Turning to another view of the subject, it will no doubt be remembered that in 1884 the late Mr. McGill, of Leeds, published a method of proceeding whereby more or less of the hypertrophied and obstructing prostate was removed through a suprapubic incision into the bladder. For a supplementary record of this work, I have to express my thanks to Mr. Moynihan, the resident surgical officer of the Leeds Infirmary. Mr. McGill's communication to the Clinical Society of London attracted considerable attention. Amongst other advantages claimed for it was that it gave persons who had been dependent on the catheter by reason of an enlarged prostate, either partly or entirely, a reasonably good chance of being able to dispense with the use of this instrument. As the possibility of such a result has been called in question, Guyon, for instance, maintaining, "that prostatic enlargement is but a local manifestation of a general senile sclerosis which pervades the entire urinary tract," I have taken pains to ascertain from some surgeons who I knew had been engaged in the performance of this class of operations what their observations in reference to this particular point had been. The result of these inquiries is that I have received, and am receiving, a large amount of information from at home and abroad affording undoubted evidence that the function of micturition is not infrequently restored both after prostatotomy and prostatectomy. But as the subject opens up under the light thrown upon it by the accumulated experience of many observers, there are points which arise on which it would be desirable to obtain further information. These points have reference to many aspects of the questions that are involved in these records. For instance: (1) whether the loss of power was gradual or sudden, if partial or complete; (2) the selection of cases appropriate for such treatment; (3) the choice of operation, whether perineal or suprapubic; (4) the mode of dealing with the obstructing prostate, whether by incision or extirpation: and, lastly, the degree of catheter independence that is subsequently obtained, whether temporary or permanent.

As illustrating the desirability of keeping the subject open for a time before attempting to narrow it down to conclusions, I would quote from some of my correspondents. Dr. Belfield, of Chicago, one of the earliest advocates of these operations, and the author of a most interesting paper on the subject,³ writes me under date of July 6th, after giving the particulars of a case where the restoration of the voluntary power of micturition was known to have continued for two years and a-half after the removal of a portion of the prostate:

I could, probably, by correspondence with other patients, adduce at least six cases where such operation has been followed by complete restoration of the vesical function for over a year. I happen to have received, only two weeks ago, an unsolicited letter from a patient operated on last January by combined suprapubic and perineal incision, who had been absolutely dependent on the catheter for nearly two years, and who states that he can now pass a strong and full stream, and has given up his catheter. Almost a duplicate case is one that I operated upon last April. These two cases, however, are too recent for your purpose.

Again, Dr. Keyes, of New York, in a very interesting letter on this subject, writes dated July 7th, 1892:

CASE III.—Solely dependent on the catheter, which he uses every two hours, night and day. Operation four months ago. Horse-collar enlargement and general hypertrophy. Two ounces and a-half of prostate removed. This gentleman is now at his house in the country. His doctor writes me that he urinates voluntarily, and has given up the catheter. Whether he empties his bladder or not I cannot say, as I have had no personal opportunity to test him. His case is remarkable, in that his atony was complete. He had a very thin, flabby bladder, and had been using his catheter exclusively for about six years.

Other evidence of this kind is adduced.

It is for reasons such as I have suggested as arising out of these records that I would ask you to regard this in the light of a preliminary communication. In the meantime I shall be glad to receive the particulars of cases, or of observations which seem to throw light on the many points, some of which I have mentioned, that surround the pathology and surgery of this affection. Apart, however, from the direct evidence that is thus afforded as to the possibility of restoring the function of micturition by the operative measures referred to, an analysis of the causes of death in cases of progressive prostatic obstruction, treated either by casual or regular catheterism, indicates what is only a matter of time in many cases of this kind. By the back pressure of the urine, under the in-

fluence of more or less continuous spasm which the prostate as it encroaches on the interior of the bladder provokes, the whole urinary apparatus above becomes converted into little else than suppurating sacs, or tubes, as may also be seen in connection with the ordinary forms of advanced urethral stricture. As the secreting portion of the kidney is gradually absorbed under this constant hydrostatic pressure, the solid material, in the process of time, disappears from the urine, the specific gravity falls, and under these circumstances, as Sir James Paget long ago pointed out, the patient is endangered by the slightest interference, accidental or otherwise, with his urinary apparatus.

It must not, however, be assumed that the restoration of the function of micturition can only be brought about by strictly operative measures, for this I am sure is not the case. When the bladder either gradually or suddenly strikes work, as we so often see in connection with prostatic obstruction, no one I think would feel disposed to recommend the adoption of such measures merely because it necessitated the use of a catheter as the alternative for normal micturition. It is only when ordinary catheterism is rendered impossible, or nearly so, either by the degree of obstruction or the inadequateness of the relief, that operative measures are to be considered. A word may here be said in reference to the purely medical treatment of the weak bladder. Much more might often be done in the early stage of regular catheterism in promoting power and restoring lost function. To abandon all hope, and hand over the case to the instrument maker, especially in the acute form of prostatic obstruction, is often to throw away almost the only chance that remains short of operative interference. Muscle, whether in the form of a bladder or a biceps, will soon cease to work effectually when the necessity for its doing so is brought to an end.

I have found the long continued use of ergot of much benefit in these cases. There is a combination of ergot, cantharides, and nuxvomica, which often seems to assist the return of power. The late Professor Gross remarks⁴: "Ergot is a favourite remedy with Dr. Atlee in the treatment of this affection. Several patients, whose ages ranged between 60 and 90, were enabled under this treatment to lay aside the catheter after having been the victims of its daily use. A gentleman aged 89, by the methodical evacuation of the bladder, and whose death appeared imminent, has for the last three years maintained his general health and his urinary organs in excellent condition by the evening dose of the remedy."

In my own work I have now the case before me of a member of our profession, who, after many weeks of complete catheter life, has entirely recovered his lost power—a result which he attributes to the long continued use of ergot in conjunction with the judicious employment of the catheter.

SUPRAPUBIC PROSTATECTOMY.¹

By G. BUCKSTON BROWNE, M.R.C.S.

PROSTATECTOMY means the actual removal, by knife, scissors, or forceps, of part of the prostate. At the outset of an inquiry into the merits of this operation it is desirable to have a clear idea of the anatomy and function of the prostate. For surgical purposes it is well to recollect that the prostate is only arbitrarily divided into lobes, it is really one single organ. As Ellis says: "Three lobes are described in the prostate, namely, a middle and two lateral, though there is no fissure in the firm mass." With regard to its function, I believe it is a sexual organ, and nothing more. To my mind it is quite sufficient to remember that in the female the act of micturition is perfectly well performed without a prostate, in order to reject all theories that it performs any urinary function. In adult and advanced life, in a certain number of cases, that is to say, exceptionally, the organ enlarges or hypertrophies, and by so doing frequently, but not always, interferes with the act of micturition. This affection is met with in all sorts and conditions of men, and this has led to great difference of opinion regarding its causation, but it certainly does seem very frequently to follow sexual activity in middle and advanced

⁴ *Annales des Mal. des Org. Gén.-Urin.*, March, 1885.

⁵ Operations on the Enlarged Prostate, with Summary of Cases, *Amer. Journ. Med. Sciences*, November, 1890.

⁶ *Diseases of the Urinary Organs*, Philadelphia.

¹ Read before the Medical Society of London, March 6th, 1893.

life. I am more and more struck by the fact that prostatic hypertrophy often follows a second marriage, or a marriage contracted late in life. The results of youthful sexual excess are doubtless usually outlived. It is remarkable how rarely urethral stricture accompanies prostatic enlargement, and it may be presumed that men with urethral stricture have usually been sexually active in youth. When the prostate enlarges the hypertrophy may be (1) extravascular, or (2) intravesical, or (3) both extra- and intravesical. It is the intravesical growth which chiefly causes difficulty in micturition. This intravesical growth is often like an egg projecting into the bladder, with the vesical urethral orifice at the apex of the egg. In such cases the projection is usually equal to an eighth, or a quarter, or even half of an ordinary hen's egg. This ovoid projection may be deficient at any part of the urethral circumference. When wanting anteriorly and laterally, we have the so-called middle lobe enlargement with which all are so familiar, where from behind the urethral orifice there is a projecting prostatic mass acting like a bullet valve, and often causing the bladder to be entirely dependent upon the use of a catheter for the voidance of its urine. More rarely we have the ovoid projection, only wanting in front, and we have a prostatic growth continuously surrounding the vesical urethral orifice on both sides and behind, or the projection may be only on one side; in such cases it is nearly always continuously combined with a posterior enlargement. While so rarely as practically to be never met with, the intravesical growth is only found anterior to the urethral orifice. Intravesical prostatic outgrowths may be associated with considerable extravascular enlargement, and the latter may exist without the former, and cause the patient so afflicted to be partially or completely dependent upon his catheter.

In my opinion it is the intravesical growth alone which can be removed with reasonable safety, and with a fair prospect of recovery of the power of natural micturition. As therefore so much depends upon this form of hypertrophy, the answer to the question, Can we during life diagnose the existence of intravesical prostatic growth? is a very important one. Without digital examination after suprapubic cystotomy the presence of such growth can only be approximately diagnosed. In making this approximate diagnosis we must remember that we are dealing with a form of urinary disease where all unnecessary or excessive urethral interference is to be deprecated. It is precisely these cases which Sir Andrew Clark had in view when he so ably drew the attention of the profession to urinary fever following catheterism, or, as he called it, "catheter fever." This fever is unfortunately sometimes a fatal fever, and elsewhere I have attempted to prove that its severity is usually in direct proportion to the amount of urethral disturbance. The electric cystoscope, the use of which is never free from risk, is therefore particularly dangerous in the cases now referred to. In many its employment is impossible, or almost impossible, for there are cases in which the shape of the instrument is an absolute bar to its introduction, and in other cases the introduction is attended with so much difficulty that the very limited range of vision is obscured by blood. Several remarkably severe cases of cystitis, which I have met with in practice, after endoscopic examination, where the prostate has been enlarged, have created a strong feeling in my mind against the use of this instrument in these cases. Again, the use of instruments which may be classed as urethrometers has not commended itself to me. They are all very trying to the urethra, which in this complaint we particularly desire to preserve from injury, and even when used they really do not appear to throw light upon this important point, whether there is or is not intravesical prostatic hypertrophy. There are, however, two simple means of examination, not trying to the patient and within the range of every surgeon, which, combined, will throw considerable light upon the question, namely, digital rectal examination and the careful measuring of the length of the urethra by means of the simple passage of the catheter. Any undue length of urethra will be an argument in favour of intravesical hypertrophy, and particularly so if by the rectum the prostate is felt but little enlarged. If much extravascular growth is found, this must be allowed for in estimating the importance of the length of the urethra. If the urethra is 9 inches long or more, and if not much growth can be felt by the rectum, there is

almost sure to be intravesical hypertrophy. Should it be deemed desirable to sound the patient for stone further evidence for or against the presence of intravesical growth will be obtained, for, if such growth exists, it will be found that the sound has to travel very much uphill into the bladder.

Practically the consequence of all the forms of prostatic hypertrophy is almost invariably more or less difficulty and imperfection in the act of micturition. In some cases the prostate is enlarged without really causing urinary trouble, but these cases are rare. It is, however, most important to bear in mind that, even where there is great urinary difficulty, due to prostatic enlargement, the difficulty may be only temporary, due to congestion, and may pass away entirely in the course of days, weeks, and even months. This fact has an important bearing upon the question of prostatectomy. The following case is instructive in this connection:

—aged 68; February, 1889. On a railway journey, owing to the presence of ladies, he did not leave the carriage. When arrived at his destination he could pass no water. Catheters were used unsuccessfully, and he was treated for suppression and not retention of urine. I saw him sixty-three hours after the last act of micturition, performed before starting on his journey. A catheter was passed and 3 pints of urine drawn off. The urethra was 10 inches long, and by the rectum the prostate felt enlarged. He recovered, but for three months all his urine was passed by catheter. Towards the end of April he began to pass water naturally, and in another month the retained urine—that is, water left behind in the bladder after a natural act of micturition—had come down to 2 ounces. In July the retained urine was only 1 ounce, and in February, 1890—a year after the retention—there was no retained urine. He is alive and well now, holds his urine from three to five hours, and does not use a catheter.

The explanation of the case is that the prostate was hypertrophied, but not sufficiently so to cause any real difficulty in micturition. The railway journey produced congestion of the already enlarged gland, and the confinement to the carriage without urinary relief caused over-distension of the bladder, producing temporary atony of its muscular coat. It would have been a surgical blunder to have subjected this patient to a suprapubic prostatectomy, from which operation he might easily have died. On the other hand, had he recovered from the operation, and recovered with full power of natural micturition, he would have been no better off, his life would have been risked, and prostatectomy would have obtained credit for what would have been brought about by far simpler methods. Such cases are by no means uncommon, and they are not unknown in the records of prostatectomy.

Unhappily, however, prostatic retention, whether partial or complete, generally comes prepared to stay, and we may next ask, What are the prospects of a man obliged to pass his urine entirely, or in part, by catheter? I would reply, that the prospect is a perfectly tolerable one, provided he becomes a master of the art. *Quoad* this particular complaint, there is no reason why he should not reach a good old age, and the chances are in favour of his not dying of his urinary complaint, but of some other disease or accident in the end. There is certainly nothing in his prospects to make him as it were lead a forlorn hope and rush into a grave and even dangerous operation such as prostatectomy, at the beginning of his catheter life. Instances are numerous all round us of elderly men, active in all the pursuits of ordinary life, and many of them exceptionally highly placed in the conduct of affairs, who are obliged to pass all their urine by catheter, and who lead comfortable, useful, and happy lives. This state of comfort depends in the first place upon there being only a moderate amount of intravesical prostatic growth, and happily this is the rule and not the exception, and secondly upon the amount of attention paid by the patient to his condition. I shall not go into the details of this attention, but will only point out that such care consists: (1) In the choice, and proper skilful use of the best kind of catheter for the individual case; (2) the sufficiently frequent use of such an instrument; and (3) the immediate renewal of all instruments when they become cracked, rough, or otherwise worn. Also in (4) the use of an antiseptic lubricant; and (5) in the proper washing out of the bladder, and application of medicaments to its mucous membrane in certain cases. All this may be spoken of as the proper toilet of the bladder. Taking everything into consideration, it is wonderful how tolerant the bladder usually is of neglect in many of the details of its toilet, but sometimes it is not tolerant, and neglect leads to such a state of vesical irritability, that is to say a state of

chronic cystitis, that life soon becomes a burden, because of the constant and imperious calls for the use of the catheter. This painful condition may also occur from causes over which the patient has no control, and which he cannot avoid by the greatest cleanliness and niceness in his self-management. One of these causes I would particularly refer to, for it is a condition which has almost escaped notice, but which has an important bearing upon the subject of this paper, namely the growth into the bladder of the prostate to such an extent as to act as a foreign body causing constant desire to pass water, and adding terribly to the trials of an elderly man already obliged to pass all his urine by catheter. Such a case I record in the *Transactions of the Clinical Society*, vol. xxii, where I removed 4 ounces of purely intravesical prostate, giving the patient great relief. He is alive and well now, in his 92nd year, four years after the operation.

There are other cases where comfortable, or even tolerable, catheter life is impossible. In some very rare cases catheterism, I mean regular habitual autocatheterism, is practically impossible, owing to the extreme curve of the prostatic urethra forwards, the patient being supposed to be standing up, and, but not so unusually, there are cases where autocatheterism is so difficult that life under such conditions is not worth having. This difficulty may arise from the great curve of the prostatic urethra, the existence of false passages, and sometimes from the great ease with which the prostate will bleed if impinged upon and injured by the catheter, filling the catheter with blood clot, thus preventing the emptying of the bladder, and causing vesical spasm, as well as exhausting the patient by the constant loss of blood. Occasionally, also, we meet with patients whose hands are crippled by rheumatism, or by nervous affections, or who only possess one hand, or whose special occupations make autocatheterism difficult, or even almost impossible.

In all these cases where regular, habitual, autocatheterism is so frequent as to threaten to exhaust the patient, and where all palliative and other treatment has failed to bring relief, and in cases where from the patient's urethral condition or want of manipulative power, such catheterism is impracticable, the question has long been—What are we to do? Up to 1886 we could only offer such sufferers a tied-in catheter, or a perineal or a suprapubic vesical puncture or incision, followed by the permanent wearing of a tube through which the urine could drain away. Sir Henry Thompson in 1874 devised a special instrument for the suprapubic puncture, and I published² a description of an apparatus for these patients to wear after the suprapubic opening. This apparatus acts as an external receptacle for the urine, and patients can wear it and move about, fully dressed, with a fair amount of comfort. Many surgeons had before 1886, and have since, proposed the incision, and the excision of the intravesical prostatic obstruction, and also the burning of a groove in it by instruments introduced through the urethra, or by means of perineal incision, with the view of radically doing away with the obstruction, but no evidence has been brought forward which commends these operations to the surgical mind at large. The revival of suprapubic cystotomy, however, in the last decade suggested an attack upon the prostate from within the bladder from above, and independently of each other, Dr. Belfield, of Chicago, and the late and much regretted Mr. McGill, of Leeds, in 1886, became the pioneers in this important new surgical departure.

There is now no doubt amongst all surgeons that the obstructing prostate can be excised from above the pubes, but the surgical mind is not entirely satisfied that the operation, which is undoubtedly a severe one in itself, and necessarily performed upon those ill able to bear surgical interference, is justified because some doubt that even if the obstruction is entirely removed the bladder can regain its powers. Many surgeons believe that the prostatic hypertrophy is secondary to vesical changes, while others believe—and I do—that the prostatic enlargement is entirely primary. Sir Henry Thompson has expressed his doubts as regards the results of prostatectomy in the following sentences, and I need not say how weighty his authority is, and how clear and logical his mind. He writes in his *Clinical Lectures*: "I am entitled to require that if it does happen, or has happened, to any surgeon to divide or remove any part of an enlarged prostate for a

patient who had previously been compelled to pass all his urine by catheter—say, for a period of twelve months, and that after the division in question he was enabled to dispense with the instrument, or at any rate to pass, say, only half his urine by natural effort, the case ought to be seen and examined by others. I desire extremely to see such a result from any of the proceedings alluded to. I have long wished to see this sight, and have travelled considerable distances abroad and elsewhere expressly seeking it, but at present without success."

In answer to Sir Henry Thompson I will briefly relate the following case; the patient is here to-night, and the facts are absolutely beyond dispute.

R. H., a gentleman, aged 70, tall and spare. He began to use a catheter in 1872, or twenty years ago. My first note of him is in April, 1886. All urine had then been drawn by catheter for four years. He now used his catheter seven times in twenty-four hours. The urine was clear and healthy. Catheterism was not easy; the instrument had to be well bent in order to go in. In 1887 he called on me complaining of bearing down of the rectum and much pain when he wanted his catheter. In May, 1890, he had bloody urine, and catheterism was necessary every hour and a half to two hours. On sounding his bladder the sound had to pass very much uphill in order to reach the bladder. During June the bleeding was so profuse that I feared a vesical growth. He was next seen in June, 1891. There was now great suffering and much vesical spasm and constant bleedings. He continued in this state until January, 1892, when I saw him with Dr. Cunningham of West Hampstead. The catheter was necessary every half hour. There was considerable trouble from hæmorrhage and blocking of the catheter by clot. The urethra was $\frac{3}{4}$ inches long. By the rectum the prostate felt only moderately enlarged. On sounding him a small vesical calculus was found. All his pain was before catheterism; he had none afterwards until the next call for the catheter. His life was quite unbearable and perfectly miserable.

On March 10th, 1892, Dr. Frederic Hewitt administered ether. I could easily with tube and aspirator make the stone rattle against the former, but could not possibly seize it with the lithotrite, owing to the deep post-prostatic pouch in which it lay. The bladder was then opened above the pubes, and an intravesical prostatic subgrowth found, as large as a tangerine orange, below and on both sides of the vesical urethral orifice. I removed the stone with a scoop; it resembled an orange pip and weighed 9 grains, and then proceeded to remove all the prostate which projected into the bladder with forceps. Everything was twisted off, nothing torn or cut away. The pieces removed weighed 1 ounce. The bleeding was very severe; it was partially arrested by hot water injections, applied through the urethra, by means of an enema syringe attached to the end of the penis. For forty-eight hours much blood came away with the urine. In three weeks some urine began to come by the penis. By the end of April the wound was closed, and all urine passed naturally by the penis except 3 ounces which he drew off by catheter night and morning. Then came an attack of influenza in June, and the suprapubic wound slightly opened for a time, and we had some trouble in bringing a small suprapubic leakage to an end. Early in August all was perfectly healed, and by the middle of September we found the bladder able to empty itself to the very last drop, proved on several occasions by passing a catheter after a natural act of micturition, and no catheter has been used since. Of his own accord he wrote, under date January 3rd, 1893, "It is fifteen weeks since I saw you, when you advised me to do without the catheter. I have not used it since. I can now go in the daytime on the average three hours, and at night from four to six hours; indeed the last two nights I went fully nine hours each night, and this has happened twice before during the last three weeks. I cannot express the relief I feel from the dreadful pain and hæmorrhage I had so long endured, now I have not even inconvenience. I can now go about with more comfort than at any time during the last ten or twelve years; indeed it is twenty years since I first had to use the catheter."

This case speaks for itself. The patient had used a catheter for twenty years, and for ten years had made no water except by catheter. He submitted to prostatectomy, and had full natural power of micturition restored to him, an unspeakable boon, but to obtain which he undoubtedly risked his life. Such a case proves beyond all question that the habitual use of the catheter does not necessarily permanently destroy the power of the bladder to empty itself, as has been asserted upon great authority, and also proves that prostatic enlargement is the cause, and not the result, of troubles in micturition. With regard to the dangers of prostatectomy, I am just as sure that in a fatal case of suprapubic lithotomy in my practice, the result would have been different had I left the projecting prostate alone, as I am that in several others the successful results were largely due to my non-interference with the prostate, although in several instances it offered itself temptingly for removal.

With reference to the details of the operation of suprapubic prostatectomy, I believe that the operation should always be extraperitoneal; all intraperitoneal operations must add largely to the risk, and all that is necessary can be done through an extraperitoneal incision. The bladder should always be opened upon a staff; if not—since the body of the prostate in these cases is frequently very large—it is very likely to be incised, instead of the bladder, when the surgeon thinks he is puncturing that organ with his knife, and mis-

² BRITISH MEDICAL JOURNAL, August 4th, 1882.

chief is done. The presence of a staff prevents such an accident. I believe in removing the projecting prostate with forceps and twisting it off in one piece if small, piecemeal if large. By twisting or torsion hæmorrhage is lessened. The intravesical growth should alone be attacked; no good will come of trying to remove the lateral lobes even in part. In clearing the vesical urethral orifice of all surrounding projecting prostate tissue much assistance will be obtained by the presence of a metal sound in the urethra. Hæmorrhage is usually very free, and will be all the more so if the prostate has been attacked with knife or scissors, the use of both of which instruments I deprecate. Dr. Keyes, of New York, has had much experience of prostatectomy, and has suggested a lint tampon drawn into the prostatic urethra by a thread through the urethra, but I have found the bleeding sufficiently controlled by hot water irrigation, and all plugs must add to the patient's pain. My space is limited, and I make no special reference to perineal prostatectomy as compared with suprapubic, because the former operation is performed, practically and metaphorically, in the dark. The parts concerned are almost always beyond the reach of the finger, hæmorrhage is usually severe, and the risk of that most distressing condition, a perineal urinary fistula, resulting is very appreciable. I am also obliged to omit noticing the results obtained by the suprapubic route by Belfield, McGill, Mayo Robson, Jessop, Atkinson, Keyes, Southam, and Moullin; their works, however, speak for themselves.

In conclusion, I would express my present opinions as follows:

1. Suprapubic prostatectomy should never be undertaken at the outset of catheter life unless regular catheterism is impossible.

2. The operation should never be undertaken as long as the ordinary catheter life is a tolerable one.

3. If, from any of the causes I have detailed, catheter life becomes intolerable, suprapubic cystotomy should be resorted to. By means of this proceeding the bladder can be thoroughly explored, and any stone removed, which in these cases may easily have escaped detection by the more usual methods of examination. The intravesical growth, if it is found to exist, and of this existence we can never be sure until the finger is in the bladder, can be fully examined, and removed if the operator thinks right to do so. If he deems removal inadvisable, or if there is nothing which can be removed, he can leave the patient with a suprapubic tube, for permanent after-wear, with the certainty that he will have materially improved the condition of the patient.

4. Should the operator decide to remove the prostatic obstruction, there is a very good prospect, but not a certainty, of the power of natural micturition being restored to the patient.

CHEMICAL VACCINE AGAINST RABIES.¹

By PROFESSOR TIZZONI

AND

DR. E. CENTANNI.

(From the Laboratory of General Pathology of the University of Bologna.)

In a previous publication we described the results of the researches we had made concerning the extraction from the central nervous system of rabid animals of a principle for vaccination against rabies. By means of this principle we succeeded in every case in securing for rabbits immunity even from subdural infection.

Later on we propose to communicate the methods for the extraction and preparation of this substance, and a series of experiments to determine its nature and properties, which have already been begun in this laboratory, will be published. We desire now, in view of their great importance both scientifically and practically, to make known the results of the antirabic vaccination obtained in rabbits by means of this substance.

The vaccine is extracted from the central nervous system of a rabbit which has died from *virus fixe*, though even that

taken from a rabbit of the first generation after direct inoculation has given us absolutely positive results. We confine ourselves, however, to the use of the first named in order to have a material to deal with the strength of which is definitely determined. We employ this vaccine in solution made always under exactly the same conditions, and the same designation, thus enabling us to obtain results both constant in themselves and comparable with each other. The proportions we have selected as most convenient for our purposes are so regulated that every 10 c.c. of the liquid contains dissolved the active principle of about 1 gramme of the rabic nervous system. This solution has a limpid appearance, is colourless like water, or very slightly tinted of a straw colour, without odour, with neutral reaction, and aseptic in the most restricted sense of the word.

By a series of preliminary experiments, we have several times satisfied ourselves that the vaccinating substance we employ is deprived of all virulent properties. Whether injected under the dura mater or introduced in fairly large quantity (5 c.c.) under the peritoneal cavity in the rabbit, it never gives rise to any of the phenomena of rabies.

Further, we have been able to demonstrate that it is without hurtful action of any kind, whether local or general. In fact with inoculation under the skin of large quantities of the solution (20 c.c.) in a single dose, or of still larger quantities (50 c.c.) during several days, no local irritation or general disturbance of any kind has ever been observable in the animals thus treated, no alteration of the temperature beyond the normal limits, no diminution of the ordinary liveliness of the animal nor of its weight, which even in the case of young animals follows its usual course of gradually increasing.

Further, this antirabic vaccine not being in the form of an emulsion, but in that of complete solution, spreads rapidly and becomes completely absorbed in a few seconds when injected even in large quantities or several times in the subcutaneous connective tissue. With this vaccinating substance we have, since the month of January, been carrying on numerous experiments. The animal we selected was invariably the rabbit; the virus used for infecting them was taken from three different dogs, and its virulence was previously conclusively established by numerous control experiments. Our researches may be divided into two series, those in which the vaccination was performed before infection, and those in which it was performed afterwards.

PREVENTIVE VACCINATION.

The animals belonging to this series received by subcutaneous inoculation varying quantities of the vaccinating solution repeated during a varying number of days. The day after the final inoculation the animal was infected (always under the dura mater) with the virus of "street" rabies. After which all further injections were discontinued, and the development of the experiment carefully followed.

In 3 animals the vaccination treatment was prolonged during two weeks, each animal being inoculated with 40, 30, 25 c.c. of the vaccinating solution on several occasions. In 8 other animals the time of the treatment was shortened to eight days, and they were respectively inoculated with 30, 30, 20, 20, 15, 15, 10, 7 c.c. of the vaccinating solution distributed over daily doses. In another animal the treatment lasted five days with 20 c.c. of the solution administered in five equal doses each day. One more animal also received 20 c.c. of the vaccinating solution, but in two doses on the two days preceding the infection. Finally, 1 animal received the dose of 20 c.c. at one single time on the day preceding the infection.

To sum up, therefore, we see that the treatment before infection was carried out in 14 cases; that the quantity of the vaccinal solution employed has ranged from 40 to 7 c.c., and that the time elapsing between the commencement of the vaccination to the moment of infection has varied from two weeks to one day. The whole number of control animals all inoculated under the dura mater was 6, and they died between the fifteenth and twenty-first day after infection. Twelve of the animals treated are alive and in excellent health, and a considerable time (five months already for the first ones) having elapsed since their infection, we may regard their recovery as definitive. Of the 2 remaining animals, 1 died of rabies the fifteenth day after inoculation, that one

¹ Read in the Section of Pathology at the Annual Meeting of the British Medical Association held at Nottingham, July, 1892.