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N° échantillon : **08E011098-003**
Version du : 04/11/2008 16:37

RAPPORT D'ANALYSE

Date de réception :	28/10/2008
Référence dossier :	Demande d'analysesdu 20/10/08 selon devis N°FVBA200803490 - Métaux sur sols et eaux souterraines
Référence échantillon :	PAC
Matrice :	Sol
Début d'analyse :	28/10/2008

Résultats

Paramètres	Méthodes	Résultats	Unités	LQI
Préparation pour analyses physico-chimiques	NF ISO 11464			
* Préparation physico-chimique (séchage à 40°C)		-	-	
* Refus pondéral à 2 mm		35.0	% P.B.	1
* Minéralisation Eau Régale - Bloc chauffant après préparation	NF EN 13346	-	-	
Métaux par ICP/AES après minéralisation	NF EN ISO 11885			
Aluminium		7830	mg/kg M.S.	5
* Baryum		70.2	mg/kg M.S.	1

LQI : Limite de Quantification Inférieure. Les LQI sont fournies à titre indicatif, elles sont sous la responsabilité du laboratoire et fonction de la matrice.

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N° échantillon : **08E011098-002**
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RAPPORT D'ANALYSE

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Référence échantillon :	PGB
Matrice :	Sol
Début d'analyse :	28/10/2008

Résultats

Paramètres	Méthodes	Résultats	Unités	LQI
Préparation pour analyses physico-chimiques	NF ISO 11464			
* Préparation physico-chimique (séchage à 40°C)		-	-	
* Refus pondéral à 2 mm		36.5	% P.B.	1
* Minéralisation Eau Régale - Bloc chauffant après préparation	NF EN 13346	-	-	
Métaux par ICP/AES après minéralisation	NF EN ISO 11885			
Aluminium		837	mg/kg M.S.	5
* Baryum		14.4	mg/kg M.S.	1

LQI : Limite de Quantification Inférieure. Les LQI sont fournies à titre indicatif, elles sont sous la responsabilité du laboratoire et fonction de la matrice.

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RAPPORT D'ANALYSE

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Référence échantillon :	PTE
Matrice :	Sol
Début d'analyse :	28/10/2008

Résultats

Paramètres	Méthodes	Résultats	Unités	LQI
Préparation pour analyses physico-chimiques	NF ISO 11464			
* Préparation physico-chimique (séchage à 40°C)		-	-	
* Refus pondéral à 2 mm		34.5	% P.B.	1
* Minéralisation Eau Régale - Bloc chauffant après préparation	NF EN 13346	-	-	
Métaux par ICP/AES après minéralisation	NF EN ISO 11885			
Aluminium		878	mg/kg M.S.	5
* Baryum		31.2	mg/kg M.S.	1

LQI : Limite de Quantification Inférieure. Les LQI sont fournies à titre indicatif, elles sont sous la responsabilité du laboratoire et fonction de la matrice.

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APPENDIX 24

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Aerotoxic syndrome: a descriptive epidemiological survey of aircrew exposed to in-cabin airborne contaminants

C WINDER

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J-C BALOUET

The term "aerotoxic syndrome" was proposed in 1999 to describe the association of symptoms observed among flight crew and cabin crew who have been exposed to hydraulic fluid or engine oil vapours or mists. A descriptive epidemiological study was conducted to investigate the health effects of aircrew through a questionnaire mail-out. Most of the respondents (88%) reported that symptoms occurred after exposure to engine oil or hydraulic fluid leaks which caused odours and/or visible contamination in the cabin. Invariably, aircrew directly attributed their symptoms to exposure to in-cabin airborne contaminants. A comparison between 18 respondents from the United States and the 50 Australian respondents shows significant similarities in reported symptoms. There was sufficient commonality in reported symptoms to conclude a symptom basis for aerotoxic syndrome.

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KEYWORDS

- AVIATION INDUSTRY
- AEROTOXIC SYNDROME
- NEUROTOXICITY
- NEUROPSYCHOLOGICAL DYSFUNCTION
- AIRBORNE CONTAMINANTS

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Introduction

The oils and hydraulic fluids used in aircraft engines can be toxic, and specific ingredients of oils can be irritating, sensitising and neurotoxic (including phenyl-alpha-naphthylamine, and tri-aryl phosphates such as tri-ortho-cresyl phosphate).[1,2] If oil or hydraulic fluid leaks occur, this contamination may be in the form of unchanged material, degraded material from long use, or combusted or pyrolised materials. These materials can contaminate aircraft cabin air in the form of gases, vapours, mists and aerosols. There are a number of possible situations that can arise whereby cabin air can become contaminated.[3] Significant contaminants include: aldehydes; aromatic hydrocarbons; aliphatic hydrocarbons; chlorinated, fluorinated, methylated, phosphate and nitrogen compounds; esters; and oxides.[4-6] An additional problem is the lower partial pressure of oxygen in the cabins of aircraft flying at altitude.[7]

To date, most studies that have been carried out to measure atmospheric contamination in aircraft as a result of engine oil or hydraulic fluid leaks are sufficiently flawed on procedural and methodological grounds so as to render their conclusions invalid. Further, no monitoring has occurred during a leak.

International aviation legislation such as the United States Federal Aviation Regulations and the airworthiness standards for aircraft air quality state that "crew and passenger compartment air must be free from harmful and hazardous concentrations of gases or vapors".[8] Where contamination of the air in flight decks and passenger cabins occurs that is sufficient to cause symptoms of discomfort, fatigue, irritation or toxicity, this contravenes such standards and legislation.

Inhalation is an important route of exposure, with exposure to uncovered skin being a less significant route (for example, following exposure to oil mists or vapours). Ingestion is unlikely.

Occasionally, such exposures may be of a magnitude to induce symptoms of toxicity. In terms of toxicity, a growing number of aircrew are developing symptoms following both short-term and long-term repeated exposures, including dizziness, fatigue, nausea, disorientation, confusion, blurred vision, lethargy and tremors.[9-11] Neurotoxicity is a major flight safety concern, especially where exposures are intense.[12]

The earliest case found in the literature was reported in 1977.[13] A previously healthy member of an aircraft flight crew was acutely incapacitated during flight with neurological impairment and gastrointestinal distress. His clinical status returned to normal within a day. The aetiology of his symptoms was related to an inhalation exposure to aerosolised or vapourised synthetic lubricating oil arising from a jet engine of his aircraft.

Other studies of chemical exposures in aircraft can be found in the literature, including a 1983 study of 89 cases of smoke/fumes in the cockpits of US Air Force aircraft, a 1983 study of Boeing 747 flight attendants in the US (this article linked the symptoms to ozone), a 1990 study of aerospace workers, and a 1998 study of BAe 146 flight crews in Canada over a four-month period.[9,14-16] A recent report of seven case studies considered to be representative of the common symptoms of irritancy and toxicity described similar symptoms.[10] They investigated different exposures and situations, and the range of symptoms in these studies was quite broad, affecting many body systems. However, there are common themes in symptom clusters in these studies, as shown in Table 1.

While Table 1 shows a long list of symptoms, it is possible to characterise many symptoms more consistently. For example, different studies may describe the same symptom as dizziness, loss of balance, light-headedness, feeling faint, feeling intoxicated, or disorientation. It would be incorrect to regard such symptoms as being entirely different from each other — they point to a basic neuropsychological dysfunction affecting balance. But, rather than dismissing such symptoms as being multitudinous and variable, it may be more appropriate to re-categorise symptoms with clearer definitions, so that the artificial distinctions between symptom reporting can be clarified, and a shorter list developed.[17]

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TABLE 1

Studies reporting signs and symptoms in aircrew

	Number of cases/reports				
Symptoms	*89*[14]	*248*[15]	*53*[16]	*112*[9]	*7*[10]
Irritation of eyes, nose and throat					7/7
Eye irritation, eye pain	35%	74%	57%	24%	4/7
Blurred vision, loss of visual acuity	11%	13%		1%	4/7
Rashes, blisters (uncovered body parts)			36%		4/7
Sinus congestion	35%	54%		5%	2/7
Nose bleed		17%			1/7
Throat irritation, burning throat, gagging and coughing	2%	64%	57%	43%	2/7
Cough		69%			2/7
Difficulty in breathing, chest tightness		68%			3/7
Loss of voice		35%			1/7
Chest pains	7%	81%		6%	2/7
Respiratory distress, shortness of breath, breathing problems requiring oxygen		73%		2%	4/7
Fainting, loss of consciousness, "grey out"	4%	4%			3/7
Shaking, tremors, tingling	9%			3%	3/7
Numbness (fingers, lips, limbs), loss of sensation			8%	2%	4/7
Dizziness, loss of balance	47%			6%	4/7
Light-headedness, feeling faint or intoxicated	35%	54%		32%	7/7
Disorientation	26%			15%	4/7
Severe headache, head pressure	25%	52%		26%	7/7
Trouble thinking or counting, word blindness, confusion, coordination problems	26%	39%	42%		6/7
Memory loss, memory impairment, forgetfulness			42%		7/7
Behaviour modified, depression, irritability	26%	20%	60%		4/7
Nausea, vomiting, gastrointestinal symptoms	26%	23%	15%	8%	6/7
Abdominal spasms, cramps, diarrhoea	26%				3/7
Change in urine		3%	6%		
Joint pain, muscle weakness, muscle cramps		29%			2/7
Fatigue, exhaustion					7/7
Chemical sensitivity			32%		4/7

Against this background, a descriptive epidemiological study was conducted of aircrew, which investigated the development of symptoms during flight through the mail-out of a self-administered questionnaire. Because of industry sensitivities with regard to such a survey, it was designed to be independent of the aviation industry (that is, aircraft manufacturers, airline operators and unions were not involved in the design or conduct). Therefore, there was no formal process of requesting nominations and a description of survey objectives was not provided prior to nomination.

One of the aims of the present study was to identify whether aerotoxic syndrome was definable and, if so, the symptoms that might be considered indicative of such a condition.

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Methodology

The survey

Selection process: The survey was voluntary. Survey participants were those aircrew who took the effort to identify themselves to the research project team as being interested in the survey, and who then agreed to complete and return the survey.

As noted above, there was no information or publicity prepared or circulated by the research team about the proposed survey. Officers in both flight attendants and pilots unions were aware of the study, and a statement was issued by the Flight Attendants' Association of Australia that it was not involved with the survey. Further, information flows rapidly within the Australian aviation industry and the principal investigator received many telephone and email inquiries. Some inquirers were suspicious about the independence of the survey, about the source of research funding and about the possibility that the survey had any undue influence from companies or unions. Many nominations were made only when guarantees of funding independence and assurances of nominator anonymity were provided by the research project team.

The aircrew volunteer database was compiled over a four-month period in late 2000. It was originally proposed to survey between 30 and 50 nominations, but it became apparent that this was an underestimate of those interested in participating. Eventually 117 aircrew volunteered to be part of the survey. Of these, 100 were nominations from Australian aircrew.

Survey mail-out: Survey questionnaires were sent out in January 2001. A response period of four months was specified. After this time, no further responses were included. Other responses have been received since the cut-off date, including 18 from two US airlines. Because the highest response rate was from Australian aircrew, data from Australian respondents are presented in this article, with a comparison between the Australian and US findings discussed later.

Response rate: Ultimately, 100 survey forms were sent out to Australian nominations and 50 replies were received (a response rate of 50%). As distinct from many other surveys, the research team did not send follow-up reminders to non-respondents. It is not known why 50 volunteers initially planned to be involved in the survey but then later declined. A response rate of 50% to a single mail-out is considered excellent, and could have been higher if there had been a follow-up to non-respondents.

Development of questionnaire

A three-page structured questionnaire was developed to survey aircrew volunteers. The questionnaire consisted of open-ended and closed questions, with extra space to add other comments.

The questionnaire was derived from pre-existing questionnaires that had been developed for collecting information at interviews to assess the experience of aircrew following adverse health outcomes from exposure to contaminants while flying.[10] Additions and modifications were made to the questionnaire to suit the present study. The questionnaire used in the present study was reviewed by the University of New South Wales Ethics Committee. It was considered that the questionnaire should not "lead" or prejudice the respondent, and extensive modifications were made to early drafts to ensure neutral language. The final questionnaire did not contain concepts such as air leaks, contamination or aerotoxic syndrome. The questionnaire was then trialled with 10 aircrew. Further, mainly editorial, modifications were made as a result of the trial.

Aircrew were initially asked to identify what, if any, health symptoms they had experienced while flying and the duration of these symptoms. These questions were open-ended and invited opportunities for in-depth qualitative responses. Respondents were asked to describe factors that may have contributed to any adverse health symptoms and outcomes.

The second part of the questionnaire consisted of a relatively long list of signs and symptoms within the following symptom categories: neuropsychological;

neurological; senses; eye and skin; respiratory; cardiovascular; gastrointestinal; renal; endocrine; immunological; and reproductive. Respondents were asked to report whether they had experienced any of the listed symptoms.

Data analysis

Qualitative data were analysed by using the Statistical Package for the Social Sciences.[18] Given the possibility of selection and reporting bias, statistical analysis was not conducted on these data.

Qualitative open-ended responses were documented and descriptive quotations are included in this article.

Results

Demographic characteristics

Table 2 contains a demographic overview of respondents. Of the 50 crew surveyed, 28% were male and 72% were female. The majority of respondents were cabin crew (70%), with flight crew comprising the remaining 30%.

The age of respondents ranged from 26 years to 59 years, with a mean age of 40±8 years (the median was 38 years).

Years of experience in the industry ranged between two and 40 years. The mean number of years of experience in the aviation industry was 16±10 years.

Ansett employed 72% of respondents and National Jet Systems 22%. Most flew on BAe 146 aircraft (92%), with 56% flying the A320 aircraft. Several cabin crew flew both types of aircraft.

The vast majority of respondents (92%) reported that they were non-smokers and tended to abstain from alcohol (16%) or consume small quantities of alcohol occasionally (72%).

Contributing factors

Aircrew were asked to describe any factors that may have contributed to their symptoms. These questions were unprompted and individual open-ended comments were requested. Most of the respondents (88%) reported that their symptoms occurred after an assumed exposure to oil gases and fumes in the cabin. The common use of the word "fume" was often incorrect on technical grounds. Technically, a fume is an aerosol of solid particles generated by condensation from the gaseous, volatile or oxidised atomic state — not what were almost certainly vapours (the gaseous phase of a liquid at room temperature) or mists.

Invariably, respondents attributed these gases and "fumes" (vapours and mists) to possible oil leaks. As the nature of these exposure events cannot be adequately described in statistics and graphs, a few extracts from some of the respondents are reproduced below. These sometimes better describe the more alarming aspects of such exposures:

— Pilot, age 59: "I consider the symptoms suffered are a direct result of cockpit fumes on the BAe 146 aircraft. The greater the incidence of detectable fumes, the more apparent the symptoms ... also related to rate of flying. On leave, the symptoms reduced."

— Flight attendant, age 48: "I had an increased exposure of fumes on the BAe 146, when the cabin filled up with smoke, I could not see past row two on the aircraft. Since that incident both the Captain and First Officer have developed lung disease, I had breast cancer and another flight attendant has sued the airline because of health problems."

— Flight attendant, age 37: "Following the fume occurrence on the BAe 146 I had a metallic taste in my mouth, headache over the right eye, sore throat. Short-term symptoms included nausea, dizziness, lack of concentration, memory loss, stiff neck, stinging/itchy, weepy eyes, difficulty in concentrating while driving, 'heavy' head, unable to stand in the shower without falling over."

Over half of the respondents (54%) cited airconditioning problems as a reason for adverse health symptoms. Other factors included hypoxia (18%) and pressurisation problems (16%).

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TABLE 2

Overview of the aviation employees surveyed

Aviation employee characteristics	*Categories*	*Number of responses* n	%
Gender	Male	14	28
	Female	36	72
Age	20–29	4	8
	30–39	25	50
	40–49	13	26
	50–59	8	16
Years of experience in aviation industry	1–9	13	26
	10–19	19	38
	20–29	11	22
	30–39	5	10
	40+	2	4
Occupation	Flight crew	16	32
	Cabin crew	34	68
Airline	Ansett	36	72
	National Jet Systems/Airlink	12	24
	Northwest Airlines	2	4
Type of aircraft*	BAe 146	46	92
	A320	28	56
Alcohol	None	8	16
	Mild	36	72
	Moderate	5	10
	Heavy	1	2
Smoking	Current smoker	4	8
	Non-smoker	46	92

* This was a multiple response question, so the percentage was calculated by each item as a total of 50 responses.

Onset of symptoms

Adverse health symptoms as a result of exposure to oil fumes were reported by 47 (94%) of the respondents.

Almost all respondents (96%) reported adverse symptoms immediately while flying or on the same day as flying. A large number of respondents (82%) also experienced adverse symptoms that continued for at least one month from the time of exposure. Many respondents (74%) reported that they experienced symptoms for at least six months after exposure. The term "long-term effects" indicates an effect(s) persisting over a long period of time; however, the duration of what might be considered "a long period of time" has generated debate in this industry. Some view this as being at least over six months, others over decades. For the purposes of this article, an effect is considered long-term if it has been present for over a year. Long-term symptoms that remained or developed after at least one year of exposure were reported by 76% of respondents.

Amelioration of effects of exposure

Data on the manner in which effects of exposure were ameliorated are shown in Table 3. Under half of the respondents (42%) had mild symptoms that reduced on vacating the plane and subsided further after extended rest.

Those with more moderate symptoms (32%) used the oxygen on board the aircraft:

— Flight attendant, age 37: "At times, due to maintenance problems, aircraft are flown with one

TABLE 3
Amelioration of effects of exposure (including gender differences)

	What happened					
Gender	*Fresh air/ sleep on landing*	*Oxygen used*	*Hospitalised*	*Doctor attended*	*N/A or no symptoms*	*Total %*
Male*	10 (20%)	2 (4%)	0	0	2 (4%)	14 (28%)
Female*	11 (22%)	14 (27%)	8 (16%)	3 (6%)	0	36 (72%)
Total*	21 (42%)	16 (32%)	8 (16%)	3 (6%)	2 (4%)	50 (100%)

* Data expressed as number of respondents (%) (total n = 50).

airconditioning pack in service. I usually feel hypoxic on these flights and use oxygen. On other occasions, the problem is with oil leaks and then my symptoms re-occur. As I have removed myself from flying on the BAe 146 my symptoms have subsided."

— **Flight attendant, age 40:** "After the mechanical failure, hydraulic fuel leaked into the cabin. All of the cabin crew and four passengers became ill. Flight deck was on oxygen when the crew reported dizziness, nausea and confusion and extreme head pain."

One pilot was so affected by exposure that the aircraft was grounded until the symptoms subsided. Almost one quarter of respondents (22%) experienced severe symptoms and collapsed after exposure. Hospitalisation was necessary for 16% who were taken off the aircraft on a stretcher or wheelchair suffering from exposure to toxic fumes:

— **Flight attendant, age 40:** "All the cabin crew and some passengers were exposed to the fumes. My legs gave way ... I had to harness myself into my jump-seat. After landing, the crew were taken by company van to an emergency room. Hospitalised, the physician's diagnosis five hours after landing was probable inhalation injury — cognitive problems, speech slurred, headache, nausea. Twenty-four hours after exposure the Internist Doctor noted ataxia, coordination problems — diagnosis toxic encephalopathy. Day 3, the Neurologist documented toxic encephalopathy with significant cognitive dysfunction, memory loss, speech disorder — I cannot set a clock and cannot draw a cube. An MRI was given two days after incident, tissue damage was found in white matter, high signal intensity spots on the frontal lobe of the brain. Still experience long-term effects."

— **Flight attendant, age 24:** "On the day of the incident, within the first hour of smelling the fumes I had difficulty breathing and talking. I had spasms in my legs, was faint and felt very hot. On disembarking I fell to the floor, they put me on oxygen and wheeled me off in a wheelchair. I was on oxygen for the first hour in the first aid room and was unable to talk for the first hour. I was taken to the medical centre during which time I was in and out of consciousness."

On a gender basis, fresh air and sleep reduced symptoms for almost equal numbers of males (20%) and females (22%); however, females generally experienced more severe symptoms that required greater medical intervention. Females (28%) were over five times more likely to use oxygen than males (4%). Hospitalisation was required for 16% of females in comparison with no males requiring hospitalisation. Three women (6%) required attendance by a doctor, as opposed to no reported requirements for males seeking medical assistance (see Table 3).

Data on signs and symptoms

Data on symptoms are presented below on the basis of grouped symptoms or organ systems. Data are presented in graphical form, with the same axis

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dimension for respondents showing symptoms to make comparison easier. Where possible, data on the background incidence of such symptoms in the Australian population are provided to allow a comparison with background incidence, although comparison of the data below with the other forms of data may be problematic (for example, self-reported as opposed to physician-collected data). There are also problems with comparing total populations with workers in that the "healthy worker" effect may bias results, as would comparing males with females.[19,20]

Irritancy symptoms in eyes, skin and respiratory system

There are high levels of irritancy symptoms in the data presented in Figure 1, including eye irritation (76%) and skin problems (58%). These are consistent with exposure to an irritant, but this may not be the only cause (for example, they could also be caused by the low humidity in aircraft during flight). There are some gender differences, although these could be related to gender sample sizes.

Similarly, a number of the symptoms in Figure 2 show respiratory irritation, with 64% of respondents reporting breathing problems (75% in females) and 48% reporting chest tightness/wheezing.

There are problems in categorising self-reported symptoms such as breathing problems or respiratory irritation. There are some gender differences in the data, with apparently high rates of respiratory irritation in females.

Adverse respiratory health effects from exposures to, among others, oxides of nitrogen, ozone, sulphur dioxide and particulates either singularly or in combination, such as in exposure to aviation fuel or jet stream exhaust, have been known for some time.[1,9,11,14] Tunnicliffe et al found an association between high occupational exposures to aviation fuel or jet stream exhaust and excess upper and lower respiratory tract symptoms — in keeping with exposure to a respiratory irritant.[21] In their study, 51% of aviation workers had upper and lower respiratory symptoms, including cough with phlegm and runny nose.

Gastrointestinal/renal signs and symptoms

Nausea and vomiting are relatively common symptoms, and were reported by 58% of respondents.[22] In most cases these symptoms were associated with intensifying gastrointestinal symptoms (mainly in females) of abdominal spasms (20%), abdominal pain (10%) and diarrhoea (28%) (Figure 3).

Neuropsychological and neurological signs and symptoms

Symptom reporting rates were high for many neuropsychological symptoms, including intense headache (86%), dizziness and disorientation (72%), performance decrement (including changes in cognitive function) (70%), memory and recall problems (66%), and balance problems (62%) (Figure 4). Other symptoms, such as anxiety (50%) and depression (40%) are more global and harder to interpret. The consistency of neurological symptoms is quite striking, suggesting neuropsychological impairment of a general nature, as seen, for example, in exposure to volatile organic compounds, organophosphate compounds or carbon monoxide.[23-25] The significance of such phenomena remains problematic.[26]

While neuropsychological effects are often dismissed as being subjective or unquantifiable, intense headache at 86%, dizziness/disorientation at 72%, performance decrement at 70% or memory problems at 66% are not symptoms that should be dismissed in aircrew while performing their duties. The high rate of respondents reporting such effects is difficult to interpret, owing to the self-selection of respondents to, and reporting bias in, this survey. However, the incidence of neuropsychological symptoms in aircrew, especially in females, appears excessive.

While self-reporting of neuropsychological or neurological symptoms may contain elements of subjectivity, the incidence in both genders of neuropsychological or neurological symptoms such as tingling (40%), tremors (30%), seizures or loss of consciousness (14%) was based on the reporting of symptoms after a respondent had been examined by

FIGURE 1
Data on eye and skin irritation signs and symptoms

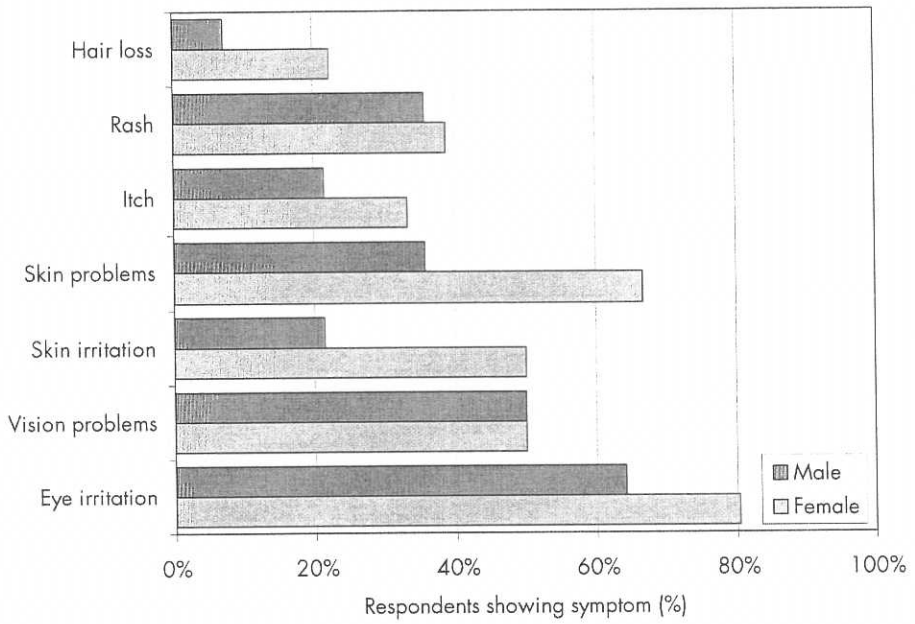

FIGURE 2
Data on respiratory and cardiovascular signs and symptoms

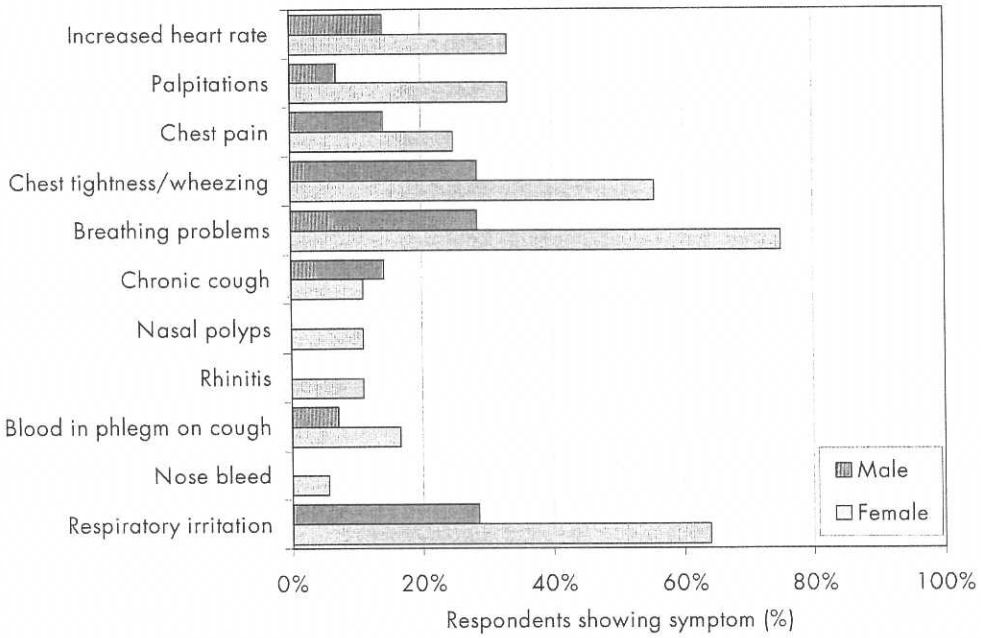

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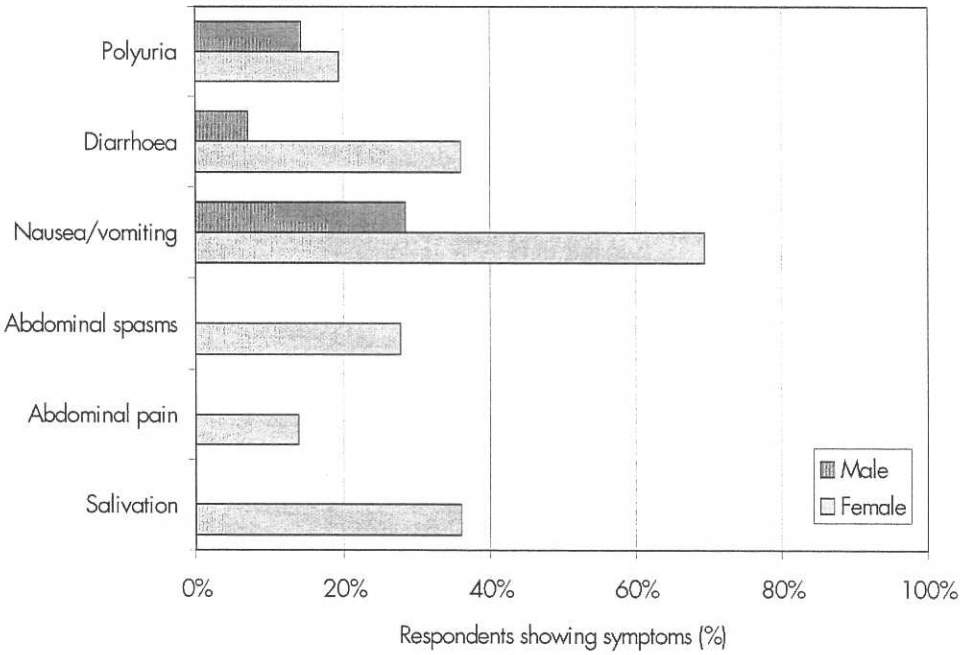
FIGURE 3
Data on gastrointestinal/renal signs and symptoms



their medical practitioner (Figure 5). These are significant symptoms that point to a toxic aspect of the exposures reported by respondents. Further, there may be a neurotoxic component to other symptoms, such as vision problems or disorientation or balance problems.

Reproductive signs and symptoms

There were 36 female respondents. All were of reproductive age, and many were planning to have or were having families during the time of their employment. Working women tend to have a lower fertility rate than non-working women, although this is for employment rather than biological reasons.[27] Fertility rates are falling in the developed nations for a range of reasons, and are estimated at 7–10%.[28] The data from respondents for reproductive symptoms are shown in Figure 6. Infertility was reported by 33% of respondents. This appears to be above population norms.

Menstrual dysfunction (variously reported as heavy periods, irregular periods or dysmennorrhoea) was reported by 28% of female respondents, miscarriage by 14% and multiple miscarriage by two respondents. Of particular significance is the problem of neonatal death in two respondents and genetic problems in the offspring of three respondents. While the sample size is small, these are noteworthy findings.

General signs and symptoms

As well as signs and symptoms in specific organ systems, a range of multi-organ or general symptoms was reported (Figure 7).

Joint pain (arthralgias) and muscle pain (myalgias) are common symptoms resulting from a variety of disease processes.[29,30] Despite the poorly understood pathogenetic mechanisms underlying myalgia and arthralgia, they are common in chronic fatigue and chemical sensitivity syndromes.

FIGURE 4
Data on neuropsychological signs and symptoms

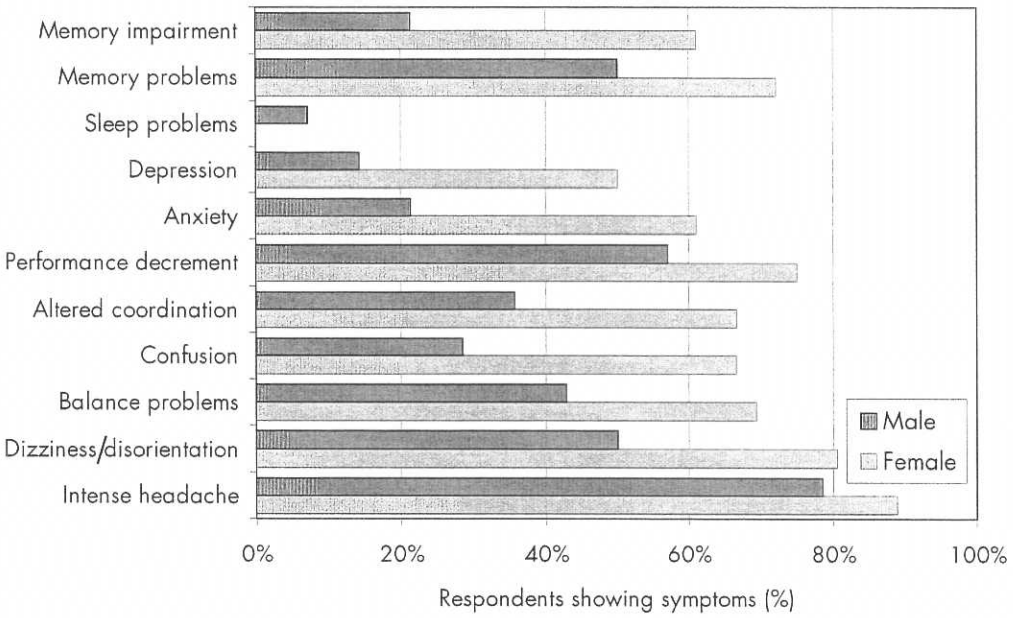


FIGURE 5
Data on neurological signs and symptoms

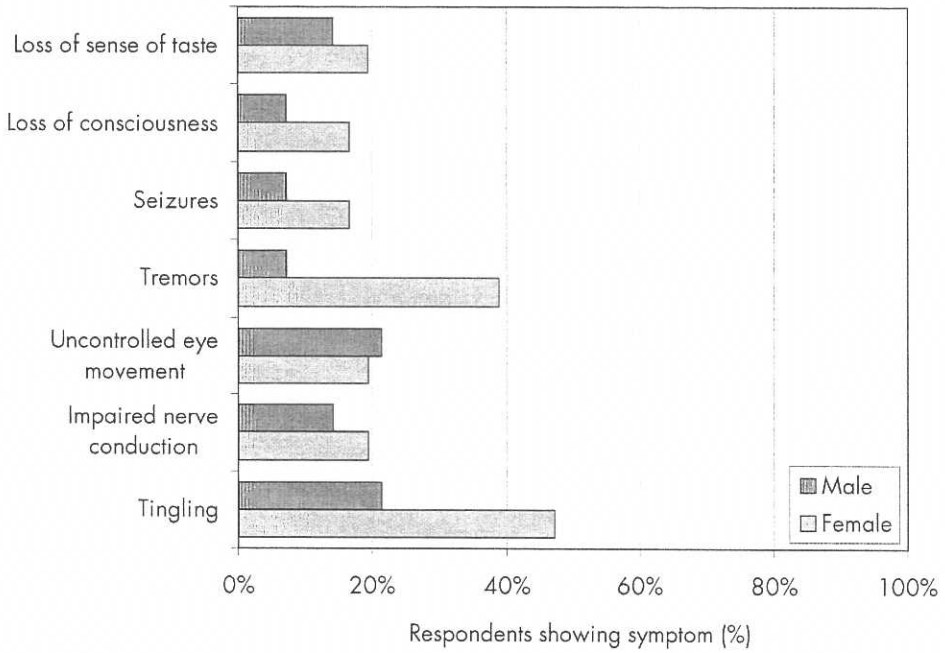


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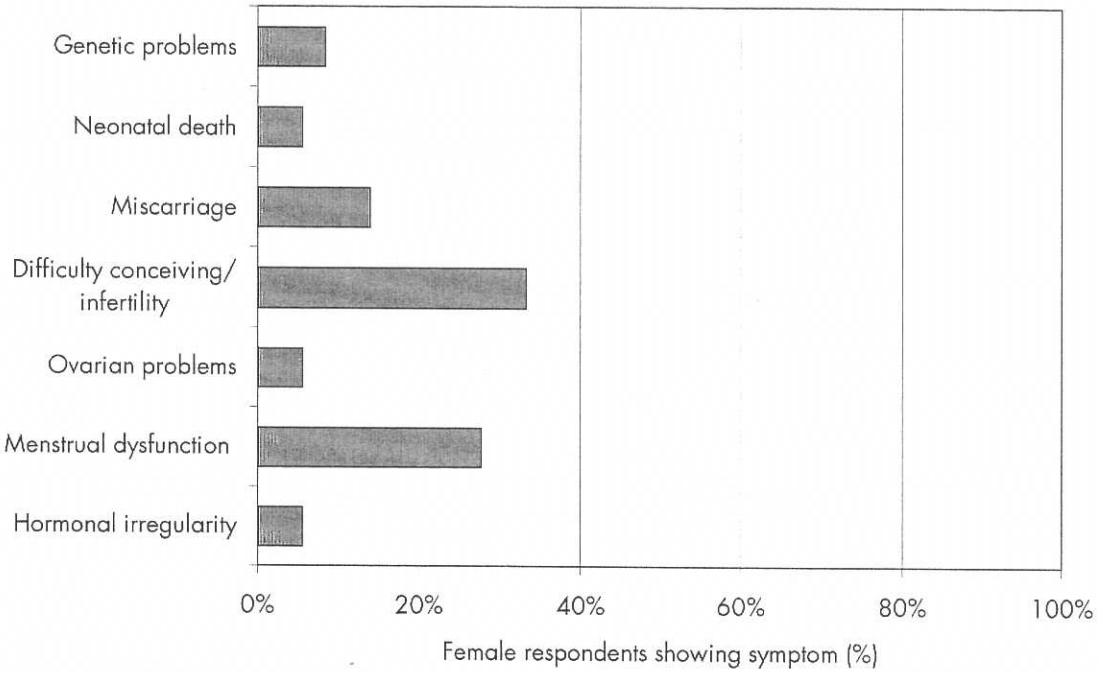
FIGURE 6
Data on reproductive signs and symptoms

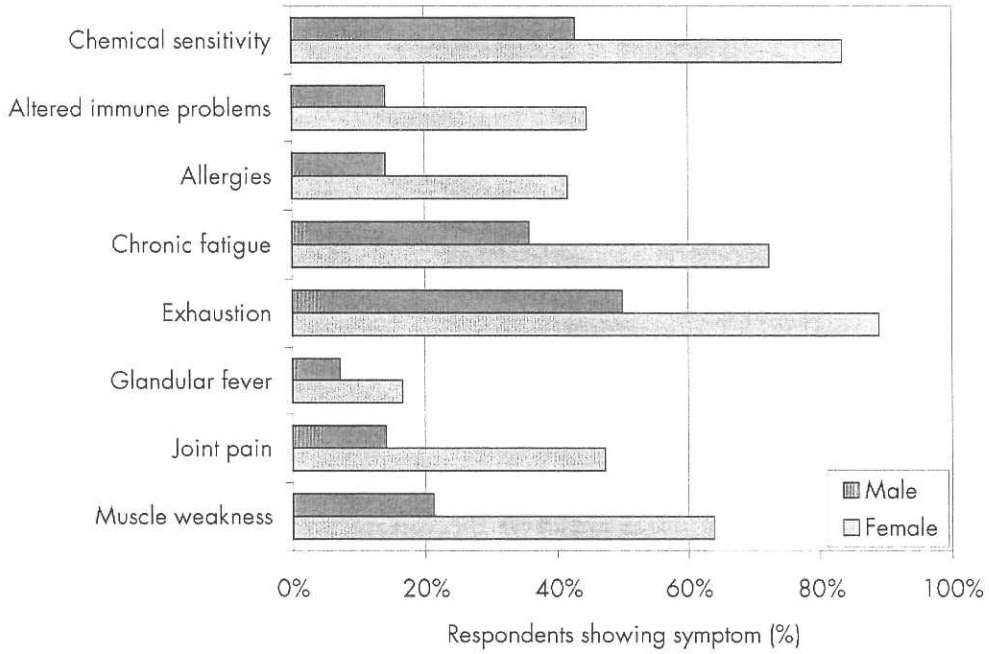


Of the symptoms reported in this survey, exhaustion was the second most common, being reported by 78% of all respondents (89% of female respondents). Fatigue is an established hazard in aviation — from the perspective of the impairments in alertness and performance that it creates in pilots.[31] The exhaustion reported by respondents escalated into 72% of respondents reporting chronic fatigue. Prolonged or chronic fatigue is reported by about 25% of all patients presenting to Australian general practice.[32] Such fatigue states represent a continuum of severity ranging from the mild and transient symptoms through to the more rare, severe and prolonged fatigue disorders. In about 1% of patients attending general practice in Australia, the fatigue state will meet diagnostic criteria for chronic fatigue syndrome.[32] Figure 7 shows chronic fatigue at 36% for males and 72% for females. While there may be differences between diagnostic criteria for, and self-reporting of, chronic fatigue, these rates (particularly in females) are still very high.

A second cluster of symptoms was observed with chemical sensitivity. Allergies were reported by 34% of respondents, altered immune problems by 36% of respondents, and chemical sensitivity by 72% of respondents (83% of female respondents). Again, these are high rates that would almost certainly be well above any population background rate.

The co-occurrence and overlapping of many of the symptoms reported by the respondents is in keeping with comparable investigations. Co-morbidity of chronic fatigue, irritable bowel syndrome, chemical sensitivity, chronic headache and other unexplained conditions has only recently been systematically studied.[33] Comparative investigations in referral clinic populations have reported that in 53–67% of persons with chronic fatigue syndrome, illness worsens with exposure to various chemicals. Many patients with chronic fatigue syndrome also have irritable bowel syndrome (63%), multiple chemical sensitivity (41%) and other unexplained illness.[33]

FIGURE 7
Data on general signs and symptoms



The US questionnaires

Eighteen questionnaires were submitted from respondents with addresses in North America (16 female; two male). Again, these were analysed descriptively. Rather than presenting the same data again (as in Figures 1 to 7), the symptom incidence for each symptom was plotted using an X,Y scatterplot, with the horizontal axis (X-axis) being the Australian symptom percentages and the vertical axis (Y-axis) being the US percentages (Figure 8).

These data show a number of symptoms where there is some difference between Australian and US symptom incidences, although in a few cases these outliers suggest diagnostic differences between the two countries (for example, chemical sensitivity/allergy). Nevertheless, there is a remarkable correlation between these data (correlation coefficient $r = 0.859$, $r^2 = 74\%$).

Discussion

The term "aerotoxic syndrome" was proposed in 1999 to describe the association of symptoms observed among aircrew who have been exposed to hydraulic fluid or engine oil smoke/fumes.[10,34]

With regard to the use of the term "syndrome", this is used to describe a set of symptoms that occur together, although generally there is no specification for the type and number of symptoms. Further, experience would suggest that the range and types of symptoms in such a symptom cluster would not be large.[17]

With regard to exposure to contaminants, while such exposures were not common, they were relatively frequent in certain models of aircraft. This study found two main types of exposure:

1. an "exposure event", where there was at least one self-reported intense exposure to contaminated air from an engine oil or hydraulic fluid leak; and

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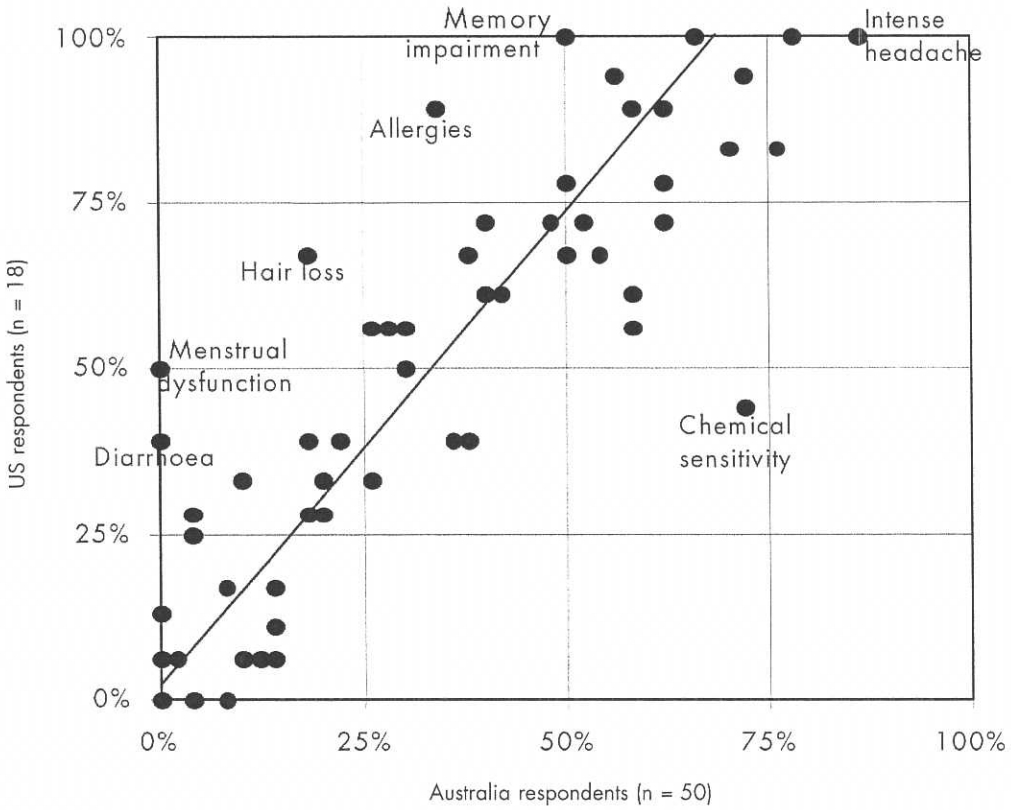
FIGURE 8
Comparison of Australian and US symptom incidences



2. self-reported residual exposure to odours and non-visible contamination.

While the majority of exposure events occurred during flight, it should be stressed that a number of leaks and exposures occurred on the ground. Engine seals are less efficient during engine warm up, during ground manoeuvring, and during transient operations (acceleration/deceleration). Further, prior to 1998, an operational procedure on some models of aircraft called an auxiliary pack unit burn out was carried out every day, whereby heated engine air was pumped through the passenger cabin to decontaminate heat exchangers, air ducts and filters. While operational procedures expressly excluded any person from being on the aircraft during pack burns, from 1992 to 1997 it was common for flight attendants to carry out early morning pre-flight checks on aircraft during pack burns — therefore, aircrew were exposed to contaminants. So, although major exposure events occurred during flight, ground operations should not be excluded as a source of exposure.

Although it was not possible to quantitatively assess exposure during exposure events, descriptions from visible haze to dense smoke suggest significant exposure.

Immediately after exposure, the symptoms are essentially those that can be observed in individuals who have been exposed to toxic irritants, such as eye irritation, respiratory irritation, headache and other short-term neuropsychological effects, skin problems and nausea. These symptoms usually recede after

cessation of exposure. At least two Australian airlines have admitted that exposure events are significant enough to produce symptoms of irritation.[35,36]

However, it became apparent during this study that not all symptoms receded following cessation of exposure. Some existing symptoms became more debilitating, for example, headaches became so intense that they lasted for weeks and would not respond even to the most powerful over-the-counter analgesics. Neuropsychological symptoms became more generalised and affected more functions, with cognitive symptoms and recall problems becoming more significant. Skin itch became skin rash. Respiratory irritation became chest pain and/or difficulty in breathing. The intensification process was more likely to occur if exposure continued but, occasionally, would intensify even if exposure had ceased.

In addition, new symptoms began to emerge, including chronic fatigue, parathesias and numbness, myalgias, arthralgias, alcohol and food intolerances, and chemical sensitivity. Most of these symptoms continued even after exposure had ceased. Further, these and many of the neurological and neuropsychological symptoms worsened.[9,11]

The number of cases that emerged over the 1996 to 1999 period in Australia, North America and Europe became significant — to the extent that an appropriately designed epidemiological survey of aircrew was needed. The possibility of an industry-sponsored study seemed unlikely. Therefore, the present independent survey was conducted.

This survey comprised 117 individuals who nominated themselves to be entered into a database to receive a copy of the survey questionnaire. There were no criteria used to select study participants. The survey was carried out after a well-publicised Australian Senate Inquiry into air quality in the aviation industry, and this may have increased interest in some individuals to self-nominate.[37] The fact that so many respondents who had flown on those aircraft where engine leaks had occurred returned questionnaires was not intrinsically part of the survey. It is almost certain that self-nominations occurred through word of mouth as a result of contacts in the Australian aviation industry, and it is for this reason that there is a selection bias in the study respondents. No claim is made to suggest that the respondents in this survey are representative of any group in the aviation industry. The respondents represent themselves.

The survey questionnaire was designed to be neutral and contained no leading or biased questions. It was finalised after a trial with 10 aircrew. Eventually, 50 individuals from Australia returned completed surveys. Analysis of their surveys established similar findings to earlier studies (for example, see Table 1) with a moderate-sized group of respondents. Eighteen respondents returned questionnaires from North America — these were analysed separately.

In most cases it is not known whether the respondents' self-reporting was subjective or based on objective clinical or laboratory findings. This is a shortcoming of the survey. For example, the number of synonyms that exist for fatigue, that is, lack of energy, weakness, sleepiness, tiredness, lassitude, exhaustion, and so on, indicate the problems of assessing just one symptom.[38] In many cases, objective criteria exist for physicians to use in the diagnosis of such conditions. In some cases, respondents knew this and reported accordingly.

Patient diagnosis may also have been influenced by practice patterns in which their physicians specialised, that is, they reported symptoms diagnosed by specialists (not themselves). In other cases, agreement on case definitions of certain symptoms is not universal.[38] This overlap of symptoms and syndromes makes diagnosis complex.[33]

Conclusion

The range of epidemiology studies varies, and the predictive power of each type of study varies depending on design and methodological, analytical and interpretational factors. This survey was a descriptive survey of a group of non-representational individuals who qualitatively described workplace exposure scenarios and self-reported symptoms from such exposures. For this reason, no attempt has been

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made to ascribe causality or make inferences of a general nature. However, even with such procedural limitations, it was possible to draw a number of conclusions from this survey:

1. The hydraulics and lubricants used in the aviation industry contain a number of irritating and toxic ingredients.[6]

2. This study has shown that exposure to such contaminants, if they get into aircraft cabin air, can produce symptoms of toxicity.

3. The symptom clusters in aerotoxic syndrome can be described. These are:

— symptoms of dysfunction in neurological function immediately after intense exposures, including loss of positional awareness, vertigo and loss of consciousness. If these symptoms occur in a pilot, they are a significant aviation safety problem;

— symptoms of skin, eyes, nose and respiratory irritation immediately after exposure. Further exposures exacerbate the symptoms, often leading to other respiratory and cardiovascular effects;

— symptoms of gastrointestinal discomfort immediately after exposure. While these recede with cessation of exposure, there is a suggestion that nausea and diarrhoea can persist;

— some symptoms of impairment of neuropsychological function immediately after exposure, such as headache, dizziness, disorientation and intoxication. These symptoms become more debilitating after time, with problems of loss of cognitive function and memory problems emerging;

— general symptoms of exhaustion progressing to chronic fatigue. It was common for respondents to spend layovers, weekends and holidays sleeping for days to overcome the symptoms of exhaustion; and

— general symptoms of immune suppression developing some time after exposure, including food and alcohol intolerances, allergies and chemical sensitivity. These symptoms worsen with continuing exposure and may worsen even after exposure ceases.

Where symptoms of discomfort, irritation or toxicity occur, this breaches airworthiness legislation.

4. Many surveys of workers report that working populations generally enjoy a higher level of health than the populations from which they arise. This is the "healthy worker" effect, a commonly observed phenomenon by which lower death rates (or injury or disease rates) are observed in workers relative to the general population.[19,39] While this may be due to a selection bias problem, the aircrew in this survey had incidences of symptoms at much higher rates than population backgrounds — suggesting (in many cases) that they were unhealthier than the general population. However, as aircrew undergo regular health checks (pilots regularly, flight attendants less so), the levels of fitness and health in such individuals should be better than population norms.

5. There are a number of results from this study that require further investigation — particularly the findings of neurological impairment, respiratory system effects, reproductive dysfunction and other long-term effects.

Aerotoxic syndrome presents significant issues with regard to the health of pilots, cabin crew and passengers, but most notably with regard to air safety if pilots are incapacitated and cabin crew cannot supervise cabin evacuations during emergencies. Health effects include short-term irritant, skin, gastrointestinal, respiratory and nervous system effects, and long-term central nervous and immunological effects. Some of these effects are transient, others appear more permanent. The exacerbation of pre-existing health problems by toxic exposures is also highly probable.

There is also a hidden issue. Airline staff in Australia are worried about job security and what might happen to them if they complain about working conditions and make their symptoms public. This is especially apparent following the demise of a major Australian airline. At present, with only a few cases proceeding in

the courts, little compensation has been awarded to airline workers affected by toxic gases, vapours and fumes. Therefore, many crew are flying while further compromising their health and safety, and will only come forward when they become concerned that they may not be able to continue flying, or worse, when they are no longer able to fly.

Acknowledgments

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APPENDIX 25

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2. HEALTH EFFECTS

2.1 INTRODUCTION

The primary purpose of this chapter is to provide public health.officials, physicians, toxicologists, and other interested individuals and groups with an overall perspective of the toxicology of jet fuels JP-4 and JP-7 and a depiction of significant exposure levels associated with various adverse health effects. It contains descriptions and evaluations of studies and presents levels of significant exposure for JP-4 and JP-7 based on toxicological studies and epidemiological investigations.

A glossary and list of acronyms, abbreviations, and symbols can be found at the end of this profile.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the information in this section is organized first by route of exposure- inhalation, oral, and dermal-and then by health effect-death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods-acute (14 days or less), intermediate (15-364 days), and chronic (365 days or more).

Levels of significant exposure for each route and duration are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELs) or lowest observed-adverse-effect levels (LOAELs) reflect the actual doses (levels of exposure) used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear. They should also help to determine whether or not the effects vary with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the tables and figures may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons may be interested in levels of exposure associated with "serious" effects. Public health officials and project managers concerned with appropriate actions to take at hazardous waste

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2. HEALTH EFFECTS

sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) may be of interest to health professionals and citizens alike.

The jet fuels JP-4 and JP-7 are liquid military aviation turbine fuels whose composition varies slightly with the nature of the crude petroleum from which they were derived (Dukek 1978). Jet fuels derived from crude oil, the common name for liquid petroleum, are referred to as petroleum-derived jet fuels. Jet fuels derived from an organic material found in shale that can be converted by heat to shale oil are called shale-derived jet fuels. JP-4 is a wide-cut fuel; this is a refinery term indicating that it is distilled from crude oil using a broad temperature range and consists of hydrocarbons in a wide range of chain-lengths (4 to 16 carbons long) (Air Force 1989b; CONCAWE 1985). It was developed by the U.S. Air Force in order to ensure fuel availability in times of war (Dukek 1978; ITC 1985). JP-7 is a kerosene with a high flash point and is used in advanced supersonic aircraft. The jet fuels are blends of various hydrocarbons, including alkanes (paraffins) and cycloalkanes (naphthenes), aromatics, and olefins, as well as small amounts of compounds such as benzene, n-hexane, and polycyclic aromatic hydrocarbons.

The purpose of this chapter is to consider the toxicological effects of exposure to the mixture JP-4 or JP-7. Exposure to jet fuel components, exhaust, or combustion products will not be discussed. For information concerning the possible toxicity associated with exposure to some of the individual components of jet fuels, the reader is referred to the ATSDR toxicological profiles for benzene (ATSDR 1991a), toluene (ATSDR 1990), total xylenes (ATSDR 1991c), and polycyclic aromatic hydrocarbons (ATSDR 1991b). In addition, because of the variable composition of the jet fuels, the molecular weights are unknown (Kinkead et al. 1974).

2.2.1 Inhalation Exposure

2.2.1 .I Death

No studies were located regarding death in humans after inhalation exposure to JP-4 or JP-7.

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2. HEALTH EFFECTS

Exposure of Sprague-Dawley rats to concentrations as high as 5,000 mg/m^3 shale- or petroleum derived JP-4 for 4 hours did not result in any mortality or apparent toxic signs during the 2-week post exposure holding period (Clark et al. 1989).

Intermediate-duration exposure of rats and mice to concentrations of JP-4 as high as 5,000 mg/m^3 resulted in death in 1 of 40 exposed mice and 1 of 50 exposed rats, between 4 and 6 months after the exposure was begun (Air Force 1974). It was concluded that exposure to the test substance was probably not responsible for the deaths of these animals since two unexposed mice and one unexposed rat also died and because there were no abnormal histological findings in the rat. No deaths occurred when dogs or monkeys were exposed to similar JP-4 concentrations for 8 or 6 months, respectively (Air Force 1974).

No increase in mortality was seen in chronic studies in which mice and rats were exposed intermittently (6 hours/day, 5 days/week) to as much as 5,000 mg/m^3 JP-4 (Air Force 1981i; Bruner et al. 1993) or in studies where rats were exposed to 750 mg/m^3 JP-7 (Air Force 19828, 1983e, 1991). Additionally, no increase in mortality was observed in rats or mice 12 months after chronic intermittent exposure (6 hours/day, 5 days/week) to 5,000 mg/m^3 JP-4 (Bruner et al. 1993).

2.2.1.2 Systemic Effects

No studies were located regarding cardiovascular, gastrointestinal, musculoskeletal, dermal or ocular effects in humans or animals after inhalation exposure to JP-7. No studies were located regarding gastrointestinal, musculoskeletal, dermal or ocular effects in humans after inhalation exposure to JP-4. No studies were located regarding musculoskeletal or dermal effects in animals after inhalation exposure to JP-4.

The highest NOAEL values and all reliable LOAEL values for systemic effects for each study and end point are recorded in Table 2-l and plotted in Figure 2-l.

Respiratory Effects. No studies were located regarding respiratory effects in humans after inhalation exposure to JP-7.

TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
INTERMEDIATE EXPOSURE							
Systemic							
1	Monkey (Rhesus)	6 mo 5 d/wk 6 hr/d	Hemato	5000			Air Force 1974 JP-4
			Hepatic	5000			
			Bd Wt	5000			
2	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Hemato	1000			Air Force 1980 JP-4 (PET)
			Hepatic	1000 F	500 M (9% decreased liver weight)		
			Renal	500 M	1000 M (22% increased kidney weight)		
				1000 F			
			Bd Wt	500			
3	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Resp	1000			Air Force 1984b JP-4 (PET)
			Hemato	1000			
			Hepatic	1000			
			Renal	1000 F	500 M (hyaline degeneration of renal tubular epithelium, renal tubular casts related to alpha-2μ-globulin nephropathy)		
			Bd Wt		500 (unspecified decreased body weight)		

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TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
4	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Hemato	1000			Air Force 1984c JP-4 (SH)
			Hepatic	500 F	1000 F (5% increased liver weight) 500 M (11% increased liver weight)		
			Renal	1000 F	500 M (19% increased kidney weight, 26% decreased urine osmolality)		
			Bd Wt	1000			
5	Rat (Fischer 344)	90 d 7 d/wk 24 hr/d	Resp	1000 M			Newton et al. 1991 JP-4 (SH)
6	Mouse (C57BL/6)	90 d 7 d/wk 24 hr/d	Resp	1000 F			Air Force 1984b JP-4 (PET)
			Hepatic		500[b] F (fatty degeneration)		
			Renal	1000 F			
7	Dog (Beagle)	8 mo 5 d/wk 6 hr/d	Resp	5000			Air Force 1974 JP-4
			Gastro	2500	5000 (emesis)		
			Hemato	5000 M 2500 F	5000 F (unspecified increased red blood cell fragility)		
			Bd Wt	5000			
8	Dog (Beagle)	90 d 7 d/wk 24 hr/d	Resp	1000			Air Force 1984b JP-4 (PET)
			Cardio	1000			
			Renal	1000			
			Other	1000			

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TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
Neurological							
9	Monkey (Rhesus)	6 mo 5 d/wk 6 hr/d			2500 (unspecified depressed activity)		Air Force 1974 JP-4
10	Dog (Beagle)	8 mo 5 d/wk 6 hr/d			2500 (unspecified depressed activity)		Air Force 1974 JP-4
Reproductive							
11	Rat (F-344, S-D, Wistar, O-M)	90 d 7 d/wk 24 hr/d			1000 M (at day 90: 3% increased testis weight for Fischer 344 rats)		Air Force 1984d JP-4 (SH)

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TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
CHRONIC EXPOSURE							
Systemic							
12	Rat (Fischer 344)	1 yr 5 d/wk 6 hr/d	Resp	750			Air Force 1991 JP-7
			Hemato	750 F	150 M (16% decreased WBC count)		
			Hepatic		150[c] (21and 29% increased alkaline phosphatase in males and females respectively, 9% increased absolute liver weight in females)		
			Renal	750 F	150 M (hyaline droplet formation, hydronephrosis,tubular mineralization and 13% increased BUN)		
			Ocular	750			
			Bd Wt		150 (unspecified decrease "throughout the study period")		
13	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hemato		1000 (23 and 24% reduced mean WBC in females and males, respectively)		
			Hepatic	5000			
			Renal	1000 M	5000 M (mild progressive nephropathies, medullary mineral deposits)		
				5000 F			
			Bd Wt	5000			

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TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
14	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hepatic	5000 F	1000 M (11% decreased liver weight - 12 months post-exposure)		
			Renal		1000 (4 and 10%decreased kidney weight in males and females respectively, increased medullary mineral deposits in 14% of males - 12 months post-exposure)		
			Bd Wt	1000			
15	Mouse (C57BL/6)	1 yr 5 d/wk 6 hr/d	Hepatic	750 M	150 F (inflammation after 12-month post-exposure period)		Air Force 1991 JP-7
16	Mouse (C57BL/6)	1 yr 5 d/wk 6 hr/d	Endocr	750 M	150 F (43% increased incidence of adrenal capsular cell hyperplasia)		Air Force 1991 JP-7
17	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d	Resp		1000 (M: 38% increased nasolacrimal duct hyperplasia. F: 27% increased mild pulmonary inflammation)		Bruner et al. 1993 JP-4
			Hepatic	5000 M 1000 F	5000 F (37% increased lymphocytic inflammatory infiltrates)		
			Renal	5000			
			Bd Wt	5000			

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TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
18	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d	Resp	5000			Bruner et al. 1993 JP-4
			Hepatic	5000			
			Renal	5000			
			Bd Wt	5000			
	Immuno./Lymphor						
19	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d		5000 M	1000 F (24% increased spleen weight)		Bruner et al. 1993 JP-4
	Reproductive						
20	Rat (Fischer 344)	12 mo 5 d/wk 6 hr/d			5000 (increased cystic degeneration of the prostate in 52% of males; increased cystic hyperplasia of the mammary glands in 35% of females - 12 months post-exposure)		Bruner et al. 1993 JP-4
21	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d		5000			Bruner et al. 1993 JP-4

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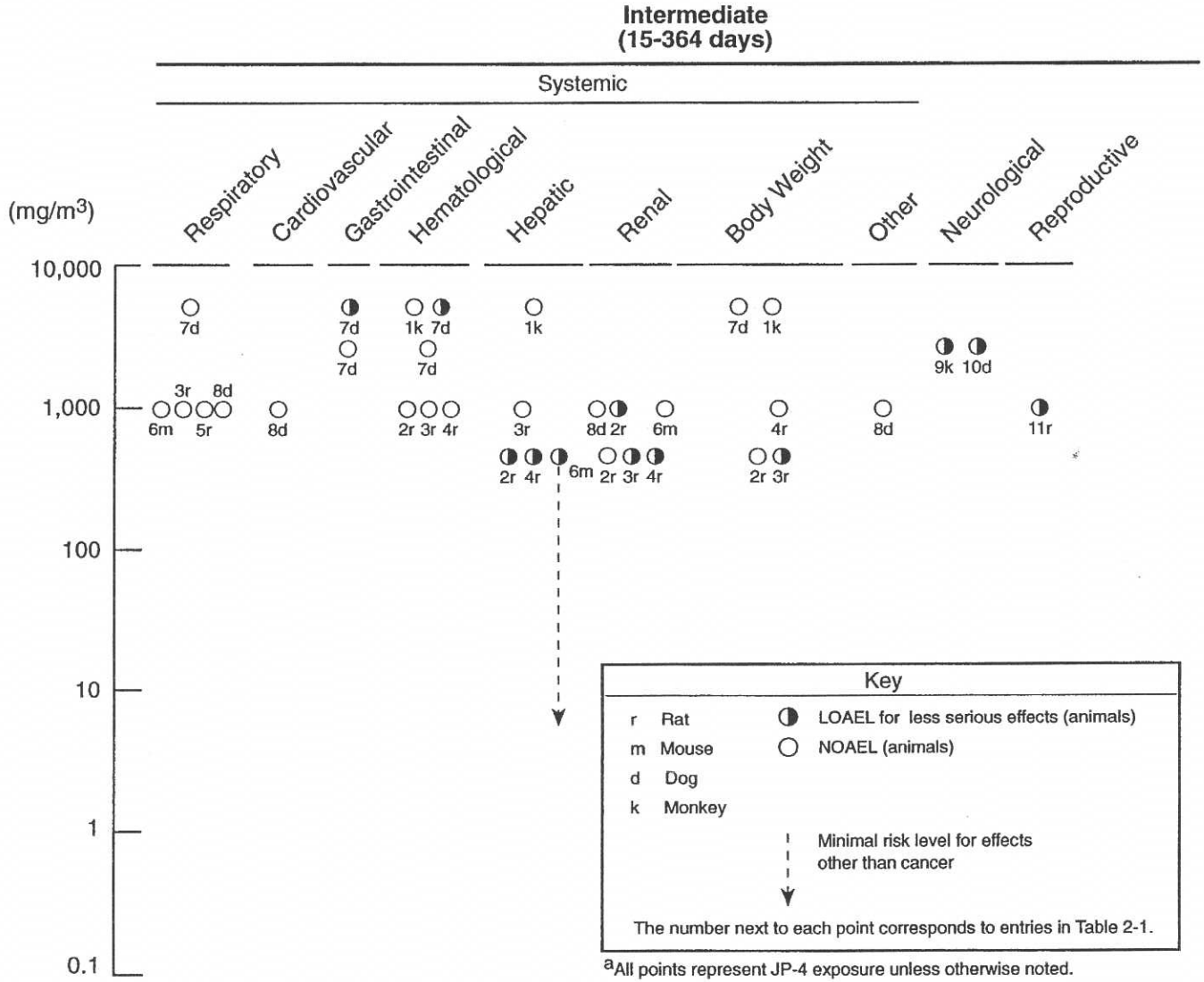
TABLE 2-1. Levels of Significant Exposure to Jet Fuels/ JP-4 and JP-7 - Inhalation (continued)

Key to[a] figure	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (mg/m3)	LOAEL Less serious (mg/m3)	LOAEL Serious (mg/m3)	Reference Chemical Form
22	Mouse (C57BL6)	12 mo 5 d/wk 6 hr/d		5000 F	1000 M (increased testicular atrophy in 47% of males - 12 months post-exposure)		Bruner et al. 1993 JP-4

[a]The number corresponds to entries in Figure 2-1.
[b]Used to derive an intermediate inhalation minimal risk level (MRL) of 9 mg/m^3, concentration divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) and multiplied by a factor of 5.7 for converting from animal to human exposure.
[c]Used to derive a chronic inhalation MRL of 0.3 mg/m^3, concentration adjusted from intermittent to continuous dosing (150 mg/m^3 x 5 d/7 d x 6 hr/24 hr); adjusted concentration divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) and multiplied by a factor of 3.3 for converting from animal to human exposure.

Bd Wt = body weight; BUN = blood urea nitrogen; Cardio = cardiovascular; CEL = cancer effect level; d = day(s); F = female; F-344 = Fischer 344; Gastro = gastrointestinal; HCT = hematocrit; Hemato = hematological; HGB = hemoglobin; hr = hour(s); Immuno./Lymphor = immunological/lymphoreticular; JP-4 = jet propellant-4; JP-7 = jet propellant-7; LOAEL = lowest-observable-adverse-effect level; LT50 = time to 50% kill; O-M = Osborne-Mendel; M = male; MCH = mean corpuscular hemoglobin; mo = month(s); NOAEL = no-observable-adverse-effect level; PET = petroleum-derived; Resp = respiratory; SH = shale-derived; S-D = Sprague-Dawley; WBC = white blood cell; wk = week(s).

Figure 2-1. Levels of Significant Exposure to Jet Fuels[a] – Inhalation



[a]All points represent JP-4 exposure unless otherwise noted.

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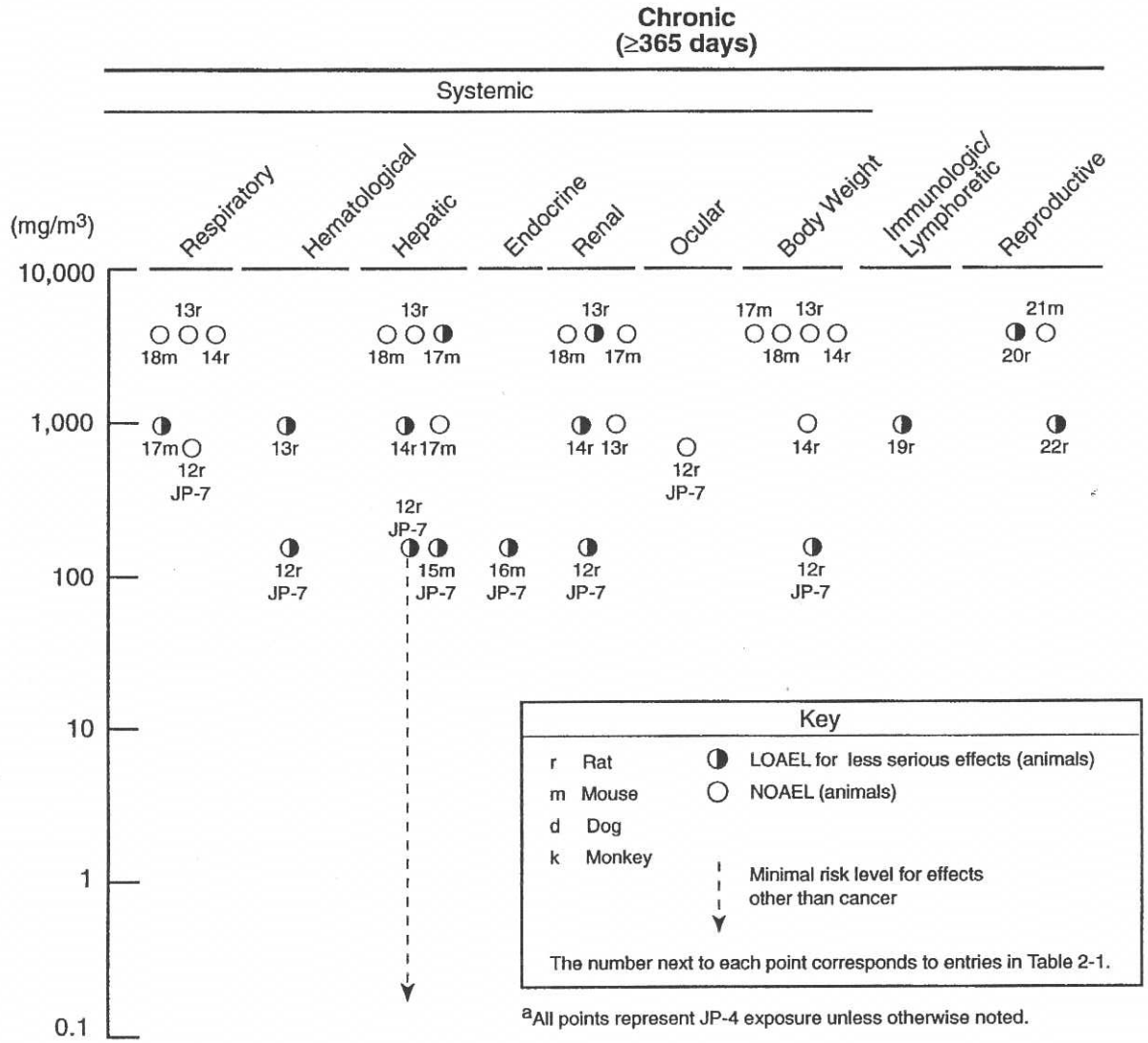
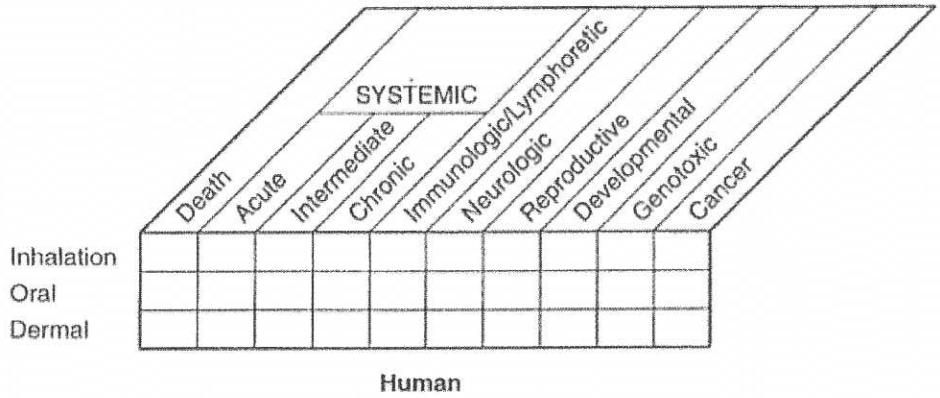
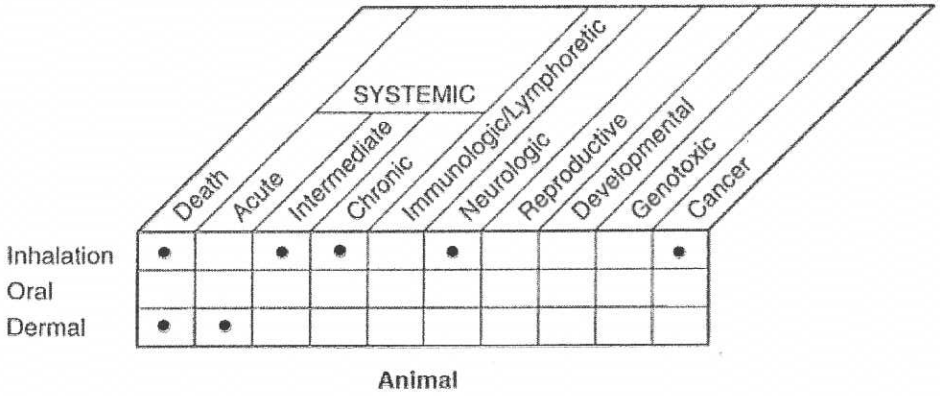
Figure 2-1. Levels of Significant Exposure to Jet Fuels[a] – Inhalation (continued)



[a]All points represent JP-4 exposure unless otherwise noted.



Human



Animal

● Existing Studies

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