

Toxic Triggers Exposure Assessment and Timeline of the gradual loss of tolerance to chemical substances.

Teaching Paper – Case Study

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Abstract

Toxic exposure can have occurred unnoticed for many years in the past—some toxic substances deposit in the organs and bones, and others in fatty tissues. The presence of synthetic chemicals in the body's fat cells slows down the natural detoxification process. Over time, this can lead to the body carrying a toxic load, also known as *toxic body burden*. Chemicals vary widely in the timescale it takes for their potency to reduce - known as the *chemical half-life*.

Even at low levels, chronic exposure to toxic substances increases the body's *toxic inflammatory reaction*. The body will do its best to deal with foreign or 'xenobiotic' invaders. However, at some stage, it will run out of steam and ill-health results.

A person's susceptibility to chemicals depends on many factors. Some cases by the genes they inherit and others by epigenetic effects that can be changed by environmental factors. Whether a person is ill or not and whether a toxic event has happened in the organism can be shown scientifically by finding a metabolite or original substance in human biomonitoring or fatty tissue biopsies. Alternatively, by provocation tests. A validated analysis and exposure assessment that explicitly prove the relationship of the substance type or noxious agent (pollutant) and the provocation effects are required.

Case Study

Female, caucasian, age 55, region USA

From the age of 6 to 9, the patient shared living quarters with her grandparents. She recalls the mobile home reeking of formaldehyde. She remembers her eyes burning, feeling nauseated and being short of breath from the overwhelming fumes - she also felt tired all the time. This was before the MHCC (Manufactured Housing Consensus Committee) raised questions in 1984/1985 following the many complaints about health issues related to the formaldehyde fumes in these mobile homes. They were debating the use of warning notices concerning formaldehyde¹.

At the age of 10, she moved into a house, situated right beside soybean fields on either side of the house. Crop dusters would spray pesticides² on those fields while she was playing in the garden, oblivious to the danger. She also played with children at a nearby farm where the crop dusters were again often spraying the very fields they would play in. She remembers the smell of the spray.

At the age of 18, she started work in the State Agriculture Soil Testing Laboratory where she was exposed to pesticide-laden soil as it was being washed; a process used to reveal the nematodes for counting by the laboratory assistants.

At the age of 19 to 20, she began working in a toxicology laboratory. At that time, this Animal Disease Laboratory had toxicology facilities. Her job as a Toxicology Laboratory Assistant included helping out in other sections, such as bacteriology, histopathology, virology, serology and specimen intake, where she was exposed to many chemical substances. She developed sinus issues and nose bleeds, which was one of the more notable exposure symptoms, and appeared whenever she washed selenium³containing testing glassware. Shortly after washing this glassware for which she had to use nitric acid⁴, the nosebleeds began. The nosebleeds included substantial blood clots coming out of her nose. Often the clots would be the size of a dime or bigger. She was diagnosed with sinus issues, and later had surgery to remove her tonsils and reconstruct a deviated septum. Her ENT told her that he had only seen a septum nearly as bad as hers in a patient who had a cocaine addiction for ten or more years. She had never used drugs and told the ENT about the chemicals used in the lab she worked in, and about the nitric acid, to which he said *"That would explain it! Your septum has been melted!"* He explained that those clots were parts of her septum deteriorated by the fumes.

At the age of 22, she was still working in the laboratory. She had her first child, and only months later was suffering horrible depression. She went to a counselor, thinking she may be suffering from PD/Postpartum Depression. She was advised to self commit to a mental health hospital/clinic. There her blood work was run, and subsequently was diagnosed with a hypothyroid condition. She then was told that it was most likely the thyroid condition and the related hormone imbalance, causing the depression. She was prescribed thyroid medication and stayed in the clinic's 30-day program to be counseled and have her thyroid monitored. She felt that her hypothyroid condition might have been caused by the chronic exposures to so many toxins⁵ and possibly her own body's inability to process some chemicals. Shortly after having her first child, she built her own home in Fuquay-Varina, NC. Years later the community were told that their water well that serviced 39 homes was poisoned and the EPA banned its use. The people suffered health issues as a result; some were stricken with tumors and cancer.

After leaving her job at the Animal Diagnostic Laboratory, she went to work for a Laboratory in Raleigh/N.C. That laboratory raised animals for laboratory use: rats, mice, and rabbits. She worked directly in the rat and mice laboratory. The rats and mice are kept in a vacuum-sealed room to maintain a sterile environment to ensure laboratory „pure“ animals. To enter those rooms, employees went through several airlocks. She would spend 8 to 10 hours a day, five days a week, in that air-tight room. Duties in that room included scraping and cleaning of the cages. The workers would take turns scooping up waste out of huge push tubs into a vacuum shoot that would then carry the

waste out of the room. Rat and mice waste (pee & poop) is very high in ammonia. The laboratory workers spent all day in that room breathing in the strong ammonia fumes⁶.

Household water contamination with Ethylene Dibromide⁷ (Dibromoethane). In 1996 she was made aware that the community well that provided water to her home was contaminated with ethylene dibromide (EDB) at 20 times the acceptable level. The United States Environmental Protection Agency (EPA) left a notice on her door warning all residents of the contamination and to avoid all use of this water: no drinking, cooking, washing with or in any way exposing the body to the water until the issue was found. The notice advised they would be supplying home water dispensers for consumption, and they further advised to use only bottled water for all other needs and shower elsewhere. A few community members had been experiencing skin rashes, eczema, headaches and nausea. Some children in the neighborhood had been found to have kidney, stomach and other intestinal issues—some with tumors.

In 1996/1997 she began her career as a Flight Attendant, where she was exposed to carbon monoxide⁸ fumes, jet fuel fumes⁹ and hydraulic fluid fumes¹⁰, in the end causing her to suffer from „Aerotoxic Syndrome“¹¹. The chronic exposure to these lingering fumes, as well as several exposures to acute „fume events“ with visible fumes, added to the accumulation of her toxic body burden. And, in her own words, these exposures were the “ nail in the coffin” for her health.

She was still a young woman but no longer had a high energy body or mind. After her first known exposure to an acute fume event¹² in 2010, she struggled to do what was once normal and easy for her. She would arrive home exhausted and spend off-days resting to gather the strength and energy to work the next flight. Mentally she became stumped, frustrated and depressed because she could not understand what had happened to her or how to fix it or recover from it.

Because she continued to fly, she continued to be sick. She learned that she was likely being re-exposed at such a rate her body could not fully detox. Her last aircraft-related work exposure was in January 2018. Shortly after that, she was diagnosed with Chronic Ethmoid Sinus Disease, RADs and non-alcoholic cirrhosis of the liver. She was told that if she hoped to walk away from this job rather than be carried out on a stretcher, she would need to stop flying. The health reaction from the last flight scared her into action. It was way too similar to an anaphylactic shock she had had a few years earlier following an insect sting to be ignored.

Her second to the last job was in a Zoo Gift Shop. There she would occasionally have headaches and dizziness from breathing in the fumes from perfumed¹³ customers. She also noticed that she often felt nauseated and could not figure out the trigger at first. One day her boss told her that most (85%) of their merchandise was imported from China, India and Africa¹⁴. She began wondering if the warehouses or Customs & Health authorities sprayed the boxes and containers with pesticides upon either leaving or entering the countries. She often experienced sneezing, runny nose and sinus headaches, and often got sinus infections when unpacking the boxes. More and more when at work, she became overwhelmed with fatigue, brain fog and dizzy spells. She changed jobs.

In her final job, she again experienced issues that were triggered by working close to people wearing strong perfumes and the excessive use of sanitizers in the shop area and

deodorizer dispensers¹⁵ in the washrooms. She again experienced dizziness, fatigue, brain fog and sinus issues every time she was in that work environment. She had to leave when the use of sanitizers increased due to the Covid19 outbreak as the fumes made her feel sick non-stop.

Effects of chemical substances on the organ system:

Systemic Effects	Target Organ Effects	Other Health Hazards
<ul style="list-style-type: none"> • Carcinogens • Toxic agents • Highly toxic agents • Corrosives • Irritants • Sensitizers 	<ul style="list-style-type: none"> • Hepatotoxins • Nephrotoxins • Neurotoxins • Blood/hematopoietic toxins • Respiratory toxins • Reproductive toxins • Cutaneous hazards • Eye hazards 	<ul style="list-style-type: none"> • Cardiovascular toxicity • Gastrointestinal toxicity • Immunotoxicity • Skeletal/muscular effects • Connective tissue effects • Endocrine system toxicity • Sensory organ toxicity (sight, hearing, taste)

Some possible symptoms, not all may apply and depend on point of entry:

Skin Absorption	Ingestion	Inhalation	Eye Contact
<ul style="list-style-type: none"> • Itching • Redness • Burns • Blisters • Rash/Hives 	<ul style="list-style-type: none"> • Abdominal Pain • Nausea • Vomiting • Diarrhea • A warm sensation in the stomach (halogenated hydrocarbons) • Dark-colored (black water) urine (arsenic) • Dehydration 	<ul style="list-style-type: none"> • Drowsiness • Dizziness/Vertigo • Headache • Confusion/Lethargy • Clear drainage from nose • Cough • Dry/Scratching/Burning Throat • Blurred vision • Shortness of breath • Rapid breathing (tachypnea) • Rapid heart rate (tachycardia) 	<ul style="list-style-type: none"> • Redness of the eyes • Burning sensation in eyes • Constant tear production • Mucous discharge from tear ducts • Blurred vision / blindness (partial or complete)

Diagnosis

Our patient was diagnosed with CRS (Chronic Ethmoid Sinus Disease), RAD (Reactive Airways Disease), Hashimoto disease and multiple chemical sensitivity¹⁶ (MCS, or TILT¹⁷) and non-alcoholic cirrhosis of the liver. A small thyroid nodule remains under observation.

Summary of effects of chemicals the patient was exposed to and short conclusion:

¹ **Formaldehyde** is a colorless, strong-smelling gas used in making building materials and many household products.

² **Pesticides** can cause short-term adverse health effects, called acute effects, as well as chronic adverse effects that can occur months or years after exposure. Examples of acute health effects include stinging eyes, rashes, blisters, blindness, nausea, dizziness, diarrhea and death. Examples of known chronic effects are cancers, congenital disabilities, reproductive harm, neurological and developmental toxicity,

³ **Selenium** is a trace mineral needed in small amounts for good health, but exposure to much higher levels can result in neurological effects, brittle hair and deformed nails. Occupational inhalation exposure to selenium vapors may cause dizziness, fatigue, irritation of mucous membranes, and respiratory effects.

⁴ **Nitric Acid** Exposure to nitric acid can cause irritation to the eyes, skin, and mucous membrane; it can also cause delayed pulmonary edema, pneumonitis, bronchitis, and dental erosion. Nitric acid is highly corrosive.

⁵ **Toxic** - Chronic exposures to chemicals

A chronic health effect is an adverse health effect resulting from long-term exposure to a substance. Symptoms do not usually subside when the exposure stops. Examples of chronic health effects include asthma and cancer. A chemical may cause both acute and chronic effects. Health effects can vary depending on the organ, the dose level, frequency, duration, and exposure route (inhalation, skin contact).

⁶ **Ammonia fumes**

Exposure to high concentrations of ammonia in air causes immediate burning of the nose, throat and respiratory tract. This can cause bronchiolar and alveolar edema, and airway destruction resulting in respiratory distress or failure. Inhalation of lower concentrations can cause coughing, and nose and throat irritation.

⁷ **Ethylene Dibromide**

is a mucous membrane, skin, and eye irritant. It may also cause respiratory distress and pulmonary non-cardiogenic pulmonary edema, liver and kidney toxicity, drowsiness, coma, and death. Dermal absorption may contribute to systemic toxicity.

⁸ **Carbon monoxide**

Breathing CO can cause headache, dizziness, vomiting, and nausea. If CO levels are high enough, you may become unconscious or die. Exposure to moderate and high levels of CO over long periods of time has also been linked with increased risk of heart disease.

⁹ **Jet fuel fumes**

Acute exposure to jet fuels has been associated with neurologic effects in humans, including headache, nausea, vomiting, dizziness, fatigue, in coordination, irritability,

problems with attention and memory, narcosis, and gait disturbances (Klave et al. 1976.)

¹⁰ Hydraulic fumes

Hydraulic fluids are complex mixtures of many chemical components, some of which may be toxic. Each hydraulic fluid should be considered equally hazardous. Exposure to these fluids mainly occur in workers using and maintaining equipment. Exposure to hydraulic fluid can occur through touch, injection, ingestion, and inhalation. Touching some hydraulic fluids may cause weakness in the hands or burns to the skin depending on the chemical make-up of the fluid. Injection injuries may result in poisoning, severe burns, and loss of limbs. Inhaling toxic fumes because of burning hydraulic fluid may cause respiratory or nervous system damage, such as lung disease, asthma, or chronic bronchitis. (Hydraulic Training Associates, llc. 866-432-9771 "Dangers of Stored Hydraulic Energy" by J. Eric Freimuth)

¹¹ Aerotoxic Syndrome information <https://www.aerotoxiciteam.com/fume-events-aerotoxic-syndrome.html>

¹² Contaminated Cabin Air Events (CACE) = toxic fumes in aircraft cabin air

„There is strong evidence that some people experience acute symptoms as a consequence of fume events. Some of the chemical contaminants that are present during such events are irritant, and may cause itching or soreness of the eyes, nasal discharge, sore throat or coughing.“ (CAA/UK)

12a) Adverse Health Effects of Fume Events and Air Quality Incidents on Commercial Aircraft Axel F. Sigurdsson, MD, PhD | 2018

<https://www.docsoption.com/2018/07/02/fume-events-air-quality-incidents-commercial-flight/>

12b) Contaminated Cabin Air Events -CACE-Teaching Paper – 2019 Bearnairdine Beaumont <https://bearnairdinebeaumont.academia.edu/research>

¹³ Perfumes/ Fragrances Exposure to fragrance chemicals can cause headaches; eye, nose, and throat irritation; nausea; forgetfulness; loss of coordination; and other respiratory and/or neurotoxic symptoms. Many fragrance ingredients are respiratory irritants and sensitizers, which can trigger asthma attacks and aggravate sinus conditions. Perfumes or fragrances are a cocktail of usually undeclared ingredients, which often comprise toxic ingredients including hormone disruptors.

¹⁴ Freight/container spraying and disinsection in aircraft passenger cabin

Spray pesticide for the regulated disinsection of aircraft cargo holds and maritime, shipping containers. Active ingredients usually used are d-phenothrin and permethrin.

14a) Airlines are facing new complaints, union trouble and possible lawsuits over pesticide spraying on aircraft. 1999 – ongoing <https://www.flightglobal.com/airlines-face-lawsuits-for-pesticide-spraying/24824.article>

¹⁵ Deodorised/fragranced dispensers (see also „Perfumes/Fragrances“)

Compounding the risks posed by formaldehyde, most major brands of plug-in air

fresheners contain a chemical known as naphthalene. Naphthalene has been shown to cause tissue damage and cancer in the lungs of rodents in laboratory studies. It's plausible to assume that it causes similar effects in humans.

¹⁷ **MCS, multiple chemical sensitivity**, also known as Idiopathic Environmental Intolerance (IEI) or Environmental Illness (EI). MCS is a chronic, physical illness affecting people of all ages and backgrounds. It causes sufferers to have allergic-type reactions to very low levels of chemicals in everyday products. Put simply the immune and detoxification systems stop working properly and the body cannot process toxins efficiently.

¹⁸ **TILT Toxicant-Induced Loss of Tolerance (TILT)** is a two-stage disease process initiated by a one-time major exposure, or a series of low-level chemical exposures (Stage I, Initiation). Affected individuals experience symptoms triggered by everyday chemicals, foods, and drugs that never bothered them before (Stage II, Triggering). Exposure examples include chemical spills, pesticides, cleaning agents, solvents, combustion-related products, drugs and medical devices, and indoor air contaminants associated with materials used in construction or remodeling.

Conclusion

After working for a while as a Flight Attendant, our patient noticed that she became more sensitive than ever to chemicals and fumes. Her toxic body burden finally seemed to overflow after several acute fume events (CACE) and the build-up from long-term exposure to lingering poisonous fumes in the aircraft cabin. Her system lost all tolerance to any toxic (chemical) exposures, also known as Toxicant-Induced Loss of Tolerance TILT.

A person's susceptibility depends on many factors. Inherited genetic makeup may be a reason or more often than not, environmental factors as described in the timeline. Whether a person is ill or not, and whether a toxic event has happened in the organism can be shown by searching for particular metabolites or original substances in human biomonitoring and in fatty tissue biopsy samples, alternatively, by provocation tests. Validated analysis and exact exposure assessments and time-lines are necessary to explicitly prove the relationship of the substance type or noxious agent (pollutant) to the provocation effect and symptoms, depending on the immune system or/and susceptibility of the individual's tolerance.

The WHO (World Health Organisation) declares on their website:

„Occupational exposures, exposure to (lead) and acute poisonings resulting from unsound management are estimated to account globally for 1 303 100 million deaths (2.3% of total) and 43 109 000 DALYs (1.6% of total). **Health effects considered include poisoning, leukaemia, lung cancer, ischaemic heart disease, stroke, intellectual disability and chronic obstructive pulmonary diseases.**“ Source: <https://www.euro.who.int/en/health-topics/environment-and-health/chemical-safety/data-and-statistics>

Available as pdf: **WHO Human Health Risk Assessment Toolkit: Chemical Hazards**

Department of Health N.Y. City help and information :

Armed with some basic facts about toxic substances, you can reduce your exposure to chemicals and lower the chance of harmful health effects.
https://www.health.ny.gov/environmental/chemicals/toxic_substances.htm

ECHA - Guidance for Human Health Risk Assessment

https://echa.europa.eu/documents/10162/23492134/biocides_guidance_vol_iii_part_b_v10_superseded_en.pdf/8ce06b02-2a0b-a348-7a44-162a8c83e633

First Aid/ First Emergency Procedures

If you think you have been exposed to a hazardous compound, and you know the name, consult the Safety Data Sheet (SDS). Section 4 of the SDS will contain first aid information. If you seek medical attention for a chemical exposure, be sure to bring the SDS with you to show medical staff.

For many chemicals, the following first aid measures are appropriate:

Skin Contact

Remove contaminated clothing and rinse off affected skin immediately with copious amounts of water at a shower station for 15 minutes or until pain is relieved. Seek medical attention, especially if skin is irritated or damaged.

Eye Contact

Use the eyewash to rinse the eyes thoroughly for at least 15 minutes, occasionally lifting upper and lower eyelids, moving the eyeballs around. Seek medical attention.

Inhalation

Move to fresh air immediately. Seek medical attention if symptoms persist. Provide the medical team with the SDS for the chemical to which you were exposed.

For Clinicians and ER staff in case of CACE (bleed-air fumes exposure in aircraft cabin)

- 1) https://www.aerotoxicteam.com/uploads/6/0/3/8/6038702/med_staff_info_update_2019.pdf

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- 2) https://www.academia.edu/attachments/65106572/download_file?s=portfolio

Note: names and locations of the patient's employers are known to the author.