# Multiple chemical sensitivity as a result of exposure to heterogeneous air pollutants

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## Abstract

To understand the relationship between health and the environment, we must study a series of events that might begin with the release of pollutants into the environment and might end with the development of disease in an individual, or a population. Noticeably, many studies have demonstrated an association between environmental exposure and certain diseases or health problems. Amongst all pollutants, Cadmium, Mercury, Arsenic, Nickel and Lead are emitted from several industrial processes, energy production processes and most vehicles. Methyl-Mercury is a poisonous industrial derivative of Mercury, enters the food chain and is toxic to the nervous system. Cadmium, Arsenic, Nickel and Lead are considered carcinogenic. Lead also causes digestive problems and damage to the nervous systems, especially in children.

Assessing the relationship between exposure to air pollutants and disease is complicated by the problem of multiple exposures to multiple pollutants. In fact, a controversial condition, known as Multiple Chemical Sensitivity (MCS), is thought to arise only through the combined effects of a number of chemicals in concentrations that might not be harmful on their own. In this first Italian pilot study, sufficiently large population groups have been considered to evaluate levels of toxic trace metals stored in the body by means of a hair analysis technique. For a majority of toxic trace metals the hair analysis technique has proved to be a well-suited biological marker of environmental exposure of general population to such toxic metals. The results suggest that there is an explicit correlation between exposure to air pollutants and high levels of toxic metals in the body with consequent development of diseases.


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# 1 Introduction

Health effects originated by air pollutants range from subtle biochemical and physiological changes to difficult breathing, wheezing, coughing and aggravation of existing respiratory and cardiac pathologies. Many health effects are directly associated with breathing of polluted air, but air also transports pollutants and deposits them onto soils or surface waters, where they can potentially affect plants, crops, property, and animals. Toxic substances in plants and animals can move through the food chain and pose potential risks to human health.

Toxic chemicals enter the water (and, therefore, the fish) from the atmosphere, tributaries, and sediments. Plants and animals can retain these chemicals through the food chain thus increasing their concentration. This process is known as “bioaccumulation.

Bioaccumulation results from a dynamic equilibrium between exposure from the outside environment and uptake, excretion, storage, and degradation within an organism. The extent of bioaccumulation depends on the concentration of a chemical in the environment, on the amount of chemical entering the organism through food, water, and air, and the time the organism necessitate to acquire the chemical and then excrete, store, and/or degrade it. The nature of the chemical itself, such as its solubility in water and fat, affects its uptake and storage. The ability of the organism to degrade and excrete a particular chemical is equally important. When exposure ceases, the body gradually metabolizes and excretes the chemical. The contaminants (namely Aluminium, Mercury, Iron, Lead, Cadmium) can be accumulated into the body and become a source of excess free radicals. Natural detoxification pathways of the body cannot eliminate them and the build-up can eventually reach toxic and dangerous levels. Too much Iron can give rise to heart problems and high levels of Lead and Cadmium can cause high blood pressure. In addition high levels of toxic metals can cause chronic fatigue and Multiple Chemical Sensitivity (MCS) syndrome also known as Environmental Illness.

MCS is a disorder triggered by exposures to chemicals in the environment. Individuals with MCS can have symptoms due to exposure to concentrations far below the levels tolerated by most people. Symptoms occur in more than one organ system in the body, e.g. nervous system and lungs. Exposure may be from the air, from food or water, or through skin contact. The symptoms may look like an allergy because they tend to go with exposures, though some people's reactions may be delayed. As MCS gets worse, reactions become more severe and increasingly chronic, often affecting more bodily functions.

Over the last years a group of 2346 Italian patients has been observed. Hair samples from 1627 women and 719 men were analyzed for Aluminium (Al), Mercury (Hg), Cadmium (Cd), and Lead (Pb).

Those who reported MCS symptoms were later interviewed to understand how the syndrome affects their daily lives. In all cases, we found uptake of heavy metals. These patients were studied under various degrees of environmental control.

Head-hair analysis is only the first step in a comprehensive evaluation and treatment that should proceed if the preliminary head-hair analysis gives plausible reasons for concern. The next step is an accurate analysis including urine, blood, for those with dangerous findings in the first screening test, and specialized biochemical intervention to treat the effects heavy metal poisoning.

## 2 Human health and exposure to heavy metals

The term heavy metal refers to any metallic chemical element that has a relatively high density and is toxic or poisonous at low concentrations. Examples of heavy metals include Mercury (Hg), Cadmium (Cd), Arsenic (As), Chromium (Cr), and Lead (Pb). Metals are notable for their wide environmental dispersion due to human activity, their tendency to accumulate in select tissues of the human body and their overall potential to be toxic at relatively minor levels of exposure.

Inter alia, combustion processes, cars, trucks, and industrial processes, release heavy metals and other elements. Cu, Cr, Zn, Sb and Pb can be partly attributed to traffic sources. Many heavy metals are also emitted into the atmosphere as a consequence of industrial processes: Cr and Ni are required for metal refinement in the steel industry while Pb, Ni, Zn, Cd, Hg are present inside accumulators. Through reaction with other substances and condensation processes, submicron aerosol particles develop from the emitted heavy metals, and are taken up by other particles and can be transported over large distances.

These particles are incorporated into the water drops in the precipitation process and washed out of the atmosphere with rainfall. Some metals, such as Copper and Iron, are essential to life and play irreplaceable roles, for example, in the functioning of critical enzyme systems. Other metals are xenobiotics, i.e., they have no useful role in human physiology (this also occurs for most other living organisms) and, as for Lead and Mercury, may be toxic even at trace levels. Even essential metals have the potential to turn harmful at high levels of exposure.

Exposure to metals can occur through a variety of routes. Metals may be inhaled as dust or fume (tiny particulate matter, such as the Lead oxide particles produced by the combustion of leaded gasoline). Some metals can be vaporized (e.g., Mercury vapor in the manufacture of fluorescent lamps) and inhaled. Metals may also be ingested involuntarily through food and drink. The amount that is actually absorbed from the digestive tract can vary widely, depending on the chemical form of the metal and the age and nutritional status of the individual. Once a metal is absorbed, it distributes in tissues and organs. Excretion typically occurs primarily through the kidneys and digestive tract, but metals tend to persist in some storage sites, like the liver, bones, and kidneys, for years or decades.

Heavy metals are dangerous because they tend to bio-accumulate. Bioaccumulation denotes an increase in the concentration of a chemical in a biological organism over time that is not due to an increased concentration of the chemical in the environment. Many compounds accumulate in living things any time they are taken up and stored faster than they are broken down (metabolized) or excreted.

An individual with metal toxicity, even if high dose and acute, typically has very general symptoms, such as weakness or headache. This makes the diagnosis of metals toxicity in a clinical setting very difficult. Chronic exposure to metals at such high levels to cause chronic toxicity effects (e.g. hypertension in individuals exposed to Lead and renal toxicity in individuals exposed to Cadmium) can also occur in individuals who have no symptoms. Much about metals toxicity, such as the genetic factors that may render some individuals unusually vulnerable, remains a subject of intense investigation.

Heavy metals that are more toxic include Lead, Cadmium, and Mercury. Lead in the environment arises from both natural and anthropogenic sources. Exposure can occur through drinking water, food, air, soil and dust from old paint containing lead. In the general non-smoking, adult population the major exposure pathway is from food and water. Food, air, water and dust/soil are the major potential exposure pathways for infants and young children. In humans exposure to lead can result in a wide range of biological effects depending on the level and duration of exposure. High levels of exposure may result in toxic biochemical effects in humans which in turn cause problems in the synthesis of haemoglobin, effects on the kidneys, gastrointestinal tract, joints and reproductive system, and acute or chronic damage to the nervous system.

Mercury is a global pollutant with complex and unusual chemical and physical properties. The main natural sources of Mercury are degassing of the Earth's crust, emissions from volcanoes and evaporation from natural bodies of water. Mercury is mostly present in the atmosphere in a gaseous, relatively unreactive, form. The rather long atmospheric lifetime (about 1 year) of this gaseous form means the emission, transport and deposition of mercury is a global issue. Natural biological processes can cause methylated forms of Mercury to form, to bio-accumulate up to a million-fold and to concentrate in living organisms, especially fishes. Some forms of Mercury such as Monomethyl-Mercury and Dimethyl-Mercury are highly toxic, causing neurotoxicological disorders. The main pathway for Mercury to humans is through the food chain and not by inhalation.

Cadmium is produced as an inevitable by-product of Zinc (and, occasionally, Lead) refining, since these metals occur naturally within the raw ore. The most significant use of Cadmium is in Nickel-Cadmium batteries, as rechargeable or secondary power sources exhibiting high output, long life, low maintenance and high tolerance to physical and electrical stress. Cadmium is also present as an impurity in several products, including phosphate fertilizers, detergents and refined petroleum products. In general, for non-smoking population, the major exposure pathway is through food, via the addition of Cadmium to agricultural soil from various sources (atmospheric deposition and fertilizer application) and uptake by food and fodder crops. Additional exposure arises due to Cadmium present in ambient air and drinking water. Cadmium derives its toxicological properties from its chemical similarity to Zinc, which represents an essential micronutrient for plants, animals and humans. Cadmium is bio-persistent and, once absorbed by an organism, remains resident for many years (over decades for humans) although it is eventually excreted. In humans, long-term exposure is associated with renal dysfunction. High exposure can lead to obstructive lung disease and has been linked to lung cancer, although data concerning the latter are difficult to interpret due to compounding factors.

## 3 The bioaccumulation process

Bioaccumulation is a normal and essential process for the growth and nurturing of organisms. All animals, including humans, daily bio-accumulate many vital nutrients, such as vitamins, trace minerals, essential fats and amino-acids. What concerns toxicologists is the bioaccumulation of substances up to levels that can result harmful. Bioaccumulation is the net result of the interaction of uptake, storage and elimination of a chemical. It begins when a chemical passes from the environment into an organism's cells.

Uptake is a complex process that is still not fully understood. It is well known that chemicals tend to move, or diffuse, passively from a place at high concentration to a place at lower concentration. The force or pressure for diffusion is called the chemical potential, and it can move a chemical from outside to inside an organism. The same factors affecting the uptake of a chemical continue to operate inside an organism, hindering a chemical's return to the outer environment. One factor important in uptake and storage is water solubility, the ability of a chemical to dissolve in water. Usually, compounds that are highly water-soluble have a low potential to bio-accumulate and do not leave water readily to enter the cells of an organism. Once inside, they are easily removed unless the cells have a specific mechanism for retaining them. Heavy metals like mercury and certain other water-soluble chemicals are such an exception, because they bind tightly to specific sites within the body. When binding occurs, even highly water-soluble chemicals can accumulate. This is illustrated by cobalt, which binds very tightly and specifically to sites in the liver and accumulate there despite its water solubility. Similar accumulation processes occur for mercury, copper, cadmium, and lead.

The storage of toxic chemicals in fat reserves also operates to detoxify the chemical, or at least to remove its most harmful forms. However, when fat reserves are called upon to provide energy for an organism, the materials stored in the fat may be re-mobilized within the organism and may again be potentially toxic. If appreciable amounts of a toxin are stored in fat and fat reserves are quickly used, significant toxic effects may be seen from the remobilization of the chemical.

Another factor affecting bioaccumulation is whether an organism can break down and/or excrete a chemical. The biological breakdown of chemicals is termed metabolism. This ability varies among species and individual organisms and also depends on characteristics of the chemical itself.

Chemicals that dissolve readily in fat but not in water tend to be eliminated more slowly by the body and thus have a greater potential to accumulate. Many metabolic reactions change a chemical into more water-soluble forms called metabolites that are readily excreted.

## 4 Multiple chemical sensitivity

Multiple Chemical Sensitivity (MCS) is a disorder triggered by exposures to chemicals in the environment. Individuals with MCS can have symptoms from chemical exposures at concentrations far below the levels tolerated by most people. Symptoms occur in more organ systems in the body, such as the nervous system and the lungs. Exposure may be from the air, from food or water, or through skin contact. The symptoms may look like an allergy because they tend to go with exposures, though some people's reactions may be delayed. As MCS gets worse, reactions become more severe and increasingly chronic, often affecting more bodily functions. No single widely available medical test can explain symptoms.

An increase in the numbers of people having adverse physical reactions to low levels of many common chemicals (ranging from congestion to sneezing to more severe reactions such as rashes and breathing problems) is becoming more evident. These reactions are often non-specific and hence dismissed. In brief, chemicals damage the immune system and the liver, and suppress the cellular mediation that controls the way the body protects itself from foreign materials. MCS is, in fact, an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects.

Measuring the metal load in the body is an important approach in diagnosing MCS syndrome and assessing its degree (level). Heavy metals in the body may accumulate in hair, which can be considered a valuable specimen for diagnosing heavy metal poisoning. Hair analysis is a very useful tool [1] in detecting what causes MCS chronic symptoms.

A hair analysis acts as a timeline for exposure to various elements and so can be considered a good screening test when heavy metal toxicity is suspected. A growing number of peer-reviewed publications support the considerable value in elemental analysis of hair specimens, especially for the toxic metals [1]. For example, elevated levels of Arsenic in both hair and urine confirmed Arsenic toxicity from pesticide exposure in an individual with peripheral neuropathy and macrocytosis but without anemia [2]. There is also evidence linking hair levels of Lead, Manganese, Cadmium, and other toxic metals with psychological conditions and deviant/violent behaviors [3]. Lead, Cadmium and Mercury levels in children’s hair have also been correlated with childhood intelligence.

An important advantage of hair analysis is that the collection of samples is simple and non-invasive. Hair analysis provides a useful initial screening for trace element status. Studies have demonstrated a correlation between element hair concentration, environmental exposure, and pathological effects [4,5]. Hair analysis is an excellent indicator of long-term risk as well as a barometer for early, chronic exposure, often reflecting excess exposure before symptoms appear.

## 5 Data analysis

A group of 2346 adults was considered in this study. The treated group consisted of 1627 (69%) women and 719 (31%) men. All patients have had some chemical sensitivity symptoms, namely headaches, flu-like symptoms, asthma or other respiratory problems, visual disturbances, ear, nose and throat problems, persistent skin rashes, inflammation, food allergies, bloating and other digestive problems, genital-urinary problems, Candida, auto-immune disorders, cardio-vascular irregularities, fatigue and depression.

These symptoms often develop after an exposure to a toxic substance or after an infection or other illness and they can be considered as a stress overload condition. The immune system can be seen like a barrel that continually fills with chemicals until it overflows and symptoms appear. A single serious episode of infection, stress, or chemical exposure can trigger “immune system dysregulation”. The first cause of chemical sensitivity syndrome can be considered the total body load, today often dubbed as Body Burden.

The Body Burden is the patient’s total pollutant load due to sources such as air, food, and water. The body must cope with this total burden; usually, it must be utilized, expelled, or compartmentalized. Total body load includes toxic chemicals (e.g., inorganic elements such as Pb, Cd, Hg, Al, Br, etc. and organic elements such as formaldehyde, phenols etc., present, for example, in pesticides and car exhausts) [6,7], and biological factors (bacteria, viruses, parasites, moulds etc.) [8].

Identifying offending chemicals and/or toxic elements represents a challenge for the clinician. Many chemicals exert their effect at such low concentrations that they elude detection whenever tests are not performed through very sophisticated laboratory methods. While measuring effects of toxicity by observing symptoms is a time-honored procedure, a preferred approach is to use laboratory methods that measure biomarkers that are specific indicators of the toxicant’s action.

Hair has been used in many studies as a bio-indicator of heavy metals exposure for human populations [9]. As hair growth is approximately 1 cm each month, heavy metal exposure over time is recapitulated in hair strands.

Eighty-four percent of all patients presented the total toxic representation over the normal range (see Figure 1).

A more detailed analysis (see Figure 2) has revealed that Mercury appears to be the most common significant toxic exposure. Sixty-six percent of patients presented Mercury values over the reference range (0.4 ppm). Thirty percent presented Lead values over reference range (0.1 ppm). About Cadmium and Aluminium, 14% and 28% had values over the upper normal limit respectively.

In this analysis Mercury appears to be the “kingpin” in the cascade of events in which metals become pathogenic. Mercury can be present as metallic Mercury (HgO), as Mercury salt (e.g. Mercury chloride HG+), or as Methyl-Mercury (HG++). Methyl-Mercury is 50 times more toxic than metallic Mercury. Methyl-Hg is so firmly bound to the body that it has to be first reduced to HG+ before it can be removed from the cell. This is achieved through injection of reducing agents (antioxidants), namely intravenous vitamin C and reduced Glutathione.

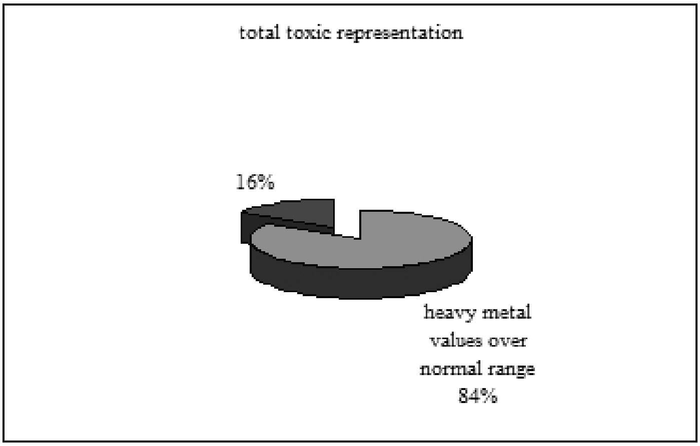


Figure 1: Percentage of heavy metals within or over normal range.

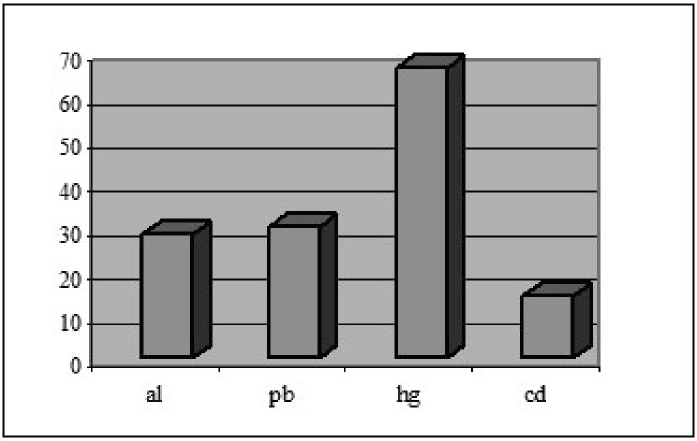


Figure 2: Percentage of Al, Pb, Hg, Cd over normal range.

Cadmium is a toxic, heavy metal without positive metabolic function in the body. Cadmium levels in hair provide an excellent indication of body burden. Moderately high Cadmium levels are consistent with hypertension, while severe Cadmium toxicity can cause hypotension.

In most cases, mineral analysis has revealed a slow oxidizer pattern with very sluggish adrenal gland activity. This is not surprising, as the adrenals are a primary defense against allergic phenomena. Cortisone and adrenalin, adrenal hormones, are often administered to stop allergic reactions. If our bodies produce enough of these hormones, they can protect us from many allergens in the environment. Slow oxidizers often have low energy levels, impaired digestion and an accumulation of toxic metals due to their slow rate of metabolism. All this can contribute to environmental illness.

Hair analysis can be considered a "screening test" and should be followed by confirmatory testing in blood or urine.

In the end, the diagnosis of chemical sensitivity can be achieved through the concurrent analysis of patient history, physical examination and immune tests - including IgE, IgG, complements- blood levels of pesticides, organic compounds and heavy metals.

## 6 Conclusions

Toxic chemicals, at any level of chronic exposure, affect human biochemistry. The body has mechanisms for transforming, eliminating or compartmentalizing many toxic chemicals absorbed over a lifetime. Nonetheless, these 'safety' mechanisms may be inadequate or even inappropriate in our modern industrialized society, especially for susceptible people such as the elderly, individuals with poor nutritional habits, and others who are physiologically stressed.

The heavy metals that are most often implicated in human poisoning are Lead, Mercury and Cadmium. Measuring the metal load in the body is an important approach in diagnosing heavy metal load and assessing its severity.

Hair acts as a depot of toxic metals; therefore, their analysis provides information of element storage over time and is an excellent indicator of long-term risk as well as a barometer for early, chronic exposure, often reflecting excess exposure before symptoms appear.

A group of 2346 patients was analyzed in this first pilot study. In most cases we have verified an alarming toxic load. Heavy metals, in fact, tend to accumulate leading to a cascade of chronic events and illness.

Diagnosis of environmental illness has to be made only after meticulous investigation. It is essential to confirm abnormal hair analysis results by further investigation methods, such as blood, serum, or urine analyses.

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