

## TETRAETHYLTHIURAM DISULFIDE (ANTABUSE®) AND THE ANESTHETIC AGENTS \*

B. M. COOPER, M.D.,† H. C. SLOCUM, M.D., AND C. R. ALLEN, M.D.

*Galveston, Texas*

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TETRAETHYLTHIURAM disulfide (antabuse®) is used in the present day treatment of chronic alcoholism. If patients receiving this drug are given a small amount of ethyl alcohol they exhibit acute distress, as evidenced by marked flushing, redness of the eyeballs, difficulty in breathing, palpitation, vomiting and low blood pressure. Chemical examination of the blood during such a period shows a marked increase in acetaldehyde content. The physiologic disturbances in these individuals is believed to be due to this substance.

Some patients on antabuse therapy carry cards warning against

**EMERGENCY NOTICE TO DOCTOR**  
**I \_\_\_\_\_ am**  
**taking Antabuse. Administra-**  
**tion of Chloroform, Ether,**  
**Cyclopropane, Paraldehyde**  
**or Alcohol would be danger-**  
**ous. I can tolerate**  
**Pentothal or Procaine.**

Fig. 1. The card carried by some patients on antabuse therapy.

the administration of such general anesthetic drugs as ether, cyclopropane and chloroform for fear that these agents will produce a response similar to that of ethyl alcohol. These cards state that pentothal or procaine may be given (fig. 1). We were unable to determine the origin of these cards and the reasons for designating some agents as harmful and others safe. Therefore, we decided to investigate the effect of anesthetic agents upon the acetaldehyde content of the blood in the presence of antabuse.

\* From the Department of Anesthesiology, University of Texas Medical Branch, Galveston, Texas.

† Presently at The Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee.

## METHOD

Adult rabbits were used for the experiments because rabbits show an elevation of blood acetaldehyde when given ethyl alcohol following treatment with antabuse. Each rabbit was given antabuse by gastric tube in a dose of 0.5 Gm. per kilogram of body weight sixteen hours before each period of anesthesia. Blood samples were taken for the determination of acetaldehyde before and during anesthesia. Blood acetaldehyde was determined by the spectrophotometric method of Stotz (1). Each rabbit received from one to five periods of anesthesia with at least three days between successive anesthetics. The anesthetic agents used were nitrous oxide, cyclopropane, sodium pentothal, procaine, ether, chloroform and avertin®. To be sure that a significant increase in blood acetaldehyde would develop in each animal when given alcohol after being treated with antabuse, each rabbit was given intravenously 2 cc. of 20 per cent ethyl alcohol per kilogram of body weight.

## RESULTS

It was found that the control blood acetaldehyde level in the rabbit is subject to rather wide variation both from one rabbit to another and from day to day in individual rabbits. The values ranged from 26

TABLE 1  
BLOOD ACETALDEHYDE IN RABBITS TREATED WITH ANTABUSE\*

Agent	Number of Rabbits	Change in Blood Acetaldehyde*, micrograms/100 ml. of blood		
		Minimum	Maximum	Average
Control with alcohol	18	74	771	291
Nitrous oxide	15	3	139	9
Cyclopropane	7	3	- 81	- 10
Pentothal	6	0	- 61	- 10
Procaine	6	0	129	30
Ether	8	- 4	100	23
Chloroform	4	15	71	36
Avertin	4	- 7	- 52	- 32

\* A negative sign indicates that the change was a decrease from the control level.

micrograms to 240 micrograms per hundred milliliters of blood, with an average blood level of 92 micrograms per cent. The variation in individual rabbits was as great as 189 micrograms per cent with an average variation of 73 micrograms per cent.

With nitrous oxide, cyclopropane, pentothal, procaine and ether there was no constant change in the blood acetaldehyde during anesthesia. In about half of the animals there was a small increase and in the other animals a decrease in acetaldehyde. During chloroform anesthesia all the animals showed some increase in acetaldehyde, but

the maximal increase was 71 micrograms per cent. With avertin anesthesia there was a consistent decrease in acetaldehyde with a disappearance of acetaldehyde from the blood in 3 of 4 animals. All animals showed a marked increase in acetaldehyde when given ethyl alcohol. Table 1 is a summary of the changes in blood acetaldehyde of the rabbits during anesthesia and following the administration of ethyl alcohol. Figure 2 is a graphic representation of the average changes in blood acetaldehyde during anesthesia compared to the marked rise in acetaldehyde with alcohol.

THE AVERAGE ACETALDEHYDE RESPONSE TO ANESTHETIC AGENTS COMPARED WITH ETHYL ALCOHOL

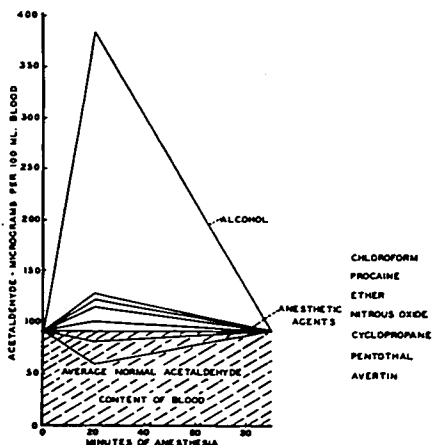


Fig. 2. The average change in blood acetaldehyde with anesthetic agents compared to the change with ethyl alcohol in rabbits treated with antabuse.

Statistical analysis of the changes occurring in blood acetaldehyde in rabbits shows that the changes during anesthesia with each of the anesthetic agents used are not statistically significant at the 0.05 level of probability but that the increases with alcohol are significant.

#### DISCUSSION

Antabuse is insoluble in water, slightly soluble in ethyl alcohol, and readily soluble in ether and chloroform. The formula of tetraethylthiuram disulfide is  $(C_2H_5)_2 N-C-S-S-C-N (C_2H_5)_2$ .



In antabuse treated animals given ethyl alcohol, the alcohol disappears from the blood at the normal rate, but the metabolism of acetaldehyde is retarded, allowing this substance to accumulate in the blood to toxic levels (2). It has been shown by Warburg experiments that antabuse reduces the oxygen consumption of rat liver homogenates with alcohol substrate and that the addition of ascorbic acid reverses this effect in proportion to the amount of ascorbic acid added (3, 4).

It has also been shown that the administration of high concentrations of oxygen reduces the severity of the symptoms of the antabuse-alcohol response (5).

For those reasons, in the anesthetic management of patients on antabuse therapy it is recommended that a continuous intravenous drip of saline or glucose solution which contains ascorbic acid be given and the anesthetic agent be administered with a high concentration of oxygen. Any of the commonly used anesthetic agents may be employed with relative safety (6).

#### SUMMARY

Rabbits treated with tetraethylthiuram disulfide were given periods of anesthesia during which the blood level of acetaldehyde was determined. The anesthetic agents used were nitrous oxide, cyclopropane, sodium pentothal, procaine, ether, chloroform and avertin. In contrast to the marked elevation of blood acetaldehyde when ethyl alcohol was given, there was no significant elevation when any of the anesthetic agents were employed.

#### REFERENCES

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