Cabin Air Contamination Events

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Teaching Paper: A Diagnostic Workup for the clinician to follow in order to determine the correct diagnosis for patients presenting with ‚undefined' symptoms and without immediately recognisable links, but with a pattern of signs and symptoms that could be from inhalation poisoning after a flight on which a Cabin Air Contamination Event (CACE) occurred.

This paper presents the main strategies used to date by physicians who have diagnosed CACE patients. It is a useful tool for *diagnosis* and *follow*-up of a patient presenting with a list of symptoms that could be mimicking many other illnesses. *When patients present* with *symptoms such as, i.e. blood pressure, brain fog and dizziness,* it is vital to *listen to them as they may mention that they are coming directly from the airport and a flight, which is essential information. The patient's symptoms must not be diagnosed as simple ‚jet-lag', the possible reason being:*

An increasing number of so-called "cabin air quality events "or "fume" events in aircraft happen daily worldwide. The cabin air becomes polluted with unfiltered emissions from the engines. These fumes entering the cabin air contain substances from various chemical families (i.e. organophosphates) that are known to be harmful to the endocrine system and nervous system or listed as cancerogenic.

The patient (aircrew and/or passengers) may have experienced such a CACE, either as visible mist or as a strong chemical smell or pungent odour, to which they react with, i.e. immediate headaches, palpitations and nausea. The description given by the affected person can be ‚wet dog', ‚smelly socks', ‚stuffy gym air', ‚burnt oil', ‚exhaust' fumes.

Patients exposed to toxic fumes can present with a variety of symptoms, depending on the time frame and the amount that has been inhaled. They may be presenting with symptoms such as nausea, dizziness, pounding headache, blurry vision, focusing problems, concentration issues, tingling hands/ feet, balance problems, confusion, muscle soreness, coughing, breathing problems, balance and gait issues, fatigue. Such symptoms are common in other poisoning scenarios as well.

One will not know what type of toxic substance they have been exposed to; for this reason, a list of substances determined in biomonitoring of aircrew after flights with acute CACE, at the University of Göttingen/Germany. Verifying that the patient is reporting directly after a flight is a good indication for a CACE exposure.

The **three main leads** that can cause toxic fumes inside the aircraft are:

1. **Pyrolised jet engine oils/ hydraulic oils** (which can contain among hundreds of other substances, TCP from the chemical family of organophosphates)

2. **Aircraft exhaust fumes/ kerosene fumes poisoning** (carbon monoxide)

3. **Pesticide/ insecticide poisoning** (from 'disinsection', which contain substances from the chemical family of pyrethroids, mostly if the flight was to/from a country requiring onboard spraying with passengers and crew present.)

Carbon monoxide occurs from incomplete combustion. The CO pollution from jet engines can happen both from the ingestion of jet engine exhaust from outside of the aircraft and inside, from the thermal breakdown and incomplete combustion of engine lubricating oil that bypasses the engine bearing seals and enters the cabin breathing airflow.
A particular combination of chemicals can indicate a so-called "finger-print" particular to jet-engine kerosene, jet-oils and hydraulic fluids and have been detected in aircrew's biomonitoring regularly as mentioned above. Specific substances are listed further down can be tested.

Note: Body fluid tests should be taken straight after, or at the very latest within 48 hours of exposure. Blood should be drawn (2 samples at 5ml) and save three samples of urine on the same day. Storage: in the deep freeze. **The CO tests must be done within 2 – 3 hours of exposure.**

Blood Pressure - While many people may be familiar with the risks of hypertension in everyday life, hypotension "or low blood pressure" is a common symptom in poisoned patients and can result from a variety of factors, including dehydration or anaphylaxis (severe allergic reaction).

Seizures - Some toxins may cause seizures. Since the stability of our bodies depends on the balance of excitatory and inhibitory neurotransmitters and if this delicate balance is upset by poisoning, seizures can occur.

The following should be examined and documented – and repeated if the symptoms persist after a couple of weeks.

Heart rhythm disorders
1. ECG recording
2. Shortness of breath
3. Lung function disorders

Brain related symptoms (cognitive test) :
4. Confusion/ word-finding issues/memory and concentration issues
5 Dizziness/ brain fog
6. Hearing problems/sudden tinnitus
7. Vision problems/ i.e. tunnel vision/ blurred vision

After an incident with suspected cabin air contamination, it is in the patients best interest to compile complete medical documentation, including diagnosis in case of subsequent medical problems that may require a work-related injury record. If the patient wishes to take legal action, it is imperative to get the tests done within a couple of hours, best straight after the flight/disembarkation.

Please bear in mind that if a patient is suffering from poisoning, their intellectual functions can be affected, so making decisions may be difficult. Advice: run the tests and

determine a diagnosis for the records by using the ICD list (below) - there is always the danger of a later onset of health problems following poisoning and the need to be able to prove it may arise!

Immediate Action after Exposure

As mentioned, some of the tests must be done within the 2-3 hours brackett since those particular values tend to change quickly - they can sink to 50% of the initial value within 4-5 hours (i.e. CO) and could be back to normal by the next day.

The following list shows which values should be analyzed within a 2-hour frame:

- Complete blood count (CBC)
- White blood count (WBC) and differential
- Liver transaminases
- Creatine kinase with isoenzymes *(AChE determination)*
- COHb (Carboxyhemoglobine) determination for forensic purposes *(within 2 hours, more info below)*
- Blood gas analysis/earlobe blood gas analysis *(within 2 hours)*
- Oxygen saturation *(within 2 hours)*
- AChE *(read info further down)*

Note: Metabolic parameters such as cholesterol and insulin can be omitted. Smoking may impact the measurements.

Examine and record all symptoms such as, i.e. change of heart rhythm, shortness of breath and vision problems. These fumes can affect all organs, not only the central nervous system.

COHb - Carbon monoxide-saturated haemoglobin for forensic purposes.
In forensic investigations, there are occasional incidents in which the circumstances seem to point irrefutably to carbon monoxide poisoning, but the blood analysis shows low or normal COHb levels. For the investigation of low-level exposure, more sensitive methods involving the release of carbon monoxide and its measurement by gas chromatography will be required. For this type of measurement, the blood must be sampled on the day of the event, since the half-life is only 245 minutes, and therefore the values may be back to normal the following day. Samples that are not to be dealt with immediately must be stored correctly. As little air as possible should be in the tube, and the samples placed in a deep freeze without delay, irrespective of the anticipated degree of carboxylation.

AChE - *(= red blood cell acetylcholinesterase activity)* this measurement should not be an issue in a larger clinic/emergency room/university hospital who can deal with it on the same day. Preferably previous measurements without/before exposure are available for comparison; however, this will most often not be the case.

How to take and store blood & urine samples

Important: Disinfection of the skin area should not be carried out with solvent-containing disinfectants before sample collection, but, e.g. with a three-per cent aqueous hydrogen peroxide solution. (AMR 6.2); if not available, please note the name of the disinfectant used.

Blood:
2 x 5 ml EDTA blood should be taken in clinical chemistry tubes and stored in the **deep-freezer (should be minus 20°C/ -4°F)** for further (resp. later) toxicological analyses.

Urine:
Each sample should have about 15ml. Three (3) urine samples on the first day - then over the next five days one (1) sample per day, (on these days the first urine in the morning after getting up), these are also to be stored in the freezer. Special sterile cups can be obtained in pharmacies.

Long Term Effects - an Overview
Some, or all symptoms may disappear within hours or days, and the patient will feel okay again. Nevertheless, there is also the possibility of symptoms persisting 'on and off', especially if aircrew are flying as usual. So-called 'low level' contamination, meaning: exposure to some frequently present residues in air, carpets, seats and on the interior walls, and/or unnoticed small leaks can build up a 'toxic body burden' and symptoms reappear - often these symptoms will, when the patient is at home and has a few days off, or is on holiday, will seem to disappear, and they appear to feel better. Symptoms should be continuously documented and medically supervised. Some long-term symptoms can be:

- Fatigue
- Memory loss
- Concentration issues (brain fog)
- Word finding problems
- Vision issues
- Headaches (recurring)
- Muscle weakness
- Sleep disorders
- Mood swings
- Tinnitus

When long-term effects/symptoms persist, tests can be made for (within +/-30 days):

- Small Fiber Neuropathy
- Cognitive testing (i.e. memory, word-finding issues, concentration)

When respiratory function tests become necessary due to ongoing respiratory issues:

- Respiratory orientated exercise test with spirometry pre and post
- Lung Ventilation (TLC, RV, FRC AND VC).
- Diffusion (TLCO and TLNO).
- Blood gas analysis/earlobe blood gas analysis
- Oxygen saturation
- ECG (i.e. cardiac arrhythmia)

BIO-MONITORING (samples taken on the same day). The following substances could be present:

In the blood:

- 2-Butanone/MEK
- Isopropanol
- n-Heptane
- Isohexane/2-Methylpentane
- n-Hexane
- n-Octane
- n-Decane
- 2-Heptanone
- Toluole
- Acetone
- Formaldehyde
- Erythroid Acetylcholinesterase
- Insecticides (d-phenothrin, permethrin and metabolites)

In the urine:

- 2,5-Hexandion (a metabolite of n-hexane)
- o-cresol (Metabolite of Toluol)
- Acetone
- Tricresyl-phosphate
- Triphenyl-phosphate
- Tributyl-phosphate
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(This protocol may not be all-inclusive).

<u>Additional possible tests to check for exposure</u>

Clothing:
Worn uniform shirts/blouses (also ties): do not wash, fold well and place it in an airtight packing. Pack samples separately. They can be tested for engine oil, hydraulic oil and glycol residues at various laboratories if necessary.

Hair:
Tricresyl-Phosphate and specific metabolites can be detected in hair samples.

Blood:

Determination of organophosphate exposure and injury to the nervous system - by Professor M. Abou-Donia: Glial Auto-Antibodies.

Some more critical information and tips
The half-life of most VOCs (volatile organic compounds) is typically a few hours; therefore, laboratory results reflect very recent exposures such as within hours or days. If the patient was exposed a month ago, even every day, VOCs will most likely not be detected.

Laboratory tests for VOCs are technically challenging to perform due to the preparation and storage of test tubes. When some chemicals enter the body, they are partially broken down – or 'metabolized' – before they are excreted. Thus, when testing occurs, it is the 'metabolite' and not the chemical itself that can be detected; also, the levels might be lower than they would have been initially!

Various chemicals may have the same metabolite. Consequently, the results of the testing may be misleading and must be analyzed well. Not every laboratory can perform these tests, as specific technology and training are needed. Governmental and Military laboratories are the best option. Also possible if a laboratory advertises:

- Biological Monitoring for Exposure to Volatile Organic Compounds or
- Clinical Occupational Medicine or
- Occupational Toxicology & Immunology
-

And laboratories specializing in 'analytical laboratory for occupational toxicology and immunology'. Examples to look for in their services:

- Air & biomonitoring of volatile toxic substances, fumigants, solvents & metabolites in blood & urine
- Biomonitoring of isocyanate, metals, cotinine, pesticides
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Samples sent to a laboratory must be delivered in an uninterrupted cooling /frozen condition (e.g. on lots of dry ice in a Styrofoam box by special courier).

A consult with the local Poison Control Center in order to confirm that the treatment applied is the most effective could be advisable, as well as checking in with neurologists/toxicologists and lung specialists.

Classification and diagnostic keys: ICD International Classification of Diseases

The term „Aerotoxic Syndrome“ has been used since coined by three scientists in 1999; still, it is a medically „non-existent“ problem. Doctors can find classification keys, not under „aerotoxic syndrome“, a term often mentioned by aircrew, but instead, under, i.e. „toxic effects of other specified gases, fumes and vapours “ (as per above-listed substances) with the search word „aircraft“.

It is not easy to navigate the classification listings and takes time, of which medical staff usually have very little. Some of the helpful pointers using the term inhalation or toxic effects could be:

- inhalation of engine oil/kerosene fumes inhalation of toxic fumes
- toxic effects of gas
- toxic effects of carbon monoxide
- aircraft gases and VOC

Examples

T59.91XS is a billable ICD code used to specify a diagnosis of toxic effect unspecified. Example: even if one knows one is looking for „tricresyl phosphate“ (TCP) which is one of the substances crew and passengers can be exposed to, the search can be difficult. Who would have known that it is listed under „drugs“?
https://icd.codes/icd10cm/drugs-index

Acetylcholinesterase/anticholinesterase (AChE) which can be inhibited after exposure to various chemical substances, such as organophosphates, and is also listed under „drugs“: https://icd.codes/icd10cm/drugs-index/anticholinesterase .

Neither TCP nor AChE appeared directly when the searching with the term „aircraft“ or „toxic fume effects“ – one has to know that a) TCP is an organophosphate and a substance in the aircraft engine oil, resp. can be present in the fumes, and that b) organophosphates (TCP) inhibit AChE.

Type the word “aircraft” in the search bar and these examples pop up amongst many concerning aircraft accidents:

Toxic effect of other specified gases, fumes and vapors, accidental (unintentional)

- https://icd.codes/icd10cm/T59891
- https://icd.codes/icd10cm/drugs-index/combustion-gas

Toxic effect of unspecified gases, fumes and vapors, accidental (unintentional), sequela

- https://icd.codes/icd10cm/T5991XS = ICD-10-CM Code T59.91XS = gases, fumes and vapors, accidental (unintentional), sequela. Note: A 'billable code' is detailed enough to be used to specify a medical diagnosis.

Aircrew can have respiratory problems following acute and chronic exposure to bleed-air fumes this would be the (or one) necessary code to use:

ICD-10-CM Code J68.4 Chronic respiratory conditions due to chemicals, gases, fumes and vapours. **J68.4** is a billable ICD code used to specify a diagnosis of chronic respiratory conditions due to chemicals, gases, fumes and vapours. *A 'billable code' is detailed enough to be used to specify a medical diagnosis.*
https://icd.codes/icd10cm/J684

Useful scientific and technical information concerning aircraft cabin air quality

Some helpful information to refer to if and when medical staff and the public wish to have more background around "fume events" / "aircraft cabin air quality" can be found here **:**

- CACE (Cabin Air Contamination Event)Prof. D. Scholz https://www.fzt.haw-hamburg.de/pers/Scholz/CabinAir.html
- Technical https://www.aerotoxicteam.com/fume-events-aerotoxic-syndrome.html
- Science: https://www.aerotoxicteam.com/science.html
- Medical Info https://www.aerotoxicteam.com/medical.html
- Time Line/General info: https://www.aerotoxicteam.com/time-line.html
- Documentaries/reports: https://www.aerotoxicteam.com/evidence.html
- List of substances in cabin air https://www.aerotoxicteam.com/easa-list.html > *Update from 2019: a list of over 300 substances has been compiled by Jean-Christophe Balouet Phd, which are available upon written request.*

This paper presents the main strategies used to date by physicians who have diagnosed and treated CACE patients. The author adds updates when they become available.

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Science/Research:

An extensive list of peer reviewed science papers and research on the subject matter "Aerotoxic Syndrome" and "Cabin Air Contamination Events":
https://www.aerotoxicteam.com/science.html

Research on the subject ICD-Classification:

TCP (tricresyl phosphate)
https://icd.codes/icd10cm/drugs-index

Acethylcholinesterase
https://icd.codes/icd10cm/drugs-index/anticholinesterase
https://icd.codes/icd10cm/T441X1
https://icd.codes/icd10cm/drugs-index/acetylcholine

Science Direct a study
https://www.sciencedirect.com/topics/medicine-and-dentistry/international-classification-of-diseases

CDC
https://www.cdc.gov/nchs/icd/index.htm?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fnchs%2Ficd.htm

ICD Neurology application
https://www.amazon.com/Application-International-Classification-Diseases-Neurology/dp/9241547464

EU
https://ec.europa.eu/eip/ageing/standards/healthcare/e-health/icd-10_en

Wikipedia
https://en.wikipedia.org/wiki/ICD-10

WHO revision 11
https://www.who.int/classifications/icd/en/

Abstracts of the European Association of Poisons Centres and Clinical Toxicologists XXII International Congress*
https://www.tandfonline.com/doi/full/10.1081/CLT-120005494