

citrate. It should be particularly noted that the ratio between calcium and citrate is approximately the same as that observed in the previous experiments on coagulation of oleate, toxicity to mice and interference with complement hemolysis, a fact which lends further support to the theory that the liberation of thrombin is associated with a disturbance in the colloidal equilibrium of fatty substances present in the cell membrane.

These experiments prove, furthermore, that the membrane contains substances other than fats and lipoids and, in the absence of the latter, is apparently uninfluenced by the addition of an excess of calcium to the system. In the light of these experiments, it should be possible to greatly simplify the existing theories regarding blood coagulation and to reduce the whole question to one of the liberation of thrombin as a result of a disturbance in the colloidal equilibrium of the platelet membrane under the influence of electrolytes and the subsequent precipitation of fibrinogen by adsorption of thrombin.

#### 4 (821)

#### **On analogous effects exerted by anesthetics in physical and biological systems.**

By G. H. A. CLOWES.

[From the Biological Chemical Department of the State Institute for the Study of Malignant Diseases, Buffalo, N. Y.]

Lillie has recently demonstrated that anesthetics used in certain concentrations are capable of functioning in a manner similar to calcium salts, protecting *Arenicola* larvæ from the destructive effect of pure salt solutions. Since calcium, on the one hand, and anesthetics, on the other, are capable of rendering a concentration film of fatty acid salts or lipoids relatively more soluble in oil and less soluble in water, it appeared possible that the agents in question protect the cell protoplasm by counteracting the destructive effect of negative ions on similar surface films formed between an external lipid phase of protoplasm, and adjacent aqueous phases. If this theory were correct it should be possible to counteract the effect of negative ions in purely physical

systems by means of anesthetics and to obtain curves corresponding with those observed by Lillie on *Arenicola* larvæ.

To test this question an aqueous solution of NaOH of suitable concentration was delivered from a Traube stalagmometer into olive oil with and without the addition of various anesthetics at varying concentrations. The number of drops formed from a given volume of solution served as an index of the extent to which the anesthetic inhibited or promoted the destructive effect of the OH ions on the film of fatty acid salts formed at points of contact between water and oil. In all cases the curve obtained showed with increasing proportions of anesthetics, first a fall in the number of drops, and subsequently a rise, the number of drops finally exceeding that of the system employed. The fall in the number of drops indicating protection of the membrane reached a maximum with each anesthetic at approximately that concentration at which Lillie observed a maximum protective effect for *Arenicola* larvæ. Furthermore on increasing the proportion of anesthetic above this optimum, the number of drops increased and finally passed the normal at approximately that point at which Lillie found no further protective effect for larvæ. The curve indicating the effect of MgCl<sub>2</sub> corresponded almost exactly with that of an organic anesthetic, but CaCl<sub>2</sub>, instead of exhibiting an optimum, was found to counteract the destructive effect of OH ions not only at low but also at high concentrations, and also to exert a protective effect against Mg and organic anesthetics used at high concentrations. The accompanying diagram illustrates the effect of propyl alcohol on this purely physical system, and on *Arenicola* larvæ.<sup>1</sup>

C <sub>3</sub> H <sub>7</sub> OH.	Drops.	Larvæ.
nil . . . . .	52	Killed.
2½ per cent. . . . .	18	Uninjured.
10 per cent. . . . .	76	Killed.

As a further confirmation of this point, it was found that propyl alcohol added in suitable proportions to a solution of *n*/10 NaOH would protect mice from a lethal dose of this substance injected intravenously, and furthermore that it was possible to protect to a certain extent corpuscles suspended in salt solution from the destructive effect of negative ions by the addition of optimum

<sup>1</sup> See Lillie, *Am. J. of Physiology*, 1913, 31, p. 255.

proportions of certain anesthetics. The close relation between curves obtained in purely physical systems and those observed by Lillie on *Arenicola* larvæ suggests the probability that anesthetics exert their effect on the cells by increasing the solubility in a fatty or lipid phase and decreasing the solubility in the water phase of the film formed by contact between the fatty or lipid phase and adjacent internal and external aqueous phases. If protoplasm be considered for the moment as an aqueous lipid system in which the lipid phase is continuous or external (a by no means impossible contingency in view of the preparation of emulsions containing 99 per cent. or more of the dispersed phase), and the water phase internal, it will easily be seen that anesthetics functioning in the manner indicated above would tend to promote the continuity of the external lipid phase, protecting it from the destructive effect of negative ions present in the adjacent aqueous phases. In the absence of protective kations or anesthetics, negative ions adsorbed on this film or membrane would presumably induce a series of spherical curvatures with consequent contraction in length. Ultimately the film in question would be broken up into globules which would now constitute the dispersed phase. The original interior aqueous phases by uniting with the exterior aqueous medium would afford a continuous aqueous phase which would permit of the ready diffusion of any water-soluble substances originally present in the interior aqueous phase. Lillie particularly notes that *Arenicola* larvæ show violent muscular contractions, separation of fatty globules and the diffusion of water-soluble pigments into the surrounding water when subjected to the influence of pure salt solution. These effects are entirely inhibited when suitable proportions of calcium salts or anesthetics are employed.

From the above considerations it appears possible that protoplasm is an aqueous fatty system, and that anesthetics function by promoting the continuity of an external fatty or lipid phase. The solubility of this lipid film in adjacent aqueous phases being lowered, its permeability to water-soluble substances would be diminished. Since certain vital processes presumably depend upon intermittent intercommunication between adjacent aqueous phases, it may well be imagined that a temporary interruption in this communication would result in anesthesia.