LETTERS TO THE EDITOR

INFLUENCE OF TRICHLOROETHYLENE IN EACH PROCESS OF AGEING OF RATS

Many experiments using animals have been carried out to clarify the effect of various toxic substances. In most of these experiments except the tests for carcinogenicity, however, the toxicity in acute or subacute poisoning has been investigated only in a stage of the ageing of animals, particularly in young mature stage, because in the stage the toxic effect on body weight or organs' weight would appear more clearly than that in older stage. Since metabolic pattern and physiological functions in the body change with ageing, the effects of toxic substances on the body would perhaps differ with ageing. In other words, the results obtained in a stage of ageing are not always general in the animal species used in the experiment. By taking into account the results of animal experiments, we assume customarily the effects on human body. In this sense, it is necessary to perform the animal experiments in careful consideration of the ageing process of animals.

In this report, the effect of trichloroethylene was studied at various stages of ageing of rats. JCL-SD female rats of three weeks old were purchased from Nippon Clea Co., and they were bred in a barrier system. When the rats came of age of 1, 3 or 12 months they were exposed to 0, 40, 80, 160 or 400 ppm of trichloroethylene, respectively, throughout a month. At the final day of the exposure, body weight of each animal was measured and then they were abstained from food but water for a night. On the next day, they were killed by decapitation. After organs' weight was recorded, blood, heart, liver, lung and brain samples were analysed biochemically.

Three of 5 rats of 12 months old exposed to 400 ppm of trichloroethylene died during the exposure. It has been shown in other experiments that all of 5 rats of 8 weeks old exposed to 800 ppm of trichloroethylene for a month were alive¹⁾ without any apparent significant sign of functional disturbance, and further, 4 weeks old rats exposed to the same concentration eight hours a day for over a year were alive.²⁾ This ageing experiment is yet proceeding, and the conclusion how the toxicity of trichloroethylene relates to the ageing process will be discussed in a following paper.

Some results were shown in Table 1. In this table, the values for normal rats of the ages of 4 and 13 months were given as percentage comparing with 2 months old rats.

Fig. 1 shows the ratio of body weight before and after the exposure in each stage of ageing. This figure indicates that body weight of rats of 1 and 12 months old was severely influenced by trichloroethylene, while rats of 3 months old were not. Effect of trichloroethylene on organs' weight was observed in 1 and 12 months old animals but almost no effect in 3 months old rats. Enlargement of the liver seemed to be most

Table 1. Normal values of 2, 4 and 13 months old rats and effect of trichloroethylene exposure on the rats of each age group.

Age (months old)	Normal value			Effect of trichloroethylene		
	2	4	13	2	4	13
Body weight	100* ¹	137* ¹	170* ¹	↓ * ²		↓
Organ's weight						
Heart	100	127	143	↓		↓ (400 ppm ↓)
Liver	100	110	131	↑	↑	↑
Lung	100	111	103	↓		(400 ppm ↑)
Kidney	100	104	118	(↓)		(400 ppm ↑)
Adrenal gland	100	100	100	↓		
Spleen	100	115	130			(400 ppm ↑)
Serum						
LDH-isozyme	100	173	193		↓	↓
ALP	100	35	22	↑	↑	↑
Ch-E	100	323	191	↓	↓	↓
CPK	100	43	31	↑		
red. GSH	100	460	767			
Glucose	100	100	83	↓	↓	↓
Lactate	100	261	634	↓	↓	↓
Hb	100	106	104	↓	↓	↓
Pi	100	83	69		↑	↑
Alubumin	100	124	112			
FFA	100	167	140		↓	↓
Phospholipids	100	126	141		↓	↓
Triglycerides	100	197	278			↓
Free-cholesterol	100	114	161			↓
Liver						
Triglycerides	100	100	100			↑
red. GSH	100	260	400	↑	↑	
Glucose	100	150	157			↓
Glycogen	100	141	393	↑	↑	↑
Lactate	100	95	304			↓
Heart						
Glycogen	100	71	86	↑	↑	↑
Lung						
ALP	100	100	100			(400 ppm ↑)
ACP	100	100	100			(400 ppm ↑)
γ-GTP	100	75	165		(400 ppm ↑)	
red. GSH	100	157	428	↑	↑	↑
Collagen	100	83	191	↑	↑	

*¹: These are relative values represented as the value in 2 months old is 100.*²: The effect of trichloroethylene exposure was shown as follows:

↑ increase ↓ decrease ↑↑ remarkable increase ↓↓ remarkable decrease

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Fig. 1. Ratio of body weight before and after trichloroethylene exposure in each ageing process.

- : 2 months old rats (Rats of 1 month old were exposed to trichloroethylene for a month)
- △—: 4 months old rats (Rats of 3 months old were exposed to trichloroethylene for a month)
- : 13 months old rats (Rats of 12 months old were exposed to trichloroethylene for a month)

remarkable in 12 months old rats exposed to trichloroethylene over 200 ppm as shown in Fig. 2.

On the other hand, the results of biochemical examination of serum and liver were not always considered to indicate the damages of the liver when the following facts were taken into consideration. There was observed any change in neither serum GOT nor GPT activity in the rats exposed to trichloroethylene, though the increase of ALP and the decrease of choline esterase in serum were recognized. In the rats of 1 month old, the weight of kidney decreased by the exposure, while in 12 months old rats the weight increased. The increase of inorganic phosphate in serum was observed in the rats over 3 months old. Lipids, especially triglycerides, in serum also decreased in older rats by the exposure. From the above findings, it may be reasonable to consider that trichloroethylene exposure causes a latent abnormal state of the liver rather than some damages of the liver and bile duct.

Remarkable increase of creatine phosphokinase (CPK) activity in serum was observed only in 1 month old rats, but no change in either of the two other age groups, as shown in Fig. 3. It has been considered that the increase of CPK activity has some

Fig. 2. Effect of trichloroethylene on the ratio of liver weight to body weight in each ageing process.

- : 2 months old rats (Rats of 1 month old were exposed to trichloroethylene for a month)
 —△—: 4 months old rats (Rats of 3 months old were exposed to trichloroethylene for a month)
 —□—: 13 months old rats (Rats of 12 months old were exposed to trichloroethylene for a month)

relations with the diseases of voluntary muscle. Above finding indicates that trichloroethylene may have some effects on the growth process of muscle rather than the muscle itself.

It is generally known that the central nervous system is sometimes disturbed by trichloroethylene and other organic solvents. In the present study, several chemical components in the brain were measured. The content of 5-hydroxytryptamine in brain cortex and hippocampus was observed to be significantly lower ($p < 0.05$) in 12 months old rats exposed to 400 ppm of trichloroethylene than that in the control rats of the same age. Dopamine in striatum showed a similar tendency, but not significant comparing to the control. The level of noradrenaline in hypothalamus and the other areas of the brain showed no change by the trichloroethylene exposure. Details of the results will be presented in a next paper.

Disorders in the liver and those of neurological functions have been reported as symptoms of acute or subacute trichloroethylene poisoning in animal and human bodies.³⁻⁸⁾ In the present study, it was demonstrated that liver enlargement and the change of neurotransmitter concentration in the brain were induced by trichloroethylene exposure.

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Fig. 3. Change of creatine phosphokinase activity in serum by trichloroethylene in each ageing process.

- : 2 months old rats (Rats of 1 month old were exposed to trichloroethylene for a month)
- △—: 4 months old rats (Rats of 3 months old were exposed to trichloroethylene for a month)
- : 13 months old rats (Rats of 12 months old were exposed to trichloroethylene for a month)

The liver enlargement perhaps indicates a latent abnormal state of the liver as mentioned above. Some of these findings were observed only in 1 and 12 months old rats but not in 3 months old. This may suggest some age-difference in the toxic effects of trichloroethylene on the animals. Further investigation is necessary in order to clarify the relation between the toxicity of trichloroethylene and ageing.

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