LUNG-HEART REFLEXES IN AMPHIBIA

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It is known that in sick persons the heart may sometimes stop when an anesthetic is first administered (when the stomach tube, laryngoscope or intratracheal tube is introduced, or when the patient inhales the vapors of the anesthetic, etc.). The effect is attributed to reflex action from the upper respiratory pathways on the heart [16, 18]. There are numerous experimental and clinical reports on reflex influences arising in the lungs and affecting various organs and systems [2-6, 10-13, 15, 17, 19].

In a study of the action of various anesthetics exerted on the heart via the lungs [1, 7, 8] an unusual action on the heart was found to be exerted by the vapors of ether and chloroform. The effect was that when air containing a high concentration of anesthetic was introduced under pressure into the lungs of a frog heart-lung preparation, the heart stopped immediately, at the first inspiration.

In our experiments air containing a constant concentration of the substances to be investigated was introduced into the lungs of a heart-lung preparation; with the anesthetic concentration used, to stop the heart, not less than 5-10 inspirations were required. The change in the work of the heart was greater the more inspirations of the anesthetic mixture were made.

In the kymogram shown in Fig. 1a, the action of the vapors of ether on the heart of the heart-lung preparation can be seen.

In many experiments we increased the anesthetic concentration 2-3 times, and in some cases we found the heart stopped in diastole at the moment the anesthetic entered the lungs (Fig. 1b). The arrest might be due either to the rapid penetration of the saturated vapors of anesthetic through the pulmonary membrane into the blood, or to the stimulating influence of the anesthetic on a pulmonary receptor apparatus connected reflexly along nerve fibers contained in the vessels of the lesser circulation and ending on the heart. In the latter case we would infer the presence of a viscero-visceral (lung-heart) reflex. Note that the effect was not consistent, but occurred only with very careful setting up of the heart-lung preparation: when ligature of the inferior vena cava (damage to the sinu-auricular node may occur) did not affect the heartbeat; when the vessels on the lung pulsated distinctly during removal of the preparation from the thorax; and when the pulmonary veins were not damaged. Some authors [19] have insisted that this care in the preparation is necessary also in order to demonstrate the lung-heart reflexes.

It is important to note that in cases when ether or chloroform vapor in the usual concentration has been passed through the lung of a heart-lung preparation and then, when the heart recovered, a single inspiration of a high concentration of anesthetic was given, no cardiac arrest occurred. Probably the effect of the low concentrations was to bring about adaptation of the nervous apparatus, so that subsequent actions of the vapors did not cause the expected cardiac arrest. We observed a similar phenomenon previously [1] when studying the action of chloroform, formalin, or ether vapor in the so-called heart-lung-brain preparation. V. V. Parin [6] also observed that the blood pressure in the carotid artery fell less when the receptor zones of the pulmonary arteries were stimulated repeatedly.

In order to study the effect described we replaced the heart in a heart-lung preparation by another heart taken from a second frog. By this method, which was worked out by N. P. Sinitsyn [8], we at first transplanted the heart completely, and then prepared from it a heart-lung preparation.* This method ensured that there was no possible

* The method of setting up a heart-lung preparation and its use has been described previously [1, 7].

nervous connection between the lungs and the heart, and that humoral transmission alone remained. We carried out 18 experiments by this method.

After ether vapor had been passed through the lungs of a preparation made by the method described, cardiac activity was suppressed almost to the same extent as in a normal heart-lung preparation (from the heart of the same frog). The difference was that at the start the reduction of the contraction was somewhat delayed, and the general effect of the drug upon it was therefore somewhat smoothed over. When the concentration of ether was increased 2 or 3 times and passed through the lungs of the preparation with the transplanted heart, in none of the 18 experiments did cardiac arrest occur. There was a change only in the heartbeat (a reduction either of the rate or the amplitude of the contractions). But the effect could have been caused by a change of the diffusive capacity of the pulmonary membrane with a reduction in the permeability of the alveolo-capillary complex, a change related to the operation of transplanting the heart (insufficient concentration of ether in the lesser circulation), or to damage of the conducting system of the heart caused by transplantation.

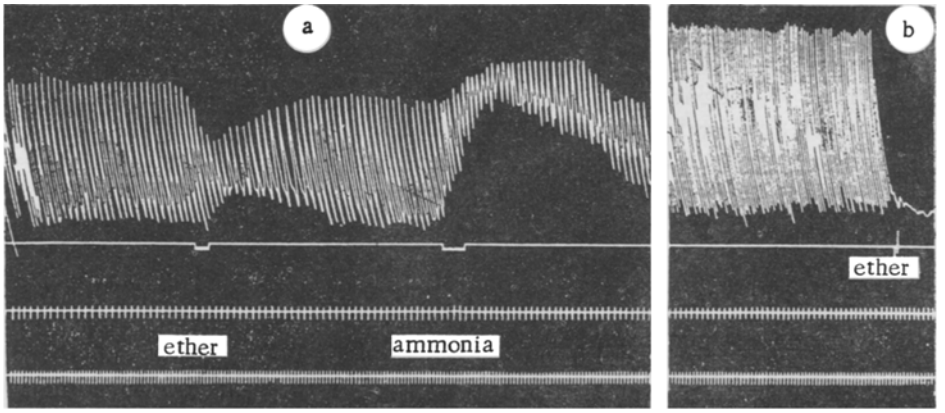

Fig. 1. Kymogram showing cardiac contractions in a frog heart-lung preparation. a) 3 Inspirations of ether vapor (normal concentration), followed by 5 inspirations of ammonia; b) single inspiration of ether vapor (increased concentration). Curves, going downwards: cardiac contraction; marker indicating introduction of vapors into the lungs; respiration frequency; time marker (2 seconds).

In order to exclude these possible causes, we passed ammonia vapor through the lungs of the heart-lung preparation incorporating a transplanted heart, at the moment when it had just "breathed" ether. The effect was to produce a rapid and marked cardiac reaction (Fig. 2). Precisely the same effect of ammonia was observed in experiments with the normal heart-lung preparation (see Fig. 1a). Evidently there was no disturbance of either the functional capacity of the transplanted heart or of the pulmonary membrane, and the diffusive capacity was completely preserved; the small reaction of the heart to massive doses of ether appeared to result from the absence of nervous connections between lung and heart.

In control experiments made on an intact frog in which artificial respiration was maintained, we produced no cardiac arrest of the type observed in response to a single "inspiration" of massive concentrations of ether vapor by the preparation (Fig. 3). In these experiments we observed only a gradual increase in the suppression of cardiac contractions proportional to the number of "inspirations" of anesthetic vapor, and subsequently the contractions returned to normal (after inhalation had ceased).

We also carried out a number of experiments on a heart-lung preparation in which the nervous connections with the brain had been preserved. De Burgh Daly et al. [14] used a similar preparation for a warm-blooded animal (the dog). For our heart-lung-brain preparation we used the frog [1].

Passage of ether or chloroform vapor through the lungs of this preparation caused a cardiac response similar to the one observed in the intact frog, and quite different from what we observed in the heart-lung preparation. A single lungful of air saturated with ether or chloroform vapor did not cause cardiac arrest. However, destruction of the brain, which caused a transformation into the usual heart-lung preparation, almost always produced the desired effect, i.e., the heart stopped in diastole.

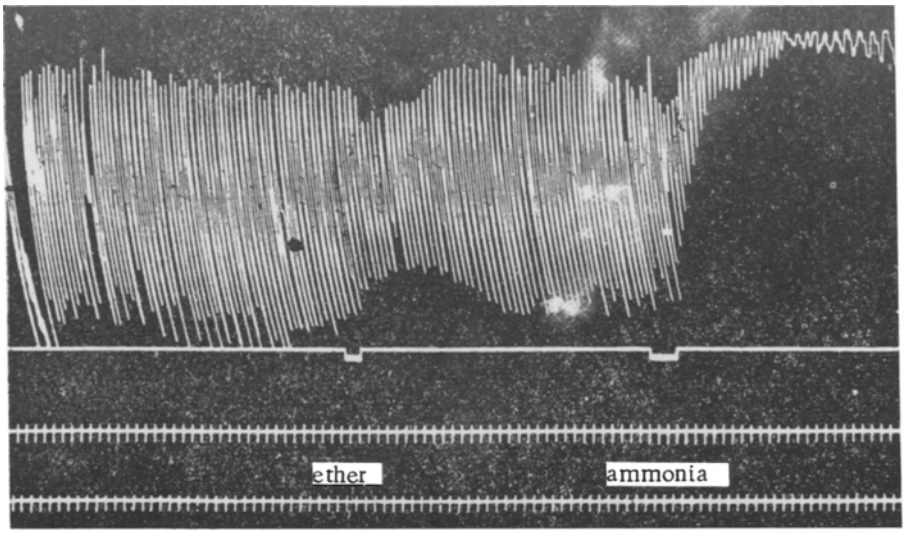

Fig. 2. Kymogram showing cardiac contractions in a heart-lung preparation incorporating a transplanted heart: 2 inspirations of ether vapor (increased concentration), then 4 inspirations of ammonia. Curves as in Fig. 1. (Time marker 3 seconds).

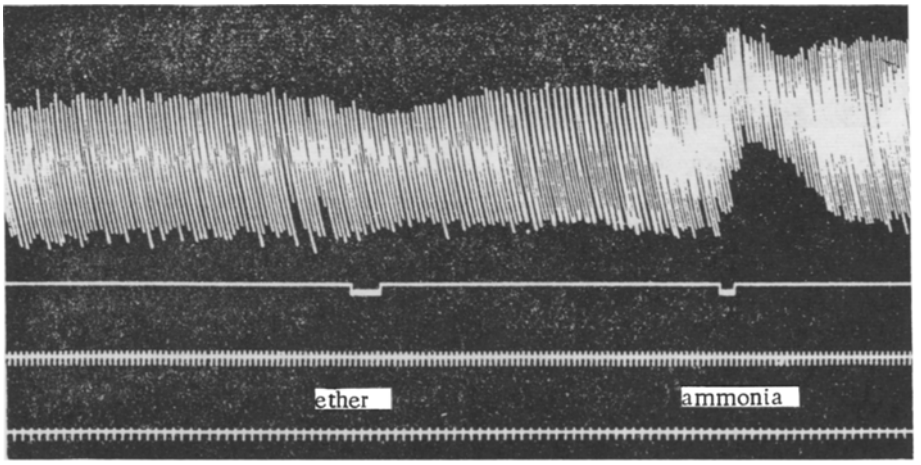

Fig. 3. Kymogram of cardiac contractions from an intact frog: 5 inspirations of ether vapor (increased concentration), then 3 breaths of ammonia. Curves as in Fig. 1.

There is therefore every reason to suppose that when high concentrations of anesthetics enter the lung the arrest of the heart in a frog heart-lung preparation is a reflex event induced by strong stimulation of the pulmonary receptor apparatus by the anesthetic. The absence of any such effect in the intact organism must be attributed to the function of the central nervous system.

SUMMARY

Cardiac arrest in diastole occurs immediately after once filling the lungs of a frog-heart lung preparation with a high concentration of ether or chloroform vapor. When the heart of such a preparation is replaced by one from another frog, no such effect is observed, and only the rate and amplitude of the heart contractions are changed. Cardiac arrest doesn't occur (a) if the nervous connections between the heart-lung preparation and the CNS are preserved (so-called heart-lung-brain preparation), or if intact or spinal animals are used or (b) if the anesthetics

are applied repeatedly to the preparation. Evidently cardiac arrest in the first case must be regarded as resulting from an interoceptive lung-heart reflex. The failure of this action to occur in an intact animal must be due to a central nervous action.

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