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# COVID.19 : Man Made Pandemic: Lead and Cadmium Mutate Influenza Virus Produce: SARS COV-2

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Cadmium and lead toxicity is a newly emergence problem particularly in industrial countries, beside pollution of air with industrial fumes, water with sewage contained heavy metals especially cadmium and lead, soil pollution by using of inorganic fertilizers contained those poisonous heavy metals, furthermore contamination of food chain with them increase their danger. Vegetarians are at great risk of cadmium toxicity, beside those whom depend in meat and animal based food. Lead induces changes in C-U bases of influenza virus, and cadmium replaces zinc and copper in sulfhydryl group of it and produces what is known as SARS COV-2. Olfactory dysfunction due to invasion of virus to the olfactory nerve lead to transitional loss or reduction of smell and taste, while taste returns rapidly, smell takes longer time to act properly, this attributed to role of influenza virus in loss of smell which makes dysfunction of this sense more severe than taste. Low hemoglobin lead to absorption of more cadmium which is important for viral replication and lead to severe complications. Women are enriched with cadmium in comparison to men, and that explains why they suffer from serious complications.



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Mosab Nouraldein Mohammed Hamad

## COVID-19: Man-made pandemic

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**June, 2021**

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## **Dedication**

**To the soul of my father**

**To my mother**

**To my sisters, brothers**

**To my sons**

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## **Acknowledgement**

I am very grateful to the administration and all of the staff of Banoon fertility center, Khartoum, Sudan, for their continuous support and guidance. Also to all people whom support and help me throughout my life.

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## Summary

Cadmium and lead toxicity is a newly emergence problem particularly in Industrial countries , beside pollution of air with industrial fumes , water with sewage contained heavy metals especially cadmium and lead, soil pollution by using of inorganic fertilizers contained those poisonous heavy metals , furthermore contamination of food chain with them increase their danger.

Vegetarians are at great risk of cadmium toxicity, beside those whom depend in meat and animal based food. Lead induce change in C-U bases of influenza virus , and cadmium replace zinc and copper in sulphhydryl group of it and produce what is known as SARS COV-2.

Olfactory dysfunction due to invasion of virus to the olfactory nerve lead to transitional loss or reduction of smell and taste, while taste return rapidly, smell take longer time to act properly, this attributed to role of influenza virus in loss of smell which make dysfunction of this sense is more severe than taste.

Low hemoglobin lead to absorption of more cadmium which is important for viral replication and lead to severe complications. Women enriched with cadmium in comparison to men that explain why they suffer from serious complications. Highest concentration of lead and cadmium occur in elderly, then viral mortality see among this age group.

Trump decisions in 2017 enhance pollution and accelerate emergence of SARS COV-2 pandemic, which is pure result of man-made pollution in air, soil, water and even their food. Beginning of the pandemic in Wuhan, due to heavy cadmium and lead pollution in water and air, also high content of seafood with these elements promote emergence of it.

Indian SARS COV-2 crisis occur because of that most population are vegans and high usage of that metals in aqua-agricultural farm.

## Introduction

Coronaviruses derive their name from the Latin word “corona” meaning crown. The name refers to the unique appearance of the virus under an electron microscope as round particles with a rim of projections resembling the solar corona. They are enveloped, positive-sense, single-stranded RNA viruses which were first isolated from humans in 1965. Coronavirus belongs to the family Coronaviridae which is known to produce mild respiratory diseases in humans. In recent times, there have been three major coronaviruses leading to disease outbreaks, beginning with the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, followed by the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, and now the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) [1].

It seems that coronaviruses take an important place in the 21st century history. Five of seven human coronavirus was isolated in this century. Unfortunately, last three of them entered our life with a fear of outbreak, pandemic or death. Last human coronavirus which emerged world from Wuhan China, SARS CoV-2 and its clinical expression, Coronavirus disease (COVID-19) recently taken a significant place in our daily practice [2].

At the end of 2019, a cluster of pneumonia patients with an unidentified cause emerged in Wuhan, Hubei Province, China [1]. Through the analysis of sequence, this unidentified pneumonia was considered to be caused by a novel coronavirus (CoV) named 2019-nCoV. Subsequently, the World Health Organization (WHO) announced a standard format of Coronavirus Disease-2019 (COVID-19), according to its nomenclature, for this novel coronavirus pneumonia on February 11, 2020. On the same day, the International Committee on Taxonomy of Viruses (ICTV) named this novel coronavirus as SARS-CoV-2[3].

On 26 February 2020, the rate of new cases begin to decline in China, but the tendency changed outside China, where new cases occurred, such as in Italy, South Korea and Iran; and for the first time the number of new cases outside China surmounted those reported in China. After China, Italy had the second largest number of Covid-19 case-fatality rate. Unfortunately, the infection spread also to all other European countries. Covid-19 is also spreading in US, mainly a high concentration in New York City, with a higher fatality rate. Other countries such as Iran, Turkey, Canada, South Korea, Brazil, Israel, have also unfortunately experienced a large spread of the infection. African countries are at particular risk because of the density of the communities and insufficient diagnostic and therapeutic capacities [4].

Official COVID-19 deaths reached 1 million in late September 2020. Marked differences in overall mortality rates exist across countries and locations. As of early October 2020, 66 countries recorded <1 death per 100 000 population (including 21 mostly small countries without any deaths), while 17 countries exceeded 50 deaths per 100 000. These stark differences are mostly genuine, reflecting massive variability in viral spread, substantial variability in infection fatality rate (IFR), and both under- and overcounting of deaths across locations [5].

It is now a pandemic affecting various countries globally. 213 countries /territories have registered COVID-19 cases. Some countries are now considering whether to ease the measures, others have already decided to keep them in place over the following weeks. The WHO estimates one person in 20 will need intensive care treatment, which can include being sedated and put on a ventilator.

With the phenomenal increase in cases and deaths in top 10 countries various interventions are being undertaken. New countries are coming up in the list of top 10, and all are showing an increasing trend in terms of mortality and morbidity [6].

Pollution in the environment is the price we have paid for growth in industrialization and urbanization. While advancement in technology has improved the standard of living, it has also released unwanted substances into the environment, thereby raising issues with public health. Ineffective regulations on pollution and emission controls due to increasing urbanization and industrialization have put humans at risk. Heavy metals are persistent environmental pollutants and humans are exposed to them through water, air, food, or industrial settings. Biological buildup in the food chain allows multi-heavy metal pollutants to increase. Heavy metals are extensively used to uphold the standard of living in developed nations and they enter the environment through natural and anthropogenic sources, including artisanal mining, illegal refining, inadequate disposal of waste, and the constant increase in industrialization and urbanization.

Thus, the risk of human exposure continues to increase as a result of the prevalence of heavy metals in the environment. Insufficient control of reclaim plans has led to unplanned exposure in the past. Metal poisoning from various sources is a significant problem, from evolutionary, natural, and dietary perspectives.

The ubiquity of heavy metals poses major public health threats to adults and children. While toxicity from industrial exposure usually affects several organ systems, the severity of the health outcomes is dependent on the nature of the metal, the method of exposure, the age of the individual, and finally, the person's individual susceptibility. Humans are exposed to heavy metals, either voluntarily or involuntarily, from various sources resulting from an increase in industrial pollution, manmade or natural activities, and there is a constant increase in heavy metal contamination around the globe and this has posed serious health concerns.

The increase in population, urbanization, and industrialization, coupled with the rapid growth of buildings as a result of inadequate planning, have caused an increase in the production of waste without proper disposal systems [7].

The most polluting countries seem to be aware they must reduce their emissions, but, despite agreements such as the Kyoto Protocol, these carbon dioxide emissions continue to rise. To a greater or lesser extent, almost all the world's countries are responsible for the high level of global pollution, but there are five that stand out from the rest, as shown below:

#### **1. China (30%):**

The world's most populated country has an enormous export market, which has seen its industry grow to become a serious danger to the planet. In just five provinces, which that host most of these industries, more dioxide is emitted than in any other country in the

world. As a consequence, Beijing has experienced, in recent years, constant red alerts for environmental pollution.

**2. United States (15%):**

The world's biggest industrial and commercial power. **Although in recent times it has led the most important initiatives to combat climate change**, in practice the great majority have been shown to be insufficient. Neither are its pollution levels limited to big cities; many rural areas are also beginning to notice the consequences.

**3. India (7%):**

Fourteen out of the world's 15 most contaminated cities are in India, says the World Health Organization. The country has had a law protecting air quality since 1981, but the burning of fossil fuels has grown significantly and as a consequence India occupies third place in the ranking of the most polluting countries in the world.

**4. Russia (5%):**

The biggest country in the world geographically appears in this ranking for its high dependence on products such as oil, coal, gas and fossil fuels.

**5. Japan (4%):**

Finally, the other great Asian power after China completes the list. Japan is the biggest consumer of fossil fuels in the world and the fifth largest emitter of greenhouse gases. This situation is due to its high level of urban development and industry that seems to care little for nature [8].

## Trump impact on the environment



**Figure 1:** *President Donald Trump signs a presidential memorandum to "minimize unnecessary regulatory burdens" on October 19, 2018. Since his earliest days in office, President Trump has been taking steps that increase emissions of the heat-trapping greenhouse gases that are warming the planet to dangerous levels.*

Since the Trump administration took office, it has been fighting what they call an “anti-growth” agenda put in place by the Obama administration. Regulations that required businesses to spend time and money to meet the former administration's environmental standards were swiftly reviewed and, in many cases, rolled back.

National Geographic has been tracking the decisions that will impact America's land, water, air, and wildlife. What started with curtailing information when the president took office in 2017 has evolved into actions like executive orders that open public land for business.

## **Influential decisions made by the Trump administration impact the future of United States:**

1. *U.S. pulls out of Paris Climate Agreement:*

This is perhaps the decision that set the tone for the Trump administration's approach to the environment: when he moved to withdraw from the Paris Climate Agreement in June of 2017.

2. *Trump EPA poised to scrap clean power plan:*

The Clean Power Plan was one of the Obama's signature environmental policies. It required the energy sector to cut carbon emissions by 32 percent by 2030, but in October 2017 it was rolled back by Trump's EPA.

3. *EPA loosens regulations on toxic air pollution:*

This regulation revolved around a complicated rule referred to as "once in, always in" or OIAI. Essentially, OIAI said that if a company polluted over the legal limit, they would have to match the lowest levels set by their industry peers and they would have to match them indefinitely. By dropping OIAI, the Trump EPA forces companies to innovate ways to decrease their emissions, but once those lower targets are met, they're no longer required to keep using those innovations.

4. *Rescinding methane-flaring rules:*

Under the Affordable Clean Energy rule issued in August 2018, states were given more power over regulating emissions. In states like California, that means regulations would likely be stricter, whereas states that produce fossil fuels are likely to weaken regulations. The following month, the EPA announced they would relax rules around releasing methane flares, inspecting equipment, and repairing leaks.

5. *Trump announces plan to weaken Obama-era fuel economy rules:*

Under the Obama administration's fuel economy targets, cars made after 2012 would, on average, have to get 54 miles per gallon by 2025. In August 2018, the Trump Department of Transportation and EPA capped that target at 34 miles per gallon by 2021. The decision created legal conflict with states like California that have higher emission caps.

6. *Trump revokes flood standards accounting for sea-level rise:*

In August 2017, President Trump revoked an Obama-era executive order that required federally funded projects to factor rising sea levels into construction.

7. *Waters of the U.S. Rule revocation:*

Trump issued an executive order in 2017 ordering the EPA to formally review what waters fell under the jurisdiction of the EPA and Army Corps of Engineers according to the 1972



Clean Water Act. The proposed change narrowed the definition of what's considered a federally protected river or wetland.

8. *NOAA green lights seismic airgun blasts for oil and gas drilling:*

Five companies were approved to use seismic air gun blasts to search for underwater oil and gas deposits. Debate over the deafening blasts stem from concerns that they disorient marine mammals that use sonar to communicate and kill plankton. The blasts were shot down by the Bureau of Energy Management in 2017 but approved after NOAA found they would not violate the Marine Mammal Protection Act.

9. *Interior Department relaxes sage grouse protection:*

The uniquely American sage grouse, a bird resembling a turkey with spiked feathers, has become the face of the debate between land developers and conservationists. In both 2017 and 2018, the Trump administration Department of Interior eased restrictions on activities like mining and drilling that had been restricted to protect the endangered bird.

10. *Trump officials propose changes to handling the Endangered Species Act:*

In July of 2018, the Trump administration announced its intention to change the way the Endangered Species Act is administered, saying more weight would be put on economic considerations when designating an endangered animal's habitat.

11. *Migratory Bird Treaty Act reinterpretation:*

Companies installing large wind turbines, constructing power lines, or leaving oil exposed are no longer violating the Migratory Bird Treaty Act if their activities kill birds. This controversial change was declared by the Trump administration in December of 2017.

12. *Trump unveils plan to dramatically downsize two national monuments:*

Unlike national parks, which have to be approved by Congress, national monuments can be created by an executive order, which the president said means they can be dismantled just as easily. Such was the case for Bears Ears and Grand Staircase-Escalante in Utah, which President Trump reduced and opened for mining and drilling companies in 2017.

13. *Executive order calls for sharp logging increase on public lands:*

Just a day before the longest government shutdown in U.S. history, Trump issued an executive order that called for a 30 percent increase in logging on public lands.

14. *Trump drops climate change from list of national security threats:*

The Trump administration's decision to delist climate change from national security threats in December of 2017 meant less Department of Defense research funding and a nationalistic viewpoint on the potential impacts of wildfires, droughts, hurricanes, and other natural disasters.

*15. EPA criminal enforcement hits 30-year low:*

The size and influence of the EPA has shrunk under the Trump administration, and it's illustrated by their diminished prosecuting power. Criminal prosecutions are at a 30-year low, and many violations that would have been prosecuted in the past are now being negotiated with companies. The administration says this is streamlining its work, but environmentalists have warned it could lead to more pollution [9].

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## **Lead Pb pollution**

Lead is a naturally occurring element found in small amounts in the earth's crust. While it has some beneficial uses, it can be toxic to humans and animals, causing health effects.

Lead can be found in all parts of our environment – the air, the soil, the water, and even inside our homes. Much of our exposure comes from human activities including the use of fossil fuels including past use of leaded gasoline, some types of industrial facilities and past use of lead-based paint in homes. Lead and lead compounds have been used in a wide variety of products found in and around our homes, including paint, ceramics, pipes and plumbing materials, solders, gasoline, batteries, ammunition and cosmetics.

Lead may enter the environment from these past and current uses. Lead can also be emitted into the environment from industrial sources and contaminated sites, such as former lead smelters. While natural levels of lead in soil range between 50 and 400 parts per million, mining, smelting and refining activities have resulted in substantial increases in lead levels in the environment, especially near mining and smelting sites.

When lead is released to the air from industrial sources or spark-ignition engine aircraft, it may travel long distances before settling to the ground, where it usually sticks to soil particles. Lead may move from soil into ground water depending on the type of lead compound and the characteristics of the soil.

Federal and state regulatory standards have helped to reduce the amount of lead in air, drinking water, soil, consumer products, food, and occupational settings.

Lead is particularly dangerous to children because their growing bodies absorb more lead than adults do and their brains and nervous systems are more sensitive to the damaging effects of lead. Babies and young children can also be more highly exposed to lead because they often put their hands and other objects that can have lead from dust or soil on them into their mouths. Children may also be exposed to lead by eating and drinking food or water containing lead or from dishes or glasses that contain lead, inhaling lead dust from lead-based paint or lead-contaminated soil or from playing with toys with lead-based paint.

Adults may be exposed to lead by eating and drinking food or water containing lead or from dishes or glasses that contain lead. They may also breathe lead dust by spending time in areas where lead-based paint is deteriorating, and during renovation or repair work that disturbs painted surfaces in older homes and buildings. Working in a job or engaging in hobbies where lead is used, such as making stained glass, can increase exposure as can certain folk remedies containing lead. A pregnant woman's exposure to lead from these sources is of particular concern because it can result in exposure to her developing baby [10].

Sources of lead emissions vary from one area to another. Lead is persistent in the environment and can be added to soils and sediments through deposition from sources of lead air pollution. Other sources of lead to ecosystems include direct discharge of waste streams to water bodies and

mining. Elevated lead in the environment can result in decreased growth and reproduction in plants and animals, and neurological effects in vertebrates.

Once taken into the body, lead distributes throughout the body in the blood and is accumulated in the bones. Depending on the level of exposure, lead can adversely affect the nervous system, kidney function, immune system, reproductive and developmental systems and the cardiovascular system. Lead exposure also affects the oxygen carrying capacity of the blood [11].

*Due to the ability of birds to travel long distances in the air, the potential feeding area of each individual is much larger than that of typical terrestrial animals. This makes birds a convenient indicator of environmental lead (Pb) pollution over large areas, in particular areas of inland and coastal waters.*

The highest levels of lead pollution can be observed in China and Korea, related to their high level of industrialization. In Iran too, environmental lead pollution is high, likely due to the developed petrochemical industry. Lead pollution in Japan, as well as in Western European countries (Spain, France, and Italy), seems to be much lower than in China, India or Iran. The USA and Canada appear to be the areas with the lowest lead pollution, possibly due to their low population densities. [12].

In South Africa lead Pb concentrations in water samples from all the rivers were significantly higher than the values for the other metals in both the wet and dry seasons. The high levels shown by Pb may be attributed to the deposition of Pb particulates on the roads next to the rivers especially during precipitation. Other investigations. Lead Pb emissions from motor vehicles produce elevated concentrations of the element in roadside vegetation and soil. High levels of Pb on vegetation and soil as a result of the use of leaded petrol in Thohoyandou River. The high concentrations of Pb in Madanzhe and Mvudi Rivers, may have been influenced by the effluent from a nearby sewage treatment plant and a waste dumping site, respectively. The observed high levels of Pb is followed by that of Cd, particularly in Mvudi River. The agricultural activities around the rivers may have contributed to the observed high levels of Pb and Cd levels, since these metals can occur as impurities in fertilizers and in metal-based pesticides and compost and manure. *The Cd and Pb exceed the WHO and South African water quality guidelines* [13].

*Lead (Pb<sup>2+</sup>)-induced TAR–RNA cleavage experiment, strong and selective cleavage of the C24-U25 phosphodiester bond is observed* [14].

Tohoku University immunobiologist Emi Furusawa-Nishii and colleagues investigated the genome sequences of almost 8,000 SARS-CoV-2 viruses from an international database. They specifically looked for 'point mutations', in which a nucleotide base within the virus's RNA is switched to another base.

*Their analyses found that virus strains that had evolved from the original one isolated in Wuhan, China had a disproportionate number of cytosine bases that were switched to uracil, in addition to a number of other nucleotide base switches. Further analyses of the nucleotide bases preceding and following these point mutations suggested they were caused by two types of human editing deaminase enzymes, called APOBECs and ADARs* [15].

Non-cytotoxic concentrations of Pb, detected in human blood, can induce oxidative stress in human lymphocytes. Pb changes GSH and GSSG levels through the induction of oxidative stress, and furthermore triggers lipid peroxidation. Pb also affects lymphocytes organelles such as mitochondria, which have an important role in cell survival and death [16].

Lead represses the anti-EMCV protective effects of an RNA picornavirus encephalomyocarditis (EMCV), (PIC), which, in other reports, were shown to induce IF in radio-resistant macrophages (PIC). It represses IF induction in two kinds of cells (macrophages and lymphocytes), however, it does not inhibits IF action. [17].

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## **Cadmium pollution**

Cadmium (Cd) is a soft, ductile, silver-white metal that belongs together with zinc and mercury to group IIb in the Periodic Table. It has relatively low melting (320.9 °C) and boiling (765 °C) points and a relatively high vapour pressure. In the air cadmium is rapidly oxidized into cadmium oxide. However, when reactive gases or vapour such as carbon dioxide, water vapour, sulfur dioxide, sulfur trioxide or hydrogen chloride are present, cadmium vapour reacts to produce cadmium carbonate, hydroxide, sulfite, sulfate or chloride, respectively. These compounds may be formed in chimney stacks and emitted to the environment. Several inorganic cadmium compounds are quite soluble in water e.g. acetate, chloride and sulfate, whereas cadmium oxide, carbonate and sulfide are almost insoluble.

Cadmium is a relatively rare element (0.2 mg/kg in the earth crust) and is not found in the pure state in the nature. It occurs mainly in association with the sulfide ores of zinc, lead and copper. Cadmium has only been produced commercially in the twentieth century. It is a byproduct of the zinc industry; its production is thus determined essentially by that of zinc. Before the First World War cadmium was not usually recovered from zinc plants or other nonferrous metals plants, which resulted in an uncontrolled contamination of the environment for decades. The average annual production of cadmium throughout the world increased from only 20 tonnes in the 1920s to about 12 000 tonnes in the period 1960–1969, 17 000 tonnes in 1970–1984; since 1987 it has fluctuated around 20 000 tonnes.

In the past cadmium was mainly used in the electroplating of metals and in pigments or stabilizers for plastics. In 1960, the engineering coatings and plating sector accounted for over half the cadmium consumed worldwide, but in 1990 this had declined to less than 8%. Nowadays, cadmium-nickel battery manufacture consumes 55% of the cadmium output and it is expected that this application will expand with the increasing use of rechargeable batteries and their potential use for electric vehicles. For instance, the demand for cadmium in nickel-cadmium batteries moved from 3000 tonnes in 1980 to 9000 tonnes in 1990. This rapid growth has more than offset declining trends for pigments (20%), plating (8%) and stabilizers (10%). In many respects cadmium has become a vital component of modern technology, with countless applications in the electronics, communications, power generation and aerospace industries.

In the European Union and worldwide, approximately 85–90% of total airborne cadmium emissions arise from anthropogenic sources, mainly from smelting and refining of nonferrous metals, fossil fuel combustion and municipal waste incineration.

In European Union Member States, atmospheric emissions of cadmium in 1990 amounted to 158 tonnes/year distributed as follows: natural, 9.3%; nonferrous metal industry, 20.4%; oil combustion, 17.9%; waste incineration, 17.5%; iron and steel industry, 15.3%; coal combustion, 13.4%; cement manufacture, 4.4%; and others, 1.8%.

### **Routes of exposure:**

#### **1. Air:**

Assuming a daily inhalation of 20 m<sup>3</sup> of air and indoor concentrations similar to those outdoors, the average amount of cadmium inhaled daily by humans in rural, urban and industrialized areas should not exceed 0.01, 0.2 and 0.4 µg, respectively. Deposition of inhaled cadmium in the lungs varies between 10% and 50% depending on the size of airborne particles. Absorption of cadmium in the lung depends on the chemical nature of the particles deposited. It is around 50% for cadmium oxide but considerably less for insoluble salts such as cadmium sulfide.

Cigarette smoking may represent an additional source of cadmium which may equal or exceed that from food. Depending on the brand (i.e. mainly on the origin of the tobacco), cigarettes produced in Europe or the United States of America contain cadmium at a concentration of 0.5–2 µg/g (dry weight) of tobacco, of which 10% can be absorbed.

## 2. **Water:**

Drinking-water contains very low concentrations of cadmium, usually in the range 0.01–1 µg/litre. In polluted areas, well-water may contain very high concentrations of cadmium (exceeding 25 µg/litre). Such unusual situations excepted, the intake of cadmium via drinking-water, based on a water consumption of two litres per day is thus very low.

## 3. **Food:**

For nonsmokers, food constitutes the principal environmental source of cadmium. The lowest concentrations are found in milk (around 1 µg/kg). The concentration of cadmium is in the range 1–50 µg/kg in meat, fish and fruit and 10–300 µg/kg in staple foods such as wheat, rice and potatoes. The highest cadmium levels (100–1000 µg/kg) are found in the internal organs (kidney and liver) of mammals and in certain species of mussels, scallops and oysters. When grown on a cadmium-polluted soil, some crops, such as rice, can accumulate considerable amounts of cadmium (more than 1000 µg/kg). The average daily intake of cadmium via food in European countries and North America is 15–25 µg but there may be large variations depending on age and dietary habits. In Japan, the average intake is generally 40–50 µg but may be much higher in cadmium-polluted areas. The gastrointestinal absorption of cadmium in humans amounts to about 5% but may be increased by nutritional factors (up to 15% in iron deficiency). The average amount of cadmium absorbed via food can thus be estimated at about 1 µg/day.

Assuming a mean absorption of 15% for inhaled cadmium, and excepting special circumstances, such as living close to a cadmium emission source, the amount of cadmium absorbed daily by the pulmonary route in nonsmokers does not exceed 0.0015 µg in rural areas, 0.03 µg in urban areas and 0.06 µg in industrialized areas.

Cadmium in food comes to a large extent from atmospheric cadmium as a result of foliar absorption or root uptake of cadmium deposited on soils. Foliar absorption is determined by dry or wet deposition rates of cadmium and uptake of cadmium by plants from soils is primarily controlled by the concentration of cadmium in soil solution. In rural areas, 20–60% of the total plant cadmium may originate from foliar absorption. It is important to

stress that excessive levels of cadmium in soil ( $>1$  mg/kg) presently found in some industrialized areas are largely the result of emissions in the past when smelters were operating under less stringent conditions and when cadmium was not recovered during zinc production. In Belgium, for instance, airborne cadmium emissions were estimated at 125 000 kg in 1950 and dropped to less than 130 kg in 1989.

The transfer of cadmium from soil to the food-chain depends on a number of additional factors, such as the type of plant, the type and pH of the soil, and the zinc and organic matter content of the soil. These factors explain why a transfer of cadmium from soil to plants and humans has been demonstrated in some polluted areas in Europe but not others.

Another important source of contamination of soils is the use of commercial fertilizers derived from rock phosphate and sewage sludge. Studies in Denmark and the Netherlands indicate that current inputs of cadmium to the soil from this source exceed that of atmospheric deposition by 35–184% depending on the area. The yearly increases of cadmium in soil in Denmark and the Netherlands are estimated at between 0.4% (sandy soils) and 0.79% (clay soils) corresponding to doubling times of 250 and 125 years, respectively. The direct contribution of airborne cadmium to human exposure is very low and has probably declined during the last decade in parallel with the reductions in atmospheric emissions [18], but Trump administration altered this equation [9].

#### **Toxicokinetics:**

The main metabolic feature of cadmium is an exceptionally long biological half-life resulting in a virtually irreversible accumulation of the metal in the body throughout life. In blood, more than 90% of cadmium is found in cells. In adults not exposed to cadmium at work, the cadmium level in blood is usually less than  $0.5 \mu\text{g}/100$  ml. During exposure to cadmium, the blood concentration of cadmium is mainly an indicator of the absorption over the previous few months. In persons with previous high exposure (e.g. retired workers) the blood concentration may be predominantly influenced by the body burden if the amount of cadmium released from storage sites exceeds the amount currently being absorbed.

The two main storage sites for cadmium in the body are the liver and the kidney. Newborn infants are virtually free of cadmium but during their lifetime there is a considerable accumulation of cadmium in these two organs, which contain about 40–80% of the body burden.

In the case of low-level exposures, such as those occurring in the general environment, about 30-50% of the cadmium body burden is stored in the kidneys alone, with concentrations in the cortex about 1.25 times higher than in the kidney as a whole.

In nonoccupationally exposed subjects, the concentration of cadmium in the liver increases continuously with age. The concentration also increases in the renal cortex but only until the age of 50-60 years, after which it levels off or even decreases.

However, when the integrity of renal structures is compromised by cadmium itself or by other factors (e.g. ageing), the cadmium concentration in the kidney decreases.



In the tissues, cadmium is mainly bound to metallothioneine, a low-molecular-weight protein (MW 6.6 KD) rich in cysteine residues. The synthesis of this protein probably represents a defense mechanism against the toxic cadmium ion.

It is also hypothesized that, by virtue of its small size, metallothioneine is involved in the transport of cadmium from the liver to the kidney, the cadmium-metallothioneine complex released from the liver being rapidly filtered through the glomeruli then reabsorbed by the tubules. Such a mechanism could explain the selective accumulation of cadmium in the renal cortex.

Cadmium is eliminated from the organism mainly via urine. The amount of cadmium excreted daily in urine is, however, very small; it represents only about 0.005-0.01% of the total body burden which corresponds to a biological half-life for cadmium of about 20-40 years. In subjects non-occupationally exposed to cadmium, the urinary excretion of cadmium is usually less than 2 µg/g of creatinine. A substantial body of evidence derived from numerous human and experimental studies indicates that in the general population and in workers moderately exposed to cadmium, the urinary excretion of cadmium on a group basis is a reliable indicator of the cadmium body burden.

#### **Health effects:**

##### *Effects on experimental animals and in vitro test systems:*

In experimental animals, cadmium can produce acute toxic effects on various organs, such as the kidney, liver, pancreas, testes and lung (by inhalation). In chronically intoxicated animals, cadmium gives rise to a nephropathy very similar to that described in humans and characterized functionally by the appearance of a tubular or mixed-type proteinuria, aminoaciduria, glucosuria and hypercalciuria and, morphologically, by lesions predominantly involving the tubules. It is noteworthy that the critical concentration of cadmium in the renal cortex associated with these changes in rats is around 200 mg/kg, as in humans. Other chronic effects which have been described in animals treated with cadmium include lung emphysema and inflammation (by inhalation), disturbances in calcium and vitamin-D metabolism resulting in bone lesions, hepatic damage and effects on the pancreas, testes or cardiovascular system. Cadmium can also produce embryotoxic, teratogenic and carcinogenic effects.

##### *Effects on humans:*

###### Toxicological effects:

Short-term exposure to moderate concentrations (200-500 µg/m<sup>3</sup>) of freshly generated cadmium fume during less than 1 hour may cause symptoms similar to those of the metal fume fever, usually with a complete recovery within a few days. More intense or prolonged exposure may lead, again after a latency period of several hours, to a chemical pneumonitis with death in 15-20% of cases. Chronic respiratory effects consisting of bronchitis, obstructive lung disease or emphysema have been described in the past in workers heavily exposed to cadmium (more than 20 µg/m<sup>3</sup> for more than 20 years).

The kidney is the critical organ after long-term occupational or environmental exposure to cadmium. Since the first report by Friberg in 1948, numerous epidemiological studies on industrial workers or on inhabitants of cadmium-polluted areas have documented the constellation of renal effects that may be produced by this heavy metal. Because of intrinsic differences in their sensitivity or the sequential involvement of specific sites of the nephron, these indicators become abnormal at different levels of cadmium body burden. This variable response is reflected by the thresholds of urinary excretion of cadmium (CdU) associated with an increased probability of renal changes.

With respect to occupational exposure (which occurs mainly by inhalation), a recent study has identified three main groups of thresholds: one at around 2  $\mu\text{g/g}$  of creatinine mainly associated with biochemical alterations; a second at around 4–5  $\mu\text{g/g}$  of creatinine for the onset of high-molecular-weight proteinuria and of some cytotoxicity signs (tubular antigens or enzymes); and a third at around 10  $\mu\text{g/g}$  of creatinine for the development of tubular proteinuria. These findings have led to a reassessment of the critical concentration of cadmium in the renal cortex, which was estimated at about 200  $\text{mg/kg}$  in the early 1980s. The recent reassessment was based on the relationship between urinary cadmium and the cadmium concentration in the renal cortex of workers, as determined by neutron activation analysis.

The average concentrations of cadmium in the renal cortex corresponding to CdU thresholds of 2, 4 and 10  $\mu\text{g/g}$  of creatinine are 110, 139 and 182  $\text{mg/kg}$ , respectively. Only the effects associated with the CdU threshold of 10  $\mu\text{g/g}$  of creatinine (182  $\text{mg/kg}$  in the renal cortex) are known to be irreversible and to predict a faster decline of the renal function with age in occupationally exposed workers.

#### Carcinogenic effects:

In 1993, IARC classified cadmium and cadmium compounds as group 1 human carcinogens, having concluded that there was sufficient evidence of cadmium being carcinogenic to humans and animals. The evidence for carcinogenicity in humans was mainly based on the observation of excess lung cancer mortality among cohorts of workers in a United States cadmium recovery plant and from United Kingdom cadmium processing plants. In the United States cohort, a dose–response relationship was demonstrated between estimated cumulative exposure to cadmium and lung cancer risk. The latter was not thought likely to be due to confounding by cigarette smoking or exposure to arsenic. Excess mortality from prostatic cancer was found initially but the relative risk diminished and became insignificant during further follow up. In the United Kingdom cohort, there were suggested trends with duration of exposure and with intensity of exposure. The mortality from prostatic cancer was decreased. IARC took into consideration the evidence that ionic cadmium produces genotoxic effects in a variety of eukaryotic cells, including human cells [18].

Study on characteristics and origin of air pollutants done in Wuhan, the city from which SARS COV.2 pandemic emerged showed, that the annual average concentrations for  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{NO}_2$ ,  $\text{SO}_2$ ,  $\text{O}_3$ , and CO during the whole period were 89.6  $\mu\text{g m}^{-3}$ , 134.9  $\mu\text{g}$

$\text{m}^{-3}$ ,  $54.9 \mu\text{g m}^{-3}$ ,  $32.4 \mu\text{g m}^{-3}$ ,  $62.3 \mu\text{g m}^{-3}$ , and  $1.1 \text{mg m}^{-3}$ , respectively. The monthly variations revealed that the peak values of  $\text{PM}_{2.5}$ ,  $\text{PM}_{10}$ ,  $\text{NO}_2$ ,  $\text{SO}_2$ , and  $\text{CO}$  occurred in December because of increased local emissions and severe weather conditions, while the lowest values occurred in July mainly due to larger precipitation. [19], the concentrations of Cd from indoor air and water and Pb concentrations in outdoor air and water are the highest in Wuhan in comparison to other Chinese regions [20].

It is well known that many toxic effects of cadmium (Cd) action result from interactions with essential elements, including zinc (Zn). These interactions can take place at different stages of absorption, distribution in the organism and excretion of both metals and at the stage of Zn biological functions. Exposure to Cd leads to disturbance in Zn in the organism on the one hand, while dietary Zn intake has an important effect on Cd absorption, accumulation and toxicity on the other. The Zn status of the body is important in relation to development of Cd toxicity. Numerous data show that increased Zn supply may reduce Cd absorption and accumulation and prevent or reduce the adverse actions of Cd, whereas Zn deficiency can intensify Cd accumulation and toxicity [21].

Thrombosis can be caused by endothelial disorders due to the presence of heavy metals such as cadmium (Cd). These amino acid residues can bind Cd metal covalently with the -S-S-, -C-S-, -SH, and phenyl groups, which are present in the amino acid residues. This situation causes changes in the structure of the protein, so that it becomes modified and forms a blood clot [22]

Cadmium increased cell death and lowered the survival of the host in a dose dependent manner. In search of the reason we found increased expression of the pro-apoptotic proteins p53 in splenic lymphocytes. Here we showed that cadmium induced p53-dependent apoptosis through cooperation between Bcl-x1 down regulation without changing the Bcl-2 and Bax expression, the common target of p53. The down regulation of Bcl-x1 strongly indicating mitochondrial involvement in apoptosis. It is confirmed by the release of cytochrome *c* and activation of caspase-3. All of these findings establish an important role of p53 and mitochondrial function in cadmium induced toxic environment in the host [23].

Zinc counteracts or prevents some toxic effects induced by cadmium (Cd). Selenium has also been reported to decrease arsenic, Cd, and lead (Pb) toxicity.

Cd-induced oxidative stress directly increases the ability of influenza virus to replicate in the host-cell, thus suggesting that exposure to heavy metals, such as this, could be a risk factor for individuals exposed to a greater extent to the contaminant, resulting in increased severity of virus-induced respiratory diseases [24]. The cadmium content is more highly enriched in women than in men [25]. Estrogen like effect of cadmium [26] and low level of zinc may enhance growth of yeast (such as black yeast in SARS COV-2 Patients).

## Coexposure to cadmium Cd<sup>++</sup> and Lead Pb<sup>++</sup>

Nowadays Cadmium and Pb s commonly occur together in the environment and simultaneous exposure is likely. Cadmium and Pb occur together as natural ore deposits, and the process of smelting Pb simultaneously releases both metals into the terrestrial, atmospheric, and aquatic environment surrounding refineries.

The metabolism or action of a toxicant may be modified by the presence of a similar toxic compound through utilization of common metabolic pathways. Lead and Cd exert toxic effects on hematopoietic and nervous systems, in addition to causing lesions in the liver and kidneys. Each metal has also been reported to suppress immune responses in mammals.

Because of the potential for simultaneous exposure to Pb and Cd in the environment and their common sites of toxicity in the body, it is important to study the effects of coexposure to these compounds [27].

Exposure to lead and cadmium, induce suppress both humoral and innate immunity result in an increased susceptibility to chronic infections. While the mechanisms of immunotoxicity vary by metal type, exposure dose, and genetic factors, increased environmental contamination with heavy metals will likely contribute to an increased incidence of chronic infections in human populations [28].

Study done by Exon H. J Showed that; Mortality was greater in all groups of mice exposed only to Pb than in controls or mice given Cd, Mortality was less in all groups of mice exposed to Cd than in controls. In groups of mice given Pb and Cd simultaneously, mortality was lower than in Pb-exposed groups, greater than in Cd-exposed groups (except at 600 Cd: 2600 Pb) and slightly lower than in the controls. Mice which received Cd with or without Coexposure to Pb, demonstrated decreased body weights. Mice given only Pb had body weights similar to controls throughout the experiment.

Tissue concentrations of Pb and Cd increased as exposure levels of the metals were increased in the drinking water. Cadmium residues in liver and kidney tissue of mice given either Cd or Cd + Pb simultaneously, were greater than Pb residues, even though the dietary concentration of Pb was as much as 4 times that of Cd at comparable doses.

Lead concentrations in heart, liver, spleen, testes, and lung were generally decreased in mice coexposed to Pb and Cd, compared to residues in mice which received only Pb .Kidney Pb residues of mice coexposed to Pb and Cd were increased except at the 600 Cd: 2600 Pb exposure level where residues were decreased. Corresponding liver Pb residues were increased at that exposure level.

Cadmium residues were increased in tissues of mice coexposed to Pb and Cd at the three lower interaction levels (3 Cd: 13 Pb, 30 Cd: 130 Pb, and 300 Cd: 1300 Pb) compared to mice which received only Cd. Cadmium tissue residues of mice simultaneously exposed to Pb at the high interaction dose were decreased compared to Cd residues in tissues of mice which received only

the high Cd dose. Cadmium levels were greatest in kidneys of mice in the two lower Pb: Cd interaction groups (3 Cd : 13 Pb and 30 Cd : 130 Pb) and the two lower Cd-only exposed groups (3 Cd or 30 Cd). However, liver Cd residues were greater in the two higher Cd: Pb interaction groups.

Lead and Cd each possess a divalent cation and are grouped together in the periodic table. Due to the similarities of these metals, it is reasonable to assume that common pathways may be utilized for gastrointestinal absorption and transport within the body.

Decreased absorption of Pb due to competition with Cd for transport pathways or binding sites in the intestine could explain why Pb residues are decreased and Cd levels are increased in tissues of mice coexposed to these metals. Utilization of common intestinal absorption-transport pathways is indicated by alteration of Pb<sup>29</sup> and Cd<sup>30</sup> absorption in the intestine by calcium, vitamin D, and zinc. Cadmium has been reported to reduce intestinal absorption of iron which indicates that gastrointestinal absorption of metal ions is affected by the presence of other metals.

Lead residues were generally decreased in all tissues (except kidney) of mice coexposed to Cd. This could result from a general decrease in tissue binding sites for Pb in the presence of Cd. Lead content in kidneys could be due to decreased retention of Pb in other tissues and resultant increased transport of Pb via blood to the kidneys for excretion.

Kidney Pb residues were decreased, however, in mice coexposed to 600 Cd: 2600 Pb. The combined toxic effects of Pb and Cd on kidney cells at these high doses could result in an inability of these cells to synthesize protein which complexes with Pb to form the intranuclear inclusion bodies, a form of Pb storage in kidney cells. Inability to synthesize the protein necessary to complex Pb could result in decreased renal Pb storage. Alternate pathways of storage or excretion of Pb could be utilized which could account for increased Pb residues in the liver and testes of these mice.

Increased Cd residues in tissues of mice coexposed to Pb could result from interference by Pb with metallothionein synthesis or binding of Cd. Lead interference could occur via damage to hepatocytes where metallothionein is synthesized. Impairment of metallothionein-Cd binding could result in increased "free" Cd in the blood that could accumulate in tissues to a greater degree than metallothionein-bound Cd. Decreased Cd residues in all tissues of mice treated with 600 Cd: 2600 Pb could occur from a combined toxicity of Pb and Cd on kidney cells at these high doses causing decreased retention and increased excretion of Cd [26].

High levels of blood lead and cadmium increase in both genders of elderly populations [29].

Vitamin C, B<sub>1</sub> and B<sub>6</sub> deficiencies have been reported to enhance sensitivity towards Cd and Pb toxicity [30].

## Viral metals ions

Among the many roles of metal ions in biological processes are bridging distant residues or domains of proteins, mediating interactions between proteins and ligands, and serving in the active site as a nucleophilic catalyst and in transfer of electron. Biological processes are often metal ion specific, although more than one metal ion can play each of these roles. For example the coagulation cascade is  $\text{Ca}^{2+}$  specific, protein biosynthesis is primarily  $\text{Mg}^{2+}$  specific, several enzymes are  $\text{Zn}^{2+}$  ion specific and oxidative processes are often iron specific.

A number of trace metals are essential micronutrients and their deficiency and infectious diseases often coexist and exhibit complex interactions. Several trace metals such as zinc, copper and manganese, etc. influence the susceptibility to, the course and the outcome of a variety of viral infections. Deficiency of trace metals is known to alter the genome of the viruses and the grave consequences of this may be the emergence of new infections [31].

$\text{Zn}^{++}$ ,  $\text{Cd}^{++}$ , and  $\text{Cu}^{+}$  tend to form similar chelates and have similar affinities for ligands such as sulfhydryl groups, presumably present in intestinal as well as body tissues. These chelate affinities might well be the basis of mutual effects of these metal ions on liver or tissue turnover as well as on absorption. From this point of view, site of absorption must also be considered in evaluating interacting effects. For example, results with rats show that copper, unlike cadmium and zinc, is absorbed to a large extent from the stomach rather than from the small intestine [32].

It was clear from SEM-based elemental maps and EDS graphs that elevated lead levels were associated with low levels of zinc. The results suggest that lead absorption is highly influenced due to zinc levels in body which has an impact over DNA damage, blood cell aberration and oxidative stress caused by lead exposure. [33]. Cadmium and lead cause zinc deficiency in synergistic way.

## Transposable elements TE

They are an important component of eukaryotic genomes, making up approximately 15% of the total DNA. They occur as families of dispersed repeat sequences scattered throughout the genome, with the number of copies varying from less than ten to several hundred thousand depending on the element and species concerned. They can be classified according to their structure and presumed mechanism of transposition, and fall into two main classes: Class I elements that transpose by reverse transcription of an RNA intermediate; and Class II elements that transpose directly from DNA to DNA.

There are two groups of Class I elements. Class 1.1 elements resemble retroviruses in having long terminal repeats (LTRs) and open reading frames (ORFs) with the potential to code for polypeptides similar to the gag- and pol-encoded proteins [34].

Transposable elements comprise at least 45% of the human genome while coding sequences occupy <3%. These highly repetitive strands of “junk” DNA are capable of generating new copies in the human germline and certain somatic tissues.

Transposable elements (TE) can be classified as either DNA transposons or retro (RNA) transposons. The mobilization of these elements is referred to as either transposition or retrotransposition. DNA transposons, known as Class I transposons, are flanked by terminal inverted repeats and transpose with a “cut and paste” mechanism whereby the sequence is excised from one region, catalyzed by a transposase enzyme, and integrated into a separate region in the genome. DNA transposons constitute 3% of the genome and are no longer active in most mammals.

Retrotransposons, also referred to as Class I transposable elements, integrate into the genome via an RNA intermediate, utilizing a “copy and paste” mechanism; this allows the active retroelements to retain their original location in the genome while accumulating copy numbers elsewhere. These retroelements can be further classified based on the presence of long terminal repeats (LTR) in the sequence. Elements such as Mammalian apparent LTR-retrotransposons (MaLR) and human endogenous retroviruses (HERV) both contain LTR sequences that flank internal coding regions. LTR retrotransposons comprise about 8% of the human genome.

Non-LTR retrotransposons can be further classified into two subtypes: LINE (Long Interspersed Nuclear Elements)

and SINE (Short Interspersed Nuclear Elements). Together, LINE and SINE comprise ~33% of the human genome [35].

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## Human Endogenous Retroviruses HERV

A characteristic feature of retroviruses is their ability to persist as integrated proviruses in cellular genomes. While exogenous retroviruses are spread horizontally in their natural hosts, endogenous retroviruses are transmitted genetically and can therefore be detected in the genome of all cells of all members of the host species.

In human DNA, endogenous retrovirus sequences (HERVs) are well known genetic elements. They all seem to be defective due to multiple termination codons, deletions, or the lack of a 5' long terminal repeat.

HERVs are grouped into single and multiple copy number families and are classified according to the tRNA they may use as primer for reverse transcription [36].

HERV copies comprise 5–8% of the human genome, with some lower estimates at 1%. HERV elements possess similar genomic organization to that of exogenous retroviruses, such as HIV. Briefly, HERV elements include gag, pol, and env regions that are flanked by LTR sequences on either side.

The gag and pol genes encode a retroviral capsid protein and enzymes (protease, reverse transcriptase and integrase) required for viral replication and integration, respectively. HERVs also contain the presence of a gene encoding an envelope protein (Env), a remnant of their exogenous retroviral origin prior to their insertion and endogenization into germline cells.

Functional env proteins have been shown to initiate innate and adaptive immune responses. Transcriptionally active HERV subfamilies have more recently been implicated as pathophysiological contributors to various disorders [37], mentioned below:

### Multiple sclerosis (MS):

It is a chronic autoimmune, inflammatory neurological disease of the central nervous system (CNS). MS attacks the myelinated axons in the CNS, destroying the myelin and the axons to varying degrees. The course of MS is highly varied and unpredictable. In most patients, the disease is characterized initially by episodes of reversible neurological deficits, which is often followed by progressive neurological deterioration over time. 50% of patients will need help walking within 15 years after the onset of the disease. Twice as many women are affected as men, and persons of Northern European descent appear to be at highest risk for MS.

The disease is diagnosed on the basis of clinical findings and supporting evidence from ancillary tests, such as magnetic resonance imaging (MRI) of the brain and examination of the cerebrospinal fluid (CSF). MS typically presents in adults 20 to 45 years of age; occasionally, it presents in childhood or late middle age.

The cause is a retrotransposon human endogenous retrovirus named HERV-W , but it appears to involve a combination of genetic susceptibility and a nongenetic trigger, such as a virus, metabolism, or environmental factors, that together result in a self-sustaining autoimmune disorder that leads to recurrent immune attacks on the CNS [33], with elevated IFN $\gamma$ , IL-6, TNF- $\alpha$  [36].

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## **Type W Human Endogenous Retrovirus (HERV-W)**

In the last 15 years, great efforts have been made to provide a complete assembled sequence of the human genome, progressively revealing an unexpected, highly repetitive composition. Transposable elements (TEs) account, in fact, for >50% of our genetic material, while protein-coding regions constitute only the ~2%. TEs can be broadly divided in two general classes, based on whether DNA or RNA serves as the intermediate in the process of transposition. Human Endogenous Retroviruses (HERVs) belong to class-I TEs, also called retrotransposons, which are characterized by a RNA intermediate that is reverse-transcribed into a double stranded DNA (dsDNA). This dsDNA, commonly called a provirus, is competent for the subsequent integration into the host cell genome.

In addition to HERVs, which have 5' and 3' long terminal repeats (LTRs), retrotransposons also comprise elements devoid of LTRs and characterized by 3' poly(A) repeats that are critical for their retroposition, namely long and short interspersed nuclear elements (LINEs and SINEs, respectively). HERVs are remnants of ancient retroviral infections acquired by the host genome in several waves that occurred mostly between 100 and 40 million years ago. Hence, at the time, the proviral integration into the germline cells' DNA made HERV sequences stable components of our genome. Hence, at the time, the proviral integration into the germline cells' DNA made HERV sequences stable components of our genome.

Owing to their long-time persistence in the host genome, however, individual HERV sequences have independently accumulated nucleotide substitutions, deletions, and insertions, often leading to the loss of coding capacity.

Among HERVs, the HERV-W group is one of the most intensively investigated for its possible physiopathological effects on the host. After its initial identification as putative causative agent for multiple sclerosis (MS).

HERV-W sequence amplification in germline cells. The initial acquisition of HERV-W sequences has been due to a traditional retroviral infection process. The viral RNA was reverse transcribed and the proviral dsDNA was integrated into the host cell genome by reverse transcriptase (RT) and integrase (IN) viral enzymes, respectively. Integrated provirus expression p(i) L1-mediated retrotransposition: copy and paste mechanism in which viral mRNAs were reverse-transcribed by L1 RT and inserted into a new genomic position, generating HERV-W processed pseudogenes; (ii) reinfection: proviral mRNAs were translated and the deriving proteins assembled into a mature viral particle, that after its egress could have re-infected the same cell; (iii) cis-retrotransposition: HERV-W mRNAs could have been used as templates for further reverse transcription-integration events, leading to the acquisition of new insertions in the absence of an extracellular phase. Owing to the accumulation of mutations over time, the last two mechanisms could have required proteins provided in trans by a helper virus/rovided viral mRNAs, which generated new HERV-W insertions through [38].

### Small ubiquitin-related modifier (SUMO)

SUMO (small *u*biquitin-related *m*odifier) family proteins are not only structurally but also mechanistically related to ubiquitin in that they are posttranslationally attached to other proteins. As ubiquitin, SUMO is covalently linked to its substrates via amide (isopeptide) bonds formed between its C-terminal glycine residue and the  $\epsilon$ -amino group of internal lysine residues. The enzymes involved in the reversible conjugation of SUMO are similar to those mediating the ubiquitin conjugation. Since its discovery in 1996, SUMO has received a high degree of attention because of its intriguing and essential functions, and because its substrates include a variety of biomedically important proteins such as tumor suppressor p53, c-jun, PML and huntingtin.

SUMO modification appears to play important roles in diverse processes such as chromosome segregation and cell division, DNA replication and repair, nuclear protein import, protein targeting to and formation of certain subnuclear structures, and the regulation of a variety of processes including the inflammatory response in mammals and the regulation of flowering time in plants [39].

Primary host defenses against viruses involve specific cellular recognition of non-self-nucleic acids as pathogen-associated molecular patterns (PAMPs) that trigger induction of cytokine-mediated antiviral responses. Thus, ability to discriminate between “self” and “non-self” nucleic acids, and prevent aberrant immunopathology, is a key tenet of immunity. Here, we identify self-derived endogenous retroviral RNAs as host-encoded PAMPs that are up-regulated during influenza virus infections, and which stimulate antiviral immunity. Normally, endogenous retroviruses are tightly repressed transcriptionally by host TRIM28, but infection triggers changes in the modification status of TRIM28 to alleviate repression. This provides an example of how endogenous retroviruses integrated within the host genome have been functionally co-opted by a regulatory switch to aid defense against newly invading pathogens [40].

### **Lead and cadmium Pollution in Wuhan**

Wuhan is the capital of Hubei Province, which is located in the middle of the Yangzi River delta, at 29°58' –31°22' north latitude and 113°41' –115°05' east longitude. Its population is approximately 7.5 million people, of whom approximately 4.5 million reside in nine urban core districts within an area of 201 km<sup>2</sup>. Wuhan has a subtropical, humid, monsoon climate with a distinct pattern of four seasons. Its average daily temperature in July is 37.2°C, and the maximum daily temperature often exceeds 40°C. The major industries in Wuhan include ferrous smelters, chemical plants, power plants, and machinery plants. The major sources of air pollution in the city are motor vehicles and the burning of coal for domestic cooking, heating, and industrial processes [41]. The concentrations of Cd from indoor air and water and Pb concentrations in outdoor air and water are the highest in Wuhan in comparison to other Chinese regions [20].

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### **SARS COV.2 is a mutant Influenza virus**

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of the ongoing COVID-19 pandemic, like many other viruses, uses programmed ribosomal frameshifting (PRF) to enable synthesis of multiple proteins from its compact genome. In independent analyses, we evaluated the PRF regions of all SARS-CoV-2 sequences available in GenBank and from the Global Initiative on Sharing All Influenza Data for variations. Of the 5,156 and 27,153 sequences analyzed, respectively, the PRF regions were identical in 95.7% and 97.2% of isolates. The most common change from the reference sequence was from C to U at position 13,536, which lies in the three-stemmed pseudoknot known to stimulate frameshifting. With the conversion of the G13493-C13536 Watson-Crick pair to G-U [42]. Lead ( $Pb^{2+}$ )-induced TAR-RNA cleavage experiment, strong and selective cleavage of the C24-U25 phosphodiester bond is observed [14].

$Zn^{++}$ ,  $Cd^{++}$ , and  $Cu^+$  tend to form similar chelates and have similar affinities for ligands such as sulfhydryl groups, then due to deficiency of zinc and copper induced by lead and cadmium toxicity, cadmium binds to sulfhydryl groups of influenza virus after lead  $Pb^{++}$  induced mutation by selective cleavage of the C-U phosphodiester bond and introduce what is known now as SARS COV-2.

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### **Cadmium and lead in vegetables, cereal, fruits and seafood**

Cadmium is a toxic element ubiquitous in the environment, which damages biological systems in various ways. The major source of cadmium exposure is food. High cadmium content in the soil leads to high cadmium concentrations in certain plants such as grains (above all surface layers and germs), oil or non-oil seeds, fruit and vegetables. These food commodities are the crucial components of a vegetarian nutrition [43].

The content of cadmium and lead was measured in vegetables, fruit, cereals and soil from areas exposed and non-exposed to industrial pollution and in vegetables and soil from greenhouses. The elements were measured after dry mineralization by atomic absorption spectrophotometry following extraction of complexes from APDS into the organic phase (MIBK). Lead and cadmium were determined in 482 samples of vegetables, 101 fruit samples, and 132 cereal samples.

In the vegetables from the areas not exposed to industrial pollution lead content was below the detectability range ( $< \text{d.r.}$ ) to 576.1 micrograms/kg, and cadmium was from  $< \text{d.r.}$  to 73.5 micrograms/kg. In the vegetables from areas exposed to industrial pollution lead was from 9.3 to 1044.0 micrograms/kg and cadmium from  $< \text{d.r.}$  to 552.3 micrograms/kg and cadmium from 2.3 to 132.5 micrograms/kg.

In fruit lead was present in amounts from 12.8 to 144.0 micrograms/kg and cadmium from  $< \text{d.r.}$  to 42.0 micrograms/kg. In cereals lead was found in amounts from  $< \text{d.r.}$  to 760.0 micrograms/kg and cadmium from  $< \text{d.r.}$  to 200 micrograms/kg [44].

Spinach is rich with cadmium and China was the leading country in terms of per capita consumption, among the main consumers of spinach, followed by Belgium, Turkey, Japan and the United States [45]. Vegetarians are at high risk of cadmium toxicity, and spread of SARS COV-2 in India, may be due to dependence of most population on vegetables in their food, most of Indian are vegetarians, and pollution of air, water and soil enhance spread of viral infection among them.

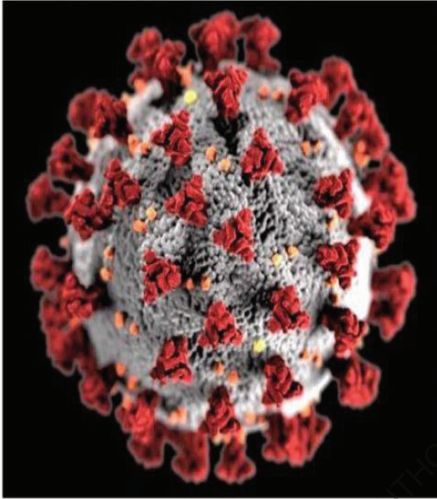
A study of aquaculture farms across 10 Indian States, which account for the bulk of India's production, has found "hazardous" levels of metals such as lead and cadmium in all of them [46].

Lead and cadmium concentrations were about 10 times higher in shellfish than in analyzed fish. The highest lead and cadmium concentrations were found in mussel and the lowest in hake [47].

Blood pressure of Indian American individuals with greater baseline levels of urinary cadmium increased at a faster rate relative to those with lower levels [48].

Important photos

SARS-CoV-2 causing COVID-19



Influenza virus causing the flu

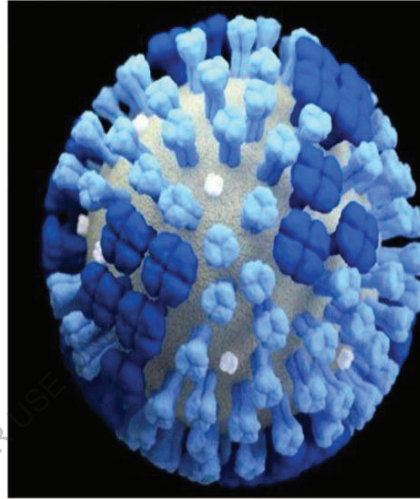


Figure (2): shows SARS COV-2 and Influenza Virus





**Figure 3: shows air pollution source, China**



Figure (4): shows consequences of heavy metals usage in industry

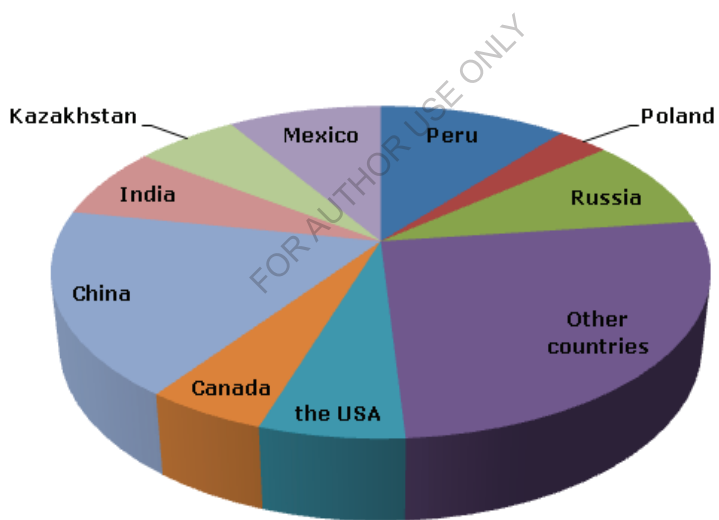
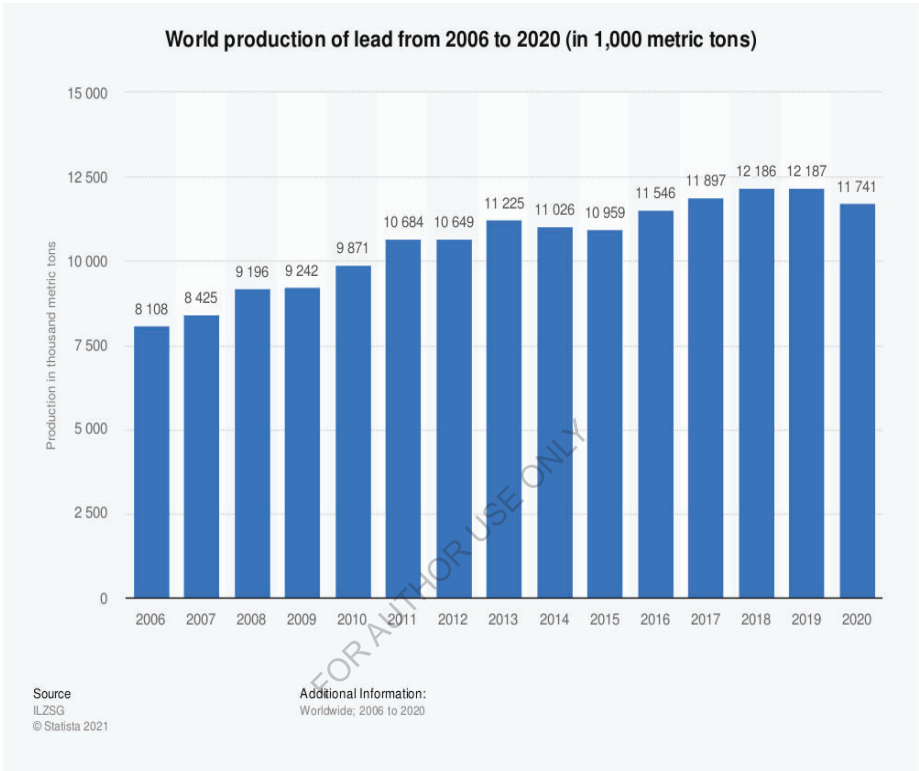


Figure (5): overall cadmium production worldwide, 2012



**Figure (6):** shows lead metal production from 2006 to 2020

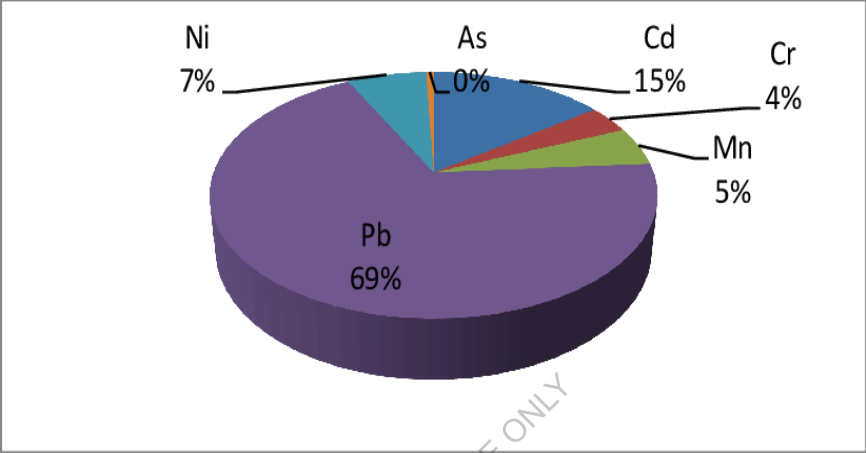


Figure (7): shows percentage composition of heavy metals

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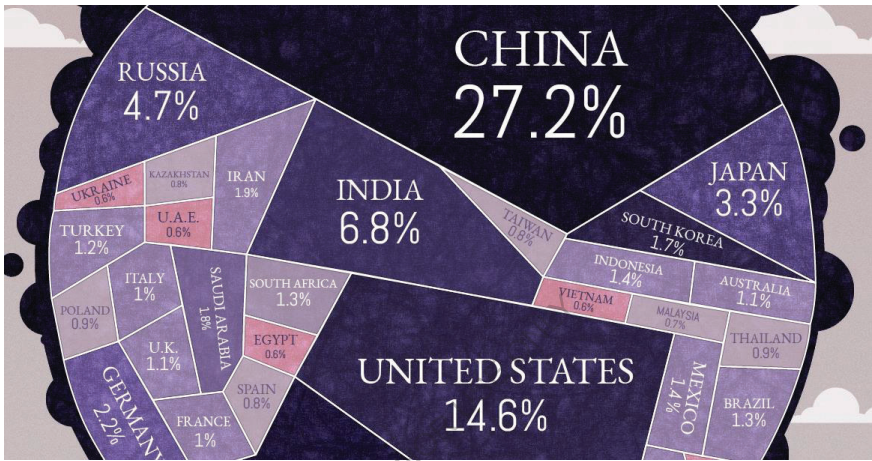
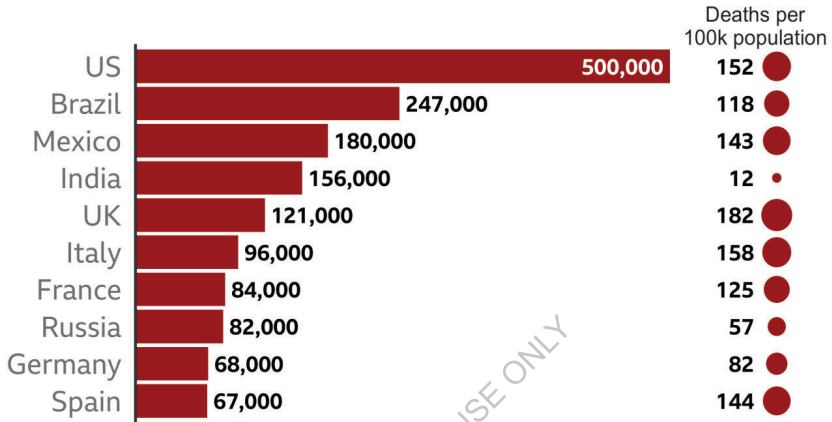


Figure (8): show global carbon emissions

# Top 10 countries by coronavirus deaths

Per capita figures show differences in the scale of outbreaks

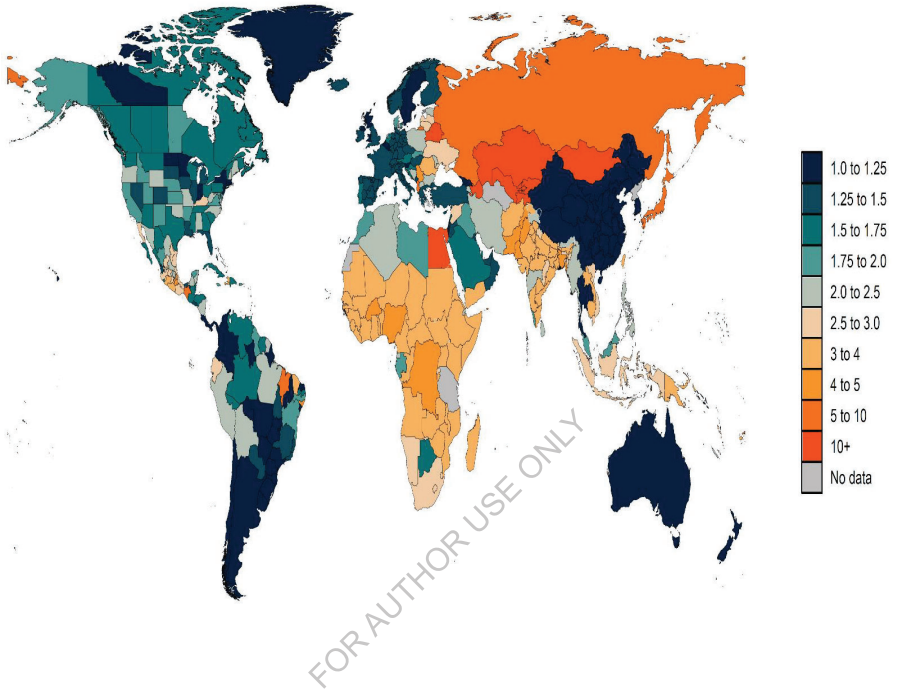


Note: Country death totals have been rounded to the nearest 1,000

Source: Johns Hopkins University, 22 February



Figure (9): shows top countries by COVID.19 mortality



**Figure (10): Shows Ratios of total COVID-19 deaths to reported COVID-19 deaths**



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