

time we could keep them alive. We show here the lungs of one of these dogs. Death occurred in this instance about four hours after the injection. The quantity of the injected pneumococcus culture was quite large—about twenty cubic centimeters. About two thirds of the right lower lobe is consolidated; as you see, it is very dark and firm, and the surface shows numerous small patches of fibrin.

19 (715)

Differences in the toxic effects of ether and chloroform, as observed under intratracheal insufflation.

By **T. S. GITHENS** and **S. J. MELTZER**.

[From the Department of Physiology and Pharmacology of the Rockefeller Institute.]

In studying the toxic effects of chloroform and ether, when administered by the method of intratracheal insufflation, we observed various differences in the course of the intoxication brought on by excessive doses of these anesthetics. We shall discuss here, however, only the differences in the toxic action of these drugs upon the functions of respiration and blood pressure. At the outset we have to point out, that when administering the anesthetics by the insufflation method one of their dangerous effects is here eliminated; it is the danger which is bound to result from a partial or complete paralysis of the respiratory function. Under the method of insufflation, life remains safe even when the animal is completely curarized. Observations may be carried on, therefore, even after spontaneous respiration is completely abolished. On the other hand, intratracheal insufflation carried on with ordinary, permissible air pressure, does not cause apnea, that is, the individual continues to carry on its own spontaneous respirations, which on tracings are easily distinguishable from the infrequent partial interruptions of the continuous insufflation of air.

The observations which we wish to report here briefly are as follows. When using ether, a certain dose may be administered which is amply sufficient to keep the animal completely anesthetized, while respiration and blood pressure may remain practically

unimpaired for several hours. When this anesthetic dose is exceeded, the first striking effect is upon the spontaneous respiration which may be rapidly abolished. For instance, if complete anesthesia has been accomplished by a dose which we term " $\frac{1}{2}$ ether" or " $\frac{3}{4}$ ether" and now "full ether" is turned on, the respiration may stop completely within one to five minutes. At this stage blood pressure is not impaired. When, however, "full ether" is continued the blood pressure begins to come down. The descent is very gradual and slow. It is rarely less than one hour, in some cases it may be even several hours, before the pressure reaches the dangerous stage. At that stage the blood pressure may not be above 20 or 25 millimeters of mercury, and the pulse pressure also considerably reduced. However, even at this stage when the ether is turned off, the pressure may begin to rise at once; although some time has to pass before the respiration returns, and there is still another interval before reflexes and consciousness return. The duration of the returning ascent is shorter than the duration of the descent. It is, however, not absolutely necessary to shut off the ether completely; a reduction to "half ether" is, as a rule, soon followed by a return to a degree of blood pressure which is sufficient to obviate danger.

The ready abolition of the respiration by ether is a practically important phenomenon; it may serve as an indication that the etherization has entered the toxic zone. It is a danger signal, and since hours may pass before the real danger will be arrived at, it is a safe and very valuable signal.

It is different with chloroform. In doses which are undoubtedly in excess of the anesthetic dose, respiration and blood pressure go down practically together, and this in a comparatively short time. When the administered dose is only slightly in excess of the reliably anesthetic dose, the impairment of respiration does not set in as early as under ether intoxication; but when this sets in, blood pressure begins to fall also, although the respiration may in some cases cease fifteen or twenty minutes before the fall of blood pressure reaches the danger point. Respiration, perhaps, resists chloroform intoxication slightly longer than that of ether, while blood pressure is affected much more rapidly and profoundly by chloroform than by ether. The zone separating the safe

anesthetic and danger lines is narrow, and there is no reliable danger sign.

20 (716)

The relation of leucocytic extract to body fluids.

By **WILFRED H. MANWARING.**

[From the Laboratories of the Rockefeller Institute for Medical Research.]

In a previous communication¹ it was shown that a comparatively strong bactericidal substance can be extracted from horse leucocytes. This substance loses its bactericidal power, in whole or in part, if it is mixed with homologous or foreign sera, with pathological exudates, with cerebro-spinal fluid, with the products of aseptic tissue autolysis, or with most of the products obtained by the bacterial decomposition of tissues. It also loses its bactericidal power if it is mixed with the products obtained by the prolonged autolysis of leucocytes themselves.

With sera that are in themselves bactericidal, not only is there a loss of the bactericidal power of the leucocytic extract in such mixtures, but there is also a destruction or inhibition of the bactericidal power of the serum itself. This gives the phenomenon of two bactericidal substances, an active serum and an active leucocytic extract, added to each other, producing a non-bactericidal substance, a good culture medium for bacteria.

An analysis of the antibactericidal action of serum shows that it is due to the combined effects of three factors: (1) the antibactericidal power of the serum colloids, (2) the antibactericidal power of sodium chloride and the other neutral diffusible serum components, and (3) the antibactericidal action of the diffusible serum alkalies.

Alkalies are very strongly antagonistic to the leucocytic bacteriolysin. The addition of 1/200 per cent. NaOH to leucocytic extract is usually sufficient to completely inhibit its bactericidal action. Acids, on the other hand, apparently have little or no antibactericidal effect.

This antibactericidal power of serum and tissue fluids can not be overcome by increasing the amount of leucocytic extract in the

¹ These PROCEEDINGS, Vol. IX, 1912, p. 74.