Health Impact of Dioxins

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Dioxins, as well as endocrine disrupters, are a group of chemicals that have received widespread publicity on a daily basis as new environmental pollutants. They are routinely described as “deadly poisons and the most potent carcinogens” resulting in fear and anxiety in the public at the mention of dioxins.

Various animal studies have shown that the lethal dose median (LD₃₀) of dioxins in guinea pigs is 1µg/kg body weight, indicating that the estimated toxicity of dioxins is 60,000 times higher than that of potassium cyanide. Long-term animal studies with dioxins have also demonstrated its carcinogenicity, teratogenicity, immunotoxicity, and reproductive toxicity. These data certainly indicate that dioxins are deadly poisons.

The concentration of dioxins is extremely low both in vivo and in the environment. The blood concentration of dioxins in the public is in the order of picograms per gram fat (pg; one trillionth of 1 g) and is much lower than that of other general environmental pollutants that are present in the order of milligrams per gram fat (mg; one thousandth of 1 g). In animal studies, dioxins are routinely used at very low doses of 1µg/kg body weight per day, whereas other common types of chemical toxins are usually used at a dose of 1 mg/kg/day. Since various harmful effects have been observed even with this low dose, dioxins have the reputation of being deadly poisonous. However, although the dose of 1µg/kg body weight per day, i.e. one thousandth of a gram appears small, it is not so small when viewed from another standpoint. It is one million times greater than 1 pg and 250,000 times greater than 4 pg/kg, the daily intake of dioxins in the public.

General Toxicity of Dioxin in Humans

An epidemiological study has been conducted recently in those involved in the accidental explosion at an agricultural chemical plant in Seveso, Italy, workers in the agricultural chemical manufacturing industry, and Vietnam veterans, in order to investigate the acute and chronic effects of dioxin exposure. The cumulative number of subjects was ca. 340,000, and the follow-up period was from 15 to 50 years. Surprisingly, no cases of acute poisoning have been reported in the study to date.

In 10 children living in Zone A, the Zone where subjects were exposed to the highest level of dioxins in Seveso, the blood level of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD; the most toxic compound in the dioxin family) immediately after exposure ranged from 828 to 56,000 pg/g fat. This is equivalent to 202 to 13,659 times the normal level found in the public.
The short-term intake estimated from the above concentration was a maximum of 168,000,000 pg or 8,400,000 pg/kg body weight, corresponding to 2.1 million times higher than the level in the public. However, even at these very high levels of exposure, the only symptom of poisoning observed was chloracne, and laboratory tests revealed no particular abnormalities.

In terms of the long-term mortality, 20 studies have been conducted in 340,000 people with follow-up periods of 15 to 50 years with blood TCDD concentrations of 38 to 56,000 pg/g fat (versus 2 to 8 pg/g fat in the public). Nineteen of these studies demonstrated no significant increase in mortality, and only one study reported a 1.3 fold increase in mortality after 20 years of exposure (Table 1).

In preventive strategies incorporating risk assessment, the level shown to be safe in animals is multiplied by various safety coefficients to calculate the standard reference value in humans (tolerable daily intake [TDI] or risk reference dose [RfD]). To obtain the standard value for TCDD in humans on the basis of the LD₅₀ in guinea pigs (1 g/kg), we need to estimate a chronic value from an acute value, a no-
Blood concentrations of 2,3,7,8-TCDD (pg/g fat) (Subject of investigation)

Kociba rats
NOISH subjects (those followed up for one year or longer)
NOISH subjects (average)
Casualties of an accident in the Netherlands (data from IARC)
Subjects from the German cohort study II (data from IARC)
Inhabitants in Seveso-Zone A (average)
Soldiers participating in defoliation
BASF casualties
Inhabitants in Seveso-Zone B (average)
Inhabitants in Seveso-Zone R

The level calculated on the basis of the TDI
General population

Liver carcinoma

Data contained within the enclosed boxed areas showed abnormalities.

Increased incidence of all types of cancer
Chloracne present
No respiratory disorders
No chromosomal abnormalities

Change in sex ratio for newborn present
Slight decrease in T-lymphocyte function
No abnormality in immunological reaction
No increase in the incidence of infection
No abnormality in immunocompetence or fat in blood
No increase in abortion rate
No liver disease or nervous disorder
No abnormality in immunocompetence or fat in blood
No decrease in sex hormone levels present
No chromosomal abnormalities
No increase in the incidence of congenital abnormalities
No abnormality in immunocompetence or fat in blood
No increase in the incidence of congenital abnormalities
No abnormality in immunocompetence or fat in blood
No increase in the incidence of congenital abnormalities

Note) The scales on this figure is logarithmic.

Fig. 1 Health impact as related to blood concentrations of dioxin (2,3,7,8-TCDD) (prepared on the basis of data from numerous reports)

Kociba rats: In this study by Kociba, the rats were fed 2,3,7,8-TCDD for two years and the development of hepatocellular carcinoma was investigated and reported.

NIOSH: National Institute for Occupational Safety and Health, which conducted a large-scale study on occupational exposure to dioxins in U.S. workers in chemical plants.

BASF casualties: Those involved in the accidental explosion at the BASF agricultural chemical plant, in the former West Germany in 1953.

Seveso-Zone A: The area polluted by the highest level of dioxins in Seveso.

Seveso-Zone B: An area less polluted than Zone A.

Seveso-Zone R: An area with a minimum of pollution considered to be less dangerous.
observed-adverse-effect-level (NOAEL) from an intoxicating level, and a value in humans from that in animals, resulting in the respective safety coefficients of 1/100, or the total safety coefficient of 1/1,000,000 at least. Accordingly, the standard value in humans can be calculated as 1 pg/kg/day, corresponding to a blood level of 10 pg/g fat. This result shows that the standard accepted TDI for TCDD in humans as determined by risk assessment is far from the actual situation.

The data above show that dioxins are not actually deadly poisonous to humans.

**Carcinogenicity of Dioxins in Humans**

A long-term carcinogenicity study in rats demonstrated that the incidence of hepatoma significantly increased after exposure to dioxins at 100 ng/kg/day for two years, and the no-effect toxic dose was 1 ng/kg/day. Multiplying this value by the safety coefficient of 1/100 gives 10 pg/kg/day, the former international TDI. However, in terms of carcinogenesis in humans, a long-term epidemiological study in people living in Seveso has shown no increase in the incidence of total cancers or hepatoma.

The International Agency for Research on Cancer (IARC) has recently accepted that only TCDD of the dioxin family is “human carcinogen”. This conclusion was based on results from a number of epidemiological surveys in humans. IARC has concluded that the incidence of cancer is significantly increased only when people are exposed to more than 100 to 1,000 times the normal blood levels of TCDD for 20 years or longer, and that the relative risk is 1.4 times. However, many animal studies and epidemiological surveys in humans have demonstrated that exposure to several times to several hundred times higher TCDD levels than that in the public exhibits an anti-promotion or anti-cancer effect. Therefore, on a scientific basis, dioxins are not considered to be the most potent carcinogen in humans.

Figure 1 illustrates various effects of dioxins on humans on the basis of their concentration in blood. The effect observed at the minimum level is reproductive toxicity, on which additional studies are needed in the future. However, no detrimental impacts on humans have been reported to be linked to exposure to normal or slightly elevated levels of dioxins.

Fortunately, the level of dioxins in the human body has decreased over the last few decades both in Japan and in other countries. At least in Japan, the major reason for higher dioxin levels in the past has been widespread use of dioxin-contaminated pesticides, and dioxins emitted from incinerators have probably not had a great influence on dioxin levels in humans.

It is important that physicians provide people with correct information in order to relieve their anxiety in relation to dioxins.