



Is there such a thing as aerotoxic syndrome?

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This paper assesses the current status of the diagnosis “aerotoxic syndrome”, namely, the cluster of characteristic symptoms reported after exposure to aviation engine oil fumes. The review begins with a short history of the diagnostic term since its introduction in 2000, and describes how the onset and characteristics of the reported symptoms are distinct from other medical conditions. While there is obvious overlap between aerotoxic syndrome and multiple chemical sensitivity, the former should not be considered a subcategory of the latter. A “nocebo effect” does not adequately explain the prevalence and consistency of the symptoms that continue to be widely reported by individuals exposed to engine oil fumes on aircraft. Currently, occupational and aviation medicine specialists largely rely on a diverse collection of diagnoses describing their patients’ neuropsychological deficits, as well as neurological, respiratory and cardiac abnormalities, among others. There is merit in a single diagnostic descriptor capturing these symptoms.

1. INTRODUCTION

The term “aerotoxic syndrome” was introduced in 2000 to describe the collection of symptoms of toxicity reported by aircrew (pilots and cabin attendants) flying in jet aircraft using bleed air to pressurize the cabin [1]. A more detailed survey of aircrew established a symptom basis for the syndrome [2]. These symptoms are partly physical (e.g., eye irritation) and partly neurological, affecting both the peripheral nervous system (e.g., tingling) and the central nervous system (e.g., memory impairment). The simple action of giving a name to a diverse collection of symptoms, many of which are quite common among the general population, has undoubtedly been useful as a “flag”, helping both sufferers and their physicians to identify the underlying cause(s), and a growing number of cases are being reported. A minority of professional aircrew seem to be aware of the syndrome, at least by description, if not by name. At the same time awareness, let alone more detailed knowledge, about the syndrome is lagging in the medical profession. Aircrew have, of course, intimate knowledge of the conditions inside the cockpit and the rest of the aircraft interior but, without having been informed about the potential health hazards associated with the ingress of fumes from the air supply system, the origin of their symptoms remained a mystery. There is ample anecdotal evidence that many physicians, including those with aviation expertise, completely fail to diagnose the neurotoxicological aspect of the complaints, instead diagnosing aircrew with depression, hyperventilation etc., leading to quite inappropriate treatment that fails to address and may even exacerbate the symptoms. Again

anecdotally, there have been reports of such physicians challenging the validity of the reported symptoms, whether referred to as “aerotoxic syndrome” or the longer list of more widely used, established diagnoses that describe the symptoms. The purpose of this article is to clarify the reality of the syndrome in the light of current knowledge.

2. SYMPTOMS

The dictionary definition of a syndrome is: “a group of symptoms or pathological signs which consistently occur together, especially with an (originally) unknown cause; a condition characterized by such a set of associated symptoms” [3, 4]. One of the difficulties facing the recognition of aerotoxic syndrome as a mainstream medical condition is the generic nature of many of the symptoms. For example, dizziness, reported as affecting 47% of aircrew [2], is also prevalent in the general population [5]. Krasnova et al. have emphasized the importance of quantifying occurrence as much as possible [6]. Even a simple binary scale (presence or absence) is a significant step towards precision; the data reported in [2] further distinguishes between occasional or mild and severe or continuous symptoms. Assuming the symptoms are independent, the probabilities of occurrence in the general population of the symptoms reported by a sufferer can simply be multiplied together [7]. Typically the overall probability of the coincidence of these symptoms among a member of the general population is vanishingly small [8]. This is an important comparison because it provides an objective basis for the identification of aerotoxic syndrome on the basis of a patient examination that any general practitioner could

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undertake without the need for special equipment or the analysis of blood or other samples.

3. IS IT USEFUL TO CONSIDER THE POSSIBILITY OF NOCEBO EFFECTS?

“Nocebo”, a relatively recently introduced medical term, is defined as: “a harmless substance that when taken by patient is associated with harmful effects due to negative expectations or the psychological condition of the patient” [9]. It has been suggested (again anecdotally) that the ill health reported by aircrew, and (now) ascribed to exposure to neurotoxic substances, originates as a psychological problem. It should, however, be borne in mind that most pilots and cabin attendants, when first reporting the symptoms grouped under aerotoxic syndrome, were quite unaware of the presence of neurotoxic substances in aircraft cabin air. Indeed, although awareness of cabin air neurotoxicity is increasing, airlines as employers are generally accused of having done very little, if anything, to educate pilots and cabin crew about the potential hazard. Furthermore, job satisfaction among aircrew is higher than average among occupations [11], suggesting that negative expectations are unlikely.

The possibility of a psychosomatic disorder has already been considered, and dismissed, by Mackenzie Ross et al. [10]. More recently, a thorough autopsy carried out on a deceased pilot revealed extensive neurological damage, including demyelination and other characteristic features of the consequences of exposure to certain organophosphates found in aircraft cabin air [12].

4. TEMPORAL ASPECTS

One of the earliest reports of pilot intoxication in-flight that was caused by exposure to engine oil fumes and reported in the medical literature only describes acute symptoms [13]. The subject apparently recovered within a day. It is possible that the pilot in question did not experience delayed and chronic neurological symptoms, although without any description of a medical follow-up, this possibility cannot be excluded. In other cases, though, persistent ill health has ensued and been documented [14]. Much more insidious than acute intoxication are the cases of chronic intoxication lasting for many years. Prediction of the consequences is presently difficult because many features of the metabolic pathways followed by inhaled neurotoxic substances still await elucidation. In any given individual, the precise genetic and epigenetic constitution will determine the efficacy of the pathways for detoxifying the body. Rates of key reactions may differ among individuals by orders of magnitude. Hence, even if

detoxification is ultimately successful, the actual rhythm of exposure (i.e., concentration, duration, frequency) will crucially determine whether bodily levels of the neurotoxic substances exceed the thresholds above which they can cause damage. Damage to the central nervous system is, of course, especially problematic, since it is well known that certain types of damage are irreparable. It is clear that more work needs to be done in this area.

5. IS AEROTOXIC SYNDROME RELATED TO MULTIPLE CHEMICAL SENSITIVITY?

Given the association between aerotoxic syndrome and the occurrence of certain known chemical contaminants in aircraft cabin air, the question arises whether the symptoms associated with aerotoxic syndrome constitute a subset of the condition known as multiple chemical sensitivity (MCS) [15, 16]. MCS is a debilitating condition affecting multiple body systems following various types of chemical exposures that do not necessarily include neurotoxic substances. Aerotoxic syndrome, on the other hand, is also a debilitating condition affecting multiple body systems, but it specifically relates to the clinical effects of exposure to a particular combination of chemicals that includes neurotoxic substances [17]. Regarding the neurotoxicity of oil fumes on aircraft, attention has tended to be focused on the tricresyl phosphates [18], which are known to be present in jet engine lubricating oil [19], some of which inevitably finds its way into bleed air [20]. The presence of tricresyl phosphates in oil fumes poses a significant concern, but the possibility of clinical effects originating from exposure to additional organophosphates in the oil fumes—compounds produced by chemical reactions between constituents of the lubricating oil upon heating in the aircraft systems—should also be considered.

6. CORROBORATING DIAGNOSES

The recognition of neurotoxicity is notoriously difficult [21, 22]. Once the concurrence of reported symptoms suggests aerotoxic syndrome, further investigations are needed. Physiological markers able to detect damage to the peripheral and central nervous systems are now available [23], damage which may persist long after the neurotoxic exposures engendering the damage have ceased. Brain function can be noninvasively assessed through new scanning technologies [24]. Higher-level psychometric investigations can complete the picture [25]. It should be noted that an extensive review of people, not working in aviation, occupationally exposed to organophosphate pesticides, chemically similar to the

organophosphates to which aircrew might be exposed, revealed that “low-level exposure to organophosphates produces lasting decrements in neurological and cognitive function” [26].

7. QUANTIFYING EXPOSURE TO THE CAUSATIVE AGENT(S)

Hitherto, attention has mainly focused on “fume events”, which may be defined as the rather sudden ingress of chemical substances into the aircraft cabin in quantities sufficient to trigger concern about the continuing safety of the flight and engendering a formal report, for example under the mandatory occurrence reporting (MOR) scheme within UK jurisdiction [27]. In such a case, should aircrew ill health ensue, there will at least be some documentation regarding the presence of chemical fumes in the work environment (e.g., pilot logbook, aircraft maintenance record, airline paperwork regarding change in flight routing, logs of medical support staff meeting the aircraft, hospital or clinic records, etc.). Nevertheless, the development of aerotoxic syndrome does not appear to require such a severe acute exposure. Following the measurement of low levels of tricresyl phosphates (and many other substances) during a significant proportion of “regular” flights on which no “fume event” occurred [28], attention is now turning to the possible clinical effects of chronic low-level exposure to neurotoxic substances.

8. CONCLUSIONS

Aerotoxic syndrome appears to be clearly identifiable on the basis of the collection of symptoms associated with it. More detailed corroborative evidence can subsequently be obtained using a variety of medical tests, although some of them are not without limitations. While the adverse effects of documented acute exposures are almost self-evident (although there appear to be no reported measurements of the actual concentrations of neurotoxic substances during such events¹), prolonged low-level chronic exposures may, in time, be equally or even more damaging to the human nervous system. The term “aerotoxic syndrome” should become a valuable vehicle for raising awareness of the clinical condition, not only among aviation medicine specialists [30] but also among general practitioners, who are often likely to have the responsibility for making the initial diagnosis.

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¹ See ref. 29 for an estimate of the concentrations.

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