A counterpoint to key misperceptions about exposure to aviation engine oil and hydraulic fluid fumes

Judith Anderson*

Air Safety, Health, and Security Dept, AFA-CWA-AFL-CIO, 501 3rd St NW, Washington, DC 20001, USA

This paper systematically reviews the most commonly encountered misperceptions regarding the crew health and flight safety hazards of breathing ventilation air contaminated with either engine oil or hydraulic fluid fumes on commercial and military aircraft. It is essential to clarify these misperceptions in order for the industry and regulatory bodies to more effectively address the underlying hazards.

Keywords: aircraft, dose–response, low dose, oil fumes, tricresyl phosphates, tri-*ortho*-cresyl phosphate

Looking back now, it all seems so clear. Rewind to the 1950s, and you can find papers published by military and industry researchers in the United States, all concerned about engine oil fumes that were reported to contaminate the outside air component of the aircraft ventilation supply (Boeing, 1953; Reddall, 1955; Treon et al., 1955). It was becoming obvious that extracting unfiltered ventilation supply air, off either the aircraft engines or the auxiliary power unit (APU), had an unintended consequence: varying amounts of engine oil smoke and fumes could contaminate the supply air. Whether the oil was leaking through engine seals or was spilled during servicing, crew members were being supplied with oil fumes to breathe in flight.

One example of an early investigation into the health effects of exposure to such fumes describes the responses to a health survey distributed to volunteer military navigators and pilots after purposefully being exposed to oil fumes: "Can you smell that? How about now?" (Loomis & Krop, 1955).

As another example of early recognition that oil fumes could contaminate pilots' breathing air, the Douglas Aircraft Company (DAC) wrote a letter in 1965 to assure the aviation regulator that, since rabbits had irritated eyes when exposed to engine oil fumes, pilots exposed to oil fumes on the DC-9 would presumably have the same experience (DAC, 1965). DAC reasoned that pilots would, thus, have sufficient warning to take corrective action before more serious symptoms developed. Hence, oil fumes were nothing to worry about.

Fast-forward to the mid-1990s and you may recall the noise that the cabin crew and their unions at Air BC and Alaska Airlines made to determine why some of them were getting so ill after exposure to fumes in the cabin on particular flights. The fumes and the illness had presumably always been there, although the presence of fumes (and, thus, the causal connexion to illness) was more obvious since onboard smoking had been banned. Also, relevant mechanical failures may have started to increase around that time, given the growing market for contract maintenance, and the growing popularity of "on-demand" maintenance (i.e., replace it after it fails).

Around the same time, front and back end crews in Australia were seeking answers to the same questions (PCA, 2000): why were they feeling dizzy and fatigued in flight? Why did they have acute flu-like symptoms, followed by delayed but chronic deficits with their speech and memory, for example?

In the early 1990s, Alaska Airlines' management representatives invited the on-site cabin crew union to join their "Unexplained Illness Committee" in order to get to the bottom of the puzzler of reported symptoms that "defied explanation" (Alaska Airlines, 1998). Subsequently, the airline's document production in response to a lawsuit brought by ill crew members showed that the airline had known the source of the problem all along.

Now it is 2014, so why are crews *still* being exposed to oil fumes, not as military volunteers, but as part of their job? The science, mechanics, and politics of exposure to oil fumes on aircraft are all better understood now, and the debate has slowly progressed. The industry no longer argues that oil *can't* contaminate the air supply system, or that the fumes don't contain *some* toxic compounds that can impair crew members in flight and compromise flight safety. But today's equivalent of the "Unexplained Illness Committee" is, unfortunately, still alive and well.

For example, in an official report regarding the potential flight safety implications of in-flight exposure to oil fumes, the UK aviation regulator claims that "[a]n average man would therefore be able to ingest 7 [*sic*] metric tonnes of pyrolysed oil per day for 74 days without effect" (CAA, 2004). Along the same lines, a major US airline recently reassured its pilot group that "[a] level of 7,000 mg/m^3 [of oil fumes] for a sustained period of time

* E-mail: judith@afaseattle.org

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is necessary in order to cause a longer term health concern" (US Airways, 2011). It seems unnecessary to comment on the absurdity of the "seven metric tonnes" assurance from the regulator, but to put the airline's claim in context, the cited exposure value for neurotoxic oil fumes is 1,400 times greater than the occupational exposure limit for mineral oil.

What follows, then, is a systematic review of what are arguably some of the most prevalent misperceptions and myths about exposure to oil and hydraulic fluid fumes on aircraft. For readers who have been exposed to fumes and have had to argue with workers' compensation claims adjusters, airline management, and even some medical professionals, much of this will be familiar ground.

MYTH #1: Bleed air contamination events are rare

If crew members were trained to recognize and respond to onboard fume events and report them to a centralized data base, "how often?" would be an easy and fair question to answer.

It is true that pilots must log all aircraft maintenance irregularities, including the presence of smoke/fumes that appear to be sourced to the aircraft air supply system. Regulations state that airlines must report incidents involving the *in-flight* "accumulation or circulation of smoke, vapor, or toxic or noxious fumes" caused by a failed or defective mechanical component, but airlines have some discretion as to whether or not to report incidents that occur *on the ground*. Further, there is evidence that airline compliance with these reporting rules for all smoke/fume events is poor (Ballough, 2006; FAA, 2006; Murawski & Supplee, 2008).

Even for incidents that meet the letter of the regulation, pilots likely underreport those that involve "just fumes" (i.e., bleed air contamination without visible smoke or haze), because airline training emphasizes smoke/fire events. And what if toxic fumes accumulate, but maintenance workers do not subsequently identify a failed/defective component; must such incidents be reported?

In addition to documented fume events that are sourced either to mechanical failures or an overserviced engine/APU, there is the potential for more prevalent but lower-level and transient oil leakage through engine/APU seals into the bleed air stream. For example, an aviation news source cites documentation from a German airline that trains its pilots to apply engine thrust slowly when possible, to minimize oil contamination of the bleed air by giving the engine seals more time to close (Flight Global, 2010). The airline appropriately notes that "for each throttle advancement from idle, there will be oil leakage around the seal until oil pressure increases to the point at which the seal becomes functional."

Still, despite the inadequacies of existing smoke/fume reporting rules, there are sufficient data to conclude that smoke/fume events involving exposure to oil/hydraulic fluid on aircraft are not rare (Michaelis, 2010). At three UK airlines, pilots reported bleed air contamination with oil/hydraulic fluid on 1% of flight segments, with some variation in frequency, according to airframe, engine type, and maintenance practices (COT, 2007).

In 2002, published oil/hydraulic fluid air supply contamination data from three Canadian airlines ranged from 0.09–3.88 events per 1,000 flight cycles, depending on aircraft type (NRC, 2002). Given the 822,776 flight segments operated by Canadian airlines in 2002,[1] this range translates into an annual low of 74 incidents and an annual high of 3,192 incidents. Likewise, applying the 1% UK estimate to the Canadian fleet translates into a yearly total of approximately 8,200 bleed air events, or 22 per day.

From 2009–12, US airlines reported a yearly average of 1,020 smoke/fume events (all types) to the US Federal Aviation Administration (FAA, 2013). These *reported* smoke/fume events are undoubtedly an underestimate of *actual* smoke/fume events because airlines don't reliably report to the regulator, as described above.

MYTH #2: "Just" an unusual smell can't make you sick—you need to be able to see smoke or haze

Clearly, many unusual smells will not make anyone sick. Anyone can retell some version of a story they heard regarding an in-flight turn-back due to onboard fumes that was ultimately sourced to a forgotten container of take-out food in a galley oven. Whether or not such incidents happen, or however representative they may be, it is the author's experience that such stories can be used to make light of the implications of exposure to onboard fumes. After all, overcooked take-out food hardly seems like a potential inflight hazard that demands crew training and education. But crew members must rely on their professional judgment daily, and they could make better and safer decisions regarding how to handle the presence of onboard fumes—whether oil or something in the oven—if they were trained to immediately assess whether the fumes are sourced to something in the cabin or to the ventilation system.

An assessment of crew-reported oil and hydraulic fluid smoke/fume events at one major US airline in 2009–10,

[1] Statistics Canada, "CANSIM data: domestic and international itinerant movements,Table 401-0013, 2002." Downloaded from www5.statcan.gc.ca on 22 August 2013.

found that only three of 87 documented bleed air events involved *visible* smoke or haze, while the remaining 84 incidents involved *"just fumes"*—namely, foul odours described as dirty socks, musty/mouldy, noxious, pungent, and more (Murawski, 2011). But on many of the 84 "just fumes" flights at that airline, there were significant crew health and operational consequences; see Table 1. If these data are representative, they suggest that exposure to oil/hydraulic fluid fumes can have crew health and operational consequences, even without the presence of visible smoke/haze. But does the airline industry recognize the potential health and operational consequences of oil/hydraulic fluid incidents involving "just fumes"? The answer appears to be, largely, no.

Table 1. Crew health/operational consequences of reported fume events at one US airline, 2009–10.

Number of flights with 1+ pilots who reported symptoms in flight (*Data not available for pilots on another 27 of 84 flights.*)	27 of 84 flights
Number of flights with 1+ cabin crew who reported symptoms in flight (*Data not available for cabin crew on 8 of 84 flights.*)	65 of 84 flights
Number of flights with 1+ crew members required emergency medical care (*Data not available for crew on 13 of 84 flights.*)	26 of 84 flights
Flight plan was changed[a]	19 of 84 flights

[a] A total of six of the 84 flights with "just fumes" were confirmed diverted/returned to gate, and another 13 of the 84 flights were confirmed as either cancelled or delayed at the gate. In addition, for 14 of the 84 flights that continued to their destination, the subsequent flight was confirmed as either cancelled or delayed. For 40 of the 84 flights, no information was available on operational impact, so the actual operational impact of "just fumes" is likely underestimated in this dataset.

First, airlines train crews to recognize and respond to onboard smoke and fire, but the author is unaware of any airline education or training programmes that explicitly describe the potential for oil/hydraulic fluid to contaminate the aircraft air supply system, and provide guidance on the importance of quickly establishing crew communications, donning oxygen, ruling out in-cabin sources of fumes, and not dispatching aircraft until the source of fumes has been addressed.

Second, as described in the previous section, there is evidence that airlines may question the applicability of smoke/fume reporting regulations to oil/hydraulic fluid in the air supply. For example, the airline referred to in the previous paragraph only reported 33 of the 87 oil/hydraulic fluid events to the regulator, even though 66 of the events appeared to meet the letter of the reporting rules, and 86 met the spirit of the reporting rules (Murawski, 2011).

Third, anecdotally, crews report that the presence of fumes is taken less seriously if neither smoke nor haze is present. Presumably, this is in part because there are many unpleasant but nontoxic sources of onboard fumes (e.g., people, food, carry-ons, lavatories), there are no chemical sensors in the air supply system, and crews are not provided with relevant education or training, as described above.

These questions of reliable recognition and reporting of "just fumes" matter, because (as described above and below) exposure to "just oil/hydraulic fumes" can cause significant short-term and long-term medical symptoms. This fact is not lost on some aviation safety investigators, who have emphasized that pilots must be trained to don oxygen, *even if* air supply contamination is *"just"* suspected.

For example, the UK aviation accident authority investigated an incident of pilot and copilot impairment attributed to the pilots breathing oil-contaminated ventilation air sourced to an APU oil leak (AAIB, 2004). The official report recommended that the UK aviation regulator publish "additional advice to the crews of jet transport aircraft on the best operational practice when there is *suspicion* of flight deck or cabin air contamination. The advice should include the *necessity* for all flight crew to use oxygen masks selected to 100% and the importance of cabin crew taking an active part in monitoring the flight crew in such circumstances." The UK aviation regulator did issue such advice seven years later (CAA, 2011), but one wonders why it took seven years, and why would such important and simple instructions not be a mandatory part of crew training?

Another pointed example of the potential toxicity of "just fumes" was published by the Australian accident investigator regarding an incident in which the pilots detected oil fumes during descent, but the pilot in command advised that it was not necessary to follow the smoke removal checklist or don oxygen, because no smoke/mist was present within the cockpit (ATSB, 1999). Then, the pilot in command became incapacitated. The report notes that oil fume events are not new, rare, or specific to one aircraft type, and expressed "particular concern" over flight safety implications of exposure.

The message not to ignore "just fumes" that may be sourced to the air supply system is vital, but the secondary message is that fumes and smoke without fire must also be taken seriously. In 2006, the Swiss aviation safety authority attributed an inflight incident of copilot incapacitation on approach to exposure to oil fumes and smoke (SAAIB, 2006). Among other things, the report highlights the need for better pilot training, noting that the copilot donned his mask during descent when he felt unwell, but

then removed the mask when his symptoms improved (which caused them to recur), and the commander did not don his mask at all because he "felt fine".

Some aircraft manufacturers have recognized the potential flight safety hazards posed by fumes, recommending appropriate precaution. For example, a technical bulletin issued by one manufacturer recommends particular inspection and maintenance procedures intended to identify and remedy oil contamination in the air supply system, and notes that "[f]light crews should be reminded of the importance of donning oxygen masks if poor cabin air quality is suspected, and reminded of the importance of reporting smoke or smells as a technical defect" (BAe, 2002).

MYTH #3: I can get my blood tested and prove that I was exposed to oil fumes onboard

The question of available blood tests is not so much a myth as a source of confusion. Researchers at the University of Washington and the University of Nebraska have published papers reporting their work to develop blood tests specific to the metabolite of particular types of the tricresyl phosphate (TCP) additives present in most aviation engine oils (Kim et al., 2010; Schopfer et al., 2010; Marsillach et al., 2011; Marsillach et al., 2012).

The University of Nebraska researchers report that they have developed a blood test for one type of TCP (Liyasova et al., 2011; Tacal & Schopfer, 2014), although that type of TCP may not be present in engine oil formulations at all and, if it is present, it would be at such low levels that (on its own, at least) it is unlikely to be a reliable marker of exposure to engine oil fumes. The University of Washington test development work continues, and hundreds of blood samples have been archived, drawn largely from crews shortly after onboard exposure to oil fumes. Once the test development is complete, the researchers intend to analyse those samples and communicate the results to each individual.

The present author is unaware of a specific blood test to reliably prove exposure to aviation oil fumes. However, available blood tests that may be helpful include: for carboxyhaemoglobin (marker of exposure to carbon monoxide; expected to clear from the blood within three to four hours, and even sooner if the crew member was administered oxygen); multiple measurements of serum butylcholinesterase post-exposure (a blood enzyme influenced by exposure to TCPs); and measurements of serum C-reactive protein (CRP, a blood marker of inflammation, which can be increased after exposure to organophosphate chemicals such as TCP).

In addition, a related "glial autoantibody" blood test is in the research phase (Abou-Donia et al., 2013). It is not specific to TCPs or engine oil fumes, but provides objective evidence of damage to the central nervous system, without the need for brain imaging/spinal tap. It does not confirm the *cause* of central nervous system (CNS) damage (i.e., exposure to neurotoxic compounds or something else) but it does confirm the *presence* of CNS damage, which may be consistent with exposure to neurotoxic compounds.

MYTH #4: Tricresyl phosphates (TCPs) are the only toxic ingredients in oil fumes

TCPs are a family of toxic ingredients added to aviation engine oils used in the commercial airline fleet globally, and are discussed in more detail in the next section. TCPs are popular oil additives because they reduce wear of the aircraft engines and improve thermal stability. According to the safety data sheets for the most widely used products, aviation engine oils contain 1–10% TCPs by weight. There is documentation to suggest that the mixture of TCPs added to these oils contains more than "just" TCPs (Michaelis, 2010). One source describes the TCP mixture (CAS Registry Nº 1330-78-5) as "consisting of … tris(dimethylphenyl) phosphates 18%, tris(ethylphenyl) phosphate 6%, other triaryl phosphates 1%", in addition to TCPs (NLM, 2014). Still, while the presence of TCPs and various other organophosphates in oil fumes is a significant concern toxicity-wise, they are not the only problem (ACARM, 2007).

Recently revised versions of the safety data sheets of some widely-used aviation engine oils explicitly report 0.1–1% trixylenyl phosphate (TXP) content (Exxon-Mobil, 2013). TXP is recognized as both neurotoxic and toxic to reproduction (NLM, 2013). Significantly, in late 2013, the European Chemicals Agency (ECHA) formally classified TXP as a "substance of very high concern" because of its toxicity to reproduction (ECHA, 2013). It is likely that many aviation engine oils contain TXPs because they are a constituent of one of the two aryl phosphate blends marketed to aviation engine oil manufacturers (ICL-IP, 2011).

In addition to TCPs and TXPs, most engine oil data sheets also report the presence of phenyl naphthylamine (PAN). PAN is an irritant compound. Interestingly, it also induces the production of a form of haemoglobin in the red blood cells that cannot carry oxygen (methaemoglobin). Thus, the symptoms associated with inhalation exposure to PAN are also the symptoms of oxygen deficiency, including blue lips/finger nails/skin, confusion, dizziness and headache (NLM, 2005). What impact does co-exposure to PAN and carbon monoxide have on the body's oxygen supply in a reduced pressure environment? Nobody knows at present.

In addition to the *reported* hazardous ingredients in most engine oils, chemical analyses of engine oil fumes

have identified many compounds not listed on the safety data sheets, such as acrolein, amines, carboxylic acid, carbon monoxide, formaldehyde, toluene, and xylene (Paciorek et al., 1978; van Netten & Leung, 2000; DERA, 2001; ACARM, 2007; ASHRAE, 2012;). Some of these compounds may be present in the bulk oil sample, and others are generated upon heating the oil to temperatures within the range of an operating aircraft engine or APU. For example, carbon monoxide can be generated when engine oil is heated to temperatures of approximately 230 °C and above. Of course, carbon monoxide is more potent in flight than on the ground, because the partial pressure of oxygen in flight is reduced as a function of cabin altitude. Carbon monoxide displaces oxygen from the haemoglobin in the red blood cells, reducing the blood's oxygen-carrying capacity and causing symptoms like mental confusion, dizziness, and headache, reinforcing the imperative to ensure that crews are trained to respond effectively to fumes.

Furthermore, there is some evidence that the TCP additives in the oils can react with other components of the engine oil at high temperatures to form new toxins. For example, one research group heated BP2380 engine oil and measured the production of the neurotoxin trimethylolpropane phosphate (TMPP),[2] starting at temperatures as low as 250 °C (Wright, 1996). In rats, TMPP exposure induced seizures (Lin et al., 2001), and repeated TMPP exposure induced long-term central nervous system sensitization (Lin et al., 1998).

On a related subject, a United States Air Force research team concluded that heating blends of TCPs to temperatures consistent with conditions in an operating aircraft engine appeared to create chemical changes to the oil, increasing its toxicity to rats inhaling the fumes (Lipscomb, 1995).

MYTH #5: Only the "*ortho* isomer TCPs" are neurotoxic and, since they comprise such a tiny fraction of engine oils, oil fumes can't make you sick

TCPs are often referred to as if they are one compound, but there are actually 10 different kinds of TCP—isomers—each with the same chemical formula and molecules, varying only slightly in structure.[3] These slight structural differences matter because they can influence toxicity. The toxicity and metabolism of the tri-*ortho* isomer of TCP (T*o*CP; see Fig. 1) has received the most attention to date, largely because of some mass accidental poisonings with T*o*CP starting in the 1930s (Morgan & Penovich, 1978). However, this does not mean that the remaining nine isomers are not toxic.

Table 2. List of all ten tricresyl phosphate isomers.

Isomer type	CH_3 ring constitution[a]	Number of each type
tri-*ortho*	o-o-o	1
di-*ortho*	o-o-m, o-o-p	2
mono-*ortho*	o-m-p, o-p-p, o-m-m	3
Total *ortho* isomers:		6
tri-*meta*	m-m-m	1
tri-*para*	p-p-p	1
di-*meta*, di-*para*	m-m-p, p-p-m	2
Total, all isomers:		10

[a] o, *ortho*; p, *para*; m, *meta* (see Fig. 1).

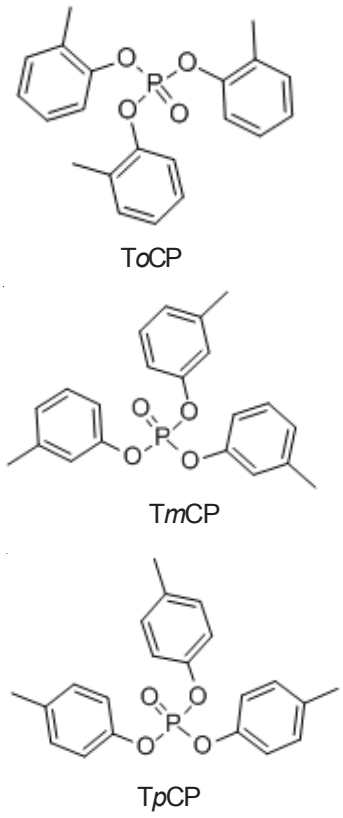

Figure 1. Chemical structures of tri*ortho*cresylphosphate (T*o*CP), tri*meta*cresylphosphate (T*m*CP), and tri*para*cresylphosphate (T*p*CP).

[2] TMPP is thought to be the product of a chemical reaction between trimethylolpropane (an engine oil base stock ingredient) and the TCP additives.

[3] The attachment location of each methyl group (CH_3) on each of the three cresyl groups attached to the phosphate molecule varies between isomers of TCP and it is a simple combinatorial problem to determine the number of each isomer type (Table 2). Evidence for the structural differences comes from the differences in boiling points (Henschler, 1958).

In 1958, a German toxicologist reported that the ingestion toxicity of TCPs is not dictated by the tri-*ortho*-isomer content alone, and that *the toxicities of the di- and mono*-ortho *isomers of TCP are, respectively, five and ten times greater than that of To*CP (Henschler, 1958). This was perhaps the first indication that T*o*CP was not the only toxic TCP isomer.

Many years later, Mobil Oil and its consultants noted that they could not explain the neurotoxicity observed amongst test animals that ingested an aviation engine oil containing 3% TCP by the small amount of T*o*CP present (Freudenthal et al., 1993). However, they did not define which engine oil constituents were to blame for the observed toxicity—whether the remaining *ortho* isomers, the dominant *meta*/*para* isomers, impurities, other ingredients, or some combination thereof.

So, everyone agrees that T*o*CP is toxic, and the *mono*- and di-*ortho* isomers of TCP are even more so. But focusing one's concern solely on the presence and toxicity of even the *combined ortho*-TCP isomer content still misses the point, and here is why: Manufacturers of aviation engine oils must ensure that the *"total* ortho *content"* of TCP—that is, the total of the six *ortho* isomers—cannot exceed 0.2% of the *total TCPs* in a given oil, by weight (SAE, 2005). So, if an average oil contains 3% TCPs (by weight), then a maximum of 0.006% of that oil can contain a mixture of as many as six *ortho*TCPs, among which T*o*CP may or may not be present.[4] All of this means that the one form of TCP that people talk about the most is barely present in oil fumes, if it's even present at all.

The industry's focus on the T*o*CP in oil fumes (while ignoring the "elephant" in the room) is not just a relic of 1950s research. The majority of industry-funded reports in the public domain still focuses on the content and toxicity of the *ortho* TCPs (Freudenthal et al., 1993; Daughtrey et al., 1996; Craig & Barth, 1999; Weiner & Jortner, 1999; Daughtrey et al., 2006).[5] This practice persists, even though the regulations dictate that 99.8% or more of the TCPs in oils must be *meta*/*para* isomers. This means that, in oil with a 3% TCP content, the concentration of the combined *meta*/*para* isomers will be 500 times that of the combined *ortho* isomers! With one notable exception (Baker et al., 2012), even the general scientific literature pays little attention to these *meta*/*para* TCPs that dominate the blend of organophosphates inhaled by exposed airline crews, other than to dismiss them as nontoxic.

MYTH #6: TCPs and oil fumes are only neurotoxic if they paralyse a chicken

The question of whether *meta*/*para* isomers of TCP in oil fumes are neurotoxic depends on one's definition of "neurotoxic". Noteworthily, *the industry promotes a definition of that term that suits its needs*, and the definition is specifically tied to inhibition of an enzyme called neurotoxic esterase (NTE), overt signs of paralysis, and spinal cord lesions.

It is well known that the *ortho* isomer TCPs significantly inhibit NTE activity (Mackerer et al., 1999), and if the inhibition is high enough, the test animal in question (usually a chicken) will eventually develop an uneven gait (if it can walk at all), lose its balance, and become paralysed. It has also been shown that the *meta*/*para* isomers of TCP barely affect NTE activity and do not cause obvious manifestations of the associated physical symptoms in test animals (Bondy et al., 1960; Mackerer et al., 1999).

Thus, the industry concludes that *ortho* TCPs are toxic (which is deemed acceptable because the *ortho* TCP content in aviation oils is so low) and the *meta*/*para* isomers are nontoxic (because they have much less of an effect on NTE activity). ExxonMobil takes this a step further: in a classic "human risk assessment" calculation, the company also assumes that the remaining 97% of oil fume constituents (i.e., non-TCPs, assuming a 3% TCP content) are effectively nontoxic (Mackerer et al., 1999). According to this way of reasoning, since only about 0.006% of the fumes are neurotoxic, the company assures anyone in potential contact with the oil that it would be "virtually impossible" to inhale enough oil on an aircraft to cause delayed neurotoxicity (Mackerer et al., 1999; Craig & Barth, 1999). However, this conclusion ignores the facts that: (1) it's inappropriate to ignore the toxicity of the non-TCP oil constituents; and (2) NTE inhibition and paralysis is only one (albeit convenient) measure of neurotoxicity.

On that second point, recent research demonstrated inhibition of two enzymes in mice that had ingested either Durad 125 (i.e., one of two blends of TCPs marketed for aviation oils) or the tri-*para* isomer of TCP (i.e., one of four isomers that dominate both commercial TCP blends added to aviation oils). Specifically, liver acyl peptide hydrolase (APH) and carboxylesterase1 (Ces1) enzymes in exposed mice were significantly inhibited (Baker et al., 2012). Assuming these findings apply to inhalation

[4] The identities and amounts of the ingredients in the TCP blends added to engine oils constitute proprietary information, although it is known that the total *ortho* content must be $\leqslant$ 0.2%, by regulation.

[5] These studies sometimes also mention the *ortho* isomers of other organophosphates that may be added to the TCP blends added to oils, such as TXPs.

exposure to these same TCPs, they are significant because the APH enzyme is implicated in cognition (Richards et al., 2000; Pancetti et al., 2007). Thus, the finding that TCPs (after being bioactivated in the liver) suppress APH activity may help to explain the prevalence of individuals who report cognitive effects after inhaling these types of TCPs during airline flights.

Likewise, the Ces1 enzyme plays a rôle in the body's detoxification processes (including the lungs and central nervous system), and the inhibition of Ces1 has been shown to suppress the activity of an important type of white blood cell that can affect overall immune function and the control of tumor cells/inflammatory processes (Markey, 2011). Thus, the finding that TCPs (after being bioactivated in the liver) suppress Ces1 activity may help to explain reports of immune system deficiencies, as well as reduced tolerance to subsequent exposures of toxic compounds, among affected airline crews. Ces1 activity is known to vary widely between people, influenced by genes, gene expression, and environmental factors (Ross et al., 2012; NCBI, 2014). It therefore appears possible that low Ces1 activity (whether naturally low or artificially depressed by a fume event) may increase a person's susceptibility to ill effects following exposure to oil fumes. Conversely, high Ces1 activity may offer some protective effect.

One should bear in mind that to be effective at spreading myths, one has to pepper them with truths. As such, the industry legitimately recognizes that exposure to sufficiently high doses of *ortho* TCPs can damage the peripheral nervous system and is associated with significant inhibition of the NTE enzyme (Mackerer et al., 1999; Craig & Barth, 1999). And it is true that it's unlikely for a crew member to inhale enough *ortho* TCPs to significantly inhibit NTE in an "average" fume event, since the *ortho* TCP content in the oils is so minimal.

But consider this: if test animals drink engine oils that contain around 0.006% *ortho* TCPs, one should not *expect* peripheral nervous system issues to dominate their symptoms, because the *ortho* TCP content is so low. Further, an early paper on TCP toxicity reported "traces of demyelination in the spinal cord" in animals given high doses of either tri-*meta* or tri-*para* TCP, suggesting that those isomers do have some effect on the central nervous system (Aldridge, 1954). Also, the absence of obvious *peripheral* nervous system damage in laboratory animals that have been fed room-temperature oil or TCPs over a period of days or weeks does not enable one to conclude that inhaling pyrolysed aviation engine oil will not cause neurological symptoms dominated by those that imply *central* nervous system damage, such as deficits in speech, concentration and information processing.

One should, therefore, not be fooled by the "logic" on the safety data sheet for the engine oil, which probably refers to toxicity research in which animals ingested oil "with a similar *ortho* TCP content" over some weeks and did *not* develop neuropathy, ataxia, and paralysis, hence implying that the oil is not neurotoxic. Remember: *focusing on the* ortho *TCPs alone ignores the elephant in the room, and it is not necessary to paralyse a test animal to be neurotoxic*.

It is important to understand this "smoke and mirrors" game because it appears to be the basis for oil manufacturers to claim that they need not warn aircrew of neurotoxicity under "normal conditions of use" (Exxon-Mobil, 2013) or "recommended industrial hygiene practices" (BP, 2012). Beyond the oil manufacturers, other part of the industry appear to accept this pseudo-science in order to justify not recognizing the neurological effects of exposure to oil fumes and not prioritizing means to prevent bleed air contamination.

To consider the bigger picture on this question of whether TCPs and oil fumes are neurotoxic, symptoms consistent with central nervous system damage have been reported after human exposure to chemically-similar organophosphates (Farahat et al., 2003; Ozyurt et al., 2008). Those same symptoms have also been reported by crews with documented exposures to engine oil fumes on board commercial and military aircraft, globally (Cox & Michaelis, 2002; Bobb & Still, 2003; Abou-Donia, 2005; Mackenzie Ross et al., 2006; Abou-Donia et al., 2013). Also, acute symptoms following exposure to aviation oil fumes are documented (Montgomery, 1977; Rayman, 1983; ATSB, 1999; CAA, 2002; FAA, 2004; SAAIB, 2006).

While neurotoxicity (acute and chronic) of oil fumes is the primary concern, it is not the only concern. TCPs have been implicated as endocrine disruptors in animal studies (Latendresse et al., 1995; Liu et al., 2012). Exposure to hydrocarbons in contaminated bleed air (Burdon, 2012) and combustion products in general (Kulling, 1992) have been associated with adverse respiratory symptoms, and organophosphate insecticides have induced airway hyperreactivity in test animals (Fryer et al., 2004).

Additional consequences of low-dose exposure to chemically-related compounds (organophosphate pesticides) include reduced testosterone levels, abnormal thyroid function, abnormal glucose and lipid metabolism, mitochondrial dysfunction, and negative effects on fetal/child brain development (Androutsopoulos, 2013). Health research to assess these types of health outcomes—as a possible consequence of inhaling the mixtures of triaryl phosphates (TAPs) in oil fumes—is needed.

MYTH #7: The dose makes the poison

This principle, enunciated by Paracelsus, the 16th century physician, chemist and founder of toxicology, was of course a very important advance in the science of poisons. Through his careful observations, Paracelsus noticed that some substances are therapeutically beneficial at low doses but toxic at higher doses. Even today, this is an important principle applicable to many substances. The enormous accumulation of knowledge about dose–response relationships has enabled the principle to be refined. For example, for substances to which the principle applies, one can distinguish between "linear no threshold" (LNT) and "threshold" behaviour. The former means that the effect of a toxin is proportional to dose right down to zero; the latter means that below a certain dose the substance has no effect at all. Further complexity has come through the realization that response cannot, in general, be predicted from dose alone; knowledge of many other factors is necessary, including genetic constitution, the status of liver enzymes active in toxin metabolism, diet and other medication.

A fairly recent observation is that for exposure to some endocrine-disrupting chemicals (like TCPs), the ill effects of low dose exposures can be different from the ill effects of higher dose exposures (Hausherr et al., 2014; Vandenberg, 2014). Also, there is evidence that low dose exposure to certain substances may elicit a response that gets inhibited at high doses—the phenomenon of hormesis (Mutch & Williams, 2006; Myers et al., 2009; Fagin, 2012; Androutsopoulos et al., 2013). To add to this complexity, for some organophosphates, there is evidence that small repeated doses can be more potent in inducing illness than a single larger dose (Abou-Donia, 2005). And yet another variable is the potential for interactions (synergistic, antagonistic, etc.) between chemical substances in a complex mixture like oil fumes. In most cases, detailed mechanisms for the observed effects are lacking.

MYTH #8: Passengers do not get sick

This myth may be best countered with eight words: "absence of evidence is not evidence of absence." Because airlines have no obligation to inform passengers of an onboard exposure to engine oil fumes that may cause delayed neurological symptoms, the apparent absence of passenger reports is not necessarily evidence that passengers don't get sick. Further, airlines are not required to forward passenger reports of chemical-induced illness to an independent third party. So, one cannot reasonably refer to *absence* of evidence, but rather, *very limited access* to evidence.

The present author has received calls from a small number of passengers who got sick after being exposed to oil fumes during various flights. Still, a reasonable person cannot expect uninformed passengers to reliably recognize the musty, "dirty socks" smell on their flight as engine oil fumes, document their subsequent neurological symptoms, and then formally report to the airline, relevant crew union, and aviation regulator. Until airlines notify and educate exposed passengers, and are required to report any passenger correspondence, there is little basis for the claim that passengers are not affected.

If a history of exposure to the chemical constituents of oil fumes can reduce a person's tolerance, then all crew members would be at higher risk of ill effects than passengers. This is because crews spend more time, proportionally, in the aircraft environment, and there is some evidence of prevalent low-level exposure to oil-based compounds on aircraft, such as the UK sampling survey that measured detectable airborne TCPs on 23 out of 100 regular flights (Cranfield, 2011; Murawski & Michaelis, 2011).

9. CONCLUDING REMARKS

In 1955, Henry Reddall of North American Aviation Inc. presented a paper at an engineering conference titled "Elimination of engine bleed air contamination" (Reddall, 1955). He reported on two possible solutions developed after two years of concentrated engineering effort, found to "greatly reduce the concentration of fumes". He wisely recommended either that aircraft be designed with an outside air compressor independent of the engines, or that engine bleed air be filtered. Fast-forward to 2011, and the bleed-free B787 with a separate air compressor entered commercial service. And in 2012, the catalytic filters recommended by Reddall were promoted at the IATA Cabin Health Conference in London, England (Bull, 2012). A less toxic antiwear additive is reportedly being formulated for aviation engine oils, and real-time chemical sensors specifically intended for early detection of oil-based compounds in cabin air are reportedly under development in several laboratories around the world. Finally, in 2013, the International Civil Aviation Organization (ICAO) published a working paper recognizing the potential flight safety implications of onboard exposure to oil fumes, and called for guidelines to ensure suitable training and education for airline workers (ICAO, 2013).

Ultimately, aviation is a business and so economic arguments must be brought to bear. One recently published paper applies a business model to estimate the dollar cost of diversions caused by reported fire and smoke incidents

at one Canadian airline (Lebbin, 2013). The estimated basic cost was $850,000 per year, but "assuming a 2% net profit, the airline would need to raise approximately $42.5 million a year in extra revenue to offset the diversion costs" (Lebbin, 2013). These cost estimates do not appear to include "fume only" events, and neither the total annual operating costs nor the fraction of diversions as a function of total number of flights are defined. Still, what is striking is the increase in financial outlay when some indirect costs of smoke/fume events are included. Thus, it is essential for airlines to define both the direct and indirect economic costs of smoke/fume events if they are to reasonably assess the economic costs and benefits of implementing preventive engineering, maintenance, and crew training measures.

Industry says it is impossible to either filter or monitor oil-based chemicals in the supply air (even if it wanted to) because the technological solutions are not available for purchase. On the other hand, suppliers are unwilling to invest in developing bleed air sensors and filters without an assured market, and regulators sit idle. In the meantime, airlines need to train crews to recognize and respond to onboard fumes, which in and of itself would help to mitigate the health, safety, and economic costs.

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