Effects of Dietary and Inhalative Cadmium on Hemoglobin and Hematocrit in Rats*

E. Prigge, H. P. Baumert, and H. Muhle

Fraunhofer-Gesellschaft
Institut für Aerobiologie
D-5948 Schmallenberg-Grafschaft
W. Germany

INTRODUCTION

It has been reported that dietary cadmium depresses hematocrit and hemoglobin, and that anemia is one of the most sensitive parameters of oral cadmium intoxication (COUSINS et al., 1972; FREELAND and COUSINS, 1973). In rats decreased hemoglobin values were detected when amounts as little as 31 ppm were added to the diet (WILSON et al., 1941). Similarly, at doses of 50 ppm dietary cadmium the hematocrit of growing swine decreased (COUSINS et al., 1972). DECKER et al. (1958) noted that hemoglobin levels had decreased considerably after only two weeks in rats given 50 ppm cadmium in their drinking water. FOX et al. (1971), FREELAND and COUSINS (1973), and MAJI and YOSHIDA (1974) believe this effect to be linked, at least in part, to a decrease in intestinal iron absorption. Dietary supplement of ferrous sulfate (FOX et al., 1971; MAJI and YOSHIDA, 1974) and parenterally - administered iron (POND and WALKER, 1972) overcame the depression of hematocrit and hemoglobin.

BERLIN and FRIBERG (1960) and AXELSSON and PISCATOR (1966), however, suggest that the anemia is caused mainly by increased destruction of the erythrocytes. This opinion is in part supported by the facts that parenteral administered cadmium also decreased the hematocrits of fowl (STURKIE, 1973) and rabbits (FRIBERG, 1950; BERLIN and FRIBERG, 1960) and that FRIBERG (1950) found a slight anemia in rabbits exposed to cadmium oxide dust.

If there is an influence on iron absorption from the intestines by cadmium or if other intestinal factors contribute to the development of anemia after

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oral cadmium uptake, the degree of anemia after inhalative resorption of cadmium should be much less pronounced.

The study was therefore undertaken to examine the difference of the effects of dietary and inhalative cadmium on hemoglobin and hematocrit.

MATERIALS AND METHODS

SPF-Wistar male rats (line TNO-W-70) were used. The animals were housed in a fully climatized room. Water and food were given ad libitum. Contamination of food by cadmium was controlled and found to be negligible.

One group of 20 rats was continuously exposed to a $CdCl_2$-aerosol (0,2 mg Cd/m^3) for 66 days, a second group of 20 rats served as control. The aerosol was produced with an ultrasonic aerosol generator. The median aerodynamic diameter of the aerosol particles was 0,32 µm and the geometric standard deviation was 1,7. Since particles of this size deposit largely in the pulmonary and tracheo bronchial compartment of man (Task Group on Lung Dynamics, 1966), STAUFFER (1975) concluded that these particles are deposited in the same regions in small animals, too.

For the dietary experiments four groups of rats were employed. Three of the groups received 25, 50 and 100 ppm cadmium as $CdCl_2$ in drinking water, the fourth got aqua dest. This experiment lasted for 48-55 days.

The following parameters were measured in all groups: The body weights of the animals, hematocrit and hemoglobin in blood, and the cadmium content in liver and kidney. The hemoglobin was determined from measurements of hemoglobin cyanide. For determination of the Cd-content approximately 1 g of the liver and one kidney was wet ashed in accordance to the standards of the "analytical methods committee" (1967) with suprapur HNO_3 and $HClO_4$. The sample was fumed until dry and remained for half an hour on a heating plate at 450° C until it became colourless.

The sample was dissolved in 1/100 M HCl which contained 2 % $(NH_4)_2SO_4$ (EDIGER, 1975). The cadmium content was determined in the graphite tube of an atomic-absorption-photometer. The sample was compared to a standard of $(NH_4)_2\ SO_4$-solution containing hydrochloride-acid with known amounts of cadmium. The background was subtracted from the signals.

The data were analyzed using a student's "t" test.

RESULTS AND DISCUSSION

The increases of body weight are shown in Table 1. In comparison to the control animals, a retardation of growth for the aerosol exposed group and the group with 100 ppm oral cadmium intake was observed.

TABLE 1

Effect of $CdCl_2$-inhalation and oral cadmium uptake on body weight (g)

	inhalation	
	control	exposed
Beginning	259,2 ± 23,4 (n=20)	256,7 ± 24,9 (n=20)
End	368,2 ± 30,0 (n=20)	311,0 ± 50,4* (n=13)

	oral cadmium uptake			
	control	25 ppm	50 ppm	100 ppm
Beginning	221,0 ± 8,6 (n=6)	231,3 ± 10,6 (n=6)	211,8 ± 18,7 (n=6)	211,5 ± 11,2 (n=6)
End	352,5 ± 9,2 (n=6)	370,8 ± 19,8 (n=6)	341,2 ± 21,3 (n=6)	295,7 ± 22,9* (n=6)

Values are expressed as mean ± SD.

*Denotes significant differences from controls ($p \leq 0{,}001$).

The cadmium concentration in the liver and kidney is shown in Table 2. The relation of the cadmium content of kidney to liver averages 1,7 for the oral exposed groups and 4,4 for the inhalation exposed groups, a result of the omission of the V. portae circulation after inhalative uptake.

The hematocrit and hemoglobin values are presented in Tables 3 and 4. For the inhalative exposed rats no significant differences are found in comparison to the controls. After dietary cadmium intake a significant reduction in hematocrit and hemoglobin values occurred in agreement with experiments reported in the literature.

Although the cadmium concentration in the organs of rats which had inhaled $CdCl_2$ particles exceeded that of

TABLE 2

Cadmium concentration in µg/g wet weight in liver and kidney in controls, cadmium aerosol exposed and orally exposed rats.

	control	oral cadmium uptake			inhalation
		25 ppm	50 ppm	100 ppm	
Liver	0,036 ± 0,014 (n=14)	5,36 ± 1,64 (n=3)	7,07 ± 0,59 (n=3)	21,57 ± 8,25 (n=3)	9,04 ± 3,08 (n=15)
Kidney	0,093 ± 0,023 (n=14)	8,81 ± 0,18 (n=3)	13,2 ± 1,36 (n=3)	36,68 ± 5,13 (n=3)	40,2 ± 12,2 (n=15)

Values are expressed as mean ± SD.

rats whose dietary intake contained 25 and 50 ppm, no anemia was found in the aerosol-exposed rats. Whereas the growth of the 25 and 50 ppm group was not different from the controls, a reduction of the increase of the body weights was found without changes in hematocrit and hemoglobin for rats after the inhalation of cadmium aerosol.

TABLE 3

Hematocrits and hemoglobin in cadmium aerosol exposed rats.

	control	Cd aerosol
Hematocrit (%)	52,65 ± 3,84 (n=20)	55,06 ± 4,09 (n=18)
Hemoglobin (g%)	16,52 ± 1,32 (n=20)	17,04 ± 2,05 (n=18)

Values are expressed as mean ± SD.

From our results the conclusion can be drawn that anemia is a sensitive indicator only for oral application of cadmium but not for inhalative uptake. This means that in generation of an anemia in rats hemolytic effects by erythocyte-destruction contribute very little because there was no anemia in the aerosol exposed rats. The reasons for a development of anemia after parenteral application are not clear.

TABLE 4

Effects of dietary cadmium uptake on hematocrits and hemoglobin.

	Control	25 ppm	50 ppm	100 ppm
Hematocrit (%)	50,50 ± 1,22 (n=6)	46,33 ± 1,21*** (n=6)	46,83 ± 0,98*** (n=6)	46,83 ± 1,60** (n=6)
Hemoglobin (g%)	17,31 ± 0,91 (n=6)	16,17 ± 0,80* (n=6)	16,10 ± 0,91* (n=6)	15,49 ± 0,78** (n=5)

Values are expressed as mean ± SD.

* Denotes significant difference from controls ($p < 0,05$)
** Denotes significant difference from controls ($p < 0,01$)
*** Denotes significant difference from controls ($p < 0,001$)

The observation of an anemia in rabbits after an exposure to CdO-dust (FRIBERG, 1950) could be possibly related to an oral uptake of larger particles which were transported upwards by cilia from the tracheobronchial regions and were swallowed.

Our results are in agreement with the observations of FOX et al. (1971), FREELAND and COUSINS (1973), and MAJI and YOSHIDA (1974) who found an inhibition of iron-resorption and a subsequent anemia after oral cadmium uptake.

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