The Independent Medical Expert Group (IMEG) 5th Report

Report and recommendations on medical and scientific aspects of the Armed Forces Compensation Scheme

February 2020

Topic 2 -The Aircraft Cockpit and Cabin Air Contamination by Bleed Air - The Evidence

Key Points

1. Some commercial aircrew have reported short and longer term non-specific, sometimes disabling, related to fume incidents and breathing contaminated cabin air. The symptoms are not accompanied by objectively verifiable clinical signs; imaging and routine laboratory tests are also negative.

2. Analysis of cabin air contaminants after fume incidents has identified more than a hundred mainly organic products but all with levels below 12 parts per billion. Organophosphates (OP) are present in jet oil but OP derivatives have not been demonstrated.

3. In 2005 the then Department of Health (DH) sponsored Committee on Toxicology (COT), reviewed evidence on the issue submitted by British Airline Pilots Association (BALPA) and concluded that it was inadequate to resolve the issue. They recommended further monitoring of fume incidents and more research.

4. The subsequent COT 2013 position paper concluded that the symptom pattern was not suggestive of an OP effect. They found that contamination of cabin air by some components of engine oil and other substances does occur and the acute illness reported by some crew members might be a chemical irritant effect. Equally given the very low levels of chemical contaminants it could also be a nocebo effect i.e. where disabling illness can arise from environmental exposures that are perceived as hazardous.

5. We examined present evidence finding an acute irritant effect plausible, but the precise environmental cause(s) was not established nor the existence of a later onset chronic disabling disorder. We will continue to monitor the literature and AFCS claims made.

Introduction and Background

1. Aircrew routinely experience unusual physical conditions at work. These include exposure to jet fuels, changes in atmospheric pressure, temperature, gravitation, exposure to ionising and non-ionising radiation and, sometimes, hypoxia. They may also undertake shift work, long hours of duty and are subject to time zone changes. In the last 20 years some aircrew have reported both short term and more lasting non-specific symptoms such as ear, nose and throat irritation, fatigue, dizzy spells, anxiety, headache and nausea and vomiting (1). They ascribe these symptoms to breathing cabin air contaminated by engine oils or other chemicals. The symptoms are not accompanied by objectively verifiable clinical signs and imaging and routine laboratory tests are also negative. At times such symptoms have been associated with reported functional compromise and several small case studies have reported evidence of neuropsychological impairment and altered cerebral white matter structure and function. Successful lawsuits against employers have followed. In 2000 the term aerotoxic syndrome was applied to these adverse health effects but since the reported symptoms are non-specific, common in the general community and there is no discrete diagnosable pathology, the term is not medically recognised (2).

2. As first introduced in military aircraft in the nineteen fifties and sixties, cockpit and cabin air in modern commercial aircraft is managed by an Environmental Control System (ECS). There are different systems for different aircraft but broadly, outside air enters the engines and is compressed, forming "bleed air", which is then used for cabin air conditioning. That air is then re-circulated before being exhausted from the cabin. Seals ensure that engine bearings are continuously lubricated with no leakage of oil into the compressed air stream. If a seal fails or is poorly maintained leakage may occur with the leaked oil or hydraulic fluid, then subject to a range of temperatures in the engine and air conditioning system thermal decomposition might then take place with release of volatile organic compounds and associated unpleasant or irritating fumes and odours.

3. Smoke or fume incidents are unfortunately not always assiduously recorded. Internationally they are considered rare and one UK estimate is that they occur in 0.05% of flights. Few data are available on products of thermal degradation of lubricant and hydraulic oils and certainly not over the range of possible temperatures experienced, where different chemical products may be formed from one primary chemical compound. Analysis of cabin air contaminants, using an engine test rig in an aircraft previously involved in a cabin air fume incident, resulted in identification of about 100 possible pyrolysis products including ketones, acids, aldehydes, esters, oxygen, carbon monoxide, carbon dioxide and ozone. Levels of these were all below 12 parts per billion (ppb). Other sources of potential contaminants in the cabin include de-icing fluid, the galley and lavatories. Any or all of these might contribute to a fume incident.

4. In the context of aircraft cabin air quality, there has been interest in organophosphates present in jet oil. Trimethylol propane phosphate (TMPP) can theoretically be formed from trimethylol propane esters and tri-ortho-cresyl phosphate (TCP), but this has not been demonstrated in experiments replicating pyrolysis conditions. While there are no monitoring data in the aftermath of a documented fume incident, it is considered unlikely that TMPP would be formed during fume incidents in commercial aircraft.

5. In theory, exposure to many of these chemicals can produce short term symptoms e.g. irritation of throat and mucous membranes. It has also been reported that in some aircrew with more prolonged exposure to cabin air there can be long term disabling symptoms, chronic ill-health and ultimately ill-health retirement. There has been no consistent pattern of symptoms reported by those affected. Short term symptoms are described with a clear temporal relationship to exposure. Symptoms include non-specific irritant effects such as itchy weeping eyes, scratchy sensation in throat, chest tightness and itchy skin. There are also reports of loss of memory, poor concentration, tiredness, confusion and headaches. There is no report of these symptoms causing safety issues or crew becoming incapacitated and unable to carry out their duties. The evidence of chronic illness and its nature is also inconsistent, with a series of case reports of symptomatic illness, often with different symptoms, without objective clinical signs, imaging or laboratory test abnormalities reported and no identified underlying pathology. While exposure to a neurotoxic substance is a plausible biological mechanism for symptoms, at least some of these symptoms are more characteristic of anxiety and hyperventilation. The current published epidemiological evidence is insufficient to resolve the issue.

6. In 2000 a group of about 20 Australian aircrew successfully applied for workers' compensation for symptoms attributed to toxic fumes on the aircraft they worked on, while in Britain there was an incident where a captain and first officer became unwell while landing at Birmingham International Airport. They landed safely but were taken to hospital where they quickly recovered with no lasting effects or cause found for the episode. It was eventually linked to a similar episode some years earlier where formaldehyde used as a cleaning agent was identified as the potential hazard. This became the subject of a Civil Aviation Authority (CAA) notification to operators.

7. Over the next few years there were a number of civil claims and international sporadic media coverage as well as, in 2000, government sponsored enquiries, including in Australia and the UK. These included

the UK Department for Transport (DfT) research, which found no link between fume exposure and long term ill-health; an Australian senate investigation, which considered the background to the workers' compensation group action, their Civil Aviation Safety Authority Expert Panel on Aircraft Air Quality considering the scientific evidence; and, in response to many complaints focused on possible organophosphate effects, an investigation by the UK parliament's Select Committee on Science and Technology. This relied heavily on the Australian Senate investigation, noting the absence of confirmed cases of TCP poisoning and going on to find that claims of ill health effects due to organophosphates were not substantiated.

Independent Expert Scientific Review by UK Committee on Toxicology

8. In 2005 the then Department of Health sponsored expert Non-Departmental Public Body (NDPB), the Committee on Toxicology (COT), was asked by the Department for Transport (DfT) to undertake an independent scientific review of data submitted by the British Airline Pilots Association (BALPA) on their concerns regarding possible health and safety effects on aircrew due to fume incidents. Following examination of the BALPA evidence and further literature scrutiny, COT concluded that the evidence was inadequate to resolve the issue although the time sequence of exposure and symptoms made an acute toxic effect plausible. They recommended further monitoring of fume incidents and cabin air contaminants and, for the long term reported symptoms, a cross-sectional study on neuropsychological symptoms in aircrew including people working on different aircraft types and who had variously reported or had not reported, fume incidents (3).

9. In 2013 COT published a position paper on cabin air (4). This commented on reports of four research projects commissioned by the DfT in response to the 2007 COT report recommendations. First, there were two on air sampling devices that might be used to monitor air quality. It was concluded that detection and monitoring was very difficult, especially quality assurance, and that in the absence of major fume events, levels of chemical contaminants were likely to be very low and certainly well below levels which cause symptoms. A third study considered surface residues, specifically four types of organophosphate. Only very low levels of chemicals consistent with those from cabin air sampling were recorded. However, none of the aircraft studied had been subject to a fume incident. The fourth project, a review of fume incidents, was limited by failure to record timing of the incident during the flight and so an opportunity to consider possible trigger events was missed. Finally, the COT literature review update again showed only low levels of pollutants in the absence of a major fume event. One 2013 study included in the review concerned urine monitoring carried out where pilots and air crew reported fumes/odour during their last flight. No samples contained detectable TCP, but the study showed that such an approach was feasible. Another study (2011) illustrated another possible biomarker by monitoring metabolites of TCP in blood using butyryl cholinesterase. This confirmed their presence at very low levels in 6 out of 12 passengers.

10. The committee recorded in its conclusions that the pattern of symptoms reported following fume events was not that expected from exposure to tri-aryl phosphates such as TCP and which itself differs from the pattern seen with over-exposure to organophosphate insecticides and nerve agents. Over-exposure to TCP might be expected to cause delayed peripheral neuropathy but only at much higher exposure levels than the current peak level recorded by air sampling in any study. Other volatile irritant or malodorous organic chemicals could be present in fume, including ketones, aldehydes, esters and ozone. To date, test rig analyses on nearly 100 compounds, simulating flight including aircraft involved in fume incidents, show contamination levels to be low, generally below 100 parts per billion (ppb).

11. The Committee on Toxicology (COT) position paper set out some overall conclusions informed by the recent investigations and the 2007 report findings:

- Contamination of cabin air by components of engine oil and other substance does occur.
- Acute symptoms and illness have been reported in close time proximity to such contamination.
- Some air crew report long term disabling illness which they ascribe to repeated chronic exposure to contaminated cabin air.
- The acute illness in close time proximity to exposure might be a chemical irritant effect of an as yet unidentified chemical or combination of chemicals, but in light of the consistent findings of only very low levels of chemical contaminants, it could also represent a nocebo effect.

Placebo and Nocebo Effects

12. There has been recent interest in the psychobiological mechanisms of placebo and nocebo effects (5). The nocebo effect was first defined in 1961 by Kennedy (6) as an adverse effect from an inert treatment (6). This compares with a placebo effect where a non-active treatment produces a beneficial health effect. While the nocebo effect has been less studied, there is much research interest in the psychological and neurobiological mechanism of the placebo effect in relation to medical treatments. Previously an aim was to reduce placebo effects but today the focus is on maximising them to enhance treatments allowing lower doses of potentially harmful or expensive medications. Placebo effects influence patient satisfaction and there is some evidence that positive expectation may also cause physiological change e.g. reduction in heart rate and blood pressure.

13. In a recent study (7), patients recovering from heart surgery were randomized to three interventions:

- Standard medical care;
- Standard care plus emotional support and encouragement; and
- Care which raised expectations of an excellent functional outcome post- surgery and good quality of life.

Six months after surgery those in the third “expectation” group reported the best outcomes for subjective working capacity and psychological quality of life. The interventions to support the “expectation” group were quite minimalist involving two face to face sessions and three phone calls of which one, six weeks after surgery served to reinforce the earlier interventions. This is a placebo effect.

14. An example of a nocebo effect is where negative expectations limit the effectiveness of a treatment. This can reduce compliance with therapy, patient quality of life and increase costs (8). The media can play an important role, e.g. a new study may be reported as showing that a widely used drug commonly causes unpleasant side effects. This may generate more reports of side effects from patients on that medication and a decision by patients to discontinue the drug. An important example is statins and cholesterol lowering. A meta-analysis of double-blinded randomised controlled primary and secondary cardiovascular prevention trials, involved 83,880 patients and compared statins against placebo for cardiovascular prevention, separately reporting information on side-effects in the statin and placebo arms. The study focused on symptoms (adverse effects). The proportions of patients reporting symptoms (such as muscle pain and fatigue) did not differ between those taking statins and those taking placebos, suggesting that only a minority of problems reported as side-effects of statins are genuinely due to statins (9). A 2017 Scandinavian unblinded statin trial of over 10,000 patients

illustrates the nocebo effect. Side-effects were reported when patients knew that statins were being used but not when the treatment was blinded (10).

Military Compensation Aspects

15. At present we are unaware of any claims for either acute or more chronic disabling symptoms under either AFCS or the War Pension Scheme. It is known that some types of military aircraft continue to use similar environmental control systems for cockpit and cabin air as in some commercial aircraft. It may be that the military working pattern, flying hours and shifts differ such that the problems do not arise.

Recommendation:

16. Current evidence has not identified an environmental basis for the reported acute discrete disorder following fume incidents in aircraft, or the existence of a later onset chronic disabling disorder. We will continue to monitor the literature and AFCS claims made.

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