activity from 50 to 100 times, or more. (6) Acetylation or benzoylation of a β-hydroxyl group does not markedly alter the activity. (7) The activity of stereoisomers involving asymmetry of the β-carbon atom of the side chain, caused by hydroxyl substitution, are not very different.

No analysis has been made of the exact mechanisms of action of these various compounds other than their general correspondence of effect with that of nicotine. Probably certain differences in the mechanisms of their effects will be found after further study but the quantitative picture of total respiratory and circulatory activities seems to be clearly related to the structure of the compounds studied and further work is in progress to define more completely these relationships.

6543

Methylene Blue as an Antidote to CO Poisoning.*

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This paper is a continuation of the study of the use of methylene blue in antagonizing the effects of CN and CO poisoning in whole animals[1,2].

In these experiments CO was administered to rabbits which had been tracheotomized. A cannula was inserted in the trachea which was then directly connected with the vessel containing the measured CO. The inspired air was separated from that expired by means of a valve. The experiments were done in two parts:

1. Injections of 1 cc. of .01% methylene blue in Ringer solution per kilo body weight were made intravenously a few minutes before CO was administered. CO (10% by volume in air) was then given until the animal stopped breathing. It was found that the peak of the variation curve for control animals was at 4.5 minutes where 39% stopped breathing, whereas the peak of the curve for those animals receiving methylene blue treatment, was at 6.5

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[1] Brooks, M. M., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1228.

[2] Brooks, M. M., *Am. J. Physiol.*, 1932, **102**, 145.

minutes where 36% stopped breathing. In other words, those animals receiving methylene blue treatment breathed 44% longer than the controls. There were 28 controls and 26 treated animals.

2. Another group was allowed to breathe air containing 8% CO until respiration had ceased. The controls were then given artificial respiration by means of an automatic respirator to see if recovery took place. The remainder were given an intravenous injection of methylene blue and artificial respiration. In the controls 20% recovered, while in the treated animals 92% recovered. In this group 25 controls were used and 20 treated animals. The dye was not effective if injected after circulation had stopped. It was made up fresh for each set of experiments and warmed before injecting.

These experiments confirm previous findings[1,2]. They show definitely that methylene blue assists the animal in overcoming the effects of CO poisoning. It is very probable that methylene blue acts as a temporary catalyst[3] in place of the bound hemoglobin[4, 5] until normal respiration is again restored.

[3] Barron, E. S. G., *J. Biol. Chem.*, 1929, **81**, 445.

[4] Warburg, O., Kubowitz, F., and Christian, W., *Biochem. Z.*, 1930, **227**, 245.

[5] Warburg, O., and Christian, W., *Biochem. Z.*, 1932, **254**, 438.