XVII. "On Organic Substances artificially formed from Albumen." By Alfred H. Smee, F.C.S. Communicated by Alfred Smee, Esq., F.R.S. Received May 27, 1864.

In a former paper which I had the honour to submit to the Royal Society, I showed that fibrin was formed by the passage of oxygen through albumen, provided a temperature of 98° F. was maintained. It was then observed that a slightly acid state of the albumen, or the absence of the alkaline salts was found to be most favourable to its formation. I noticed also that ammonia had little effect in preventing the formation of fibrin, but after the lapse of a short time caused it to swell to such a degree that its microscopic characters could no longer be determined. It was observed that albumen acted on by gastric juice and passed through a membrane, still had the capacity to form fibrin in small amount.

Since the publication of that paper, I have conducted the following experiments in addition to those before mentioned. I submitted some of the fluid drawn off from a spina bifida to the action of oxygen and heat in the ordinary manner; after the lapse of a few hours it yielded a substance which, under the microscope, presented all the characters of fibrin.

I tried to obtain fibrin from the urine in two cases in which it was highly albuminous. The urine was so loaded with albumen that it became almost solid by heat. I never have been able to transform this variety of albumen into fibrin, although the experiment was tried in many ways. I expect that on further investigation it will be found that the albumen found in urine (in most cases at least) is a substance not capable of further development.

The next experiment which I have to describe is to my mind one of the most beautiful exemplifications of the artificial formation of organic bodies under physical laws, producing results similar to those which we observe under certain circumstances in disease, the changes being produced by the action of a gas on a second body separated by a membrane, and having to traverse it before the chemical changes can be effected.

I passed a current of oxygen gas through a small portion of perfectly clean intestine, with the peritoneal coat attached. The intestine was placed in an albuminous fluid at a temperature of 98° F.; at the end of twenty-four hours I found the intestine completely invested with minute fibrinous outgrowths, similar to those seen on the intestines of persons who have died at the earliest stage of peritonitis.

It is worth noticing that although these fibrinous outgrowths take place when the peritoneum of the intestine remains, yet if this coat be stripped off they take place to a very limited extent. In many cases no outgrowths appear, even where the conditions of the experiments are equal.

It appears to me that the tendency of fibrin to be deposited on serous membranes, under favourable circumstances, may throw some light on the

frequency with which we find the surfaces of serous membranes (for instance, the pericardium) so often coated with fibrinous outgrowths.

If hydrogen is passed through albumen to which a small quantity of potash has been added sufficient to ensure a slight excess of alkali, after the lapse of some time a dense hard horny mass will be observed, especially at the point where the hydrogen comes into contact with the albumen; in fact the growth of the substance often clogs the tube to such a degree that the hydrogen is prevented from further passing through it. It also has a tendency to grow upon platinized platinum when placed in the albuminous fluid whilst the current of hydrogen is passing. The time required is, as a rule, about four days; a temperature of 98° F. rather favours its formation, but is not absolutely necessary to its production.

The following are the chief chemical and physical reactions of the substance formed by hydrogen.

It is heavier than albumen, always sinking to the bottom of the vessels. It is hard, tough, semitransparent, homogeneous, and slightly elastic. It swells up in cold water, and dissolves to a limited extent. The extent of its solubility is less the longer the time occupied for its formation. It is more soluble in hot water. Peroxide of hydrogen is not decomposed by it.

The watery solution is not coagulated by boiling; it is, however, precipitated by chlorine. Hydrochloric acid does not form a blue solution with excess of that reagent. Bichloride of mercury and bichloride of platinum, after the lapse of some time, precipitate it. Tannic acid, alcohol, acetate of lead, sulphate of the peroxide of iron, and alum also precipitate it from its solution. It is turned yellow by nitric acid and heat. It likewise contains a small quantity of sulphur. Chondrin behaves in a similar manner, in its chemical and physical relations, to the substance thus artificially produced, and hence I propose to call it "artificial chondrin."

In carrying out these experiments, I found that a very nice method of obtaining a constant and equal amount of hydrogen gas was by collecting hydrogen formed at the negative pole of a one-cell battery, and passing the hydrogen thus formed directly into the albumen. The amount of hydrogen required was regulated by increasing or diminishing the size of the negative pole.

This form of apparatus will constantly remain a week or more in action without any appreciable alteration in the quantity of hydrogen evolved.

It may be well to describe the construction of the apparatus used. I first take a common precipitating glass, and place in it a few pieces of zinc with a little mercury to amalgamate it. I then take a tube about $\frac{1}{4}$ inch in diameter, and bent in two places at a right angle; into one end I insert a platinum wire, this end I place in the glass containing the zinc; the other end I place in the vessel containing the albuminous fluid. Dilute sulphuric acid is then added to the zinc. When contact takes place between the platinum wire and the zinc, a constant stream of hydrogen is given off from the platinum wire. The amount of hydrogen required can be regulated by

making a larger or smaller surface of the platinum come in contact with the zinc. The amount of oxygen which is carried over is very limited, provided a tube is used of $\frac{1}{4}$ inch diameter; but when a tube of $1\frac{1}{4}$ inch is used, a quantity might pass sufficient to interfere with the experiment.

The amount of oxygen at times thus carried over when the large tube is used is so great, that a change in the products may take place and fibrin may be formed in the place of the chondrin, provided the albumen is not over alkaline.

As fibrin was formed by oxygen, and this new substance analogous to chondrin by hydrogen, it occurred to me that these two substances might be formed simultaneously by a simple-cell voltaic arrangement. For this purpose I took a tube with one end closed by parchment paper, or sometimes by animal membrane, filled it with albumen which had been made slightly acid by acetic acid, and inserted it into a small vessel containing albumen to which a small quantity of potash or soda had been added. I then connected the two fluids by means of a platinum wire, so that one side might become a positive and the other a negative pole. Considerable action took place after the lapse of some time, when upon examination I found the albumen in the tube was changed, not into the fibrillated fibrin, but into a granular material. The other pole, or rather the the alkaline albumen, was changed into a substance which behaved with various reagents in different ways. In some cases it was a tough, ropy and viscid substance, which was coagulated in water by a solution of acetate of lead, was insoluble in acids and in alcohol, and very slightly soluble in alkali. At other times I have noticed a substance formed having very much the appearance of the expectoration of bronchitis; and at other times the dense hard substance analogous to chondrin in its behaviour with reagents was formed.

The various states of the material into which albumen is converted appear to be influenced by the nature of the alkali employed and by the relative size of the negative pole. The temperature should be as nearly as possible constant during the time the experiment is being conducted. The amount of the surface of membrane interposed appears to have very little influence over the products. When soda was the alkali employed, the viscid and frothy mucus-like product was more frequently obtained.

The amount of water present appears to have a very decided influence on the product formed. When the viscid and frothy material is produced, it appears to form quicker than the hard and dense chondrin. The temperature of 98° F. appears to favour the production of the chondrinous material; but I must admit I have sometimes made all the varieties, the viscid, the frothy, and also the chondrin, at much lower temperatures.

In one case I succeeded after many experiments in obtaining from the acid pole, by keeping it at a temperature of 98° F., fibrin of the fibrillated form, but the greater portion of the albumen at this pole was converted into the granular form. The alkaline pole formed pretty constantly the dense hard artificial chondrin.

When hydrogen was passed through serum, after the lapse of a day or two a tough elastic product was obtained.

In experiments tried by passing hydrogen through albumen greatly diluted with water, I found, after the lapse of a few days, a flocculent deposit very similar in appearance to the deposit of mucus which often takes place when urine is allowed to stand a short time. This point, however, requires further investigation. I tried also the effect of passing hydrogen through a portion of intestine inserted into an albuminous fluid. I have not as yet been able to form either the dense hard or viscid frothy substance by this method. I repeated the experiment for the formation of fibrin from albumen, by decomposing the water of its composition by electricity. I must admit this is the most difficult, troublesome, and unsatisfactory of all the methods I have employed. I find that the great tendency of the poles to form different substances on them, and the great rapidity with which they grow together, lead, without the greatest care, to the belief that two different substances, differing only in density, are formed at one and the same pole, so intimately blended are they together. Thus I was led to believe at first sight that a dense hard substance was formed at the oxygen end, and not until I had repeated the experiment many times did I discover that the substance belonged to the hydrogen and not to the oxygen pole, and had grown across from one pole to the other.

I have obtained on several occasions fibrin and chondrin at the same time by conducting hydrogen and oxygen derived by the decomposition of water by voltaic electricity through separate tubes. The oxygen passed into slightly acid albumen formed fibrin; the hydrogen passed into alkaline albumen formed either the chondrin or else the frothy and viscid material. The temperature was kept up at 98° F. in these experiments. On one occasion, however, I happened accidentally to reverse the current (that is to say, the hydrogen was passed into the acid, and the oxygen into the alkaline albumen), when no chondrin or fibrin was formed.

The following conclusions I have arrived at after the study of the influence which oxygen and hydrogen gases exert upon albumen when submitted to their action separately at a temperature of 98° F., the normal temperature of the living body. Albumen under the action of oxygen forms, after the lapse of a longer or shorter period, fibrin. The fibrin thus artificially produced is of three distinct varieties, viz., 1st, the granular form; 2nd, a form allied to lymph incapable of being unravelled into fibrils; lastly, the true fibrillated fibrin. The law which appears to regulate the state into which the albumen is converted, as far as my observation has gone, is one of molecular aggregation, similar to the electric deposit of metals, as the slower the fibrin is formed the more organized is it in substance.

I have observed that when fibrin is rapidly formed it is almost always produced in the granular state; this is particularly the case with fibrin

formed from albumen by the decomposition of the water of its composition by voltaic means.

Lymph I consider to be imperfectly formed fibrin more highly developed than the preceding or granular form. It is possible for this artificially formed lymph, under favourable circumstances, to assume a more organized appearance.

I have no doubt that the fibrinous outgrowths on the intestine would have become larger and more developed if the experiment had been carried on for a sufficient length of time. In fact almost all the fibrin formed round a platinum wire inserted into albumen is at first covered by outgrowths of a soft structure. These outgrowths, at the earliest period of their formation, do not under the microscope present any appearance of fibrils. After the lapse of some time they appear to undergo condensation, and then to organize to such an extent that it would be difficult at first sight to determine whether the substance might not be a portion of fibrous tissue.

The alkalies, with the exception of ammonia, prevent entirely the formation of fibrin. Ammonia, although it does not retard its formation, dissolves it after the lapse of a short time. The acids and absence of alkaline salts favour its formation. The opposite, however, is the case with the hydrogen products, as an alkaline state favours their production.

The action of hydrogen on albumen, as far as my investigations have as yet proceeded, forms substances analogous to chondrin and mucin. I believe that the organic substances, chondrin and mucin, products formed in a living organism, are very closely allied to one another, if not varieties of the same substance, differing only in their mode of aggregation and stages of development, and the amount of water in their composition.

Of the exact mode in which hydrogen acts on albumen we are at present ignorant. I have noticed that in some experiments sometimes one, sometimes the other product was obtained, even when the same influences were apparently acting on experiments conducted at the same time.

Considering the important physiological part that fibrin, chondrin, and mucin play in the living body, the production artificially of substances analogous in their behaviour with reagents to those products formed in a living organism will, I trust, be taken as a sufficient excuse for submitting to the Royal Society a paper so obviously deficient in many parts, but which, nevertheless, it would require a vast amount of both time and labour to carry one step further.