correct. This, however, as I[2] pointed out, does not preclude a selective mechanism of distribution of blood brought about by the anatomical arrangements of the heart. Vandervael[1], by the injection of indian ink in *Rana*, concluded that mixing of the blood from the two auricles was complete, and I[2] have said that the mixing of the indian ink was considerable; Savolin[3], working on *Bufo bufo*, also found that mixing was considerable, although there might be some selection whereby the carotid arteries received slightly less of the blood from the right auricle than did the systemic and pulmo-cutaneous arches.

The radiographic studies referred to by Simons and Michaelis have been undertaken mainly as an illustration of the results achieved by indian ink injections. It was hoped that perhaps the densities of the shadows might have allowed of some evaluation of the degree of mixing taking place, but this has not been possible. I have never claimed to have demonstrated complete mixing; however, I believe mixing to be considerable.

I believe that in Anura we see a group of animals which have become greatly modified in many respects, not least in regard to skin respiration. In correlation with skin respiration we see also a highly modified heart, for I think it likely that in early Amphibia the division of the heart into two sides was more complete than in modern members of the group. If this is so, we are seeing a loss of division in the heart, and, in fact, it is well known that more aquatic amphibians show great reduction of the spiral valve and fenestration of the inter-auricular septum (see Noble[4]). It is therefore to be expected that certain Anura have a more selective circulation than others, and it is probable that *Hyla cærulea* is one of these. What is new is the suggestion that this selective circulation can be switched on or off according to circumstances. I shall await further reports with interest, particularly those of the actual mechanism by which selection is accomplished.

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Pharmacology of the Alkaloids of *Aspidosperma oblongum* A.DC.

A preliminary pharmacological investigation of the total alkaloids of *Aspidosperma oblongum* A.DC. obtained by classical methods has been carried out. A 6 per cent solution of the hydrochlorides in an appropriate isotonic saline at *p*H 6·8 was used.

The solution caused relaxation and loss of tone when applied to the isolated ileum of the rabbit and rat. Peristalsis was inhibited in proportion to the dose given. The characteristic actions of acetyl-choline and barium chloride were antagonized. The antagonism to acetyl-choline bore a linear relationship to the dose given. The characteristic effects of histamine and acetyl-choline on the guinea pig ileum were antagonized, the antagonism bearing a linear relationship to the dose given.

The normal movements of the isolated uterus of the rabbit, guinea pig and rat were inhibited and the actions of acetyl-choline and barium chloride strongly antagonized.

Antagonism to the action of adrenaline on smooth muscle was demonstrated on the isolated rabbit uterus.

In the frog rectus abdominis muscle preparation, a linear relationship between dose of the alkaloids and extent of inhibition of the action of acetyl-choline was demonstrated. About one-tenth of the activity of curarine chloride was shown in this respect.

In the frog gastrocnemius sciatic nerve preparation, a curare-like neuro-muscular blocking action reversible by physostigmine was demonstrated.

When tested by Sollmann's frog plexus anæsthesia method[1] as modified by Bulbring and Wajda[2], a graded local anæsthetic action was shown.

In the isolated and *in situ* frog-heart preparations the rate and amplitude of the contractions were reduced by a small dose (0·06 mgm.). A larger dose (0·6 mgm.) caused irreversible stoppage. Prior atropinization did not modify these effects. Electrical stimulation of the vagus in the latter preparation did not produce its characteristic effects.

In Langendorff heart preparations of the cat, rabbit, guinea pig and rat, the alkaloids caused a reduction in rate and amplitude followed by a well-marked auriculo-ventricular block, unmodified by previous atropinization. The block was reversible.

In the rabbit and the rat electrocardiogram, doses which caused marked slowing of the heart were seen considerably to reduce the amplitude of the *P* wave, to invert the *QRS* wave and to prolong and increase the amplitude of the *T* wave. The *PT* interval was almost doubled.

Intravenous administration of small doses to nembutal-anæsthetized rabbits and cats lowered the blood pressure and slowed the heart.

Doses of 6–30 mgm. were injected into the ventral lymph sacs of frogs. Complete paralysis was exhibited within a few minutes. The higher dose caused death within thirty minutes; at lower dose-levels there was occasional recovery.

In mice and rats parenteral administration of sub-lethal doses of the alkaloids caused the animals to become quiet and their movements sluggish. The eyelids were closed and there was an appearance of drowsiness. The limbs were extended, the heart slow and irregular. Complete recovery took about two hours. Lethal doses caused slowing and irregularity of the heart followed by violent clonic convulsions. Convulsive episodes alternated with periods of exhaustion. Death was due to heart failure.

Our investigations point to the presence of a potent cardioactive substance which antagonizes acetyl-choline or is associated with substances having this property. Studies on the chemistry and pharmacology of this substance are in progress.

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