and every member of the staff I received the greatest kindness, and I was freely permitted to examine into every detail of the method. Dr. Ruffer's address to the Association at Leeds was so full and convincing that little is left to be said with regard to M. Pasteur's method. I cannot refrain, however, from recording my testimony to the extreme care that is taken to ensure accuracy in the treatment and security to the patients from any untoward results, and my admiration for the wonderful precision that regulates each step in the preparation and inoculation of the virus. For the benefit of those who in the course of their practice are called upon to deal with cases of bites from animals supposed to be rabid, it is perhaps wise to emphasise the fact that, as Dr. Roux has shown, the freshly removed brain and cord of rabid animals may be preserved for long periods, without loss of virulence, in pure neutral, or rather non-acid, glycerine; and that, sending specimens so preserved to the Pasteur Institute, it can there with certainty be determined whether a given animal was or was not rabid.

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In concluding these notes it may be as well to mention a train of symptoms of a somewhat ambiguous nature experienced by me. I do this with no little diffidence; yet so few cases of like nature have been placed on record that I feel it wise not to pass the matter by unnoticed. Within a day or two after the cut I became aware of a sensation in the forearm of the injured extremity, by no means acute enough to be termed a pain, but rather akin to the feeling one obtains in a limb after excessive muscular exercise. In time the same sensation made itself evident along the inner side of the arm. Considering this due to the irritation of some small nerve at the seat of the wound, I paid very little attention to it. It persisted, however, for some weeks, in fact throughout the period of treatment at Paris. From about the twenty-sixth day I woke regularly in the early morning, to find the limb in a state of "pins and needles." The condition lasted for several minutes; then disappearing, it permitted me to fall asleep again. Rarely was one of the other extremities affected, and it was only after the phenomenon had occurred without fail for more than a week that I called to mind that it might be allied to the "tinglings" described as a premonitory symptom of rabies. From September 5th onwards—I had wounded myself on August 8th—I began to suffer from insomnia, not falling off to sleep until between 1 and 4 A.M., and from now I became more and more depressed. The depression was completely in spite of myself. I had no reason to doubt the efficacy of the treatment that I was undergoing, and looked upon it, not as necessary, but as precautionary, and as, on the whole, a pleasant experience. From September 8th this depression was constant; the dull heavy sensation in my arm became more marked, and soon I experienced great distaste for being alone for any length of time. On the 10th, while making my homeward journey, a tightening or constant slight constriction of the throat made itself felt. These symptoms became more and more strongly marked until the 14th, when for one short moment I found I could not swallow the saliva. That night, however, I fell asleep fairly soon; the next morning the depression had passed away, and although during the next few days I at times experienced some slight tightness of the throat, and awoke on some mornings to find my arm in the state of "pins and needles," I very soon felt myself in a state of good health, the last symptom to disappear being the heavy sensation in the arm. Taken altogether, the symptoms were at the worst not very prominent; they were, however, most decidedly uncomfortable.

What is the interpretation of these symptoms? On the whole I am inclined to believe them of nervous origin, pseudo-hydrophobic. In favour of this view it may be pointed out that certain signs of rabies which are generally well marked, such as for instance pain at the seat of the wound, were characteristically absent; other signs, for example, the tingling in the extremities were incomplete in their manifestations, and though present might be otherwise explained. But, on the other hand, not a little can be said against the purely nervous theory. I am of robust health, sound constitution, and in temperament should describe myself as the very reverse of nervous. My belief in the efficacy of the Pasteur treatment is and was throughout complete. I knew at the time that, having been inoculated, the chances were even more than ninety-nine to one that I should not be attacked. So slight did I consider my danger, that on August 22nd, but for the urgent entreaties of Professor Roy, I should have started for the Broads, instead of for Paris; and I fully acquiesced with the authorities at the Pasteur Institute, when upon the thirteenth day of treatment

they informed me that they considered my case such that they did not think it necessary to keep me for the usual fifteen days of treatment.

If indeed I passed through a most mild abortive attack of rabies, then certainly that attack was due to the cut I gave myself, and not to the treatment I underwent. The time of the first appearance of the symptoms, namely, about the twenty-sixth day after the cut, would show this. The pain, if pain it may be called, in the injured extremity only, while the region of inoculation was completely painless, would evidence the same, while the fact that it was not until the seventeenth day after the infliction of the injury that I presented myself at the Rue Dutot would again add to the probability that symptoms should manifest themselves in spite of the treatment. It is impossible to avoid the feeling that, had I not gone to Paris, the symptoms, if only nervous in origin, would, in the want of that sense of security gained by undergoing the treatment, have developed themselves to a most painful extent; if of the nature of rabies, would, failing the treatment, have become lethal; and that I owe to M. Pasteur and those at the Rue Dutot my heartiest thanks, not only for the courteous way in which I was received and treated, but perchance also for the continuance of my days.

IMMUNITY PRODUCED BY AN ALBUMOSE ISOLATED FROM ANTHRAX CULTURES.

By E. H. HANKIN, B.A.,

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THE following is a brief preliminary account of an investigation which I have recently been engaged upon under the guidance of Professor Koch at the Hygienic Institute of Berlin. The results appear to have an important bearing on the theory and practice of preventive inoculation.

It is now generally admitted that acquired immunity against a disease is in reality an acquired immunity against a poison. The phenomena of acquired tolerance of the effects of ordinary albumoses, and of snake poison which contains a poisonous albumose, show a closer resemblance to acquired immunity against a disease than is the case with any other poison. These and other facts led me to expect that if it were possible to isolate an albumose from anthrax cultures, such anthrax albumose would probably be capable of conferring immunity against the disease. Such an albumose I have now isolated from my culture fluids by ordinary chemical methods, and find that it gives the ordinary reactions for albumoses, and that it is capable of conferring immunity.

In the course of my process of preparation, it is precipitated from its solution by addition of a large bulk of absolute alcohol, and well washed in this liquid to free it from ptomaines, since it is known that all such substances are soluble in alcohol. After the addition of alcohol it is filtered off and dried, then it is redissolved, and filtered through a Chamberland's filter. A rough estimate of the percentage of albumose present in the clear solution thus obtained is made colorimetrically, by means of the biuret reaction and a peptone solution of known strength.

In one experiment four rabbits (Nos. 23 to 26) were inoculated subcutaneously with virulent anthrax spores. No. 26 served as "control," and died in about forty hours. The other three rabbits had the albumose solution injected into the ear-vein at the same time. Nos. 24 and 25 each had about the five-millionth of their body-weight, while No. 23 had only the ten-millionth of its body-weight of albumose. No. 25 died in less than forty-eight hours, but Nos. 23 and 24 survived. Ten days later Professor Koch kindly reinoculated these two rabbits for me with very virulent anthrax from an agar-agar culture. Their temperature has remained normal since then, and they are now alive and well a fortnight after this operation.

I have also succeeded in producing immunity in mice against attenuated anthrax. Dr. Fränkel kindly gave me an agar-agar culture of *deuxième vaccin*. From this I made bouillon cultures, and whenever I inoculated a rabbit from these it always died, unless it had at the same time been protected by a dose of the

anthrax albumose. Unfortunately, when, a few days later, I was inoculating mice with these cultures after a dose of anthrax albumose, I omitted to inoculate a control rabbit, so that although the culture showed itself virulent for my control mice, I have no certainty that it was still virulent for rabbits. The following experiment shows its effects on mice after treatment with anthrax albumose. Seven mice had each the millionth part of its body weight of anthrax albumose injected hypodermically. Two others had each the five-hundred-thousandth of its body weight. A week later they were all inoculated with *deuxième vaccin*. Two control mice were also inoculated, and of these one died in about thirty-six hours; the other was exceptional, inasmuch as it died only after 108 hours. Only one of the three mice, which had the five-hundred-thousandth of its body-weight of albumose, survived. Of the seven mice which had been protected by the millionth of their body-weights of albumose four died. So that in this experiment, out of ten mice inoculated, only four showed immunity against anthrax.

In another experiment, ten mice were each inoculated with the millionth part of their body-weight of anthrax albumose and with *deuxième vaccin* at the same time. Of these, three died after 108 to 116 hours; the others survived. Three others had only the two-millionth of their body-weights of anthrax albumose and *deuxième vaccin*. Two of them are now living. Four control mice were inoculated, and all died.

In my earlier experiments I gave larger doses of anthrax albumose, and on inoculation with anthrax the animals died, often before the control animals. For instance, I have had several cases of mice dying twelve to sixteen hours after the inoculation with virulent anthrax. In the spleen pulp of rabbits and guinea pigs, however, I almost always found under these conditions numerous phagocytes. In these the bacilli sometimes showed signs of degeneration, but more often appeared to be alive and growing. Sometimes the long chains of bacilli, so characteristic of the growth of attenuated anthrax, appeared to be growing out of the cells. In one case (a rabbit which died only 150 hours after inoculation) the only bacilli that I could find in the spleen were contained in phagocytes. I have found these phagocytes in rabbits not only after inoculation with *deuxième vaccin*, but also after virulent anthrax. In mice I have never found phagocytes, but often after a large dose of albumose and attenuated anthrax the bacilli in the spleen appeared to be in longer chains than in the control mouse. The appearance of these phagocytes and chains of bacilli led me to try the effect of very minute doses of anthrax albumose with the favourable results described above, for the possibility suggested itself that these phenomena were indications of a commencing immunity. In several experiments the animal received the anthrax only several days after a large dose of albumose; but in these cases also death ensued in a longer or shorter time than usual, according to the quantity of anthrax albumose injected; while numbers of phagocytes were usually to be seen. Apparently the albumose had remained in the system, or at any rate only a small part of it had been excreted. Beyond this power of conferring immunity with a small dose, or of hastening the course of the disease with a slightly larger dose, this albumose does not show clearly any physiological action in the quantities employed. I often noticed, however, that for a couple of days after larger doses the mice appeared to be sleepier than the control mouse living in the same cage.

Although the following inferences seem capable of explaining the above results more simply than any other theory, I do not pretend that they are as yet satisfactorily proved. I only wish to assert that my results make it probable that:

1. The anthrax bacillus owes its power of living in the animal body to its power of producing a poisonous albumose.
2. That this poisonous albumose is capable of suppressing the "germicidal power" of the living animal.
3. That this albumose seems to be very slowly excreted.
4. That if a large dose of this albumose is injected into an animal, the entry of anthrax bacilli into the system is aided.
5. That if a very small dose of this substance is administered, tolerance is acquired against its poisonous properties. Consequently, when after a few hours or days the anthrax virus attempts to suppress the germicidal power of the animal by means of its albumose, it is unable to do so because the animal has already acquired tolerance of its poisonous quality.
6. With a dose of anthrax albumose intermediate between that employed in the above two cases, death ensues in the usual time or (in other cases) life is greatly prolonged. Apparently in this case

complete tolerance of this comparatively large dose of albumose is unattained. Consequently the anthrax bacilli are able to live and produce more of their albumose, and at length by this means overcome the resisting power of the animal.

My observations have been made on over a hundred mice and about fifty rabbits. My best thanks are due to Professor Koch and to Drs. Fränkel and Weyl for their very kind advice and assistance.

RECENT EXPERIENCES IN THE SURGERY OF STONE IN THE BLADDER: 100 LITHO- LAPAXIES AND 32 LITHOTOMIES.¹

By SURGEON-MAJOR P. J. FREYER, M.A., M.D.,
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IN the JOURNAL of December 24th, 1887, a paper of mine was published, entitled "A Recent Series of 100 Cases of Operation for Stone in the Bladder without a Death," which brought down the record of my operations for stone by all methods—421 in number—to August 8th, 1887. Between this latter date and the present time (April, 1889) I have operated on 132 cases of vesical calculus—100 by litholapaxy and 32 by lithotomy. I now propose giving some details of these operations, and transcribing from my notebook some observations of a practical character, jotted down from time to time whilst the occurrences or reflections to which they have reference were green in my memory. I must premise, however, by saying that I shall avoid going over ground already travelled in my published writings, except in so far as it may be necessary to modify or accentuate some previously recorded observations. It is necessary to mention this, lest to some of my readers this paper should appear more or less fragmentary.

In the table (No. 1) which follows will be seen at a glance the chief features of interest in the 100 cases of litholapaxy; whilst a second table (No. 2) is added, giving details of the 32 cases of lithotomy. I shall deal first with the litholapaxy cases, to which my remarks in this paper shall mainly be confined, devoting particular attention to the development of this operation in male children.

Amongst the 100 cases of litholapaxy there were 66 adults—64 males and 2 females—and the average age of these was 48 years nearly, ranging from 18 to 25. There were 34 children—33 boys and 1 girl—and the average age was $7\frac{1}{2}$ years approximately, varying from $1\frac{1}{2}$ to 14. I notice that Mr. Cadge, in his able article on "Lithotripsy," in Heath's *Dictionary of Surgery*, in a very friendly notice of my work, in referring to my first series of 108 cases of litholapaxy in adults, in which the average age was 47, writes: "Thus there were more young and probably healthy persons than English lithotritists are accustomed to meet with." The actual average age of my litholapaxy cases is, undoubtedly, less than that recorded by some European surgeons; but, as I have never refused any patient suffering from stone the benefit of operation, this is due entirely to the fact that the normal span of life amongst natives of India is much less than that of Europeans. I do not know if there are any trustworthy statistics published on this point, but I fancy that, in round numbers, a native of India at the age of 50 is comparatively as old as a European of 60. Like the rank vegetation by which they are surrounded, the races of warm climes are reproduced more rapidly, spring up to maturity at a much earlier age, and decline and die at an earlier period than in the case of those born in cooler regions.

The average number of days spent in hospital, or, in the case of patients in private practice, under treatment, was $5\frac{1}{2}$ nearly, the average for children being practically the same as that for adults.

The average weight of calculus in the 100 cases of litholapaxy was 184 grains, the average for adults being 221 grains, and that for children 112 grains nearly.

In my paper published in the JOURNAL of December 24th, 1887, already referred to, I intimated that, influenced by the very excellent results obtained by Dr. Keegan from the practice of litholapaxy in male children, I had abandoned the position of opposition which I, in company with other surgeons generally, had

¹ This paper was written in April last, but its publication deferred, as I had at one time hoped to be able to be present at the annual meeting of the British Medical Association, and read a paper on the subject dealt with.