THIRD CONTRIBUTION TO THE LIFE-HISTORY OF CONTAGIUM.

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THIS Third Contribution to the Life-History of Contagium, the issue of which has, from various causes, been delayed from time to time, is presented in a less complete form than was originally intended. The recorded investigations extended over a period of four years; but they were several times suspended for months together, owing to the pressure of other work or the increasing demands of private practice. As regards the subjects, they were not precisely those primarily selected by us, but such as we had an opportunity of dealing with whenever we found leisure for inquiry. Thus, an abortive attempt was made to investigate the nature and mode of propagation of the contagium of scarlatina; but, after a few experiments, yielding merely negative results, the local epidemic died out, and the inquiry had to be abandoned. Next, a study of the pathology of swine-typhoid was begun; but, after a large number of *post mortem* examinations had been made and drawings executed, an important portion of the material collected was lost on a railway journey, and the lost portion will have to be made good before the remainder can be utilised.

The reports we are in a position to submit are three; viz.:

I. A record of experiments with vaccine lymph exposed to certain gases and vapours. This is an appendix to our previous experiments with vaccine lymph exposed to ozone and certain chemicals.

II. Notes on an inquiry into the morphology of the contagium of measles, its mode of reproduction, and its distribution in the tissues of the infected subject.

III. An account of an experimental research into the nature of induced septicæmia, and of a disease which presents some gross points of resemblance to it.

I.—A RECORD OF EXPERIMENTS WITH VACCINE LYMPH EXPOSED TO CERTAIN GASES AND VAPOURS.

We have already recorded, in our first and second reports, the particulars and results of our experiments with vaccine lymph subjected to the influence of ozone, quinine, salicylic acid and boracic acid, and the ordinary household disinfectants; that is to say, carbolic acid, sulphurous acid, chlorine, chloride of aluminium, liquor potassæ permananatis, and Dr. Bond's disinfectants, cupralum, ferralum, and terebene. The experiments to which we have now to refer may be considered as supplemental to those previously reported; but they differ from them in this respect, that they have for their object the testing of the effects on lymph of certain gases and vapours not usually termed disinfectants, or used as therapeutical agents in the treatment of zymotic diseases.

In the first place, the undoubted power of ozone to impair, and, if maintained long in contact, to destroy, the activity of lymph, suggested to us that oxygen might exert a similar influence; and we accordingly resolved to make an extended trial of lymph modified by being submerged in oxygen for varying periods of time. In ozonising vaccine, we had exposed it in a watch-glass to a stream of ozone generated by electricity, or in a closed vessel containing oxidising phosphorus; but how to introduce vaccine into a vessel containing oxygen was a far more difficult problem, and we were at some pains to arrange an apparatus for effecting the required exposure. An ordinary glass bell-receiver, fitted with a chambered stopper, was provided, and the chamber was carefully lined with cork. Into this lining were stuck three ivory points just charged with fresh lymph, and a piece of glass on the surface of which three tubefuls of fresh lymph were blown. The receiver was then immersed in a pneumatic trough, the stopper replaced (care being taken that the water did not touch the charged points or glass), and oxygen generated into the receiver. The gas was obtained from chlorate of potash; but, there being no black oxide of manganese at hand, it did not come off very freely, and we had to be content when the vessel was barely half-full. After two days (forty-eight hours), the stopper was removed, and the experimental vaccination of two subjects attempted. A child was inoculated in three places with the lymph on the piece of glass; and another child, also in three places, with the

charged ivory points. When the children were examined on the eighth day, it was found that vaccination in the first case had entirely failed, and in the second had produced three good vesicles. The child whose vaccination had failed was on the same day vaccinated with fresh lymph collected on a glass slip; and this not only succeeded at the three spots attempted, but developed two supplementary vesicles. These results were somewhat puzzling, especially as all the lymph exposed had been taken at the same time and from one subject. Both infants were proved to be susceptible: why had the experimental vaccination succeeded in one and failed in the other? Could it be that the lymph on the vitreous surface had been wholly within the influence of oxygen, and the lymph on the porous ivory only partially reached by the oxygen? This appeared to us the only possible explanation, and we accordingly concluded henceforth to make use of glass only for exposing lymph. The thin glass discs used as covers for microscopic preparations at once occurred to us as well suited to our purpose; and, in exposing vaccine to oxygen and some other gases and vapours, we made these discs the contagium-carriers. The precise method of procedure was as follows. Slits were cut in the cork lining of the chambered stopper, and into these two or more clean new covers were inserted. Fresh lymph, gathered with capillary tubes, was then blown on the covers. As the covers occupied very little space, when the receiver was plunged in the pneumatic trough, the water was allowed almost up to the stopper, so that the proportion of air mixed with oxygen was inconsiderable. The gas was generated from chlorate of potash as before; but a little black oxide of manganese was added, and care was taken to fill the receiver. Three tubefuls of fresh lymph was the charge for each cover, and each cover was used for the experimental vaccination of one subject. One cover was exposed to oxygen for seven days; four covers were thus exposed for five days, three for two days, and two for one day. In each of the subjects vaccinated, the lymph was inserted at three places; the scarifications were made with a clean lancet kept for the purpose; and the covers were used to apply the lymph. All these experimental vaccinations failed; and, on subsequent vaccination, all but two succeeded. The oxygen being delivered from a heated flask, we wished to be quite certain that its temperature had nothing to do with its effect on the lymph. On one occasion, therefore, when exposing three covers, we inserted in the lining of the receiver-stopper a small clinical thermometer. It stood at a little below 90° Fahr.; and, although the gas was played upon it, it did not rise one degree. Lymph from the same source as that exposed was in each instance tested by being used for vaccinating, so that the activity of every tubeful up to the time when it was immersed in oxygen is beyond dispute. Thus, out of twelve experimental vaccinations with vaccine exposed to oxygen, but one was successful; and in this case, as has been stated, there is reason to believe the exposure was imperfect.

Carbonic Oxide being a gas singularly inimical to even low forms of animal life, its effects on vaccine lymph seemed to us an interesting subject for study. If this type of contagium should prove able to resist the poison, it would be evidence of its possessing a vitality more persistent than the organisms with which it is assumed to be allied. If, on the other hand, the specific properties of the vaccine, as tested by its results when inoculated, were found to be destroyed by the poison, it would be *pro tanto* evidence of its being, if not exactly a protozoon, at least something higher than protoplasm. We do not wish to press this, as we are well aware that facts may be as readily made to appear in favour of one theory as another; but, in any case, the behaviour of vaccine after being exposed to carbonic oxide is deserving of investigation, and forms a necessary part of an inquiry into the conditions of life of contagia.

The bell-receiver used in the experiments with oxygen was again made use of. Into the cork lining the stopper were stuck two glass covers, and three tubefuls of fresh lymph were blown on each *in situ*. The receiver was then plunged into a trough, and the stopper replaced. Carbonic oxide was then generated from yellow ferrocyanide of potassium and sulphuric acid. The vaccine remained in the gas twenty-four hours; and two children were then vaccinated, each at three points. They were examined on the eighth day, when it was found that all the points of insertion had failed. Both children were forthwith revaccinated, and with success. Six tubefuls of lymph were then exposed on covers, in the same manner, for twenty-four hours; and, on vaccinating two subjects from them, one succeeded at all the points of insertion, and the other at two out of three points. Another six tubefuls of lymph were exposed, on two covers, for twenty-four hours; and with this lymph two children were vaccinated each at two points. One child succeeded at one point only; and the other wholly failed, and was forthwith revaccinated successfully. A fourth sample (six tubefuls) of fresh lymph was exposed on two covers as before, but for three days. The vaccination of two children with

this, each at three points, was unsuccessful. Revaccination immediately afterwards was also unsuccessful; but, on being again revaccinated, both children yielded vesicles, five out of six points of insertion succeeding. Thus, out of eight experimental vaccinations of children with lymph exposed to the influence of carbonic oxide, three succeeded; out of twenty-two points at which the lymph was inserted, six produced vesicles. Vaccine may, therefore, endure at least twenty-four hours' exposure to carbonic oxide without losing its specific properties. It comes out of the ordeal weakened and uncertain in action, as lymph diluted with much glycerine or water.

Carbonic Acid appears to affect vaccine in the same way as carbonic oxide, though more feebly. Three tubefuls of fresh lymph were blown on a slip of glass, which was placed at the bottom of a deep beaker, the side which received the lymph being uppermost. Carbonic acid was then disengaged from marble chips by means of nitric acid, and, by a long "down", carried right on the lymph for the space of three hours. A child was then vaccinated with the lymph at three points, and all succeeded. Further, two slips of glass were charged with fresh lymph, receiving three tubefuls each, and retained in carbonic acid, disengaged as above, one for twenty-four hours, the other for two days. Each slip was made use of for an experimental vaccination, and all the points of insertion succeeded. Thirdly, two slips of glass were charged with lymph, three tubefuls each, and retained in carbonic acid two days. This time the gas was specially dried, by being delivered through a long drying chamber containing chloride of calcium. The acid was disengaged from chalk by sulphuric acid. Two children were vaccinated with the lymph thus treated, each at three points, and all the points failed. Our results with carbonic acid are, therefore, that, of five experimental vaccinations with lymph subjected to the influence of this gas, three succeeded. It is curious that, in the children successfully vaccinated, all the insertions succeeded; and, in the children inoculated unsuccessfully, all the insertions failed. The latter were revaccinated at three points each, and produced three good vesicles each. Could it be that the drying of the carbonic acid gave it a sterilising power which it would not otherwise have possessed? In view of two experiments to be hereafter recorded, we incline to think that the drying probably did not influence the results.

Hydrochloric Acid.—This gas, prepared in the usual way from chloride of calcium and sulphuric acid, was collected in a jar, in which slips of glass charged with vaccine lymph had previously been placed. The slips, having three tubefuls of lymph on each, were retained in the gas for four days; and, on vaccinating with them, all the six points of insertion failed. A charged slip exposed in the same manner for two days, and four charged slips exposed in the same manner for one day, were used for experimental vaccination, and not a single vesicle resulted. Lastly: lymph on a slip, immersed for two hours in the gas, was tested, and also entirely failed. In all, twenty-four tubefuls of lymph were subjected to the influence of this gas, and used for the vaccination of eight subjects, each subject being vaccinated at three points, and every insertion failed. They were forthwith vaccinated, and all but two succeeded—one of these being revaccinated successfully. Hydrochloric acid gas is, therefore, like chlorine, a perfectly reliable destroyer of the contagium of vaccine.

Camphor, from its proved power of postponing or arresting decomposition in such a typically putrescible liquid as blood-serum, appeared to us not unlikely to act as a contagicide, if only it could be thoroughly incorporated with the contagium liquid. Certainly it is popularly believed to be efficacious in warding off contagious diseases, and, with that object, is often carried about the person by ministers, nurses, etc. We accordingly made use of the bell-receiver, with the chambered stopper previously referred to. A thermometer and two glass covers were fixed in the lining of the stopper, and on each of the covers were blown three tubefuls of fresh vaccine lymph. The receiver was then placed over a drachm of camphor on a bed of hot sand. The temperature did not at first exceed 110° Fahr., and soon fell to the normal temperature of the room. After fifty hours' exposure, the lymph thus camphorised was used for vaccinating two subjects, the lymph on each cover being inserted at three points. On examining them a week later, one child showed no results, and the other but a single vesicle. Next, we tested the effect of three tubefuls of lymph exposed in the receiver to camphor, but for twenty-four hours only, and no hot sand being used. The experimental vaccination succeeded at all the three points inoculated. Thirdly, we exposed in the receiver, for two days, three covers, each holding three tubefuls of lymph; and vaccinated a child from each cover. The hot sand was not used. All the nine points inoculated succeeded. Our fourth exposure was for a period of seven days. The covers were charged as before from three tubes each, and the camphor was placed under the receiver, no hot sand being used. The experimental vaccination of two children with this lymph, each at

three points, entirely failed. Lastly, we exposed in the same receiver three tubefuls of lymph for four days, and three for five days. In the former, vaccination succeeded at all the points attempted; in the latter, it succeeded at one point only. It should be mentioned that the ground-glass rim of the receiver fitted closely to the marble slab on which it was placed. In the later experiments, the rim was well greased. The gross results, as regards camphorised lymph, are therefore that, out of ten children vaccinated, seven succeeded and three failed; and, out of thirty points vaccinated, seventeen succeeded and thirteen failed. However, on referring to the table of particulars annexed, it will be seen that the experiment (the first in the series), in which lymph exposed to camphor for upwards of two days failed, is unsatisfactory, owing to the age of the subject, and her refusing to submit to a test revaccination. If, therefore, we set this aside, the outcome of the experiments is, that camphor is not a contagicide, except only where the contagium is retained, for at least a week, in an air-chamber saturated with the volatile oil. No better demonstration could be given, than is afforded by these experiments, of the vanity of expecting that a little camphor, exposed in a sick-room, or carried about the person, will "keep off infection".

Chloroform.—Three tubefuls of lymph were blown on a cover stuck in the cork lining of the chambered stopper of a bottle. Half an ounce of chloroform was then placed in the bottle, and the stopper replaced. After four days, the cover was withdrawn, and used for vaccinating a child at three points. All the points failed. A cover, holding three tubefuls of lymph, was exposed for twenty-four hours; and on another occasion a cover, similarly charged, was exposed for twenty-three hours. With each cover, a child was vaccinated at three points, and all failed. A fourth and fifth cover were charged as before, and exposed—one for six hours, the other for three and a half hours. The subjects vaccinated from them, each at three points, wholly failed. Only three of those children were revaccinated by us. In one, revaccination was postponed owing to a smart attack of diarrhoea; and, in the other case, mother and child moved away, and could not be traced. We, however, hold that these experiments show that a comparatively brief exposure to chloroform vapour does entirely sterilise vaccine lymph.

Ether.—The exposure of lymph to anhydrous ether was effected in precisely the same manner as lymph was exposed to chloroform. Half an ounce of anhydrous ether was placed in a bottle having a chambered stopper, in the cork lining of which the covers were inserted. A cover exposed for two days, two covers exposed for one day each, and finally two covers exposed for one hour each, were used for experimental vaccinations. Each cover held three tubefuls, and each child was vaccinated at three points. Not a single vesicle resulted, and all the children were revaccinated with success. Ether vapour is, therefore, a contagicide, so far as regards its action on vaccine lymph, and a brief exposure to the vapour is sufficient to kill.

With reference to the last three groups of experiments, it may be noted that, according to Dr. John Dougall, neither camphor, nor the vapour of chloroform or ether, impairs the action of vaccine.

On two occasions, we essayed to expose lymph to bromine; but a sufficiently low temperature for the purpose could not be readily obtained, and the experiment was for the time abandoned.

We have only to add, that the activity of the lymph used in these experiments was, in every instance, tested on the human subject, and found efficient. The experiments extended over a period of seven months—namely, from January to July 1878.

The age and sex of the subjects operated on, and other particulars, are given in the annexed table.

Experiments with Desiccated Vaccine Lymph.—As a complement to the above experiments with vaccine lymph exposed to certain gases and vapours, it was necessary to test the effects of thorough desiccation; and it appeared to us desirable to allow the desiccating agent to be in operation for at least seven days, the extreme period of time lymph was subjected to the influence of any gas or vapour. Accordingly, three tubefuls of fresh vaccine lymph were blown on the under surface of a ground-glass stopper, belonging to a bottle just filled with concentrated sulphuric acid. When the lymph was apparently dry, the stopper was replaced—the acid in the bottle reaching to within an eighth of an inch of the lymph. After seven days, the stopper was withdrawn; and, an infant's arm being scarified at three points, the desiccated lymph was applied to the points with the stopper. When the infant was examined in due course, it was found that vaccination had succeeded at all the points attempted. This experiment was repeated, and with exactly the same results. Again, three scarified points were inoculated directly from the stopper of the desiccating bottle, and again all succeeded. Both the subjects experimented on were males—one was three months old, the other two years old.

TABLE.

No.	Initials of Subject.	Sex.	Age.	Gas or Vapour in which Lymph was Exposed.	Age of Lymph when Exposed.	Age of Lymph when Used.	No. of Points Vaccinated.	Result.	No. of Points Re-vaccinated.	Result.	REMARKS.
1	P. H.	M.	4 y.	Oxygen	Fresh	2 days	3	Failure	3	3 succeeded	
2	G. G.	M.	11 y.	Ditto	"	2 "	3	3 succeeded	—	—	
3	M. N.	F.	2 y. 3 m.	Ditto	"	7 "	3	Failure	3	3 succeeded	
4	J. M.	M.	"	Ditto	"	5 "	3	"	3	"	
5	M. M.	F.	7 m.	Ditto	"	5 "	3	"	3	Failure	
6	J. L.	M.	2 y.	Ditto	"	5 "	3	"	2	2 succeeded	
7	H. M.	M.	4 y.	Ditto	"	5 "	3	"	3	2 "	
8	M. M.	F.	7 y. 6 m.	Ditto	"	2 "	3	"	3	3 "	
9	T. B.	M.	5 m.	Ditto	"	2 "	3	"	3	3 "	
10	C. C.	M.	2 y.	Ditto	"	2 "	3	"	3	3 "	
11	F. W.	F.	1 y. 4 m.	Ditto	"	1 day	3	"	3	2 "	
12	T. L.	M.	3 m.	Ditto	"	1 "	3	"	3	Failure	
13	E. H.	F.	2 m.	Carbonic oxide	"	1 "	3	"	3	2 succeeded	
14	T. T.	M.	2½ m.	Ditto	"	1 "	3	"	3	2 "	
15	E. D.	F.	11 m.	Ditto	"	20 hours	3	3 succeeded	—	—	
16	T. D.	M.	7 y.	Ditto	"	20 "	3	2 "	—	—	
17	W. C.	M.	11 m.	Ditto	"	1 day	3	Failure	3	2 succeeded	
18	H. S.	M.	3 m.	Ditto	"	1 "	3	1 succeeded	—	—	
19	E. N.	F.	6 m.	Ditto	"	3 days	3	Failure	3	Failure	Revaccinated at 3 points, and 3 succeeded.
20	E. W.	F.	2 m.	Ditto	"	3 "	3	"	3	"	Revaccinated at 3 points, and 2 succeeded.
21	S. M.	F.	3 m.	Carbonic acid	"	3 hours	3	3 succeeded	—	—	
22	B. D.	F.	7 m.	Ditto	"	1 day	3	2 "	—	—	
23	G. M.	M.	5 y.	Ditto	"	2 days	3	3 "	—	—	
24	G. G.	M.	11 y.	Ditto	"	2 "	3	Failure	3	3 succeeded	
25	P. H.	M.	4 y.	Ditto	"	2 "	3	"	3	3 "	
26	L. R.	F.	2 y.	Hydrochloric acid	"	4 "	3	"	3	Failure	
27	J. C.	F.	5 m.	Ditto	"	4 "	3	"	3	2 succeeded	
28	A. B.	F.	3 m.	Ditto	"	2 "	3	"	3	3 "	
29	J. W.	M.	3 m.	Ditto	"	1 day	3	"	2	2 "	
30	A. D.	F.	2½ m.	Ditto	"	1 "	3	"	2	2 "	
31	E. T.	F.	3 m.	Ditto	"	1 "	3	"	3	3 "	
32	J. C.	M.	3 m.	Ditto	"	1 "	3	"	2	Failure	Revaccinated at 2 points, and 1 succeeded.
33	E. J.	F.	4 y.	Ditto	"	2 hours	3	"	3	3 succeeded	
34	L. D.	F.	15 y.	Camphor	"	50 "	3	"	—	—	
35	J. N.	M.	5 m.	Ditto	"	50 "	3	1 succeeded	—	—	
36	J. D.	M.	3 m.	Ditto	"	1 day	3	3 "	—	—	
37	F. D.	M.	3 m.	Ditto	"	2 days	3	3 "	—	—	
38	A. G.	M.	2½ m.	Ditto	"	2 "	3	3 "	—	—	
39	C. W.	F.	3 m.	Ditto	"	2 "	3	3 "	—	—	
40	J. M.	M.	5 m.	Ditto	"	7 "	3	Failure	3	1 succeeded	
41	S. B.	M.	2½ m.	Ditto	"	7 "	3	"	3	1 "	
42	H. N.	—	7 m.	Ditto	"	4 "	3	3 succeeded	—	—	
43	J. H.	—	3 m.	Ditto	"	5 "	3	1 "	—	—	
44	J. C.	F.	7 m.	Chloroform	"	4 "	3	Failure	—	—	
45	H. S.	M.	1 y. 1 m.	Ditto	"	1 day	3	"	3	—	
46	F. U.	F.	4 m.	Ditto	"	1 "	3	"	3	2 succeeded	Success of revaccination could not be ascertained.
47	T. S.	M.	3 m.	Ditto	"	6 hours	3	"	—	—	
48	L. K.	M.	3 m.	Ditto	"	3½ "	3	"	3	1 succeeded	
49	M. D.	M.	3 m.	Ether	—	2 days	3	"	3	1 "	
50	C. R.	F.	3 m.	Ditto	—	1 day	3	"	3	3 "	
51	J. D.	M.	3 m.	Ditto	—	1 "	3	"	3	3 "	
52	E. P.	F.	2 m.	Ditto	—	1 hour	3	"	3	3 "	
53	M. S.	F.	2½ m.	Ditto	—	1 "	3	"	3	3 "	

THE ETIOLOGY OF ENDEMIC GOITRE.

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It is my lot to live in a locality where goitre is of common occurrence. I have lately taken notes of the cases I have seen; up to the present, the number is two hundred and sixty. This fact establishes the endemicity of the disease in the district. It was natural that I should turn to my books for information regarding the origin of this peculiar complaint. To my surprise, the more I looked into the literature of the subject, the more puzzling and perplexing did the matter become. My medical brethren, too, seemed to hold contradictory opinions. For this unsatisfactory state of the etiology of goitre, there must be a cause. A great philosopher once said that, if we wish to penetrate the mysteries of Nature, we must observe patiently, experiment cautiously, and generalise slowly. It appears to me that (1) medical men in goitrous districts have not observed patiently, if, indeed, they have troubled themselves to observe at all; on the other hand (2), writers on goitre have generalised far too quickly; and (3) experiments have not been attempted, except on a very small scale. The result is our present incomplete knowledge of the subject. No doubt there are great difficulties to overcome. The thyroid gland, even in health, presents a puzzle to the physiologist; its function is not yet clearly made out. It is possible that a study of its morbid conditions may throw some light on the question. To add to the general fund of knowledge should be the ambition, if not the positive duty,

of every practitioner who resides in a district where goitre is endemic. It is important that all his facts should be carefully observed and accurately recorded. It is only by the accumulation of these that, in the course of time, the true etiology will be built up. No single observer can hope by himself to solve the mystery. The rural practitioner especially, who has often the best opportunities for watching and noting obscure diseases, must be content to contribute the raw material, leaving the rest of the work to the skilled hand of the well-trained master. It is impossible for the general practitioner to find time for diving deeply into the sciences of geology and chemistry, without which the true origin of goitre cannot be traced to its source. The physician, the geologist, and the chemist must combine in the work. There is no lack of material; the difficulty is to find workers.

From inquiries I have made, I find that goitre is endemic in twenty-seven English counties; it is also found in various parts of Scotland and Ireland; in nearly every country in Europe it exists; it is common in many parts of Asia, Africa, and America—in hot and in cold countries, in moist and in dry climates, by the seashore and inland, by lakes and rivers, on plains, in valleys, and on high mountains. It has even been developed, so it is said, in a ship's crew in mid-ocean; it appears alike in the burning Sahara and in the frozen regions of the far North. With such an almost universal distribution, it is the more remarkable that there should still be this vagueness regarding its etiology. I have, during my recent studies, met with nearly fifty different theories of the origin of goitre.

Before contributing the facts I have collected, it may not be out of place, with a view to the better understanding of the subject, to refer briefly to some of the principal theories found in text-books and elsewhere. Some have expressed surprise at the idea of goitre being pre-