanisms by which they cause disease. Inspired material may take the form of solid aerosols (powders, dusts, smoke), liquid aerosols (mists, fogs, fumes) and gases or vapours, depending on their chemical and physical properties.

Broadly speaking, lung diseases can be regarded as those affecting the airways, those affecting the interstitial tissue (the substance of the lung excluding the airways), and some affecting both. The following is a list of some examples of these diseases and of their aetiological agents, and is illustrative only. Many other factors and agents can affect lung function and structure:

- ◆ Airway disorders
  - Bronchitis (smoke, mineral dusts)
  - Bronchiolitis (chlorine, ammonia)
  - Asthma (wood dusts, formaldehyde, isocyanates, grain dust)
  - Reactive airways dysfunction syndrome (chlorine, ammonia)
- ◆ Interstitial disorders
  - Pneumoconioses (dust disorders)
  - Fibrogenic dusts (i.e., scar inducing; e.g., asbestos, silica)
  - Non-fibrogenic dusts (coal dust)
- ◆ Immunological
  - Extrinsic allergic alveolitis (foreign proteins; e.g., from birds, fungi)
- ◆ Alveolar filling disease
  - Adult respiratory distress syndrome (phosgene)
  - Alveolar proteinosis (silica)
- ◆ Malignancy
  - Lung cancer (chemicals in tobacco smoke, asbestos)
  - Mesothelioma (asbestos).

3. CLINICAL ASPECTS

Fumes produced by pyrolysed engine oils have been recognized to contaminate cabin air in aircraft cockpits and cabins for more than fifty years [1, 2]. However, it is noteworthy that the toxic effects of these fumes on the health and wellbeing of aircrew has only become the focus of public scrutiny over the last decade or so, as a result of the publication of the deleterious effects on the health of susceptible aircrew [3–10]. Experience has shown that individuals who have been exposed to these fumes may develop a variety of different symptoms [3–5]. The fact that the afflicted present with a variety of different symptom complexes has proved to be a major hurdle in developing recognition of this condition by many medical professionals and, importantly, by government and industry regulators.

More than ten years ago the term “aerotoxic syndrome” was coined by Balouet & Winder [9]. It was later endorsed by an Australian Senate Enquiry [6] to describe the symptom complex prompted by the inhalation of pyrolysed aircraft oils. In this regard, it is important to recognize that the term “syndrome” is one that is loosely applied in clinical medicine to describe a range of symptoms and/or physical signs that often occur together. The existence of any one of them alerts the clearly thinking clinician to the possible presence of others and specific enquiry can then be made. Experience shows that, in any one case, not all the described features will necessarily be present. Whether aerotoxic syndrome is a real or an imagined entity has become the subject of widespread debate in recent years. Some bodies have reviewed the evidence and have concluded that the broad range of reported symptoms fails to warrant a specific diagnosis, an opinion seemingly based on the observation that not all the reported characteristics are seen in every individual. By extrapolation, this opinion leads to the inference that these bodies believe that exposure to cabin fumes does not lead to ill health. This has led to the ongoing debate with the afflicted on one side and the air transport industry and its regulators on the other, with the latter either apparently ignoring the problem or alternatively finding other seemingly more attractive explanations for the presenting symptom complex. For example, the hyperventilation syndrome has recently been informally mooted to provide an explanation for the observed complaints.

In my experience, persons who seek medical consultation for their symptoms, which followed the inhalation of pyrolysed aircraft engine oil fumes, describe a variety of different ailments. In some, the problem is very clearly related to one organ system; for example, peripheral neuropathy, which can be further related to tri-

ortho-cresyl phosphate (a constituent of aircraft oils) exposure or to one or more of its degradation products. Others present with a variety of symptoms indicating that many organ systems are affected.

Typically, affected persons are flight crew but occasionally passengers and aircraft maintenance engineers have also reported symptoms. The immediate effects of the inhalation of the possibly phosphorylated organic hydrocarbons include blurring of vision, respiratory symptoms such as cough and breathlessness, headache, nausea, dizziness, vertigo, loss of balance, a feeling of fatigue and neurocognitive impairment. The last-mentioned typically includes problem-solving disability, disorientation, memory impairment and confusion. One pilot related an experience where he had to hand over control of the aircraft to the first officer because he was fearful that he would not be able to land the aeroplane. In many cases, these symptoms resolve fairly quickly once clean air is being inhaled and, in particular, if the exposure has been of short duration.

Commonly, the symptoms indeed resolve within a short period of time. However, some people experience chronic ill health that may last for months or years and, sometimes, the condition is permanent. Furthermore, sensitivity to other inhaled irritants may be increased in the long term. Chronic complaints are typically those relating to cognitive impairment (poor short-term memory, problem solving and multitasking difficulties), lack of coördination, nausea/vomiting, diarrhoea, respiratory problems, chest pains, severe headaches, light headedness, dizziness, weakness and fatigue, parasthesiae, tremors, increased heart rate, palpitations, irritation of the ear and upper airway, muscle weakness/pain, joint pain, skin itching, skin rashes, hair loss, fatigue and chemical sensitivity, to name a few [10–15]. This may lead to a work incapacity as high as 35% [12].

Respiratory complaints among aircrew are particularly prominent. Published studies [10, 16–22] have drawn attention to respiratory abnormalities in previously healthy aircrew who were predominantly nonsmokers, who experienced symptoms following an aircraft cabin fume event. These complaints are consistent with lung injury secondary to hydrocarbon inhalation and, in many cases, the abnormalities have been irreversible. Breathlessness, cough and chest pain or tightness are reported by most subjects. Other presenting symptoms have been those of wheezing, occasionally haemoptysis and complaints of upper respiratory tract irritation; sinusitis and epistaxis are also common. Recurrence of symptoms following return to duty are frequent. A variety of diagnoses have been applied, including asthma, reactive airways dysfunction syndrome, multiple chemical sensitivity syndrome and sometimes an interstitial lung disease (e.g., sarcoidosis) is diagnosed on presentation.

4. SPECIAL INVESTIGATIONS

In general, experience shows that respiratory and other investigations are rarely undertaken at initial presentation. Unfortunately it is commonplace that appropriate tests are not considered until a later date, when symptoms continue. Delay may result in missing the opportunity to physically or chemically detect abnormality. For example, if volatile hydrocarbons are to be detected in the blood stream, serum samples need to be taken promptly before the substance is completely eliminated from the circulation. As in many cases the symptoms remit with time, special tests undertaken remotely may no longer show abnormality and, hence, the real incidence of abnormalities remains unknown. From the respiratory view point, standard tests of spirometry and diffusing capacity are commonly found to be within the normal range. Chest X-rays and high resolution CT chest scans almost never get taken at the time of injury or within a short period, so it is difficult to know whether there are any acute radiological changes. Some of those who complain of breathlessness upon exertion and who have normal standard lung function tests (spirometry, diffusing capacity) have been shown to have an elevated alveolar-arterial oxygen gradient, implying that there has been an injury to the lung at the alveolar-capillary membrane level [10]. Thus tests of greater sensitivity, in this case arterial blood gas analysis, may reveal more subtle lung injury. Finally, there are no specific diagnostic tests for the aerotoxic syndrome, which contributes to its lack of general acceptance as a real entity.

5. DISCUSSION

Experience with aircrew and others who have experienced a toxic fume event has led me to believe that the aerotoxic syndrome is real. It is a symptom complex caused by exposure to and the inhalation of toxic fumes in aircraft cabins. It is a condition with a variety of symptoms, many of which are common to most affected persons. Some clinical complaints are more sporadic, appearing to affect some and not others. In many, the complaints are temporary, but in others the illness is more prolonged and even long-term. This experience raises serious concerns about the occupational health and safety of aircrew, passengers and other potentially exposed individuals.

The fact that not all those exposed develop symptoms is not surprising. There is clearly a differential sensitivity to the effects of the contaminating fumes. This may be related to a number of factors, including the intensity of exposure, individual sensitivity and genetic predisposition. There are parallels to this experience with those affected by chemicals in the general community. For example, occupational asthma is clearly recognized, in some cases, to occur after exposure to chemical concentrations well below industry-accepted standards. The latter are, of course, set to protect most persons—complete protection can only be made by complete exclusion.

There has been speculation that the aerotoxic syndrome is caused by, or at least associated with, exposure to tri-*ortho*-cresyl-phosphate and the mono- and di-*ortho* isomers [23, 24]. These are recognized neurotoxins and whilst their effects usually follow ingestion, they may also occur following absorption through the respiratory tract mucosa or, less commonly, through the unprotected skin. Engine oils contain a considerable number of other hydrocarbon substances and it is perhaps unlikely that any one will be the sole cause of the observed deleterious health effects; it is much more likely that many of them will be toxic. Experience in clinical medicine related to the multiple chemical sensitivity syndrome, in which a broad range of substances (including organic hydrocarbons) has been implicated, would support this view [25].

As already mentioned, whether the aerotoxic syndrome is a real or an imagined entity has become the subject of widespread debate in recent years. Examination of the literature shows that a myriad of explanations and diagnoses have been suggested and many seemingly reputable bodies have reviewed the evidence. They have concluded that the broad range of reported symptoms fails to warrant a specific diagnosis. This opinion would seem to be based on the observation that not all the reported characteristics are seen in every individual, which has led to the ongoing debate with the afflicted on the one side and the air transport industry and its regulators on the other, with the latter seemingly either ignoring the problem or alternatively finding other superficially more attractive explanations [7], including the notion that the symptoms are not related to fume events, that psychological problems are the explanation and, more recently, that hyperventilation is the cause of the symptoms.

It is unquestioned that hyperventilation may occur in stressful situations but is it the cause of the symptoms reported following contaminating fume events? I do not subscribe to that view. The hyperventilation syndrome is easily recognized by experienced clinicians and, whilst commonly of short duration, may cause chronic symptoms of dizziness, light headedness and breathlessness or a sensation of dissatisfied breathing. It does not, however, lead to long-term neurocognitive disability or cardiac abnormalities as have been reported in the aerotoxic syndrome [7]. To argue that fume-affected aircrew suffer from the hyperventilation syndrome because the symptoms exhibited by them are the same or similar is facile. It is no different from saying that the breathless patient suffers from lung disease when, in fact, there are many possible diagnoses including anaemia, cardiac and neuromuscular disease. In short, a diagnosis cannot be made by forcing all the jigsaw puzzle pieces together to make a picture. A broader view taking into account the pattern of illness and the natural history (anamnesis) is required.

In summary, with current knowledge the argument that the data are inconclusive and that there is not enough evidence to reach a conclusion that the aerotoxic syndrome is a real phenomenon can no longer be sustained [2, 26]. This should be the prompt for further more detailed and broader data collection and reporting. Ignoring or providing poorly thought-out alternative explanations for the facts is at best unhelpful and, at worst, puts exposed individuals at risk of ill health, which may not be temporary. Illness does not come easily to affected aircrew. These people were otherwise exceptionally physically fit and are highly trained and dedicated to their job. They want to fly and are unable to do so.

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