Fig. 3.—After treatment.

Fig. 4.—After treatment.

the nasal apertures and extending upwards between the orbits, and spreading laterally on to the cheeks and involving also the upper and lower lids of the left eye, are seen nodulated and irregular growths of various shapes and sizes. Some of these are still covered with epidermis, whilst others are raw, bleeding, and fungating. Upon the left upper eyelid are seen typical rolled elevations characteristic of rodent cancer. Some of these are situated about the outer canthus. The disease prevents the patient elevating her eyelid, while the lower lid in its inner third is ectropic. Situated in the substance of the right cheek a lobulated growth as large as a walnut is seen. The epidermis is intact (see Photographs 1 and 2.)

Treatment.

Treatment was commenced June 23rd. X-ray exposures were continued twice weekly up to the 30th November. The duration of the treatment varied from five to twenty minutes, according to the effect produced. On July 10th the fungating growths were shrivelling up. On July 21st these were gently removed with a curette. On July 31st signs of healing and cicatrization were evident. On September 4th the other growths were reduced almost to the level of the surface. Photograph 3 shows that the growths on the nose had disappeared. The nasal apertures contracted, the right being a mere slit, and the situation of the growth in the cheek represented by an indurated scar. In November an artificial nose, made by Harry Brook, of Halifax, and attached to spectacles by Curry and Paxton, was supplied (Photograph 4).

Unfortunately I was unable to procure any portion of the growths for microscopical examination. The disease, however, in the centre of the face undoubtedly began as a rodent cancer, which after all is but a variety of epithelioma; indeed, I have seen true epithelioma develop on the site of a rodent ulcer. As to the nature of the growth in the cheek, I am unable to go further than to express the opinion that it is a form of carcinoma, and in this I am supported by Mr. F. T. Paul. There was an absence of any glandular infection.

A MICROBE PATHOGENIC TO RATS (*MUS DECUMANUS* AND *MUS RATUS*.)

AND ITS USE IN THE DESTRUCTION OF THESE ANIMALS.

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[TRANSLATION.]

EVER since Loeffler¹ first published his discovery of the bacillus typhi murium, which he isolated during an epidemic of spontaneous disease among white mice and successfully employed in the destruction of field mice (*M. agricola*), many other bacteriologists have had occasion to study epidemics of a corresponding character and have isolated microbes morphologically identical with that of Loeffler, but exhibiting considerable variety in their effect on different species of small rodents.

Thus the *B. typhi murium* proved to be absolutely pathogenic only towards ordinary mice (*M. musculus*) and field mice (*M. agricola*), that of Laser² towards the mus agrarius, that of Merechkozzski³ in the case of ground squirrels, and, finally, that of Hatchenko⁴ towards white rats. In addition, each of these different bacilli was found to vary so considerably in virulence that much difficulty was experienced in turning the powers of any of them to any practical purpose.

It was obvious that it would be exceedingly useful if any means could be discovered (1) of extending the field of action of any one of these microbes and of thus rendering it capable of attacking rodents other than those towards which it was normally inimical; (2) of maintaining its virulence after having thus raised it to the desired pitch. This is the problem which I set to work to solve, and the following is an account of how far I have succeeded up to the present date.

A cocco-bacillus which I isolated during an outbreak of spontaneous disease amongst field mice presented the general characteristics of the *B. coli*, and to that extent resembled the bacillus of Loeffler, and also from the beginning exhibited some pathogenicity towards grey rats (*M. decumanus*). Out of ten such rats fed upon a culture of this microbe I found that there died as a rule two or three, while others fell sick but recovered, and the rest remained perfectly healthy. The fact that a certain number of rats fed upon these cultures invariably died seemed to offer some hope that it would be possible to increase the virulence of the microbe by ordinary methods, that is to say, by passing the microbe a certain number of times from rat to rat. On the contrary, however, after making a great number of experiments of this character, it was found that the passage of the microbe from rat to rat, so far from exalting its virulence, always weakened it, whether the animal was inoculated with the culture hypodermically or simply fed upon it. Thus in

any series of passages of the microbe from rat to rat, it was observed that the first culture killed the animals in from seven to twelve days, though the virulence might become sufficiently increased after one or two passages to cause death in from five to ten days; nevertheless, subsequent passages resulted in constantly decreasing virulence so that finally no rats died at all. For example, after the tenth or twelfth passage, or even sooner, most or all of the rats invariably survived. The result was exactly the same, even if in any series the animals were not fed simply on cultures derived from the bodies of their predecessors, but allowed to feed on the dead bodies themselves. It was obvious, therefore, that when tracing the natural evolution of the disease caused by this microbe, it was necessary, in considering its cessation, to take into account not only the natural resistance of the survivors, but also the progressive diminution of the virulence of the microbe itself. The following is a case in point. Thirty healthy mice were placed in a large cage with two sick ones, while another lot of thirty were divided and placed in six different cages, and fed upon the same culture as the two sick ones which had been placed in the cage of the thirty healthy animals. The result was that in each of the six small cages all the mice died in from four to six days, while in the large cage of thirty rats disease did not begin until three days after the death of the two first mice and the consumption of their bodies by their companions.

This epidemic lasted twenty-three days, during which 27 mice died; the 3 which survived nevertheless died a month later after being fed on a culture of average virulence.

Messrs. T. Kirter and P. Kottjen, working in the laboratory of Professor Dunbar, obtained much the same results in experimenting on rats with a culture sent from my laboratory. Their results are sufficiently interesting to be worth citing in detail.

The original culture	killed the rats in	8 days
The second passage	"	10 "
The third	"	7 "
The fourth	"	8 "
The fifth	"	8 "
The sixth	"	9 "
The seventh	"	13 "
The eighth	"	9 "
The ninth	"	13 "
The tenth	resulted in	no deaths at all.

It is to be remembered in my experiment with mice, that the 3 mice who survived owed their immunity, not to natural resistance, but to the fact that the initial pathogenicity of the microbes had been lost; for these same 3 mice when fed a month later on a culture of average virulence died at the same time as those used as controls.

There can therefore be no doubt whatever that the virulence of this microbe diminishes progressively and constantly in the course of its passage from rat to rat, and since in this case we are dealing with a microbe which from time to time gives rise to outbreaks of spontaneous disease amongst animals, this fact would seem to throw considerable light upon the natural evolution of epizootic and epidemic disease in general, at least so far as the general group of haemorrhagic septicaemias is concerned. It may be said in short that an epidemic commences, increases in virulence, and then disappears, not only because it meets with individuals who are naturally refractory to its action, but also and in all probability mainly, because the virulence of the microbes becomes attenuated, and finally disappears altogether after passage through a certain number of bodies.

I hope soon to be able to throw full light upon this interesting point, but for the moment confine myself to stating it as a fact which has been demonstrated in indisputable fashion. The same result of diminished virulence may be obtained *in vitro* by inoculating a series of cultures one from the other or simply by leaving any individual culture untouched for a longer or shorter period of time.

The general result, therefore, is that it is difficult to maintain the virulence of the *cocco-bacillus* of the rat or to increase it when it is found to be small. It can only be effected by constantly making a large number of experiments and frequently testing the virulence of the cultures. When making experiments on a series of twenty or thirty rats at a time, it is always found that from the bodies of one or two of these animals a culture can be obtained more virulent than that from the others, and that in this case the virulence of the culture may be maintained for two or three months; it is thus possible while continuing to use this culture for current work to gain time to produce another of equal or even superior virulence. It is by working in this fashion that I

have succeeded in keeping up a supply of cultures of sufficient virulence for eight years.

During this time cultures of a sufficient degree of virulence to kill rats fed upon them in cages in my laboratory in from five to twelve days have been used for a large number of practical experiments on farms, warehouses, hospitals, workhouses, etc.

A summary of the reports which I have received, and which number several thousands, shows that in 60 per cent. of the operations undertaken the rats completely disappeared, in 15 per cent. the results were entirely negative, and in the rest, or 25 per cent., of the experiments, though dead and sick rats were found and a large diminution in the number of rodents in the places in which the experiments were conducted was simultaneously observed, complete destruction was not obtained.

In certain but not numerous cases it was observed that the epidemic extended from the locality in which it had been brought about to other localities where nothing had been done, and that sometimes the epidemic lasted for nearly a year. As an example may be quoted Odessa, where my cultures were used to destroy rats during the outbreak of plague in that city in 1902. There the rats completely disappeared after my cultures had been employed, and in 1903—or eight months after the experiment—rats brought back to the port on ships were found to be suffering from the disease which the culture causes. This extensive experiment, or rather this application of the treatment to the whole of a great town like Odessa, which with its suburbs has a radius of 10 or 15 kilometres, may well serve as a model for the use of the treatment in other places. Doubtless errors were committed which should be noted in order that they may be avoided in future, but in general the operation organized by the sanitary authorities and directed by M. Diatropoff, Director of the Pasteur Institute of Odessa, were very well conducted indeed. It was divided into two parts—one in September and the other in October. In September the proprietors of all houses were ordered to conduct matters themselves, but in October the sanitary authorities enlisted the services of the medical men and medical students of the town.

In order to prepare the 25,000 litres of virulent bouillon required by the town and its suburbs a number of large disinfecting boilers were installed in huts usually employed for storing petroleum, and in this way the whole of the infected bouillon required was supplied in the course of about twenty days. The cultures thus hastily got ready were invariably distributed for use on the day of their preparation, and crusts of bread dipped in it were used as a bait. The first supply of bouillon was inoculated with a culture brought from my laboratory to Odessa by Professor Wyrokouvic, and all the rest of the bouillon prepared from it. To keep check upon the results the Bacteriological Institute had all rats, dead or alive, which could be found after the eighth day after the first distribution collected, and paid a reward of five kopecks for each of them. Each of these rats was carefully examined with a view to deciding whether it had died as a result of the virus or otherwise.

It was not deemed necessary to exercise any special control over the way in which the directions given for the use of the virus were carried out, and reports received showed that in many cases the directions had not been sufficiently observed. Thus in certain quarters of the town, and especially in the poor ones, either the infected bouillon was kept for several days, corked up more or less tightly, or else the inoculated crusts were thrown into streets or courts or other open places, in the daytime with the result that the bread intended to be eaten by rats was devoured by dogs or other domestic animals. In the quarters thus inadequately treated the proportion of rats found to have been killed by the virus was only from 42 to 45 per cent., while in quarters where the directions for treatment had been rigorously carried out the results of the necropsy of the rats found were without exception positive.

In most of the small villages round Odessa it was observed that rodents completely disappeared, and finally, it is to be remarked that several weeks after the operations had been carried out the Bacteriological Institute was only able to procure fourteen rats alive and in good health although it offered a reward of 15 kopecks a head. In concluding his report M. Diatropoff stated that the result of the employment of the virus was far superior to that of any other measures used, and that in spite of the freedom with which the virus had been distributed, no illness either amongst human beings or domestic animals could be traced to its use. The general outcome of this report is to lead to the conclusion

that, provided a culture of this cocco-bacillus is of sufficient virulence, it is possible to count upon the destruction by its use of all the rats in a large city without causing any danger whatever to its other inhabitants, human or animal, always supposing that the operations are conducted in an orderly and methodical manner.

REFERENCES.

- ¹ *Centralbl. f. Bakt.*, 1892, Nos. 1 and 5. ² *Ibid.*, 1892, p. 184. ³ *Ibid.*, Bd. xvii p. 742. ⁴ *Ibid.*, Bd. xxiii, p. 873. ⁵ *Deut. med. Woch.*, 1901, No. 18.

ON THE ADMINISTRATION OF CHLORIDE OF ETHYL AND SOMNOFORM, ALONE OR IN CONJUNCTION WITH NITROUS OXIDE OR ETHER.

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If these newer anaesthetic agents can be shown to be almost as safe as nitrous oxide and, seeing that they possess the advantages over it, amongst others, of a longer available anaesthesia and a more prolonged period of analgesia, it is of advantage to obviate certain disadvantages in respect to some initial sensations and symptoms experienced by the patient, and also inconveniences from the point of view of the operator and anaesthetist.

It is not uncommon to hear patients complain of a choking and suffocating feeling on going under, and I venture to hold that this can, in the large majority of cases, be prevented, it being caused by the sudden application of a concentrated vapour and is more noticeable in nervous adults, in children, and those with sensitive or irritable throats.

Many patients are greatly alarmed at having a mask applied to the face filled with a powerful vapour. This not infrequently causes holding of the breath, coughing, and, in some cases, is followed by struggling with consequent delay in the induction of anaesthesia. These initial strugglings, etc., on the part of the patient may also be the cause of dreams of a disagreeable character.

In these respects, unfortunately, the anaesthetic agents now under consideration compare unfavourably with nitrous oxide, and it behoves us to use our best endeavours to minimize all disadvantages in connexion with the use of these volatile drugs if we intend to include them in our list of standard anaesthetic agents.

There is a fear in my mind that nitrous oxide, as far as the public are concerned, may have to bear the blame of some unpleasant sensations produced by these agents. This would be a calamity indeed, and I venture to think that, before administration, the patient should be told that "gas" is not the anaesthetic to be used, and also due precaution should be taken, when possible, in the preparation of the patient beforehand, to prevent after-effects, as well as a careful and skilled administration with the use of any inhaler that will obviate unpleasant initial sensations.

APPARATUS.

One of the most satisfactory methods of overcoming these disadvantages is that described by Dr. F. W. Hewitt, namely, that of administering chloride of ethyl with nitrous oxide gas, using his own special gas apparatus. This method I have used a number of times with excellent results, but unfortunately the period of available anaesthesia is shorter than when the agent is administered alone and a smaller bag is employed. In most of the inhalers I have seen and used for the administration of chloride of ethyl or somnoform alone an estimated dose is first projected on to a more or less extensive surface of lint, cotton-wool, or sponge; inside the facepiece, close to the patient's nose and mouth, and then the mask is quickly applied. In others a capsule, containing either 3 c.cm. or 5 c.cm., is broken inside an inhaler of special construction.

The objections to the first class of inhalers (besides that mentioned above) are, that a certain amount of the fluid at once evaporates and is lost for anaesthetic purposes, and consequently an unknown quantity of the agent is given. Also, freezing takes place inside the mask and often close to the patient's nose and mouth. The objection to the use of capsules is that there is too much restriction to dose. One must use either 3 c.cm. or 5 c.cm. In the case of young children, for instance, 2 c.cm. or 2½ c.cm. is often ample to pro-

duce satisfactory anaesthesia. Adults seldom require more than 3 c.cm. or 4 c.cm. for one inhalation, and further, for prolonged administration a much larger amount than 5 c.cm. may be required, when it is found both inconvenient and wasteful to be frequently breaking capsules.

An inhaler both simple in construction and use is that made by attaching together the facepiece and angle-mount of a Clover's portable ether inhaler and introducing the agent through the tap commonly found in the angle-mount, used for gas in the nitrous oxide-ether sequence. Dr. Luke has described a modification of this, in which the tap is removed flush with the angle-mount, the hole being closed with a wooden plug.

Having used this Clover method a number of times I find the following modifications and method of great advantage. Instead of the hole and wooden plug in angle-mount I prefer the tap with metal tube continuation. A tap is easier to manipulate than a plug and cannot get lost.

Also, owing to the reconstruction of some of the trigger-valved ends of the ethyl chloride bottles it is easier to get in the fluid through the projecting end of the tap than through a hole flush with the surface of the angle-mount, especially

is this so if the patient is inclined to move. At the commencement of the inhalation, instead of projecting the fluid through the tap directly from the bottle, a definite quantity is first measured out into a small tube made of thick glass, which for the sake of accuracy I have marked in 3 c.cm., 4 c.cm., and 5 c.cm. graduations. To this small measure-glass is attached a short piece of red rubber tubing, by means of which it is accurately attached to the end of the tap of the angle-mount. (Vide illustration.)

METHOD OF ADMINISTRATION.

In the case of a patient sitting up in the dentists' chair the position of the tube and angle-mount in relation to the facepiece is the reverse of that shown in the illustration. The tube being downwards, no fluid can escape and no smell will be noticed if the tap is closed. The mask having been accurately adjusted to the patient's face a short period of to-and-fro breathing is first permitted, the tap is now opened, and the angle-mount with its tube is rotated from the vertical position until it is almost horizontal. The rotation is now conducted gradually, so that the fluid will run very slowly out of the glass phial through the tap and metal tube into the bag. The patient will thus inhale a dilute vapour, which he soon gets accustomed to and will tolerate a stronger vapour in a few seconds. One should aim at producing a steady evaporation at first until signs of unconsciousness begin to show themselves, then the drug can be more quickly given. If there is a tendency to holding the breath or to coughing it is a sign that the vapour is too strong for this individual case; the angle-mount should then be rotated back again, thus limiting further evaporation of the fluid until the symptoms subside; it can then be again rotated upwards and the flow continued until the tube is empty. With a little care and practice a very satisfactory induction results in a large percentage of cases.

If the patient be in the recumbent position the facepiece may be put on first, the angle-mount and charged tube then so adjusted that the tube be in the most dependent position, the patient's head being slightly on one side. Now tip up the tube (very slowly), which is easily done on account of its rubber attachment to the tap.

The idea of the glass tube I have from Dr. F. W. Hewitt, who uses it with his special gas apparatus, as mentioned before. The metal tap and tube of the angle-mount can with advantage be made larger than those generally found,