

of the 13 dogs with part of the lung out of function may be considered to differ from the sinus arrhythmia in these cases only in degree. Both types of rhythm are seen in normal dogs, although in our experience they do not occur so frequently. We consider these arrhythmias to be due to vagal action. The inversion of the T-wave is of questionable significance when the frequency of this phenomenon in the dog is considered. The ST changes are slight, but are sufficiently unusual to suggest further investigation, including control electrocardiograms preceding operation. We do not feel that we have sufficient data to explain the ST changes at the present time.

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Rate of Elimination of Certain Toxic Substances from the Blood.*

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In certain diseases it is believed that the symptoms are due to a toxin which circulates in appreciable amounts in the blood stream. Efforts have been made to demonstrate this substance in the blood of diseased men and animals by chemical analysis, or by the injection of their whole blood, blood serum or blood extracts into healthy animals. These injections have been given intravenously or intraperitoneally. It was believed that if the individual was poisoned by such a toxin, the injection of his blood or blood serum into healthy animals would produce toxic symptoms in them. The negative results in these experiments have been considered proof of the absence of such an intoxication.

It seemed to us, however, that toxic substances might be so rapidly removed from or inactivated in the blood that although an individual was suffering from a profound poisoning, the substance might not be demonstrable in the blood stream.

The following experiment was devised to test this assumption. Dogs were matched as for size and the compatibility of their bloods and were anesthetized with sodium barbital intravenously (200 to 250 mg. per kg.) or by stomach tube (250 to 300 mg. per kg.). They were then prepared for the typical carotid-artery-jugular vein

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crossing of circulations. In addition the transfer of blood was recorded and kept equal by means of the Montgomery and Lipscomb volume flow apparatus.¹ Heparin (30 mg. per kg.) was used as an anticoagulant and the blood pressure was taken from the femoral artery. The dogs were labeled A and B. The drug to be tested was injected into the femoral vein of dog A and was allowed to circulate for varying intervals of time, after which the 2 circulations were crossed. Dog B was observed for changes characteristic of the drug.

To date only strychnine has been tested under control of blood transfer. It was found in confirmation of the chemical studies of Weiss and Hatcher² that this drug was rapidly removed from or inactivated in the blood stream. Twice the lethal dose of strychnine (1.5 mg. per kg.) for an animal under anesthesia was injected into dog A, which promptly developed severe convulsions. Within 3 minutes so much of the drug was removed that crossing of the circulations caused no convulsions, although the bloods were continued in cross circulation for over 30 minutes at the rate of 180 to 220 cc. per minute. In another experiment when the bloods were crossed 1.5 minutes after injection of a similar dose dog B developed convulsions 12 minutes after the crossing of the circulations.

Some experiments done without the control of the transfer of blood indicate that, as measured by cross circulation studies, other drugs also are rapidly eliminated. Tests with these and the toxic substances formed in or found in animals (histamine, guanidine, etc.) are now being made.

This work seems to show that it may be possible for a man or an animal to be profoundly poisoned by a substance which cannot be demonstrated in the blood by transfusion experiments and that therefore the inability to produce toxic symptoms in healthy animals by this means does not necessarily rule out the existence of such an intoxication in the diseased animals.

¹ Montgomery, M. Laurence, and Lipscomb, T. H., *Am. J. Physiol.*, 1929, **90**, 454.

² Weiss, S., and Hatcher, R. A., *J. Pharm. and Exp. Therap.*, 1922, **19**, 419.