II. BLEEDING FOLLOWED BY IMMEDIATE TRANSFUSION OF SALINE.

Weight of dog. kg.	Dose per kg. c.c.	Amount bled. c.c.	Per cent. of blood removed (approximately).	Elapsed time between dosage and bleeding. hrs.	Result. (In hours after dosage.)
7·3	0.010	200	35	22	Died within 60 hours.
3.6	"	115	50	3½	"
4.8	"	120	33	3	"
4·5	"	110	33	4	"
9.0	"	175	25	3	"

All the inoculations in the last two series were made subcutaneously.

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The effect on the normal dog heart of expressed tissue juice from hearts of dogs poisoned with diphtheria toxin.

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The injection of moderately large doses of diphtheria toxins into animals is followed by no change in arterial blood pressure until after the elapse of a certain latent period, varying from 24 hours in the rabbit to 2–4 days in the dog, when it begins to fall. The fall in blood pressure, having once occurred, rapidly proceeds, so that within a very short time the animal is dead (30 minutes in the rabbit). Both vasomotor paralysis and cardiac failure are responsible for the fall, although it is evident that the cardiac failure is the more important as the immediate cause of death, since mere isolation of the vasomotor center — as after spinal transection — is not followed by such rapid cardiac failure. The vasomotor paralysis of course accelerates the cardiac failure.[1]

Rolly further found that isolation by Hering's method of the heart of a rabbit just dying as a result of diphtheria inoculation and its perfusion with blood from a healthy animal did not in the slightest degree delay the failure.

Although a certain amount of histological change seems always to be present in the myocardium after death from the inoculation of diphtheria toxins, yet it has been considered by Rolly and others as scarcely of sufficient intensity to account for

[1] Rolly: *Archiv für experimentelle Pathologie und Pharmakologie* (1899), xlii; Romberg, Paessler, *et al.*: *Deutsches Archiv für klinische Medizin*, lxiv.

the sudden failure. Furthermore, addition of diphtheria toxins even in very large dosage to the fluid perfused through a Langendorff heart preparation does not influence the beat; nor does its perfusion with the blood of a moribund animal (from diphtheria inoculation).

It has been suggested, therefore, (by Rolly, *et al.*) that the cardiac failure is due to a functional change resulting from the gradual assimilation of toxin by the cardiac muscle until so much had been taken up as to paralyze the muscle. Hence, the long latent period and the rapid course of the failure.

From a consideration of the findings it seemed to us possible that, if any such compound of cardiac muscle substance and toxin were present in the heart, its presence could be revealed by expressing the tissue juices of the heart of a dead or dying dog after inoculation with diphtheria toxins, and then adding this extract to the blood perfused through a normal Langendorff heart preparation. A large Buchner's press was employed by us for preparing such extracts. It was found as a result of the injection of such an extract into the heart that exactly the same result is obtained as when a similar extract of the heart of a normal dog is employed; viz., a sudden and complete inhibition of the beat followed within a minute by marked fibrillation. It was found impossible by any of the numerous methods recommended to remove this latter condition.

A similar result was obtained by injecting a watery solution of the ash of the extracts (made up to the original bulk) so that there can be little doubt that the large amounts of potassium which such an extract contains is responsible for the result. It is, however, somewhat difficult to explain in the same way the marked and persistent fibrillation which occurs, for such is not usually observed after injecting pure solutions of potassium salts. The sudden cessation of circulation alone cannot explain it, else would fibrillation occur in vagus stimulation.[1]

[1] Gross: *Archiv für die gesammte Physiologie* (1903), xcix, p. 264; Braun: *Ibid.* (1904), ciii, p. 476.