

**The “AEROTOXIC SYNDROME”
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Concerns have been raised by unions representing pilots and cabin crew about the possible effects on aircrew health of oil/hydraulic fluid smoke/fume contamination incidents in pressurised aircraft. Specific concerns have been raised with respect to organophosphate compounds (OPs) in the cabin air environment and the effects on health of long term low-level exposure.

However, the epidemiological evidence is hampered by inconsistency in reporting and the numbers are small.

Organophosphates in Engine Oil

Mobil Jet Oil II is commonly used for jet engines. This contains synthetic hydrocarbons and additives, including the organophosphate Tricresyl Phosphate (TCP) which acts as a high pressure lubricant. Engine lubricating oil contains around 3% TCP.

TCP is a toxic mixture that can cause a wide array of transitory or permanent neurological dysfunction when swallowed. The toxic effect of the ortho isomer, TOCP, is impairment of neuromuscular and peripheral nerve synapse function; it has no toxic effect on brain or cognitive function. The para and meta isomers are not toxic to humans. There have been no independently peer-reviewed recorded cases of neurological harm in humans following dermal or inhalation exposure to TCP.

An unpublished report from the Medical Toxicology Unit at Guy's Hospital in 2001 stated that “the majority of cases of tricresyl phosphate poisoning have been associated with the swallowing of contaminated food or drink, not with occupational exposure. The most frequent occupational exposures occur during manufacture, packaging, shipping and storage, not at the point of product use, and reports of occupational intoxication are rare”. The report quotes documented exposures dating back as far as 1943 and all the

exposures are to high concentrations greatly in excess of the amount present in jet oil.

A Canadian study in 1998 was unable to detect TCP in-flight and another study in the USA also failed to detect TCP during in-flight measurements.

British Airways commissioned a study by an independent specialist on indoor air quality, BRE, in 2001. BRE found that the concentrations of all oil compounds detected in cabin air were well below the human toxicological threshold.

In 2004 the UK government Aviation Health Working Group commissioned BRE to analyse a wide range air quality parameters during different phases of flight, including tests for oil vapours. This supplemented an earlier 2001-2003 EU-funded research project, CabinAir, which monitored air quality on 50 European airline flights. Both surveys concluded that no air pollutant exceeded recommended health limits; hardly any trace of oil vapour was detected. A similar finding was reached by another EU-funded project, Health Effects in Aircraft Cabin Environment (HEACE), in 2001-2005.

Because of continuing concerns the UK Department for Transport (DfT) commissioned the Committee on Toxicity of Chemicals in Food Consumer Products and the Environment (COT) to undertake an independent scientific review of available data in 2007.

Summary of COT review on cabin environment and aircrew health.

- There was considerable uncertainty about the identity of volatile organic compounds (VOCs) and other pyrolysis products released into the cabin air during a smoke/fume event.
- Further specific monitoring was recommended.
- There was insufficient evidence to recommend additional epidemiological research on any acute health effects.
- The evidence available allowed no conclusion to be reached that there is a causal association between cabin air exposures and ill health in commercial aircraft crew members. However, an association remains plausible.

Following the COT review, the DfT has commissioned further in-flight studies.

HUMAN TOXICOLOGY

The human body has its own defence mechanisms which protect against harm from certain levels of hazardous substances. However, if these levels are exceeded it is possible for health to be affected, either immediately (acute effects) or some time after the first exposure (chronic or delayed effects).

Individuals can vary in their response to toxic insult because of age, health status, previous exposure or genetic differences. Some individuals are more

susceptible to adverse effects when exposed to certain chemicals; the genetic basis for differences in susceptibility is being increasingly understood. It can also be difficult to disentangle the physical, psychological and emotional components of well-being, and there is no doubt that different people may respond in different ways on different occasions.

The human senses, particularly the sense of smell, are generally very effective in detecting hazardous substances at a level well below that which causes harm (except carbon monoxide). The fact that a potentially hazardous substance can be smelt does not imply that it is of sufficient concentration to cause harm. For most volatile organic compounds, the concentration level for detection by a normal healthy human is around 1,000 times less than the concentration level which is likely to harm health.

Absorption and Distribution of Chemicals

Foreign or exogenous chemicals (xenobiotics) must be absorbed from the surrounding environment and transported to their target site in the body for a toxic effect to occur. The chemical has to cross many cell membranes which form a lipoprotein barrier to the outside as well as maintaining the integrity of the cell. Most xenobiotics are transported by simple methods and not complex carrier-associated processes.

Lipid solubility is one of the major factors determining the extent and rate of simple diffusion through a lipoprotein membrane. Lipophilic molecules diffuse more readily than those which are hydrophilic, the rate of transport being dependent on the partition coefficient (ie the ratio of solubility in octanol/water). Non-ionised molecules are often more lipophilic and ions generally more hydrophilic, so the movement of electrolytes, such as organic acids and bases, is related to the degree of ionic dissociation and the lipid solubility of the non-ionised form of the compound.

The cell membrane controls the movement of chemicals in or out of the cytoplasm.

Inhalation Kinetics

The lung tissue barrier (alveolar membrane) separating air and blood is only 0.5 - 1.0 μ thick and the 300 - 400 million alveoli provide a large surface area for diffusion. In accordance with Fick's law, the transfer of gases through the alveolar membrane depends on the area and thickness of the membrane, and the partial pressures of the gases in the blood and in the alveoli.

The media on either side of the alveolar membrane are being continuously renewed; the air is changed 12 - 15 times per minute and the pulmonary blood flows at 3.5 - 5 litre per minute at rest, at sea level. This leads to efficient absorption, and elimination, of volatile chemicals.

Factors influencing the inhalation kinetics of a volatile compound include the environmental air concentration, duration of exposure, rate of alveolar ventilation, cardiac output, blood and tissue solubility and the degree of metabolism of the chemical. Volatile compounds are usually inhaled as a gas mixture with air and most are completely miscible in all proportions. The

concentration of gases and volatile compounds in a mixture is expressed in terms of partial pressure, which is not equivalent to concentration. However, the relative concentrations of dissolved materials can be expressed in terms of partial pressures which add up to a total pressure of 100%. Solubility is inversely related to the temperature and proportional to the pressure of the chemical in the ambient gas. The partial pressures of constituent volatile compounds vary with the absolute pressure but, at a fixed pressure, the concentration of each gas or vapour varies directly with its partial pressure and indirectly with the total pressures of the gas/vapour mixture.

The rate of delivery of an inhaled mixture of air and a volatile compound depends upon alveolar ventilation. A doubling of alveolar ventilation from 4 to 8 litre/min produces a minimal increase in the blood concentration of a poorly water soluble substance but an appreciable increase for highly water soluble substances. Cardiac output has an opposing effect on alveolar concentration and this is most noticeable for highly water soluble or extensively metabolised substances rather than poorly soluble compounds. An increase in cardiac output results in a larger amount of the inhaled substance passing from the lungs to the blood. A decrease has the opposite effect and causes a rise in alveolar concentration.

AEROTOXIC SYNDROME

A syndrome is defined as a set of symptoms which occur together, or the sum of signs of any morbid state, or a symptom complex. It follows that there should be a consistent set of common symptoms which together make up a given condition.

Individuals reporting that they suffer from the so-called aerotoxic syndrome describe a wide range of individual symptoms and signs, with insufficient consistency to fulfil the requirements for the definition of a medical syndrome. Many of the reported acute symptoms are largely the same as those reported by participants in all phase 1 drug trials, being normal symptoms experienced by most people on frequent occasions. It is recognised that 70% of the population experience one or more of them on any given day.

Both the US National Academy of Science and the Aerospace Medical Association reviewed the scientific evidence and concluded that there was insufficient consistency and objectivity to support the establishment of a clearly defined syndrome. Thus the concept of the 'Aerotoxic Syndrome' is not recognised in the aviation medicine community.

Symptoms reported by some crew members who have been exposed to fumes in the cabin are similar to those seen in a wide range of conditions, including chronic fatigue syndrome, Gulf War syndrome, Lyme disease, chronic stress and chronic hyperventilation.

The UK has approximately 20,000 professional pilots. In 2008, the UK CAA Medical Department database has 21 pilots reporting symptoms connected with this issue. Of these, 10 are long-term unfit, 2 are temporarily unfit, 6 are fit and 3 have allowed their medical certificates to expire.

CONCLUSION

There has been an increase in reported incidents of in-flight smoke/fume events since 1999, with a small number of crew members reporting adverse health effects which they associate with the events.

The source of oil contamination of engine bleed air was identified in early versions of the BAe 146 and the Boeing 757 and suitable modifications were implemented. A range of chronic health effects are reported by some crew members, although there have been no payments of damages to affected individuals.

The reported symptoms are wide-ranging with insufficient consistency to justify the establishment of a medical syndrome. It has been noted that many of the acute symptoms are normal symptoms experienced by most people frequently; some 70% of the population experience one or more of them on any given day.

Individuals can vary in their response to toxic insult because of age, health status, previous exposure or genetic differences.

In addition, it can be difficult to disentangle the physical, psychological and emotional components of well-being, and there is no doubt that different people may respond in different ways on different occasions.

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