

Summary of Preliminary Observations on The Toxicity of Iron Carbonyl for Rabbits

Pure iron carbonyl was applied to the abdominal skin of rabbits, after carefully clipping off the hair or fur without injury to the skin and without wetting it. The animals were effectively restrained on animal boards and put in a fume hood with their heads turned into the air-stream so as to avoid inhalation of the volatilizing liquid applied on the skin. The volatility of iron carbonyl is such that the pure compound applied to the skin of the rabbit disappears as such in from 5 to 15 minutes leaving the skin somewhat red and apparently dry. The smoky odor of iron carbonyl can be detected on the skin for some period after the apparent disappearance of the liquid.

The following results were observed:

1. 2 cc. applied in one dose caused death of the rabbit in 36 hours.
2. 10 cc. applied in one dose caused death of the rabbit in 48 hours.
3. 20 cc. applied in two doses of 10 cc. each, with an interval of 30 minutes, caused death in 12 hours.

Pure iron carbonyl was injected subcutaneously with the following results:

3 rabbits injected with doses of 0.5 cc., 1 cc., and 2 cc., respectively, died in 60 hours, 40 hours and 16 hours respectively.

Pure iron carbonyl was injected intravenously with the following results:

5 rabbits injected with doses of 0.05 cc., 0.05 cc., 0.1 cc., 0.3 cc., and 0.5 cc., respectively, died in 22 hours, 24 hours, 23 hours, 26 hours and 40 hours respectively.

iron carbonyl was introduced at a rate of 4 liters per minute. The concentration of iron-carbonyl in the air was determined by indirect means and may be somewhat, although not grossly, in error. The following results were obtained.

1. A rabbit exposed for 4 minutes to air containing approximately 400 milligrams of iron carbonyl per liter of air died 12 hours later;
2. Another rabbit exposed for 2 hours to 20 mg. $\text{Fe}(\text{CO})_5$ per liter of air died in 12 hours.
3. Another exposed for 1 hour to 10 mg. $\text{Fe}(\text{CO})_5$ per liter of air died 17 hours later.
4. Another exposed for 1 hour to 7.5 mg. $\text{Fe}(\text{CO})_5$ per liter of air died in 12 hours.
5. Another exposed for 1 hour to 2.5 mg. $\text{Fe}(\text{CO})_5$ per liter died in 41 hours.
6. Another exposed for 1 hour to 1.0 mg. $\text{Fe}(\text{CO})_5$ per liter died in 40 hours.

The effects of iron carbonyl on rabbits was essentially the same regardless of the mode of administration although the animal killed by oral administration showed gastro-intestinal irritation in addition to the characteristic lesions elsewhere. These characteristics, however, were a striking degree of edema and acute congestion of the lungs, with occasional petechial hemorrhages; acute dilatation of the heart, and acute toxic changes -

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into the blood, the blood of sick and dead animals at no time contained carboxyhemoglobin in sufficient quantities to be revealed by the tannic-pyrogallie acid method of testing. It is apparent, therefore, that the toxicity of the material is not due to the production of carbon monoxide through a molecular decomposition in the tissues. As a matter of fact such a decomposition, although it probably occurs, does so quite slowly. Material injected subcutaneously was often found undecomposed and partly unabsorbed at the site of injection.

Animals treated with toxic amounts of the material always showed the same striking symptoms. Rapid and labored respiration developed and the animal sat with the head sharply retracted, the nose pointing upward (opisthotonus). There was no diarrhoea, and in only one instance, in which an animal was exposed to air saturated with iron-carbonyl, were convulsions seen.

Comment (Not for quotation)

There is some slight evidence that iron-carbonyl is more toxic for rabbits than for other animals, cats for example. However experimental data here are quite fragmentary.

From the experience of persons outside the United States, who have handled considerable quantities of the material,

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to reduce their toxicity. It is possible that the finely divided vapors decompose rapidly when distributed in the air in the presence of light. This, however, has not been established and can not be used as a basis for a belief that the material is less dangerous than is indicated by the above data. In any case the available heresay reports as to the occupational handling of the compound are believed to be unreliable. The writer is of the opinion that cases of acute poisoning and death have occurred among men who have been exposed to high concentrations of the vapor in the manufacture and handling of iron-carbonyl for commercial purposes. Apparently, however, measures for avoiding serious exposure were found to be feasible.

It is doubtful if there is any cumulative toxic effect from the absorption of sub-lethal doses, although there is no published evidence on this point.

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