separated and dissolved, and ready to be immediately absorbed. We may understand how in this second case the reaction of the organism under such bacteric poisons (in proportion to which the immunity is all the more assured) is more rapid, intense, and efficacious, inasmuch as immunity is all the more certain in proportion to the amount of this reaction. In order to kill the bacilli contained in his cultures, Haffkine heats them to 65° or 70° C. Now it is certain that at such a temperature the very delicate proteic substances to which in general is due the immunising power change very considerably, and may become entirely inactive. And nucleo-proteids especially (on which we have seen depends the power of the cultural liquids) suffer from the action of a temperature which almost reaches the point of coagulation of albuminoids, and lose after heating many of their chemico-biological properties. In fact all the experiments already mentioned show that the filtrates obtained from Haffkine's lymph are infinitely less toxic than the filtrates of cultures similar to those used by Haffkine, but not heated.

Another disadvantage, and a purely technical one, of the Haffkine method is the facility with which its prophylactic fluid may become contaminated. One would think at first sight that in so simple a matter it would be possible to eliminate entirely this danger, but in reality this is not so when it is a question of preparing hundreds of litres of culture and submitting this liquid so easily contaminable to several processes, of which one of the most dangerous is that of bottling. In many bottles of Haffkine's liquid were found micro-organisms of different kinds, and also sometimes pyogenic germs still capable of producing suppurations and pyæmia in the animals inoculated. In consequence sometimes abscesses and necrosis set in in the case of man, and these facts, when they came to the knowledge of the public, increased the general diffidence in regard to preventive inoculation.

With our method these difficulties are entirely eliminated, since we can reduce the immunising nucleo-proteid to the dry state, and in such a form it may be kept indefinitely and with perfect certainty of sterilisation. The most scrupulous care has to be taken only in the preparation of the cultures. The later operations may indeed be carried on with a certain amount of freedom (naturally only objects and liquids perfectly sterilised must be used), since even if it happens that some saprophytic germ gets in contact with the substance in preparation, it has no means of developing in the dried substance, and remains absolutely innocuous. It must also be noted that the nucleo-proteids possess, at least until disintegration sets in, a certain bactericidal power. In short the preparation of this immunising substance requires no greater antiseptic precaution than is necessary in the chemical preparations of other substances (such as alkaloids) destined for subcutaneous injections, and the dangers of infection liable to present themselves in the inoculations with our vaccine dried and redissolved in a sterile liquid are not greater than those which present themselves in the administration of ordinary remedies hypodermically. Besides, one of the most serious objections which have been made to the method recommended by Haffkine is that there is no dose criterion. The cultures of the plague bacilli develop in a very irregular manner, and sometimes very slight differences in the composition of the "cotton mediums" are sufficient to considerably alter the development and the virulence, and consequently also the immunising power of the prophylactic agent to be produced. Haffkine attempted to estimate the strength of the liquid contained in each series of bottles by the deposit which these bottles contained, but that this method of measurement is fallacious is self-evident. Instead, however, the dose of the immunising nucleo-proteid prepared by us in a state of considerable purity may be exactly determined by weight, since it is in the dry state, and thus we can obtain quantitative solutions just as with other medicines, and once the fundamental dose is established it may be reasonably varied according to age, sex, and constitution, and we may inject in any individual the precise quantity of active substance necessary to produce immunity without any of the inconveniences arising from an excessive dose of the toxic substance.

One other advantage, due to the fact of it being possible to preserve the immunising substance in the dry state, is the facility with which it may be distributed and sold; and this

advantage ought not to be neglected in the event of preventive inoculation requiring to be performed on a very large scale. Another great advantage which our method possesses in the event of its being applied in India, is that it in no way offends the religious sentiments of the native population of India. The difficulties which Haffkine encountered in this respect are well known, as his liquid was considered to be impure owing to its being composed, in the first place, of peptone and flesh, and even after the modifications made by him in the preparation of the broth the mistrust has not diminished. In our case, however, no objection can exist, as the active substance adopted by us contains nothing of the culture medium, and is an extract of the bodies of the bacteria, which, as is well known, are vegetable elements. Consequently, inoculation by our method would in no way offend the Vedic prescriptions. What is more, the suspicion (unjustly entertained against Haffkine's method) that the immunising liquid contained living micro-organisms could not occur. To sum up then:

1. The efficacy of our method of preventive inoculation against the plague by means of the nucleo-proteid extracted by us from the plague bacilli has been proved from the experiments made on animals—rats, rabbits guinea pigs, monkeys.

2. The immunising substance used by us is innocuous in the case of man. No troubles of any kind arise from its use, either local or general.

3. If the cultural liquids used in their entirety possess an immunising power, they owe this power to the nucleo-proteid which they contain and we have isolated.

4. The advantages of using an active substance isolated and pure in place of liquids (cultures) which contain this substance, mixed, however, with heterogeneous elements of different kinds, are at once evident.

5. The advantages which our method of inoculation possess in comparison with Haffkine's method are the following:

- (a) In using Haffkine's liquid along with the active substance are injected other toxic substances, which produce a reaction harmful to the organism and useless for producing immunity; with the use of the pure nucleo-proteid prepared by us, all the reaction produced is specific and useful for the production of immunity.

- (b) Haffkine's liquid has a very low toxic and immunising power, since it has to undergo heating so that the active substances contained in the cultures are, to a certain extent, altered. With our method this does not take place, and the active substance retains its highest immunising power.

- (c) Haffkine's liquid easily becomes contaminated, and there is no guarantee of the sterility of each separate bottle, while the active substance used by us is prepared in a thoroughly sterilised condition, and is perfectly preserved in the dry state.

- (d) It is impossible to determine an approximate dose of Haffkine's liquid; the nucleo-proteid prepared by us can be administered in perfectly well defined doses.

- (e) By the use of our method the religious feelings of the native population of India are in no way offended.

AN UNDESCRIBED FORM OF PLAGUE PNEUMONIA;

WITH FIVE CASES.

By W. C. HOSSACK, M.D. ABERD.,
Government Plague Hospital, Calcutta.

I DESIRE to bring to notice an indefinite and obscure form of plague, which, if attention is not called to it, may readily escape the recognition of the most careful and experienced physician. The ordinary classical form of plague pneumonia is known to all: its clearly marked physical signs; its rapid onset and course; its initial gravity; the severity of its general symptoms; and its rapidly fatal termination render its diagnosis all too easy. Its character, in short, is fulminant.

But there is a plague pneumonia which presents quite a different clinical character, quite another combination of general and local symptoms. Its onset is not fulminant, but

insidious, and at the end of some five to ten days the general symptoms may be little more marked than they would be in, say, a slight attack of simple bronchitis or of bronchitis complicated by a trace of broncho-pneumonia, while the lung symptoms may be so slight and vague that they are with difficulty recognised at all. The breathing may be little, if at all, quickened or laboured. On auscultation and percussion one makes out a few *râles* and rhonchi, but for the first two or three days one may fail altogether to make out any definite physical signs of pneumonia. Then one gets a small patch, —perhaps towards the apex, perhaps towards the base—where faint dulness is to be elicited, with a slight increase of vocal resonance, and occasionally a few fine crepitant *râles*. There is little if any cough, and with it very slight expectoration, clear and mucoid, or occasionally faintly mucopurulent. Expectoration at times may be almost wholly wanting. Speech and intelligence may be unaffected throughout, or if they are it is only in the latter stages; head symptoms are wanting; the eyes are not congested; the white tongue coating, may be very slight; and death, when it comes, on the fifth to the tenth day of illness, as a rule, is apt to be quite unexpected. In fact it was this unexpected death that first led me to think those cases to be plague. In addition to the culmination in death, the most striking characteristic of those cases is the pulse; it is a pulse presenting grave characters quite uncalled for by the short duration of the illness or the limited amount of lung mischief, a pulse that indicates the presence of some acutely toxic condition. In almost every case I saw it was quick out of proportion to the local or general condition, and wherever it was not found at the time of examination to be weak and running, its rapidity and general character indicated the probability of its quickly becoming so. This rapid feeble pulse, then, is an important diagnostic point. As a rule there are no enlarged glands, but if there are, they come late in the illness and are ill-developed. Every case I have seen or heard of has ended in death.

So far only 5 cases have been directly under my observation, but from the results of the 20 to 30 cases of investigations of death which passed through my hands every day, and from conversation with native practitioners I am convinced that it was far from an uncommon type in the Calcutta epidemic of the early months of 1899. In numerous cases of suspicious death, where the history obtained was reliable, it was one of seven to ten days fever, not particularly high; no delirium, no pain in the chest, no glandular swelling, and very slight cough, with almost no expectoration. Exact figures as to the number of these cases I shall not attempt to give, for it is impossible to fix the boundary line between reliable and unreliable information, and in numerous cases some such colourless history as that above was originally given with a view to concealment, when the true history, as subsequently elicited, was that of typical acute plague with well-defined buboes.

I must plead for indulgence if the record of these cases that follow is incomplete, if clinical details that ought to have been present are absent, if the ultimate scientific test of cultures and *post-mortem* examinations is altogether wanting. So manifestly deficient is the record that I do not attempt to cast my description on systematic lines; all I can do is to call attention to this undescribed variety. I feel the more justification in doing so because the cases are such that from their nature they are not likely to be removed to hospital, and so come under accurate European observation; and even were they to come under hospital observation, they would probably escape recognition as plague owing to the false histories that would be given, and the absence of that essential local knowledge, the knowledge of previous contact with plague cases, the knowledge of removal from an infected house, that knowledge so carefully withheld by relatives, that knowledge that only a district medical officer, constantly working in the huts and houses of the infected localities, can possibly obtain. The time and labour necessary to acquire that knowledge are the excuse put forward for the deficiencies of the records: only those who have worked in Calcutta can realise the difficulty with which even those were procured, scanty as they are.

In reply to the self-evident objection that the cases I give were not cases of plague at all but cases of simple bronchitis or broncho-pneumonia, I can only call attention to their clear connection with plague, the fact that they occurred in series

with indisputable plague cases, and the fact that every case proved fatal. Had they not been plague there was no reason why death should have occurred when it did.

CASE I.—Moti, female, aged 30, Chapkar, was discovered during the course of a thorough search in this bustee just as she was walking out into the street to avoid observation. The search was in consequence of repeated deaths in the bustee, of cases which before death were invariably concealed, and in which after death only vague and unsatisfactory information could be obtained. Two of the deaths were certainly plague, and the others probably so.

Condition on Examination.—The patient was well nourished, and in her general condition there was little to indicate anything seriously wrong. She answered all questions quite rationally, and her speech, if a little weak, was otherwise normal. The tongue was slightly coated with white at the back and down the middle. The eyes were not injected. Temperature 101° , pulse 140 , respiration 32 . The pulse, though so quick, was fairly full and strong; its rate was probably accelerated by the exertion of getting up and trying to get away. Respiration was a little laboured but not much. Fine *râles* distinctly heard at both bases and a few rhonchi, but no dulness or percussion could be made out. Vocal resonance perhaps a little increased. Very little cough and very little sputum; what there was was clear and mucoid. There were no enlarged glands present anywhere. This was the condition on the seventh day of illness, March 8th, 1899. The diagnosis was bronchial catarrh, with probably a little broncho-pneumonia. I suspected it might be plague, but did not report it as there was so little to go upon. Dr. H. P. Bannerjee saw her next day and found her in much the same condition. The pulse was slower and better. He made out a little dulness at the bases. We were both surprised when the Vigilance Committee reported her death on the morning of March 11th—that is, after ten days' illness. There was no opportunity of making a culture.

Remarks.—There had been no actual plague case in this particular hut, but from what has been said it will be seen that the plague connection, though not absolutely certain, had been highly probable. If the case had been simple broncho-pneumonia there was nothing to explain her sudden death. She was a healthy well-nourished woman. The pneumonia was very slight; there was nothing grave in the symptoms unless the pulse.

CASE II.—Dulal M., female, aged 52, a Hindu residing in a hut. The practitioners in charge of the case—Dr. N. L. Dey and Dr. N. Chatterjee—took me to see this woman on the morning of March 12th, 1899.

She had then had fever for three days. She was a thin, old, grey-haired woman. The pulse was 110 . The temperature 101° , respirations 30 . The tongue showed a thin white coat all over it. *Râles* and rhonchi were heard distinctly over both bases. I thought I could make out a little dulness about the point of the left scapula, but it was extremely doubtful. The diagnosis given was bronchial catarrh in an old and probably malarial subject. The other doctors failed to make out any pneumonia at all, and I could only say I had a faint suspicion of it, with nothing definite on which to state a diagnosis. No enlarged glands were detected. To the surprise of all concerned, she died the evening of the same day—that is, after three days' fever.

Remarks.—There have been suspicious deaths all round the immediate neighbourhood of the hut, and though definite connection with previous cases is not made out, it is highly probable. The subsequent death of the grandson from plague pneumonia is still more convincing.

CASE III.—Hari C. S., male, aged 8, a Hindu, grandson of Case II, living in the same hut. It turned out afterwards that he had been suffering from fever for four days until, on March 14th, two days after the death of the grandmother, he was removed to the ward hospital.

Dr. Das reported on this date as follows: Temperature 103° . Has got slight cough. No pain in any part of the body. No glandular swelling. Is quite sensible; no delirium. Pulse rather feeble. Is under treatment of Dr. N. L. Dey and Dr. D. M. Chatterjee. Hut is tiled; room on ground floor.

When seen by myself on March 17th—that is, on the seventh day of illness, his condition was as follows: Lies collapsed on the bed. Respiration 60 , nostrils dilated; temperature 104° ; pulse 120 , very weak. Low moaning cry. In the left groin there was slight tenderness, and a raisin-like gland was indistinctly felt in the inguinal region. There was no other enlarged gland. The lungs were examined only from the front. On percussion faint dulness could be made out here and there all over. It was distinct only at the right base. Auscultation gave fine moist *râles* at both bases. Towards the apices breathing was distinctly bronchial, and vocal resonance was greatly increased. Dulness there, however, was indistinct. Though rhonchi were heard, there were no moist sounds.

He lingered on for nearly a week before he died.

CASE IV.—Kanai, male, aged 32, caste Tantee, coolie employed in molasses shed.

History.—He became ill on March 15th, 1899. His is the eighth case in a series of 10 all hailing from the same hut, as will be detailed below. He was discovered on March 18th.

Condition on Third Day of Illness.—Lies in bed almost quite indifferent, but answers on being spoken to loudly. Haggard, drawn look on face. Speech is slightly affected, being rather thickened. The tongue is characteristic, that is, it is covered with a white coating, but the tip and edges are free from it. Respiration is 36 , slightly laboured. Pulse 104 , regular, and fairly strong.

Physical Examination.—No dulness made out on percussion. On auscultation moist *râles* at both apices, particularly in the right lung. The *râles* are fine. Towards the bases the breath sounds are rather bronchial, but no moist sounds are to be heard. The bases themselves seem to be clear. Cough, if any, is very slight and occasional, as is also the expectoration. No enlarged glands could be found. It was arranged by means of money compensation that the patient should be removed to the Ward Plague Hospital, and that the hut should be evacuated. The patient was, however, surreptitiously removed to 7, Joga Mohun Saha's Lane, and died March 19th, 1899, while being removed from this house to hospital by his friends.

Previous and subsequent cases from the same hut; the total population of the hut was not over twenty persons:

1. Durga, male, aged 18, Kahar, died March 8th, 1899, after five days' illness.

2. Mookta, female, aged 60, Brahmin, died March 13th, 1899. Pneumonia began March 7th, 1899.

3. Bassuntia, female, aged 11, Bindee, became ill morning of March 9th, 1899, and died 1 A.M. March 10th, 1899.

4. Agnassia, female, aged 55, Brahmin, got ill on March 10th, 1899; found with pneumonia March 13th; surreptitiously removed and died in a day or two.

5. Bindsoo, male, aged 15, Kahar, became ill on March 14th, 1899, and died on March 17th, 1899, with right femoral bubo in the Medical College Hospital.

6. Soomaria, sister of Agnassia, had nursed her, and became ill on March 16th, 1899, and was sent to the Campbell Hospital, but could not be traced.

7. Name not known, male, aged 9, Sankar, was attacked on March 16th, 1899, at noon, and died at 9 P.M. the same day.

8. Kanai, above described (Case IV).

9. Dukhee, father of Kanai, was found with pneumonia and incipient right axillary bubo on March 20th, 1899; he died in Ward Plague Hospital on March 22nd, 1899.

10. Jogoo, male, aged 8, Tantee, grandson of Dukhee; he developed pneumonia on April 14th, 1899, and died on April 19th, 1899.

CASE V.—Chumroo, male, aged 40, Kurmi.

History.—The hut is one in which two plague deaths had occurred shortly before. Hari Lal G. died with a left inguinal bubo on March 27th, 1899. Chumroo, who was a coolie in a grain shop, became ill on March 24th, 1899.

Condition on March 31st, 1899.—He was fairly nourished, but presented leucoderma on the scalp, upper and lower extremities, and several patches on the chest. He talked freely, speech not being at all affected. He could move about and sit up with ease. The tongue was dry and coated, the temperature 102.5°, the pulse 140, and the respirations 52. The eyes were not injected.

Chest.—Bronchial breathing, with increased vocal resonance, was found over both bases behind. No moist sounds were heard at bases, except one or two doubtful rales on the right side. Two inches below the point of the left scapula was a patch about 2 inches in diameter, of distinct dullness on percussion, with fine crepitant rales. Dullness was fairly marked over bases.

Raisin-like glands could be felt in both groins; these were not tender; probably they were of old standing. He was being nursed by his son in a room about 4 feet by 6 feet by 7 feet. He died quite suddenly the same night.

THE SERUM DIAGNOSIS OF MEDITERRANEAN FEVER.*

By T. ZAMMIT, M.D.,
Government Analytical Chemist.

THE object I have in discussing the bacteriology of the Mediterranean fever, is mainly to bring once more to the front the importance of having a clear and definite idea of the fever and its cause.

Knowledge of the etiology of this disease is far from being complete. Major David Bruce in 1886 discovered the micro-organism of the fever, and described its principal characters—morphological and biological. The micrococcus described by him was invariably taken from the spleen. Captain Hughes repeated the researches of Major Bruce, and added observations on the growth of the micrococcus. In his book on *Mediterranean, Malta, or Undulant Fever*, published in 1897, he gathered together all that was known about the fever. This was a step in the right direction, but the bacteriological facts were of little aid in the practical question of the causation and treatment of the fever. The micrococcus could only be discovered on the *post-mortem* table unless the spleen had been punctured during life, an operation not free from danger.

If bacteriology is to aid us in diagnosis it is imperative that we should find out a method by which the specific micro-organism can be demonstrated as soon as the patient is attacked by the fever. Everyone knows how difficult it is to give an opinion as to the nature of a fever when the patient is in the first week of his illness, and every practitioner understands the importance of a rapid diagnosis with a view of establishing a proper treatment.

Happily a practical method of diagnosis has been suggested based upon the well-known agglutination of specific micro-organisms in a solution of the blood serum from the corresponding disease. After Widal's discovery of the reaction of the typhoid bacillus when in contact with the blood serum of enteric fever patients, the method was applied to a number of diseases, among others to Mediterranean fever. In the annual report of the Public Health Department for 1898. I have endeavoured to give a summary of our attempts to use the serum reaction as a help to practitioners to come to an

* Read before the Malta and Mediterranean Branch of the British Medical Association.

early diagnosis in doubtful cases of enteric and Mediterranean fever. Our experiments were quite successful in so far as the technique was concerned, for we were able to obtain the reaction in a very short time after the sample of blood had reached us, but I am sorry to say that our enthusiasm was by no means shared by our medical colleagues, and very few of them responded to our appeal. Although this first attempt was discouraging, still the question is of such importance that I venture to repeat the appeal.

During the year 1898 the cases of fever reported to the Public Health Department were as follows:

Enteric fever	...	...	162
Mediterranean fever	...	...	510
Febricula	...	...	125

Total ... 797

Is it probable, I venture to ask, that these numbers would be the same under each heading if a bacteriological examination had been resorted to in each case? I must confess that I have grave doubts about it.

If the bacteriology of the Mediterranean fever has not been advanced further than this, I think we have at least something to work upon. Of course, not every practitioner has the time to apply himself to bacteriological researches, but everybody is able to help in his own way. Malta fever is not peculiar to our island, but the number of cases throughout the year is, most unfortunately, more than is desirable. If an effort were made by the medical community with a definite aim and purpose, I am confident that important facts would be gathered which would be of great service to us and to our patients. Knowledge of the pathology of the fever is not complete, its morbid anatomy is merely outlined, its treatment uncertain, its bacteriology in its very infancy. It is difficult, if not impossible, for a single student to grapple with these different questions, but our united efforts are bound to triumph.

In every case of fever the method of serum reaction should be used in diagnosis. It is a simple operation, easily made in the most modest laboratory. Cases with distinct reaction should then be followed closely, and some definite treatment carefully applied and recorded. In fatal cases, bacteriological and anatomo-pathological researches should be made whenever possible.

In my efforts to contribute my share to the knowledge of the fever, I submit the following facts which I have gathered during the past year:

1. The micrococcus of Bruce can be grown successfully from a culture seven months old.

2. Cultures of the micrococcus 2 years old give a clear serum reaction.

3. The micrococcus does not grow on sea water solidified with agar, not even when the sea water was taken from a sewage outfall, and was of a distinct brown colour.

4. The micrococcus grows on an aged solution of normal human faeces.

Having no connection with a hospital, I could not obtain suitable materials for further researches, but I am quite willing to help any colleague who is in a position to obtain material at *post-mortem* examinations.

A CASE OF VESICAL CALCULUS IN SIERRA LEONE: LITHOTOMY.

By W. RENNER, M.D.,

Assistant Colonial Surgeon, and Medical Officer of the Royal Colonial Hospital.

I WAS called to see Mr. P., aged 63, in May, 1899. He had recently arrived in the colony from Accra in the Gold Coast Colony, where he had been the resident keeper of the gaol for twenty-four years.

History.—His son, a druggist, informed me that his father had been suffering from hypertrophy of the prostate for some years, and that he was suffering from severe pain in the penis, and after micturition, which was very frequent both day and night, and that at times retention of urine took place suddenly. He had been passing a gum elastic catheter to relieve retention and also to wash the bladder.

Condition when First Seen.—I examined the old man *per rectum*, and found that the pelvis was occupied by a large indurated mass. On passing a large silver prostatic catheter I experienced a slight difficulty on entering into the bladder, and felt that my instrument was grazing on some hard and rough mass immediately behind the prostate, which was also en-