anastomosing branches were ligated lived only about 8 hours. If the lungs and most of the skin were excluded by tying the pulmocutaneous and anastomosing arteries, the frogs lived about 6 hours and if the mouth also were excluded by sewing this and the nostrils shut and tying the cutaneous arteries, they lived about 4½ hours. Control frogs kept at this temperature, showed no deviation from normal excepting slight over-excitability.

These results show with how little gas exchange frogs can live and also the large factor of safety with which their respiration is normally provided. Auer and Meltzer have recently shown that dogs could live with a supply of oxygen only one tenth of that which they normally consumed.

The results also show the great increase in the requisite gas exchange with rise of temperature and the inability of the skin respiration of the frog to support life at even moderately high temperatures, at which the lungs and mouth alone are still sufficient.

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Variations in the response of different arteries to blood serum and plasma.

By **HUGH A. STEWART** and **SAMUEL C. HARVEY.**

Recent work by Brodie, Sollmann, and O'Connor has shown that the blood contains substances acting on the vasomotor apparatus other than suprarenin. Even before the work of these investigators it had been noticed by Stevens and Lee that the use of defibrinated blood for the perfusion of isolated organs was often unsatisfactory because of the gradual diminution in outflow. This was not investigated thoroughly until 1900 by Brodie. He observed that the injection of blood serum into the jugular vein of a cat caused an immediate fall in blood pressure. The cat's own serum was as efficient in this respect as the serum of any other animal. The cat, however, is the only animal which responds in this manner, for Brodie's experiments were negative on the dog and rabbit. The mechanism in this case appears to be a reflex inhibition of the vasomotor center from excitation of the pulmonary branches of the vagus. The importance of Brodie's work lies in the fact that he was the first to show that plasma and

serum are not identical in their physiological activities, for, whereas the effect just described is produced by serum, plasma is entirely inactive. The process of clotting liberates some substance to which this action is to be attributed.

It was probably these experiments of Brodie which guided O'Connor in the analysis of the constrictor effect produced by blood serum on the hind limbs of the frog. He was able to show that the constriction produced by serum is not entirely due to its suprarenin content. Another substance comes into play which causes constriction and which is present only in the serum.

We have investigated the vasomotor effect of plasma and serum in different vessels of the body, especially in regard to their mode of action.

The methods we employed were the perfusion of the organ with Ringer's solution in a moist atmosphere at the temperature of the body and under a constant pressure. The outflow from the vein was recorded with a signal magnet writing on a smoked paper. Two c.c. of serum or hirudin plasma were injected close to the canula inserted in the artery.

Effect of serum.—The typical effect when injected into the vessels of the limb is to produce an immediate diminution in the rate of outflow. This usually lasts for from five to ten seconds, when it gradually begins to return to normal. The original rate of flow is regained in about five minutes.

A similar result is obtained when the heart is perfused.

Entirely different is the effect which is produced when 2 c.c. of serum are injected into the vessels of the perfused kidney. Instead of a vasoconstriction there is produced a pronounced vasodilatation.

We have first to determine whether the dilatory effect on the kidney and the constrictor effect on the limb vessels are due to the same substance. It can readily be shown that two substances are operating. If the serum is boiled and filtered through a Berkfeldt filter and injected we now get no dilatation of the kidney vessels, but instead a constriction.

As before, the effect of boiled serum is to produce a constriction of the limb vessels.

Precipitation of the protein constituents of serum by alcohol

and the injection of the dried filtrate dissolved in Ringer's solution retains the constrictor substance, but it contains no vasodilator for the kidney vessels.

We are, therefore, led to the conclusion that serum contains a constrictor substance which acts on the limb vessels, the kidney vessels and the coronaries. In addition there is also present a dilator substance acting specifically on the renal vessels. The dilator substance is a proteid, the constrictor substance is not. The perfused kidney after the injection of serum is subject to the action of both a dilator and a constrictor substance. The dilator is the more powerful and masks the action of the constrictor. The constrictor substance becomes manifest after removal of the dilator by boiling or by precipitation by alcohol.

Is the constrictor substance described above the suprarenin quotient of serum? Suprarenin, as is well known, causes constriction by stimulation of the sympathetic nerve fibers. If we add apocodeine hydrochloride to the perfusion fluid we can paralyze the sympathetics and in this way render the preparation insensitive to the strongest solutions of suprarenin. If, however, we inject serum there is still produced almost as great a diminution in the rate of outflow as before. We have thus evidenced that the constrictor substance is not suprarenin, and further, that it is a body which acts directly on the muscle coats.

In regard to the dilator substance acting on the kidney we have found that it still causes an increased outflow after the injection of serum when the perfusion fluid contains apocodeine.

Effect of plasma.—Plasma differs markedly in its action. If hirudin plasma is injected into the vessels of the limb it produces a much less constriction than does the corresponding amount of serum. This result is dependent only upon the amount of suprarenin it contains, for when the sympathetics are paralyzed the injection of serum produces no change in the rate of outflow.

On the kidney vessels, however, plasma produces an even greater dilatation than does serum.

The conclusions which we have been able to draw from these experiments are as follows.

1. That in both plasma and serum there is present a substance which causes dilatation of the renal vessels. This substance is a proteid.

2. That the process of clotting liberates a vasoconstrictor substance which acts on the coronaries, the renal vessels and the limb vessels. It acts directly on the muscle coat and it is not a proteid body.

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General physiological properties of diaphragm muscle.

By **FREDERIC S. LEE** and **A. E. GUENTHER.**

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Strips of the diaphragm of the cat, both curarized and non-curarized, have been excised after death and experimented with in moist chambers at room temperature. Their great resistance is demonstrated by the facts that they remain irritable two to three times longer than, and do several times the amount of work done by, a leg muscle, such as the extensor longus digitorum. Moreover, the diaphragm is not paralyzed by curare until long after the leg muscles have ceased to act. A most striking phenomenon is the tendency of the diaphragm strips to yield rhythmic twitches. This is much more pronounced than with the control leg muscles. It may be made manifest by the action of solutions of certain electrolytes, where the twitches are irregular in extent and duration; and by weak faradic currents, which insure more regular responses. With 40 to 100 faradic stimuli in the second, the twitches occur at a rate of from 2 to 4. They are much more marked in non-curarized muscle. When irregularities due to the stimulated current are excluded, the following factors may possibly interact in the production of the rhythmic responses: (1) There may be present the Wedenski effect; (2) the weak stimulus may affect from time to time different groups of fibers within the muscle, the irritability of the groups varying; (3) polarizing factors may be present. The relations of these and other possible factors are not yet established. A strip of diaphragm muscle as a whole has a decided power of rhythmical response, but it is not yet certain whether this power is possessed by the individual muscle fibers.