TCDD: The Deadliest Toxic Chemical Known to Science

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On Saturday July 10, 1976, it was a warm spring day filled with blue skies and normalcy. With children playing outside under the sun-kissed rays and others enjoying lunch outdoors, all were oblivious to one of the biggest man-made chemical disasters that was about to take place. What was a seemingly picturesque afternoon was soon to be history due to the foreboding thick, whitish cloud overhead. The ominous cloud that loomed over Seveso, Italy attracted rapid international media attention and became headlines everywhere during the 1980s. The mysterious cloud was the result of an explosion during the production of trichlorophenol at the chemical plant ICMESA (Industrie Chimiche Meda Società Azionaria). However, it wasn’t necessarily the explosion that kept the public’s attention, but the significant amounts of the highly toxic 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin (TCDD) that the cloud contained.

The chemical plant meant to produce 2, 4, 5-trichlorophenol (TCP), an intermediate step before the product of bactericide hexchlorophene. The reactor was supposed to be shut down and cooled down using cold water. However, it was left on its own and eventually the build-up of high temperature and pressure caused the pipe to blow up and the contents to be released in the air.

![Figure 1 a)](image1.png) A molecular representation for the production of TCP from 2, 4, 5-trichlorophenol in the Seveso accident.

![Figure 1 b)](image2.png) A molecular structure of TCDD.

Figure 2 A picture was taken after the Seveso explosion at the chemical plant ICMESA.
The TCDD story is one of pain. It exposes how health authorities and government failed to protect the people. After the release of TCDD, ICMESA officials informed the residents who lived nearby to not eat garden-produced food because the food was likely to be contaminated by the air. Nevertheless, no immediate public announcements were made to warn people about the potential dangerous because the ICMESA officials claimed that they need instructions from the municipal health officer. As a result, 3000 to 4000 livestock died within 24 hours, and it was not until five days later when 4% of the domestic animals begin to die that the health and governmental authorities start their investigation. The investigation showed that about 3000 kg of chemicals were released into the air, and among that, 100 g to 20 kg was TCDD. The investigation took about a week, and finally the mayors from Meda and Seveso declared the ban on eating local fruits and vegetables. All the animals in the area were euthanized three weeks later and people were evacuated from the exposed areas. Despite the effort, the accident raised several health problems and long term health effects.

More immediate health problems include skin lesions, which developed into a severe skin disorder called Chloracne. Chloracne is an acne-like skin inflammation, characterized by appearance of blackheads, cysts, and nodules. It could appear within 10 days after exposure to TCDD. The skin disorder may progress to more severe symptoms, such as pus-filled pimples and boils depending on the degree of exposure. A total of about 200 cases of acute Chloracne were reported. Children with less exposure were able to recover spontaneously from the disease. However, the skin disorder has been known to last for more than ten years in some children.

According to Dr. Paolo Mocarelli, who was put in charge to set up laboratory investigation to test for health problems after the accident, the most profound effect of TCDD exposure is on reproduction. Minor cases of spontaneous abortions were reported from victims after the incident. But more interestingly, in the first seven years after the accident, a surprisingly higher proportion of females than males were born to parents who were exposed to TCDD; 46 females compared to only 28 males. This is strange because the birth proportion was

Figure 3 A 3-year-old victim of the accident, who developed Chloracne after exposure to TCDD.

Figure 4 Dr. Paolo Mocarelli of the Hospital of Desio.
approximately equal in the past years in the area. As Dr. Mocarelli said, “This was the first time a chemical had been observed to change the sex ratio.” The Seveso accident is like a chance experiment on human beings. It not only changed the lives of local people, but it also shed light on the threat that TCDD can pose on human beings. In this case, the accident of Seveso may introduce a molecule that could possibly induce a change in sex ratio.

Ever since the Seveso accident, research about TCDD was initiated. However, at the time of the accident, not one scientist or technician knew how to test the TCDD concentration in people. Fortunately, Dr. Mocarelli intelligently saved the blood samples from each of the victims, and this move made later research possible. Finally in 1987 using the blood samples from Dr. Mocarelli, scientists were able to measure the concentration of TCDD in people. This is very helpful in terms of investigating at what TCDD concentration level is dangerous and thus help making more accurate risk assessments in the future.

As of now, extensive studies in the affected population from the accident are continuing in order to determine the long-term human health effects from TCDD. Scientists have categorized TCDD into the family of Dioxins. The family of Dioxins has a total of 210 compounds of similar structures, and the most toxic dioxin is indeed TCDD. Research has found that TCDD has a potent toxic effect even at a low concentration, such that a millionth of a gram is enough to kill a guinea pig. In 2001, TCDD is determined to be the most potent human carcinogen based on sufficient evidence from studies in humans. Epidemiological studies in areas with high exposure to TCDD, such as Germany, Netherlands, and the United States show an increase in overall mortality from cancer. In addition, an updated examination of the victims exposed to TCDD in Seveso incident showed to have an increased risks of all cancer combined. Even though TCDD is categorized as a human carcinogen, it does not affect genetic material. The primary reason for its toxicity and carcinogenicity is related to its structural resemblances of natural hormones. Because hormones control many important biological processes in the body, mimicking the action of a hormone is a powerful mechanism for TCDD to alter critical functions.

![Figure 5](image.png)

**Figure 5** The molecular structure of TCDD determined experimentally by single-crystal x-ray diffraction crystallography.

The mechanism of TCDD in the body starts with the binding to the aryl hydrocarbon (Ah) receptor. The Ah receptor binds to many naturally occurring contaminants such as benzene and other hydrocarbons. However, for unknown reasons, TCDD binds to the Ah receptor extremely well and forms a strong unit with the receptor. After the formation of the receptor-TCDD
complex, the complex moves into the cell nucleus and activates the gene to regulate division of cells. In this way, TCDD is able to control cell growth in the body.

**Figure 6** An accepted mechanism of TCDD getting into the cell.

The receptor-based mechanism of TCDD implies that a certain amount of Ah receptors needs to be occupied before the toxicity of TCDD can occur. This gives a chance for the industry to claim that the TCDD is probably not as toxic as they thought it would be. Therefore, the Environmental Protection Agency (EPA) has now begun to reassess its safety level. However, many scientists such as Ellen Silbergeld believe that people who are advocating a tolerable concentration level for TCDD are ignoring the complexities of TCDD. That is, people have to take into account of the different body levels, the uncertainties in real situations, and all other factors in order to assess the TCDD health effects in humans. Therefore, people should have a cautious view about the threshold of TCDD exposure.

TCDD exposure is rare because it is not produced commercially. However, a small amount of it may be formed as a by-product during processes such as incomplete combustion and production of chlorinated organic matter. Therefore, it is more likely for people working in the industry to be exposed to high concentration of TCDD as opposed to non-occupational people. Nevertheless, TCDD could still be found in trace amounts of some food products such as meat, fish and dairy products. As a result, it is toxic to eat food that is contaminated with TCDD. In addition to consumption, TCDD may be inhaled if it is in the atmosphere, but this is a not a common way for people to be exposed if no accident occurs.

The United States is one of the higher exposure countries with TCDD. Even though it has a higher level of exposure than other countries, at this current level which occurs in food and the environment, TCDD has no immediate effect on health if people are only being exposed for a short period of time. The danger of TCDD exposure comes only when victims are exposed for a long period of time. Therefore, if only the Seveso government could immediately evacuate the local residents, the cases of health problems would have been reduced.
In addition to the Seveso accident, another significant event called for TCDD research and uncovered some interesting facts about TCDD. In the past, TCDD is known for its potent lethality because it is a carcinogen and it is able to accumulate in fats, and scientists had always assumed that the human body was not able to metabolize it. However, there was a case that happened in 2004 that has changed this view. This case was the TCDD poisoning of the president of Ukraine, Viktor A. Yuschenko. After having dinner, he became seriously ill and was confirmed later that his food was laced with TCDD, possibly by his political opponents. The TCDD poisoning has plagued him for years and led to disfigurement. However, it is because of this non-fatal poisoning that researchers have found that the human body is actually able to breakdown TCDD with metabolites. In fact, a group of TCDD researchers has shown that TCDD is in fact metabolized in their three-year analysis and monitoring of Yushchenko. They have found some original form of TCDD excreted in his sweat, urine, feces and other channels. Yushchenko’s recovery from TCDD is certainly a breakthrough in the research of TCDD. This has prompted scientists to find methods in order to assess the metabolites for TCDD. Assessing TCDD’s metabolites would definitely help people gain a better understanding of TCDD poisoning.

![Figure 7 Photo of Victor Yushchenko before poisoning (A), three months after (B), and three years after poisoning with TCDD (C).](image)

In conclusion, the lesson of Seveso has simple advice to offer. This accident has taught people that it is important to have a strict control of industrial processes to reduce the chances of formation of toxic chemicals as much as possible. It is also the government and health authorities’ responsibility to oversee these industrial practices. Besides industrial practices, protecting food supply is also important because a significant chance of human exposure to TCDD is through the food supply. A rigid food monitoring system should be in practice so that public health is ensured. In addition to government’s role in preventive measure, consumers should also have awareness towards TCDD exposure. For example, because TCDD is more likely to come in food products such as meat and fish as it accumulates in fats, therefore consuming less fats from meat greatly reduces the chance of exposure to TCDD and other dioxin compounds. Before people have a deep understanding of TCDD poisoning, they should put efforts into prevention and reduction of exposure to TCDD.
Works Cited


