

**EXPOSURE TO AIRCRAFT BLEED AIR
CONTAMINANTS AMONG AIRLINE WORKERS**

A GUIDE FOR HEALTH CARE PROVIDERS

April 2009

Robert Harrison, MD, MPH¹
Judith Murawski, MSc, CIH²
Eileen McNeely, PhD³
Judie Guerriero, RN, MPH¹
Donald Milton, MD, DrPh⁴

¹University of California, San Francisco

²Association of Flight Attendants-CWA, AFL-CIO

³Harvard School of Public Health

⁴University of Massachusetts Lowell

Funding for this project has been provided by the Federal Aviation Administration Office of Aviation Medicine and is part of a collaborative project between the Occupational Health Research Consortium in Aviation (OHRCA) and the Airliner Cabin Environment research (ACER) Center of Excellence. This document is disseminated under the sponsorship of the U.S. Department of Transportation in the interest of information exchange. The United States Government assumes no liability for the contents thereof.

SUMMARY: The outside air supplied to the cabin/flight deck on commercial aircraft ("bleed air") may sometimes be contaminated with pyrolyzed engine oil and/or hydraulic fluid. As a result of this contamination, airline workers may develop acute and/or chronic health effects and seek attention from health care providers. This document provides information about the health effects that may result after exposure to aircraft bleed air contaminants, and makes recommendations regarding treatment methods. The information in this document is largely based on information that has been published in the medical and scientific literature, and also relies on the clinical experience of one of the authors (Robert Harrison, MD, MPH) who has diagnosed and treated airline workers with contaminated bleed air exposure. A more detailed discussion on the toxicity of tricresylphosphate (TCP) engine oil additives can be found in **Attachment 1**. For more information, web links to additional resources and detailed references are provided at the end of the document.

Address for correspondence

Robert Harrison, MD, MPH
University of California, San Francisco
Division of Occupational and Environmental Medicine
2330 Post Street, Suite 460
San Francisco, CA 94115
Email: Robert.Harrison@ucsf.edu

I BACKGROUND

A EXPOSURE TO PYROLYZED ENGINE OILS AND HYDRAULIC FLUIDS

During flight, high-temperature compressed air is bled off the engines and, after being cooled, is supplied to the cabin and flight deck. On the ground, airlines often rely on a smaller compressor located in the aircraft tail called the auxiliary power unit (APU). Pyrolyzed engine oil or hydraulic fluid may contaminate the air in these compressors as a result of mechanical failures, maintenance irregularities, and faulty designs (ASHRAE, 2007; van Netten, 2000; BAe Systems 2000) (**Table 1**). The most recent National Research Council (NRC) study of this subject concluded that, under certain failure conditions, toxicants such as pyrolyzed engine oils and hydraulic fluids may leak into the aircraft cabin and flight deck air supply systems, and that these toxicants may be associated with health effects (NRC, 2002). The NRC report characterized the need to define the toxicity of these airborne contaminants and investigate the relationship between exposure and reported ill health as a high priority.

TABLE 1: MECHANISMS FOR AIRCRAFT BLEED AIR CONTAMINATION

Type of fault	Example
Mechanical failures	Oil seals that otherwise separate the "wet side" of the air compressor from the "dry side" can leak or fail
Maintenance irregularities	Workers may overfill the oil/hydraulic fluid reservoirs or may spill oil/hydraulic fluid when filling the reservoir
Faulty designs	Some oil seals may be less effective during transient, high-temperature engine operations; the air supply inlet may be in the flow of hydraulic fluid that drips through bilge relief ports and is carried towards the aircraft tail

The airborne toxicants to which aircraft crewmembers and passengers may be exposed when the air supply is contaminated with pyrolyzed engine oil/hydraulic fluid form a complex mixture, including 1-5% tricresylphosphates (TCPs) (added to aircraft engine oils and at least one hydraulic fluid) and N-phenyl-L-naphthylamine (PAN) (Bobb, 2003). If the air supply system temperature is high enough, then the pyrolyzed engine oil/hydraulic fluid may also generate carbon monoxide (CO) (van Netten, 2000).

The tri-ortho isomer has been the most studied of the ten TCP isomers. It is known to cause peripheral neuropathy and is the only isomer for which there is an exposure limit (e.g., OSHA PEL: 0.1 mg/m³). One manufacturer reported that it has reduced the content of the tri-ortho isomer in engine oil formulations (Daughtrey, 2002), but there are nine other TCP isomers of toxicological concern. For more information on the toxicity of the TCPs, see **Attachment 1**.

There is a relative paucity of publicly available sampling data collected *during* bleed air contamination events on commercial aircraft. Recently, researchers commissioned by the UK Department for Transportation conducted a small-scale survey on two aircraft to test the air sampling equipment (Muir, 2008). During short-term sampling on a single flight (B757 aircraft), airborne TCPs and a wide range of aliphatic and aromatic hydrocarbons were identified as the aircraft reached the top of its climb. Ground-based data collection during APU operation on the other aircraft (BAe146) identified tributylphosphates, lubrication oil-related compounds, and ultra-fine particles.

In another study, air sampling was conducted aboard an aircraft with a history of oil odors, but the supply air was passed through a charcoal filter before it was sampled which does not reflect conditions on the vast majority of commercial aircraft. Tributylphosphates were detected on the flight deck air supply filter (Fox, 2000). An unpublished but later-released report on that same sampling survey cited the presence of some TCP isomers on that same aircraft (PCA, 2007). Some additional data refer to air sampling conducted on an aircraft (and on the engine) after a high-profile oil fume event during which the pilot was incapacitated (SHK, 2001), and include TCP isomers and triphenylphosphate (ACARM, 2007a). On military aircraft, TCPs have been found in recirculating air filters (Kelso, 1988) and in the flight deck air (Hanhela, 2005). Finally, TCPs have been identified in wipe sampling data on the cabin and flight deck walls of commercial aircraft (van Netten, 2005).

The concentration of airborne contaminants is expected to vary according to the source of contamination (engine or APU type), aircraft type, and airline maintenance practices (ASHRAE, 2007; NRC, 2002). Crewmembers report that the majority of bleed air contamination events are during taxi/take off or upon descent (Witkowski, 1999), although in airline reports to the FAA, the majority of events were identified during climb (Murawski, 2008). Crewmembers may report a visible haze or smoke in the cabin/flight deck, and/or a smell often described as "dirty socks" (carboxylic acids in burning engine oil), "chemicals", "vomit", or "burning oil". Exposure may be greater in the flight deck than the cabin because of the higher per person bleed air flow. However, pilots' exposure may be reduced as they have immediate access to 100% oxygen while cabin crewmembers do not. In the UK, there have been documented incidents where the pilots were impaired inflight as a result of breathing oil-contaminated air (AAIB, 2007; AAIB, 2004; CAA, 2002; CAA 2000). As a result, airlines have been instructed to develop and enforce operating procedures for pilots to breathe 100% oxygen if they suspect that the air supply is contaminated and ensure that pilots practice incapacitation procedures at their annual training (AAIB, 2007; SAAIB, 2006; CAA, 2002; CAA, 2001; CAA, 2000). Cabin crew have access to short-term oxygen bottles to ensure they stay functional during emergencies, but may be reluctant to use them, largely because they do not know if the source of the air contamination in the cabin is a fire.

There is no independent and standardized reporting system for air supply contamination events, for either passengers or crew. In the US, there are approximately 160,000 flight attendants and pilots in active employment. Most of these employees work at one of 13 large airlines or 14 regional airlines. Bleed air contamination events are underreported (ACARM, 2007b; FAA, 2006) and estimates are based on fragmentary data. Based on data from three airlines in the United Kingdom (UK), members of the UK Committee on Toxicity recently estimated that pilots report smoke/fume events on 1% of flight segments and maintenance workers conduct engineering investigations into smoke/fume events on 0.05% of flight segments, noting that the frequency of events may vary by airframe, engine type, and maintenance practices (COT, 2007). In the past year, US airlines served an average of 1.8 million passengers on 28,200 daily departures (BTS, 2007). So, applying the UK incident data to the US fleet (assuming comparable conditions), translates into approximately 280 bleed air contaminations events each day aboard US aircraft. A recent analysis of bleed air events on the US fleet found documentation for almost one bleed air contamination event per day over an 18-month period (Murawski, 2008). Most of these events were documented by airlines and reported to the FAA per the Service Difficulty Reporting (SDR) system regulations. This figure is an underestimate for a variety of documented reasons, including the fact that airline compliance with the SDR regulations is poor (Ballough, 2006; FAA, 2006). According to several years' data obtained from three airlines in Canada and the US, frequency estimates of bleed air contamination events range from 0.09 to 3.88 incidents per 1,000 flight cycles (NRC, 2002). Thus, the lowest estimate

of 0.09 events per 1,000 flight cycles translates into an average of two to three contaminated bleed air events each day on the US fleet. Finally, an assessment of contaminated bleed air events on one aircraft type operated by an Australian airline reported 15 oil fume events per 1000 flight cycles (PCA, 2000).

B DOCUMENTATION OF EXPOSURE TO BLEED AIR CONTAMINANTS

It is often difficult for health care providers (HCPs) to document the nature and extent of airline cabin crew exposure to pyrolyzed engine oil or hydraulic fluid. There is typically no sampling of airborne contaminants that has been performed, or any data for similar incidents that can be used for reference purposes. There are no reference criteria (e.g., PELs, TLVs, MAKs) for many TCP isomers, making evaluation of the extent of exposure difficult. Industrial exposure standards were not developed for application on aircraft (Rayman, 2002; Fox, 2000) and little is known about the health effects of exposure to mixtures of contaminants.

As noted above, in addition to the chemical constituents of pyrolyzed engine oil and/or hydraulic fluid, contaminated bleed air may also contain CO as a byproduct of incomplete combustion. Acute exposure to CO may cause symptoms of nausea, headaches, dizziness, and drowsiness. Chronic neurological sequelae have been reported after acute high-level exposure to CO (Prockop, 2007).

The HCP may obtain several sources of information that may aid in assessing exposure (**Table 2**). In addition to obtaining the Material Safety Data Sheet (MSDS) for engine oils and/or hydraulic fluids, other documents may provide clues about the mechanism and source of exposure. Each of these sources is subject to several limitations, however.

TABLE 2: INFORMATION SOURCES FOR ASSESSING EXPOSURE TO CONTAMINATED BLEED AIR

Source	Documentation	Limitations
Airline	Pilot logbook entries that describe conditions in the cabin/flight deck and possible mechanical irregularities (reportable per 14 CFR 121.563).	Pilots need not log the symptoms reported by aircraft occupants, and airlines need not release the aircraft logbook to employees or HCP.
Airline	Aircraft maintenance records, in particular those found in Air Transport Association Maintenance Manual chapters 5, 21, 29, 36, 49, 78, and 79 and covering the period 60 days prior to the event and 30 days after.	Difficult to obtain because OSHA's Access to Exposure and Medical Records Standard (29 CFR 1910.1020) does not apply to crewmembers. These records can prove air supply contamination but may require the interpretation of an airline mechanic.
FAA SDR/online	Online and searchable Service Difficulty Reporting System to which airlines are required to report smoke/fume events per 14 CFR 703(a)(5).	Airline compliance with reporting requirements is poor (Ballough, 2006; FAA, 2006).
Employee/ Online	MSDSs for particular engine oil or hydraulic fluid suspected to have contaminated air supply system. The employee should be able to obtain the name of the product in question. All aviation engine oils used in the US fleet contain 1-5% TCPs and a complex mixture of hydrocarbons. The latest version of a MSDS should be posted on the manufacturer's website. HCPs are also encouraged to identify independent product information.	MSDSs typically provide incomplete toxicity information that is based either on ingestion or dermal toxicity, or on animal data limited to assessing motor skills, not more subtle cognitive functions. OSHA's Hazard Communication Standard (29 CFR 1910.1200) does not apply to crewmembers but the MSDS for a given oil or hydraulic fluid is typically easy to obtain.

C HEALTH EFFECTS ASSOCIATED WITH EXPOSURE TO CONTAMINATED BLEED AIR

The health effects of exposure to pyrolyzed engine oil and hydraulic fluid on aircraft is difficult to assess for several reasons, including the absence of a centralized system to collect and analyze reported bleed air exposures, and the lack of a large scale epidemiological survey to systematically assess health effects and correlate these with exposures. Furthermore, symptoms are often nonspecific and may not be reported by airline cabin crew or recognized as work-related by HCPs.

Exposure to contaminated bleed air occurs through the inhalation route, and may typically result in acute respiratory, neurological, systemic, and/or psychiatric symptoms typically occur within minutes to a few hours following the contaminated bleed air event, and may vary depending on the duration and magnitude of exposure. Medical record review of airline crew members who were examined after exposure to contaminated bleed air found acute respiratory and/or central nervous system symptoms among the most commonly reported (**Table 3**).

TABLE 3: CASE SERIES – ACUTE HEALTH EFFECTS FOLLOWING EXPOSURE TO CONTAMINATED BLEED AIR*

Age	Exposure document	Symptoms	Signs/ Positive tests
26	Cabin Incident Report	muscle pain, chest pain, throat irritation, dizziness, loss of balance, L arm numbness, stuttering	PE: decreased plantar reflexes, memory loss Psychiatric evaluation: conversion disorder
38	Cabin Incident Report	Weakness, nausea, vomiting, dizziness	PE: tremor, nasal congestion, throat hyperemia and edema
39	Employee Incident Report	Myalgias, eye irritation, headache, disorientation	PE: poor serial 7s, memory loss
38	Flew MD-80	Nausea, vomiting, throat irritation, headache, lightheadedness, slurred speech, anxiety, fatigue, insomnia, wheezing, cough	PE: poor serial 7s, memory loss
42	Mechanical Report	Nausea, vomiting, diarrhea, headache, throat irritation, lightheadedness, slurred speech	Laboratory: decreased plasma cholinesterase Neuropsychological testing: attention and information processing deficits, learning and memory impairments
39	Mechanical Report	Headache, dizziness	PE: R hand tremor Psychiatric evaluation: depression, anxiety
49	Doctors First Report	Nausea, vomiting headache, chest tightness	PE: wheezing, rhonchi.
36	Flew MD-80	Headache, confusion, extremity jerks	PE: truncal movement disorder
32	Flew MD-80	joint pain, nausea, vomiting, confusion, loss of balance, anxiety	PE: ataxia
51	Mechanical report	Nausea, vomiting, throat irritation, cough, SOB, chest tightness, headache, lightheadedness, memory loss	Laboratory: decreased plasma cholinesterase
49	Pilot report	eye burning, throat irritation, headache, nausea	PE: mucous membrane erythema, abnormal Romberg, tandem gait

*** Cases examined and reviewed by author (Robert Harrison, MD). All cases met the case definition below.**

In all of these cases, airline crew submitted written reports to their airlines of in-flight exposure to airborne contaminants that they suspected to be engine oil or hydraulic fluid. The sources of exposure were often confirmed by aircraft mechanical records. All developed acute symptoms that were temporally associated with exposure and sought immediate medical care. In some cases, their symptoms persisted, necessitating long-term medical care. Many of the neurological symptoms reported by airline cabin crew following contaminated bleed air exposure are similar to those reported among other workers exposed to triarylphosphates (Schulte, 1996; Krebs, 1995). Pilot impairment or incapacitation inflight has been attributed to exposure to oil fumes (AAIB, 2007; SAAIB, 2006; FAA, 2004; CAA, 2002; CAA, 2001; CAA, 2000; Rayman, 1983; Montgomery, 1977).

A summary of acute and chronic symptoms is summarized in **Tables 4 and 5** (Mackenzie-Ross, 2006; Abou-Donia, 2005; Harper, 2005; Somers, 2005; Winder, 2005; Burdon, 2005; Singh, 2005; Michaelis, 2003; Bobb, 2003; Coxon, 2002; Cox, 2002; PCA, 2000; van Netten, 1999; Witkowski, 1999; Rayman, 1983; Montgomery, 1977).

TABLE 4: ACUTE SYMPTOMS FOLLOWING EXPOSURE TO CONTAMINATED BLEED AIR

Respiratory	Neurological	Systemic	Psychiatric	Dermal
Cough	Headache	Nausea, vomiting	Anxiety	Rash
Shortness of breath	Dizziness	Fatigue	Sleep disturbance	
Chest tightness	Lightheadedness	Muscle weakness	Depression	
Wheezing	Memory impairment	Palpitations	PTSD	
Eye, nose or throat irritation	Concentration difficulty	Diarrhea		
	Visual changes			
	Tremor			
	Gait problems			
	Paraesthesias			
	Balance problems			
	Slowed mental processing			
	Difficulty multi-tasking			

TABLE 5: CHRONIC SYMPTOMS FOLLOWING EXPOSURE TO CONTAMINATED BLEED AIR

Respiratory	Neurological	Systemic	Psychiatric	Dermal
Cough	Headache	Nausea, vomiting	Anxiety	Rash
Shortness of breath	Slowed mental processing	Fatigue	Sleep disturbance	
Chest tightness	Difficulty multi-tasking	Muscle weakness	Depression	
Wheezing	Memory impairment	Palpitations	PTSD	
	Concentration difficulty	Diarrhea		
	Visual changes			
	Tremor			
	Gait problems			
	Paraesthesias			
	Balance problems			

D SIGNS AND SYMPTOMS ASSOCIATED WITH OTHER EXPOSURES ON BOARD COMMERCIAL AIRCRAFT

In addition to contaminated bleed air, airline cabin crew may also be exposed to other environmental hazards aboard commercial aircraft (**Table 6**). The symptoms and health effects of these exposures should also be considered by the HCP in evaluating the airline cabin crew member (Murawski, 2005a).

TABLE 6: EXPOSURES AND DOCUMENTED HEALTH EFFECTS

Exposure	Source/description	Symptoms/health effects	References
Reduced oxygen	The cabin is typically pressurized between 6,000 and 8,000 feet, which can cause symptoms of hypoxia and exacerbate the effects of some chemical exposures.	Dizziness, headache, fainting, cardio/pulmonary complaints, possible increased risk of DVT	Schreijer, 2006; Muhm, 2004; Crosby, 2003; NRC, 2002; Waters, 2002; Schobersberger, 2002; Christensen, 2000; Casley-Smith, 1996; Cottrell, 1995 and 1988
Ozone	Many commercial aircraft operate within the ozone layer. Ozone levels increase with altitude and latitude and are highest in late winter and early spring. Sampling on aircraft equipped with catalytic converters reported gate-to-gate average levels of ozone ranging from < 0.05 to 0.24 ppm.	Chest tightness, wheezing, cough	Spengler, 2004; Waters, 2002; Tashkin, 1983
Insecticides	Applied for domestic insect control and to comply with foreign quarantine requirements, typically 2% permethrin or phenothrin, sometimes with piperonyl butoxide, sprayed when the aircraft is occupied or shortly before boarding and then routed domestically. History of DDT application on commercial aircraft.	Respiratory irritation, shortness of breath, wheezing, skin rash, headache, irritability, neuropathy, dizziness, ataxia, confusion, weakness, sweating	Sutton, 2007; Carlson, 2006; DOT, 2006; Murawski, 2005b; NRC, 2002; ICAO, 2001; EPA, 1996; ACAP v. USDA, 1977
Deicing fluids	Contain propylene glycol, diethylene glycol, or methylene glycol; can be entrained into the supply air during ground operations.	Respiratory irritation, headache	SAE, 1997
Exhaust fumes from ground service vehicles/other aircraft, fuel vapor	Exhaust contains nitrous oxides and ozone; can be entrained into the supply air. Fuel vapor may enter aircraft air supply systems during ground operations.	Respiratory irritation, headache	
Disinfectants, deodorizers	Cleaning staff sprays disinfectants and deodorizers in the cabin containing active ingredients, solvents, and propellants.	Respiratory irritation, skin sensitization	

II EVALUATION OF HEALTH EFFECTS

A CASE DEFINITION

Based on review of the medical literature and the case series as summarized above, the HCP may consider the following case definition for acute exposure to contaminated bleed air:

An *acute* health problem due to bleed air contaminant exposure should be considered if these factors are shown to be present:

- There is *either* a documented exposure to bleed air contaminants (based on evidence in the mechanical records, incident reports, or airborne measurements) *or* a history of flying on aircraft type(s) documented to have an increased risk of air supply contamination events;

and

- Initial symptoms occur within 48 hours following exposure;

and

- There is objective documentation of acute and/or persistent respiratory, neurological, systemic, or psychiatric symptoms that follow exposure to bleed air contaminants; see Tables 4 and 5.

In addition, chronic health effects may result from acute and/or chronic exposure to contaminated bleed air. In some cases, the individual crewmember may not recall symptoms

occurring many months or years prior to examination by the HCP. These cases should be evaluated on a case-by-case basis to determine the likelihood that health problems are due to contaminated bleed air exposure.

Whenever possible, the clinician should attempt to identify the exposure and make a precise diagnosis (e.g., avoid generic terminology such as “inhalation exposure”) based on a combination of symptoms and objective evidence of health effects (physical examination findings and/or medical tests).

B HISTORY OF ILLNESS

The clinician should obtain a complete history of the circumstances aboard the aircraft on the flight in question, including symptom onset, medical history, whether other crewmembers were affected, and any emergency treatment rendered. Acute symptoms of respiratory, neurological, and systemic toxicity, as well as psychiatric effects, should be documented. Skin rash may occur but is not likely in the absence of other symptoms.

C ASSESSING EXPOSURE AND RISK

Information about the nature and extent of the exposure to bleed air contaminants is critical to establishing the diagnosis. The clinician should attempt to collect the details listed in **Table 7**.

TABLE 7: FLIGHT-SPECIFIC QUESTIONS TO ASK THE CREWMEMBER

What was the date, flight number, aircraft number, and aircraft type?
During what phase(s) of flight was the problem noted (ground operations, taxi, climb, cruise, descent, landing, taxi in, off duty/post-flight)?
Was there a noticeable odor or any visible fumes/smoke/mist?
How long did the exposure last (if known)?
Is the employee aware of a possible cause suggested by maintenance workers or airline officials?
Is the crewmember aware of whether their aircraft had been sprayed with pesticides?

D PAST MEDICAL HISTORY

The past medical history should be obtained to determine preexisting conditions and/or risk factors that may predispose the individual to illness caused by exposure to bleed air contaminants, as well rule out alternative explanations for presenting signs and symptoms. This should include respiratory conditions (asthma, COPD), neurological problems (including headaches), psychological disorders (panic disorder, PTSD, depression), and medication use. To evaluate risk factors for neurobehavioral disorders, the HCP should obtain a history of prior head injury, prior neurological illnesses (such as meningitis), systemic disorders (e.g., diabetes, liver disease, metabolic disorders), caffeine and alcohol intake, use of recreational drugs, and family history of memory, cognitive or emotional problems. For pilots, the date of last aviation medical examination may provide useful data regarding fitness for duty. Previous medical records should be obtained and reviewed as appropriate.

Differences in individual susceptibilities to the effects of exposure to particular organophosphates may be influenced by genetics, levels of particular hormones associated with menstruation and pregnancy, liver disease, age, obesity, certain medications, and exposure to mixtures of particular chemicals that can influence the availability and efficacy of enzymes involved in their metabolism, and could thereby influence the degree of toxic effect (NRC, 2002; Haley, 1999; Gene, 1997; Mutch, 1992; Howard, 1978; Davis, 1948).

E OCCUPATIONAL HISTORY

The HCP should obtain an occupational history, including the factors listed in **Table 8**.

TABLE 8: OCCUPATIONAL FACTORS

Employment prior to airline work, including occupations in which inhalation and/or dermal exposure to chemicals may have occurred.
The duration of employment as a flight attendant or pilot.
History of previous exposure episodes (including exposures to pesticides used aboard aircraft), prior workers' compensation claims, and previous lost work time incidents due to bleed air exposures.

It has also been suggested that previous chemical exposures can increase susceptibility to toxic effects of subsequent exposures, resulting from a loss of tolerance following exposure to various toxicants, and subsequent triggering of symptoms by extremely small quantities of previously-tolerated chemicals (Miller, 1997).

F SOCIAL AND FAMILY HISTORY

Several non-occupational factors are important to evaluate in the context of examining the airline cabin crew member with contaminated bleed air exposure, as these may affect the interpretation of signs and symptoms; see **Table 9**.

TABLE 9: SOCIAL AND FAMILY FACTORS

Personal hobbies with exposures to chemicals.
Smoking status and exposure to second hand smoke (may increase the likelihood of respiratory symptoms).
Family history of asthma (if respiratory symptoms or signs are present).
Frequency of ingestion and quantity of alcohol (excessive use may contribute to neurological dysfunction).

G PHYSICAL EXAMINATION

The physical examination should focus on the respiratory tract, with attention to mucous membrane erythema and mucous discharge (upper), and wheezing, rhonchi and crackles (lower). A neurological examination should be performed, with assessment of cerebellar function, tremor and gait disturbance.

A neuropsychological screening examination may be useful if symptoms suggest cognitive dysfunction, with assessment of short-term memory function, concentration and color vision loss.

H LABORATORY DATA AND OTHER TESTS

A blood test specific to the TCP additives in aviation engine oils and some hydraulic fluids is under development but is not yet available for routine use (Furlong, 2007). Currently, the only available tests are listed in **Table 10**. These tests may provide objective evidence of exposure that will assist with confirming the diagnosis and guiding treatment. Red blood cell/acetyl cholinesterase (AChE) is not a useful blood test because the TCP engine oil additives have only a minor effect on AChE levels.

TABLE 10: TESTS TO ASSESS EXPOSURE TO BLEED AIR CONTAMINANTS

Test	Timeframe	Interpretation/limitations
Plasma cholinesterase (PChe)	Within 24 hours if suspected exposure to engine oil or hydraulic fluid that contains TCPs, although initial sample collection within seven days may still yield useful data. Proper collection and transport techniques must be followed. Repeat tests at intervals over one month to properly interpret changes.	Interpretation of PChe results are complex: PChe can be initially depressed, followed by a "rebound effect." The "normal" range of PChe is broad, and therefore an initial result within the "normal" range may be below the individual's baseline or pre-exposure level, which is another reason that subsequent testing can be helpful.
Oxygen saturation	Within an hour if crewmember took oxygen during the flight; otherwise, within four hours.	Care must be taken in interpreting results if more than a few hours have passed since the exposure has ceased, or with the prior administration of supplemental oxygen.
Arterial carboxyhemoglobin	Immediately following suspected exposure to pyrolyzed organics (likely oil or hydraulic fluid)	Carboxyhemoglobin does not provide a sensitive measure of the extent of contaminated bleed air exposure because the bleed air temperature is not always high enough for CO to be present.
Pulmonary function tests (spirometry)		Tests with pre/post bronchodilators should be obtained in the presence of respiratory symptoms or relevant physical examination findings.
Chest xray		Suggested if pulmonary edema and/or infiltrates are suspected (ARDS).

I TREATMENT AND REPORTING

The acute neurological and respiratory effects of contaminated bleed air exposure are treated primarily by prompt removal from the exposure. Some evidence suggests that

hyperbaric oxygen may reduce the risk of long-term sequelae in the setting of highly elevated carboxyhemoglobin (Weaver, 2002). Respiratory effects should be treated according to standard protocols for acute chemical inhalation; this includes the use of aerosolized bronchodilators and supplemental oxygen where bronchospasm and/or pneumonitis is present. The use of intravenous corticosteroids after acute chemical inhalation with bronchospasm may improve prognosis.

The diagnosis of work-related illness or injury should be reported to the appropriate state and/or workers' compensation authorities according to relevant requirements. A few states (e.g., CA) require pesticide illnesses to be reported separately as well. Pilots should advise their aviation medical examiner of their exposure at their next renewal examination, or as per applicable regulations. HCPs should note that crewmembers are not covered by OSHA regulations (FAA, 1975) and the FAA has not promulgated comparable occupational safety and health regulations since assuming jurisdiction in 1975 (FAA-OSHA, 2000).

J DISABILITY MANAGEMENT AND FOLLOW-UP

The course of improvement for acute respiratory, neurological, systemic, and psychiatric effects varies, but symptoms often improve and resolve within a few weeks. Exposure to contaminated bleed air may result in chronic health effects in some airline workers. Immediately following acute exposure, the airline worker should avoid exposure to contaminated bleed air. This may entail removal from work, or modified or restricted duty if available. In addition, workers should avoid exposure to other airborne contaminants such as diesel exhaust, jet fuel, and cleaning products (Miller, 1997). Follow-up medical evaluation and return to work clearance should first be performed after one to two weeks. If all respiratory, neurological, systemic, and psychiatric symptoms have resolved, the airline worker can be cleared to return to work on full duty.

If symptoms have not resolved within 1 to 2 weeks, the airline worker should continue to be examined to assess the course of recovery; see **Table 11** for additional guidance. Some airline workers may have recurrent symptoms on return to work due to re-exposure to contaminated bleed air, and/or ongoing exposure to other airborne contaminants in the aircraft environment. If symptoms have not completely resolved within 2 months following one or more contaminated bleed air exposures, the clinician should consider the likelihood that persistent health effects have occurred and will need additional evaluation and/or treatment. If symptoms persist, the airline worker should remain off work or on modified duty until complete evaluation can be performed. Depending on severity, persistent respiratory, neurological, systemic and psychiatric problems may preclude the airline worker from return to his/her usual job. Modified duty (such as a ground job) may be suitable for some crewmembers depending on their functional status.

TABLE 11: TIME COURSE FOR MEDICAL FOLLOW UP

Time course, post-exposure	Suggested medical follow up
Within 1-2 weeks	Will require follow up medical evaluation and return to work assessment. If all respiratory, neurological, systemic, and psychiatric symptoms have resolved, then the airline worker can be cleared to return to work on full duty.
Beyond 1-2 weeks	If symptoms have not resolved, airline worker should continue to be examined to assess the course of recovery.
Two months and beyond	If symptoms have not completely resolved, consider the likelihood that persistent health effects have occurred and will need additional evaluation and/or treatment. Persistent health problems may preclude the airline worker from return to his/her usual job. Modified duty (such as a ground job) may be suitable depending on functional status.

The most common chronic respiratory, neurological, systemic and psychiatric health effects are described below:

- (1) **Irritant-induced asthma** may occur after an acute, single episode of chemical inhalation where symptoms of asthma persist for greater than 3 months following the exposure episode. Airline cabin crew with acute respiratory symptoms after bleed air exposure should be advised to seek medical follow-up if their respiratory symptoms persist. Spirometry (pre/post bronchodilator administration) and methacholine inhalation challenge should be performed to document the presence of persistent asthma. Chemical bronchitis

that gradually resolves is more likely to occur after an irritant exposure than persistent asthma. Complete pulmonary function testing with lung volumes and diffusing capacity as well as chest imaging should be obtained if respiratory disease other than asthma or bronchitis is suspected. The treatment for persistent asthma is inhaled bronchodilator and inhaled corticosteroids following the Global Initiative for Asthma guidelines (GINA 2006).

- (2) **Persistent neurological problems** may occur following bleed air exposure, and can include headaches, confusion, loss of balance, lightheadedness, muscle weakness, movement disorders, numbness, and paraesthesias. Neurobehavioral problems include cognitive dysfunction, post-traumatic stress disorder, emotional lability, depression, sleep and anxiety disorders. Neurological, neuropsychological or psychiatric consultation should be obtained if symptoms persist for greater than 1 to 2 months following bleed air contaminant exposure. Testing should include visual, somatosensory, and brainstem audio evoked potentials, and color desaturation that may be sensitive measures of neurotoxic injury. A psychologist with experience evaluating brain injury following neurotoxic exposure should perform a complete neuropsychological evaluation (Coxon, 2002; Mackenzie-Ross, 2005). The neuropsychological tests may assist in the differentiation of organic brain injury and psychiatric disorder. The brain MRI can be useful to rule out the presence of space occupying lesions and demyelinating diseases, but it is not sensitive enough to characterize more subtle changes in brain chemistry or receptors, so it is usually normal after neurotoxic exposure (Menon, 2004; Meyerhoff, 2001; Haley, 2000a; Haley, 2000b). EEG results are usually nonspecific and not useful in confirming the diagnosis of neurotoxic injury, but may be helpful in excluding other conditions. Although unusual, if symptoms suggest peripheral nerve damage, NCVs, EMGs and quantitative sensory testing should be performed to assess the presence of sensory loss. A SPECT or PET scan may be helpful confirm the clinical diagnosis of neurotoxic brain injury (Heuser, 1998), but should not be utilized solely for diagnostic purposes.

Treatment for neurotoxic injury is directed by the specific diagnosis. Avoidance of any triggering agents in the general environment is recommended. Headaches are often vascular in nature and may require the use of various analgesic and other medications directed at this condition. Treatment of persistent neurological and neuropsychological problems is directed at improvement of functional status. Crewmembers who have cognitive impairment should seek advice from neuropsychologists who have expertise in rehabilitation following neurotoxic injury or traumatic brain injury. As there are limited treatment options available, some individuals may seek alternative treatment techniques that have not generally been subjected to clinical studies. Although treatment techniques such as high dose intravenous vitamin and nutritional supplementation, oxygen therapy, yoga, and sauna detoxification have been anecdotally reported to be of limited benefit in individual cases, these have not confirmed as effective in clinical trials. The HCP should encourage Improvement of functional status through exercise, adequate sleep, well balanced diet, and adequate hydration.

- (3) **Systemic symptoms.** Other long-term effects reported by some patients include persistent gastrointestinal problems, increased sensitivity to chemicals, myalgias, arthralgias, palpitations, and unusual fatigue. The presence of underlying hematological, immunological or gastrointestinal disorders should be evaluated by appropriate testing and/or referral to relevant specialists.

- (4) **Post-exposure psychiatric problems** such as PTSD, depression and anxiety should be referred for psychiatric evaluation and treatment. Pharmacological treatment and counseling may be helpful in the management of these disorders.

There are currently no tests of sufficient sensitivity and specificity to assess exposure/health affects outcomes. Various biomarkers and other assays to assess target organ and physiological effects from exposure to cabin air contaminants are currently under development (Furlong, 2007). Preliminary research suggests tests of the autonomic nervous system and autoantibodies may be useful in evaluating exposure and chronic neurotoxicity (Abou-Donia, 2005; Julu, 2005). However, these assays are not routinely available to the health care provider. In the future, these tests may prove to be useful in confirming exposure and/or risk of subsequent disease, but additional research is needed before they can be routinely used in the clinical setting.

II ATTACHMENTS

ATTACHMENT 1 – TOXICITY OF TRICRESYLPHOSPHATE ENGINE OIL ADDITIVES

III ADDITIONAL RESOURCES

Association of Flight Attendants-CWA, AFL-CIO – see <http://ashsd.afacwa.org>.

Association of Occupational & Environmental Clinics – see <http://www.aoec.org>.

Aviation Organophosphate Information Site – see <http://www.aopis.org>.

Poison Control & Prevention Center – see <http://www.aapcc.org/findyourcenter.htm>.

IV REFERENCES

AAIB (2007) Bulletin no. 4/2/07, Bombardier DHC-8-400, G-JECE (EW/C2005/08/10), UK Air Accidents Investigation Branch, UK Department for Transport

AAIB (2004) Report no. 1/2004, BAe146, G-JEAK (EW/C2000/11/4) UK Air Accidents Investigation Branch, UK Department for Transport

Abou-Donia, M. (2005) "Organophosphate ester induced chronic neurotoxicity (OPICN)" In: "Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference," pp. 59-90. Imperial College, London, 20-21 April 2005, Winder, C. ed., University of New South Wales, Sydney, Australia

ACAP v. USDA (1977) Complaint in civil court, Civil Action No. 77-1941, Aviation Consumer Action Project et. al. v. United States Department of Agriculture, US District Court for the District of Columbia, Washington, DC

ACARM (2007a) "Appendix 10: Air monitoring research summary" Aviation Contaminated Air Reference Manual, Michaelis, S., ed., p.760. ISBN 9780955567209, London, England

ACARM (2007b) "Chapter 12: Frequency of events and underreporting" Aviation Contaminated Air Reference Manual, Michaelis, S., ed., pp. 211-248. ISBN 9780955567209, London, England

ASHRAE (2007) "ANSI/ASHRAE Standard 161-2007: Air quality within commercial aircraft" American Society of Heating, Refrigerating, and Air Conditioning Engineers, Inc. Atlanta, GA

BAe Systems (2000) "BAe 146 manufacturer's operations manual: notice to aircrew, operational notice: No. OP 16 and 43 (Issue 1)" British Aerospace Systems, Hatfield, UK

Ballough, J (2006) "Smoke/fumes in the cockpit/cabin" Powerpoint presentation by the Director of Flight Standards, US Federal Aviation Administration. US/Europe International Aviation Safety Conference, 6-8 June 2006, Portland, OR

Bobb, AJ (2003) "Known harmful effects of constituents of jet oil smoke" TOXDET-03-04 Naval Health Research Center Detachment (Toxicology), Wright-Patterson AFB, OH

BTS (2007) US Bureau of Transportation Statistics, Airline activity: National summary of US flights. Washington, DC; See www.transtats.bts.gov

Burdon, J; Glanville, AR "Lung injury following hydrocarbon inhalation in BAe146 aircrew" In: "Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference," pp. 53-58. Imperial College, London, 20-21 April 2005, Winder, C. ed., University of New South Wales, Sydney, Australia

CAA (2002) "Flight Operations Department Communications (FODCOM) 21/2002" UK Civil Aviation Authority, Safety Regulation Group, Aviation House, Gatwick, West Sussex, England

CAA (2001) "Flight Operations Department Communication (FODCOM) 14/2001" UK Civil Aviation Authority, Safety Regulation Group, Aviation House, Gatwick, West Sussex, England

CAA (2000) "Flight Operations Department Communication (FODCOM) 17/2000" UK Civil Aviation Authority, Safety Regulation Group, Aviation House, Gatwick, West Sussex, England

Carlson, DA; Hogsette, JA; Kline, DL; et al (2006) "Prevention of mosquitoes and house flies from entering simulated aircraft with commercial air curtain units" *J Econ Entomol*, 99(1): 182-193

Casley-Smith JR and Casley-Smith JR (1996) "Lymphedema initiated by aircraft flights" *Aviat Space Environ Med* 67:52-56

Christensen, CC; Ryg, M; Refvem, OK; et al (2000) "Development of severe hypoxaemia in chronic obstructive pulmonary disease patients at 2,438 m (8,000 ft) altitude" *Eur Respir J*, 15:635-9

COT (2007) "Statement on the review of the cabin air environment, ill health in aircraft crews, and the possible relationship to smoke/fume events in aircraft" UK Committee on Toxicity of Chemicals in Food, Consumer Products, and the Environment, UK Department of Health, London, England

Cottrell, JJ (1988) "Altitude exposures during aircraft flight: flying higher" *Chest*, 92:81-84

Cottrell, JJ; Lebovitz, BL; Fennell, RG; Kohn, GM (1995) "In-flight arterial saturation: continuous monitoring by pulse oximetry" *Aviat Space Environ Med*, 66: 126-130

Cox, L; Michaelis, S (2002) "A survey of health symptoms in BAe146 aircrew" *J Occup Health Safety - Austr NZ*, Vol. 18(4): 305-312

Coxon, L (2002) "Neuropsychological assessment of a group of BAe146 aircraft crew members exposed to jet engine oil emissions", *J Occup Health Safety - Austr NZ*, Vol. 18(4): 313-319

Crosby, A; Talbot, NP; Harrison, P; et al (2003) "Relation between acute hypoxia and activation of coagulation in human beings" *Lancet*, 361:2207-8

Daughtrey, WC (2002) "Mobil Jet Oils" Presentation to Alaska Airlines by Exxon-Mobil Biomedical Sciences, 20 Aug 2002, Seattle, WA

Davis, ME; Yu, EA; Fugo, NW (1948) "Studies on the non-specific cholinesterase in the serum of the human female" *JCE*, Vol 8: 666-673

DOT (2006) Aircraft disinsection requirements; see <http://ostpxweb.dot.gov/policy/Safety%20Energy%20Env/disinsection.htm>
US Department of Transportation, Washington DC

EPA (1996) "Pesticide Reregistration Notice 96-3: Notice to manufacturers, producers, formulators, and registrants of pesticide products" US Environmental Protection Agency, Washington DC

FAA (2006) Flight Standards Information Bulletin for Airworthiness (FSAW) 06-05A "Guidance for smoke/fumes in the cockpit/cabin" US Federal Aviation Administration, Aircraft Maintenance Division, Washington, DC

FAA (2005) "Flight attendant fatigue" Civil Aerospace Medical Institute and Federal Aviation Administration, Washington, DC

FAA (2004) FAA (2004) Airworthiness Directives; BAE Systems (Operations) Limited Model BAe 146 Series Airplanes, Docket No. 2003-NM-94-AD; Amendment 39-13664; AD 2004-12-05, Federal Aviation Administration, Washington, DC

FAA-OSHA (2000) "Application of OSHA's requirements to employees on aircraft in operation: first report" FAA-OSHA Aviation Safety and Health Team, Washington, DC

FAA (1975) 40 US Federal Register at 29114

Fox, R (2000) " Air quality and comfort measurement aboard a commuter aircraft and solutions to improve perceived occupant comfort levels" In: Air Quality and Comfort in Airliner Cabins, pp. 161-186. ASTM STP 1393, NL Nagda, Ed., American Society for Testing and Materials, West Conshohocken, PA

Furlong, CE (2007) Personal communication with Professor Furlong, Research Professor in Genome Sciences and Medicine, University of Washington, Seattle, WA

Gene, S; Gurdol, F; Guvene, S; et al (1997) "Variations in serum cholinesterase activity in different age and sex groups" *Eur J Clin Chem Biochem*, 35(3): 239-40

GINA (2006) "Global Initiative For Asthma"; see <http://www.ginasthma.com>

Haley, RW; Marshall, WW; McDonald, GC; et al (2000a) "Brain abnormalities in Gulf War Syndrome: Evaluation with H MR Spectroscopy" *Radiology*, 215: 807-817

Haley, RW; Fleckenstein, JL; Marshall, WW; et al (2000b) "Effect of basal ganglia injury on central dopamine activity in Gulf War Syndrome" *Arch Neurol*, 57: 1280-1285

Haley, RW; Billecke, S; La Du, BN (1999) "Association of low PON1 type Q (type A) arylesterase activity with neurologic symptom complexes in Gulf War veterans" *Toxicol Appl Pharmacol* 157:227-33

Harper, A (2005) "A survey of health effects in aircrew exposed to airborne contaminants" *J Occup Health Safety – Austr NZ*, Vol. 21(5): 433-439

Heuser, G and Mena, I (1998) "Neurospect in neurotoxic chemical exposure: Demonstration of long-term functional abnormalities" *Toxicol Industr Health*, 14(6): 813-26.

Howard, JK; East, NJ; Chaney, JL (1978) "Plasma cholinesterase activity in early pregnancy" *Arch Environ Health* 277-279

ICAO (2001) "Aircraft disinsection practices survey" FALP/3-IP/1 International Civil Aviation Organization, Montreal, Canada

Jamal, GA; Hansen, S; Julu PO (2002) "Low level exposures to organophosphorus esters may cause neurotoxicity" *Toxicol*, 181-182: 23-33

Julu PO; Hansen S; Jamal, GA (2005) "Pattern of autonomic lesions and neurophysiological features of long-term exposure to the organophosphates in sheep-dip" In: "Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference," pp. 217-238. Imperial College, London, 20-21 April 2005, Winder, C. ed., University of New South Wales, Sydney, Australia

Krebs, JM; Park, RM; Boal, WL (1995) "A neurological disease cluster at a manufacturing plant" *Arch Environ Health* 50:190-5

Mackenzie-Ross, S (2006) "Cognitive function following reported exposure to contaminated air on commercial aircraft: An audit of 27 airline pilots seen for clinical purposes." Report for the UK Committee On Toxicity Of Chemicals In Food, Consumer Products And The Environment. Consultant Clinical Neuropsychologist and Chartered Clinical Psychologist, Sub-Department of Clinical Health Psychology, University College London

Menon, PM; Nasrallah, HA, Reeves, RR; Ali, JA (2004) "Hippocampal dysfunction in Gulf War Syndrome: A proton MR spectroscopy study" *Brain Research*, 1009: 189-94

Meyerhoff, DJ; Lindgren, J; Hardin, D; et al (2001) "Metabolic abnormalities in the brain of subjects with Gulf War Illness" *Proc Intl Soc Mag Reson Med*, 9:994

Michaelis, S (2003) "A survey of health symptoms in BALPA B757 pilots" J Occup Health Safety – Austr NZ, 19(3): 253-61

Miller, CS (1997) "Toxicant-induced loss of tolerance – an emerging theory of disease?" Environ Health Perspectives, 105(Suppl 2): 445-453

Montgomery, MR; Wier, GT; Zieve, FJ; et al (1977) "Human intoxication following inhalation exposure to synthetic jet lubricating oil" Clinical Toxicol, 11(4): 423-26

Muhm, JM (2004) "Predicted arterial oxygenation at commercial aircraft cabin altitudes" Aviat Space Environ Med, Vol. 75(10): 905-915

Muir, H; Walton, C; McKeown, R (2008) "Cabin air sampling study: functionality test" Report prepared for the UK Department for Transport, Cranfield University, UK

Murawski, JTL; Supplee, DS (2008) "An attempt to characterize the frequency, health impact, and operational costs of oil in the cabin and flight deck supply air on US commercial aircraft" J of ASTM International, Vol. 5(5). Paper ID JAI101640, West Conshohocken, PA

Murawski, J (2005a) "Occupational and public health risks" In: Air Quality in Airplane Cabins and Similar Enclosed Spaces, The Handbook of Environmental Chemistry, Vol. 4(H): 25-52, Hocking, MB, ed.; Springer-Verlag, Berlin, Germany

Murawski, J (2005b) "Insecticide use in occupied areas of aircraft" In: Air Quality in Airplane Cabins and Similar Enclosed Spaces, The Handbook of Environmental Chemistry, Vol. 4(H): 169-190, Hocking, MB, ed.; Springer-Verlag, Berlin, Germany

Mutch, E; Blain, PG; Williams, FM (1992) "Interindividual variations in enzymes controlling organophosphate toxicity in man" Human Experimental Toxicol, 11: 109-116

NRC (2002) The Airliner Cabin Environment and the Health of Passengers and Crew Committee on Air Quality in Passenger Cabins of Commercial Aircraft. Board of Environmental Studies and Toxicology, Division of Earth and Life Sciences. US National Research Council, National Academy Press, Washington DC.

PCA (2007) "Senate Hansard" Parliament of the Commonwealth of Australia, presented by Senator K. O'Brien, 20 Sept 2007, 10:22am, p.15

PCA (2000) "Air Safety and Cabin Air Quality in the BAe146 Aircraft" Parliament of the Commonwealth of Australia; report prepared by the Senate Rural and Regional Affairs and Transport Legislation Committee; printed by the Senate Printing Unit, Department of the Senate, Parliament House, Canberra, Australia

Prockop LD, Chichkova RI (2007) "Carbon monoxide intoxication: an updated review" J Neurol Sci. 262(1-2):122-30

Rayman, R (2002) "Cabin air quality: an overview" Aviat Space Environ Med, 73(3): 211-5

Rayman, RB and McNaughton, GB (1983) "Smoke/fumes in the cockpit" Aviat Space Environ Med, 54(8): 738-40

SAAIB (2006) "Investigation report concerning the serious incident to aircraft AVRO 146-RJ 100, HB-IXN operated by Swiss International Air Lines Ltd. under flight number LX1103 on 19 April 2005 on approach to Zurich-Kloten airport, Swiss Aircraft Accident Investigation Bureau, Geneva, Switzerland

SAE (1997) "Aerospace Information Report 1539 Rev A: Environmental control system contamination" Society of Automotive Engineers International, Warrendale, PA

Schobersberger, W; Hauer, B; Sumann, G; et al (2002) "Traveler's thrombosis: incidence, etiology, prevention" *Wien Klin Wochenschr*, 114:14-20

Schulte, PA; Burnett, CA; Boeniger, MF; et al (1996) "Neurodegenerative diseases: occupational occurrences and potential risk factors, 1982 through 1991" *Am J Public Health*, 86(9): 1281-8

Schreijer, AJ; Cannegieter, SC; Meijers, JC; et al (2006) "Activation of coagulation system during air travel: a cross-over study" *Lancet*, 367(9513): 832-838:

SHK (2001) Board of Accident Investigation Report RL 2001: 41e "Incident onboard aircraft SE-DRE during flight between Stockholm and Malmo, M country, Sweden, on 12 November 1999." Statens haverikommission, Stockholm, Sweden.

Singh, B (2005) "Inflight smoke and fumes" In: "Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference," pp. 92-99. Imperial College, London, 20-21 April 2005, Winder, C. ed., University of New South Wales, Sydney, Australia

Somers, M (2005) "Aircrew exposed to fumes on the BAe146: An assessment of symptoms" *J Occup Health Safety – Austr NZ*, Vol. 21(5): 433-439

Spengler, JS; Ludwig, S; Weker RA (2004) "Ozone exposures during trans-continental and trans-Pacific flights" *Indoor Air (14 Suppl)* 7:67-73

Sutton, PM; Vergara, X; Beckman, J; Nicas, M; Das R (2007) "Pesticide illness among flight attendants due to aircraft disinsection" *Am J Ind Med*, 50: 345-356

Tashkin, DP; Coulson, AH; Simmons, MS; et al (1983) "Respiratory symptoms of flight attendants during high-altitude flight: possible relation to cabin ozone exposure" *Int Arch Occup Environ Health*, 52: 117-137

USAF (1992) "Guide specification, environmental control airborne" MIL-E-87145, United States Air Force

van Netten, C (2005). "Aircraft air quality incidents, symptoms, exposures and possible solutions." In: "Proceedings of the BALPA Air Safety and Cabin Air Quality International Aero Industry Conference," pp. 243-253. Imperial College, London, 20-21 April 2005, Winder, C. ed., University of New South Wales, Sydney, Australia

van Netten C (2000) "Analysis of two jet engine lubricating oils and a hydraulic fluid: their pyrolytic breakdown products and their implication on aircraft air quality" In: Nagda, NL (ed) Air Quality and Comfort In Airliner Cabins. pp. 61-75 ASTM STP 1393. American Society for Testing and Materials, West Conshohocken, PA

van Netten, C (1999) "Air quality and health effects associated with the operation of BAe146-200 aircraft" *Appl Occup Environ Hyg*, 13(10): 733-739

Waters, MA; Bloom, TF; Grajewski, B; et al (2002) Measurements of indoor air quality on commercial transport aircraft. In: Levin, H (ed) *Indoor Air 2002: Proceedings of the 9th International Conference On Indoor Air Quality and Climate*, Santa Cruz, CA, pp 782-787

Weaver, KL; Hopkins, RO; Chan, KJ; et al. (2002) "Hyperbaric oxygen for acute carbon monoxide poisoning" *NEJM*, 3478: 1057-67

Winder, C; Michaelis, S (2005) "Crew effects from toxic exposures on aircraft" In: *Air Quality in Airplane Cabins and Similar Enclosed Spaces, The Handbook of Environmental Chemistry*, Vol. 4(H): 229-248, Hocking, MB, ed.; Springer-Verlag, Berlin, Germany

Witkowski CJ (1999) "Remarks on airliner air quality" Presentation at semi-annual conference of the American Society of Heating, Refrigerating, and Air Conditioning Engineers (ASHRAE), Chicago, IL

Acknowledgements: The authors thank Mohamed Abou-Donia PhD, John Balmes MD, Jonathan Burdon MD, James Cone MD, Andrew Harper MD, Steven Hecker MSPH, Captain Susan Michaelis, Goran Jamal MD, Captain Tristan Loraine, Sarah Mackenzie-Ross MA, Karen Mulloy MD, Bhupi Singh MD, Dennis Shusterman MD, Ira Tager MD and Chris van Netten PhD for reviewing the manuscript and providing suggestions for revisions.

ATTACHMENT 1

TOXICITY OF TRICRESYLPHOSPHATE ENGINE OIL ADDITIVES

Tricresylphosphates (TCPs) are added to most synthetic jet engine oils and at least one hydraulic fluid (van Netten, 2001; van Netten, 2000; van Netten, 1999) primarily because of their anti-wear properties. According to a sample of Material Safety Data Sheets of commonly used products, the total concentration of TCPs varies between 1 and 5% (Exxon-Mobil, 2006; Anderol, 2004; Exxon-Mobil, 2003; BP, 2001). Exceptions to this rule include aviation engine oils manufactured by the French oil company, NYCO SA. When it was formulating aviation engine oils in the 1970s, NYCO opted to replace TCPs with triisopropyl phenyl phosphate (TIPP) because of health concerns raised by the French health authority over exposure to TCPs (NYCO, 2008). Key product lines include Turbonycoil 160, Turbonycoil 400, and Turbonycoil 600.

The inhalation toxicity of pyrolyzed and aerosolized aircraft engine oil during commercial airline flights is a subject that has received increasing attention over the past 10 years, not only in the US, but internationally (see above "Guide for Health Care Providers"). Even though the inhalation toxicity of these products has not been published, the material safety data sheets (MSDS) typically warn the user of hazards associated with exposure to heated byproducts; for example, "toxic fumes may be evolved on burning or exposure to heat" (BP, 2001) or "the product may decompose at elevated temperatures or under fire conditions and give off irritating and/or harmful (carbon monoxide) gases/vapors/fumes" (Exxon-Mobil, 2006). The MSDS also typically cite "hazardous combustion products [such as] carbon monoxide, phosphorus oxides, aldehydes, smoke, fumes, and incomplete combustion products (Exxon-Mobil, 2006). Some of the MSDS include specific warnings about "overexposure to TCPs by swallowing, prolonged or repeated breathing of oil mist, or prolonged or repeated skin contact [that] may produce nervous system disorders including gastrointestinal disturbances, numbness, muscular cramps, weakness, and paralysis" that may be delayed (Exxon-Mobil, 2003).

The TCP additives are by no means the only toxic component of these oils, but it is important for HCPs to understand the inhalation toxicity of TCPs because it has been a source of misunderstanding and debate. The levels or nature of airborne TCPs during an air supply contamination event have not been characterized on commercial aircraft, although a recent study on military aircraft identified total TCP levels between 0.5 and 49 $\mu\text{g}/\text{m}^3$ (Hanhela, 2005). Interestingly, TCP concentrations did not correlate with visible smoke/fume or odor detection.

The three cresyl groups in a given molecule of TCP can attach to the phosphate in different configurations; these are called isomers. In total, there are ten TCP isomers (Table A1), including a tri-ortho isomer (TOCP), two di-ortho isomers (DOCP), three mono-ortho isomers (MOCP), and four meta/para isomers. The relative amounts of these different isomers can vary between brands and batches of aviation engine oil, but some combination of some or all of these isomers will be present in a given sample. Although engine oil manufacturers consider the specific isomeric blend to be proprietary, it is known that the ortho isomers make up about 0.3% of the TCP and the vast majority (99.97%) of the ortho isomers are MOCP and DOCP, while there is very little TOCP (PCA, 2000). Little is known about the relative amounts of the remaining meta and para isomers.

Table A1: DESCRIPTION OF THE TEN ISOMERS OF TCP

Category of isomer	Description of isomers
Tri-ortho: TOCP (1)	o-o-o
Di-ortho: DOCP (2)	o-o-m; o-o-p
Mono-ortho: MOCP (3)	o-m-p; o-m-m; o-p-p
Meta and/or para (4)	m-m-m; p-p-p; m-m-p; m-p-p

Probably because of some highly publicized TOCP mass poisonings resulting from adulteration of a popular alcoholic drink called "Ginger Jake" in the 1920s and a large batch of cooking oil in 1959, this single isomer has received the most attention, and it is the only isomer for which an exposure limit exists (e.g., OSHA PEL: 0.1 mg/m³). These mass poisonings involving TOCP highlighted the risk of peripheral neuropathy and paralysis, which has been confirmed in laboratory studies involving animals that ingested TOCP or absorbed it through their skin.

Symptoms of peripheral neuropathy measured in test animals following dermal or oral exposure to aviation engine oils (Craig, 1999; Mackerer, 1999; Weiner, 1999; Daughtrey, 1996), and assurances of low ambient levels of TOCP during fume events are of little relevance to the concerns raised over exposure to aerosolized engine oil on aircraft for the following reasons:

- There is little, if any, TOCP in the engine oil formulations;
- The mono- and di-ortho isomers of TCP are five and ten times more toxic (using peripheral neuropathy as an endpoint; Mackerer, 1999; Henschler, 1958) than TOCP, respectively, but are still only present at low concentrations (PCA, 2000) such that peripheral neuropathy should not be the primary endpoint of interest following inhalation exposure to pyrolyzed engine oils;
- The meta and para isomers of TCP dominate commercial engine oil formulations and are not expected to cause peripheral neuropathy, but may cause chronic neurotoxicity (The ortho isomers have been implicated in chronic neurotoxicity in addition to peripheral neuropathy.)
- Peripheral neuropathy is not the primary endpoint of concern reported by exposed aircraft crews. Of interest is that evidence of the potential for chronic symptoms of neurotoxicity associated with either acute exposures or chronic, low level exposures has been suggested for organophosphates in general (Jamal, 2002) and TCPs on the aircraft in particular (Abou-Donia, 2003).
- Aircraft occupants are primarily exposed to engine oil via inhalation with only limited potential for dermal exposure and no real potential for ingestion, but despite this, controlled studies that assess the health impact of inhalation exposure have not been published. The toxicity associated with inhalation may be different to that associated with dermal exposure or ingestion. Certainly, there is no evidence that ground-based dermal/oral research data for these oils can be applied to inhalation exposures that are often incurred in a reduced oxygen environment.

The tri-ortho content of TCP has been successfully reduced in the last few decades but exposure to the mono and di ortho isomers, as well as the meta and para isomers, are still of

toxicological concern to aircraft crews and passengers (Hanhela, 2005; Bobb, 2003). Inhalation toxicity testing in a controlled laboratory setting, with post-mortem brain analysis of exposed animals may be necessary to confirm the observations of chronic neurotoxicity among exposed aircraft occupants.

REFERENCES

- Abou-Donia, MB (2003) "Organophosphate ester-induced chronic neurotoxicity" Arch Environ Health, Vol. 58(8): 484-497
- Anderol (2004) Material Safety Data Sheet for Royco 808, Anderol Incorporated, East Hanover, NJ. Revision date, 31 May 2004.
- Bobb, AJ; Still, KR (2003) "Known harmful effects of constituents of jet oil smoke" TOXDET-03-04, Naval Health Research Center Detachment (Toxicology), Wright-Patterson AFB, OH
- BP (2001) Material Safety Data Sheet for BP Turbo Oil 25, 2197, 2380, 2389, BP Oil New Zealand Ltd, Wellington, NZ. Revision date, 3 May 2001
- Craig, PH; Barth, ML (1999) "Evaluation of the hazards of industrial exposure to tricresyl phosphate: A review and interpretation of the literature" J Toxicol Environ Health, Part B: Crit Rev, Vol. 2(4): 281-300
- Daughtrey, W; Biles, R; Jortner, BS (1996) "Subchronic delayed neurotoxicity evaluation of jet engine lubricants containing phosphorus additives" Fundam Appl Toxicol, Vol. 32: 244-249
- Exxon-Mobil, (2006) Material Safety Data Sheet for Mobil Jet Oil II, Exxon-Mobil Corporation, Fairfax, VA. Revision date, 3 Oct 2006
- Exxon-Mobil (2003) Material Safety Data Sheet for Mobil Jet Oil 254, Exxon-Mobil Corporation, Fairfax, VA. Revision date, Jan 2003
- Hanhela, PJ; Kibby, J; DeNola, G; et al (2005) "Organophosphate and amine contamination of cockpit air on the Hawk, F-111, and Hercules C-130 aircraft" Austr Government Department of Defense, DSTO-RR-0303.
- Henschler, D (1958) "Tricresyl phosphate poisoning. Experimental clarification of problems of etiology and pathogenesis" (Die Trikresylphosphatvergiftung Experimentelle Klärung von Problemen der Ätiologie und Pathogenese) Klinische Wochenschrift, Vol. 26(14): 663-674.
- Jamal, GA; Hansen, S; Julu, POO (2002) "Low level exposures to organophosphorus esters may cause neurotoxicity" Toxicol, 181-182: 23-33.
- Mackerer, CR; Barth, ML; Krueger, AJ; et al (1999) "Comparison of neurotoxic effects and potential risks from oral administration and ingestion of tricresyl phosphate and jet engine containing tricresyl phosphate." J Tox Environ Health, Part A, 56: 293-328
- NYCO (2008) Personal correspondence with Mr. Eric Piveteau, NYCO SA, 20 May 2008
- PCA (2000) "Air Safety and Cabin Air Quality in the BAe146 Aircraft." Parliament of the Commonwealth of Australia, Prepared by the Senate Rural and Regional Affairs and Transport

Legislation Committee. Printed by the Senate Printing Unit, Department of the Senate, Parliament House, Canberra, Australia.

van Netten, C and Leung, V (2001) "Hydraulic fluid and jet engine oil: pyrolysis and aircraft air quality." Arch Environ Health, Vol 56(2): 181-186

van Netten C (2000) "Analysis of two jet engine lubricating oils and a hydraulic fluid: their pyrolytic breakdown products and their implication on aircraft air quality" In: Nagda, NL (ed) Air Quality and Comfort In Airliner Cabins. pp. 61-75 ASTM STP 1393. American Society for Testing and Materials, West Conshohocken, PA

van Netten, C (1999) "Air quality and health effects associated with the operation of BAe146-200 aircraft" Appl Occup Environ Hyg, 13(10): 733-739

Weiner, ML; Jortner, BS (1999) "Organophosphate-induced neurotoxicity of triarylphosphates" Neurotoxicol, Vol. 20(4): 653-673