

DETOXICATED VACCINES

as an aid to the treatment of

GONORRHOEA.

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T H E S I S.

by

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(1) I n t r o d u c t i o n .

Perhaps the most debatable question in the treatment of Gonorrhoea is the place occupied by Vaccine Therapy. Most authorities concede that vaccine is a valuable adjuvant to the more chronic metastatic affections, but the weight of opinion is rather against its use in the acute stages.

KIDD<sup>1</sup> states that he has found vaccines irritating and dangerous in the acute stage of the trouble and that, by creating a hypersensitive state in the patient, render him more liable to the development of epididymitis and joint trouble. His chief complaint is directed against those who attempt to substitute Vaccine Therapy for clinical methods.

LUYS<sup>2</sup> would confine vaccine treatment to the complications of Gonorrhoea and is, on the whole, not greatly impressed with its achievements.

McDonagh<sup>3</sup> who used sensitised Vaccine did not advocate its use in plain urethritis but found it of the greatest value in the sequelae

Among German writers ASCH<sup>6</sup> of Strassbourg has seen most good results in joint cases, but is convinced that in uncomplicated urethritis it is useless. He looks upon vaccines administered cautiously, as the only really specific treatment of arthritis and synovitis of Gonorrhoeal origin.

LUMB<sup>3</sup> has used "Staphigon" in acute urethritis and claims for it that the disease is cut short and also the incidence of complications is lowered.

BRETT<sup>4</sup> also had remarkably good results in acute urethritis.

ALLEN<sup>5</sup> has used polyvalent vaccine in acute cases over a period of three years and is convinced of its utility.

Most physicians who object to the use of Vaccine base their objections upon the fact that a negative phase is produced which allows the disease to spread and that this spread is not entirely overcome by the succeeding positive phase. That there is some justification of this view can be seen when one considers that - in Anterior Urethritis - if a negative <sup>phase</sup> be produced which allows infection to spread to the Posterior Urethra - no succeeding positive phase is likely to repair the damage and the duration of treatment will probably be doubled. It can hardly be doubted that this does occur occasionally when a toxic type of Vaccine is used; if, during the negative phase, infection should reach the prostate the discharge is thereby decreased, with the result that a casual observer might be led to think that the vaccine ~~was~~ having a beneficial effect.

(2) Experiments in Detoxication.

Efforts of recent workers have been directed towards the production of a Vaccine which will be non-toxic and yet capable of producing anti-substances in the body fluids - they realised that if this could be accomplished the negative phase would be reduced to a minimum.

Nicolle<sup>9</sup> attempted to render vaccine less toxic by growing the cocci on special media and then making it up in a solution of Sodium Fluoride.

Dean<sup>10</sup> attempted detoxication by sterilising his Vaccine with Eusol - this however was found to become toxic on keeping.

Besredka<sup>11</sup> marked an important advance in detoxication by introducing the practice of sensitization. He treated polyvalent vaccine with immune serum, and after the vaccine was precipitated, removed the supernatant serum, washed the precipitate consisting of vaccine and fixed anti-body and used it in a solution of 5% Phenol.

Gibson<sup>12</sup> was of the opinion that sensitised vaccine did not stimulate the formation of protective substances owing to the presence of anti-bodies in the serum. He attempted in conjunction with Harvey to get rid of these antibodies.

The great disadvantages of sensitised vaccines are, the difficulty of preparation, together with the fact that they deteriorate rapidly on keeping. On the other hand the vaccine prepared by Thomson has neither of these disadvantages and is according to McDonagh far more therapeutically active in

in uncomplicated urethritis.

Thomson<sup>8</sup> working along the lines of Lustig and Calcott in their experiment with Plague Vaccine, dissolved Gonococci in a 2/10 solution of alkali. He then titrated the solution with normal H.Cl. with the result that the stroma of the germ was precipitated, the more toxic part of the coccus remained dissolved in the supernatant fluid, which was removed. The precipitate was washed with 5% Acid Sodium and 5% Carbolic Acid. He then redissolved in a slightly alkaline medium and administered intramuscularly.

Mr David Lees<sup>7</sup> tested this vaccine against polyvalent toxic vaccine in several series of cases at Rochester Row and again at Newcastle with very satisfactory results.

Lately Thomson has produced, experimentally, several modifications of his original preparation. One of these, prepared from the toxic supernatant fluid by precipitation with half saturated Ammonium Sulphate, is said to contain the capsule of the germ, and he considers it should make a good vaccine if non-toxic. He has not, however, found it so strong an antigen the complement fixation Test. He has also produced a vaccine detoxicated by alcohol, this vaccine is now on trial.

Dr. C.T. Wang following up his success in preparing a non-toxic fat-free tuberculin, has produced a fat-free gonococcal vaccine in the following manner. He took several strains of gonococci freshly isolated. The growths were then washed with saline containing 25% Phenol. After counting he centrifuged at a high

high speed. The supernatant fluid was then pipetted off. The residue was dehydrated with absolute alcohol and again centrifuged. Ether was then substituted for alcohol and the mixture placed in a mechanical shaker for one hour. The fluid was again centrifuged and the residue again treated with chloroform in place of ether and shaken as before. At the end of one hour the chloroform was mixed with three of its volume of ether and again shaken for one hour. After centrifuging the process was repeated alternately with fresh ether and chloroform until five extractions in all had been completed. The residue was dried and weighed. For use, the bacterial substance, then fat-free was ground in the dry form in a mechanical mill overnight, normal saline was then added and the mixture given another 24 hours grinding, after which it was collected for use. Knowing the number of organisms at the start and the weight of the final residue, the equivalent value by weight of the dessicated fat-free organisms was calculated on the hypothesis that one Milligram = 1000 millions of the organism.

Under the supervision of Mr. Lees, at the Lock Department of the Royal Infirmary, Edinburgh, I have used the vaccines prepared by Thomson and that of Wang in a series of unselected cases with a view to estimating their relative value as regards toxicity and therapeutic effect, also to form an opinion of the value of these Vaccines as an adjuvant to local treatment, under the somewhat difficult conditions encountered in a modern Venereal Clinic.

(3) Method of Administration.

There are three methods of administering Vaccines each of which has its supporters.

(1) Subcutaneous injection is the route Thomson advocates for his own vaccine. This has the advantage that the local reaction can be readily and accurately observed. It thereby furnishes a good deal of information as to the effect of the vaccine on the patient. It has also the advantage of being more slowly absorbed with the result that:-

- (a) The general reaction is reduced.
- (b) The action of the vaccine upon the tissues is more sustained.
- (c) A steady out pour of anti bacterial substances is evoked.

On the other hand it has the disadvantage that if the local reaction is marked, as often happens, a good deal of pain and discomfort is set up.

(2) Bruck and Somner used the intravenous method, employing large doses with the result that violent reactions were stimulated necessitating the patient remaining in bed for 2 - 3 days. Large doses of vaccine administered intravenously will cause a sharp rise of temperature, the height of which will depend upon the toxicity of the vaccine employed. Now it is a well known fact that a rise of temperature from any cause whatsoever is often followed by a disappearance of the Gonococcus. This is due to the fact that the Gonococcus is extremely sensitive to variations in temperature its optimum being 98° - 99° F. A temperature of 100° F sustained for 12 hours or more is fatal to the organism; for this reason is attributed the frequent disappearance of Gonorrhoea in the acute fevers. Bearing these facts in mind one arrives at the conclusion that vaccine administered intravenously owes its beneficial effect to the thermic ascent which it produces; as this temperature is evanescent, it is apparent that permanent improvement is unlikely to result.



((3) Among patients who are compelled to carry on their every day work throughout treatment I consider the intramuscular route is the most suitable as it causes no discomfort beyond a slight transitory stiffness. It also has the advantage of being a rapid method - an important factor in dealing with large numbers.

In my series of cases I used the intramuscular route throughout and in no case was the local reaction so severe as to impair the man's working capacity.

(4) Abortive Treatment.

On three occasions only did patients report within three days of the earliest symptoms. The abortive treatment was then administered. Of these three cases two had a definite greyish-white bead of discharge from the meatus. The third simply had pain on micturation. Gram negative intracellular diplococci were demonstrated in the discharge of the first two and in the third after massage of the urethra. All these cases were immediately given 5000 Million of the original detoxicated vaccine intramuscularly. This dose was repeated after three days interval and a third 5000 Million was administered on the sixth day. In every case all symptoms had disappeared completely before the third injection. The patients were kept under observation for 14 days and then discharged cured.

In addition to the specific treatment each patient received the following local treatment - the anterior urethra was well washed out with a solution of 1/8000 Potassium Permanganate. About  $\frac{3}{4}$  of a 5% solution of Argylol was instilled into the anterior urethra and retained there for five minutes - this was carried out once only.

The usual dietitic restrictions were observed and the patient encouraged to drink

drink large quantities of bland fluids in order to keep the urethra thoroughly flushed out.

The reaction in the foregoing doses of vaccine were as follows:-

General . A sharp rise of temperature  $101^{\circ}$  F to  $103^{\circ}$  F which lasted for 8 to 10 hours; also a feeling of drowsiness and slight general malaise.

Local. Slight stiffness at site of injection.

Focal. N i l.

Although one cannot be dogmatic on the results of three cases, yet it certainly indicates that the abortive treatment by detoxicated vaccine is worthy of a more extensive trial among a class of patients who report earlier for treatment than do those who attend a Venereal Clinic.

It has the following great advantages over the Silver Nitrate method advocated by Ulmann, Englebreth and others, namely:-

- (a) It does not cause any irritation, whereas Silver Nitrate gives rise to extensive pain and may even cause spasm leading to retention of urine.
- (b) It is perfectly sound treatment even on occasions when the disease has progressed too far to abort.
- (c) Silver Nitrate can only kill the organisms with which it comes in contact. As, even in the early stages some cocci have already penetrated between the epithelial cells to the submucous layers, it is easily seen that silver nitrate cannot penetrate to them

them without extensive damage to the lining epithelium. Vaccine on the other hand strengthens the bactericidal power of the body fluids which cannot fail to come in contact with the organism.

The Argyrol serves to kill off any organisms on the surface and also by reason of its hygroscopic power evokes a copious outpour of serum from the urethral lining - rich in agglutinins, etc.

The toxic forms of gonococcal vaccine would probably do more harm than good. The negative phase produced by their use would enable the disease to become firmly established in the submucous tissues necessitating prolonged treatment.

The abortive treatment should be employed upon all cases who report within three days of the earliest symptoms, unfortunately, the average working man notices nothing unusual until a roaring discharge coupled with a sensation somewhat picturesquely described as "like passing red hot pins and needles" compels his attention.

(5) Acute Anterior Urethritis.

Cases of uncomplicated anterior urethritis are somewhat rare, as, unfortunately, a large percentage of those who attend have received treatment elsewhere; indeed during the whole period of six months over which I conducted my observations, only six cases appeared in which infection of the posterior urethra could definitely be excluded.

One had to guard most carefully against the inclusion of cases of relapse in this category, as the latter invariably cleared up rapidly under Vaccines and were thus liable to stultify one's results.

These six cases were divided into two series, (~~of those each~~) both received the following local treatment:-

- i. Anterior irrigation with Potassium Permanganate in the strength of  $1/8000$ .
- ii. Suspensory bandage was worn.
- iii. Rest advocated as much as possible.
- iv. Diet. Alcohol, strong tea, coffee, butcher meat and all highly seasoned foodstuffs were forbidden.
- v. Patients were warned to avoid all forms of sexual stimulation.

Series 1. Treated by Thomson's Vaccine, received a preliminary dosage of 2500 Millions. This dose was increased to 7500

millions by the seventh injection. Doses were given at intervals of 3 - 5 days.

Series. 2.

Received fat free vaccine the initial dose being 125 millions and further dose-age was guided by the results and the reaction produced.

The following were the results in

## Series 1.

<u>Urethral Smear</u>	negative to Gonococci and pus.	18.3 days
<u>Urine</u>	Clear.	18,6 "
<u>Urethra</u>	Bone dry.	26 "
<u>Reaction</u>	Trifling or absent altogether.	
<u>Posterior Urethra</u>	became involved in no cases.	

One case was completely free from all signs of Gonorrhoea in seven days, after receiving a total of 7500 Millions of the Detoxicated organisms.

## Series 2.

<u>Urethral Smear</u>	Negative to Gonococci and pus cells	31 days.
<u>Urine</u>	Clear	28 "
<u>Urethra</u>	Bone dry.	36 "
<u>Reaction</u>	Usually sharp, characterised by increase or diminution of discharge, with a varying amount of general disturbance,	

Posterior Urethra became involved in one case, this case was three months under treatment before cure.

The chief points worthy of note in the foregoing cases are the following:-

1. Reaction was much less marked in Thomson's Vaccine and indeed was often absent altogether; patients almost invariably stated that the pain of micturation was definitely relieved by this vaccine.
2. Therapeutically, also, Thomson's Vaccine was undoubtedly preferable. The fact that in no case did the posterior urethra become involved is distinctly in its favour.
3. Both vaccines as a whole diminished the incidence of complications, as none occurred beyond the case already mentioned in which the posterior urethra became involved.

I was able to confirm the observations of Thomson and Lees with regard to agglutination and have devoted a special paragraph to this subject elsewhere.

Subsequent experience with cases, not included in the above series, has convinced me that I made the mistake of not increasing the dose of Thomson's Vaccine with sufficient rapidity. These later cases cleared up much more quickly when the dose was raised to 10,000 millions after the fifth injection. One case only failed to stand the "Test of Cure" (see para. on Test of Cure)

It was treated by Thomson's Vaccine. After the provocative injection of 100 millions Polyvalent Vaccine discharged reappeared, which on examination was found to contain Gonococci. What had happened here is probably that an infected follicle, just on the point of bursting, had received the required fillip from the provocative injection and had thereupon discharged its contents into the urethra. After dilatation this case quickly cleared up.

All cases in these Series were subjected to the following "Test of Cure" :-

When all discharge had disappeared and the urine had become clear, the patient was taken off all treatment and dietetic restrictions were removed. He was then told to resume his ordinary mode of life, but, of course, to refrain from coitus.

A Week later he was given a provocative injection of 100 millions polyvalent toxic vaccine and instructed to report again the following day. A Suction bougie was then passed into the anterior urethra and a suction smear taken. This was examined for the presence of gonococci or, equally important, for the presence of pus cells. If possible he was also urethroscoped, particular attention being paid to the state of the glands of Littre sinuses of morgagni, presence of submucous infiltration, etc.

The presence of a sharp general reaction after provocative injection was looked upon as strong presumptive evidence that the patient was still sensitised to the toxin of the gonococcus.



Intradermic injection of toxic vaccine, after the idea of the Schick test in Diphtheria, was attempted. The theory being that, if the patient was still sensitised to the toxin, the local reaction would be marked. This test did not work out in practice and was consequently abandoned.

Detoxicated Vaccine also I firmly believe to be useless for provocative work. After a full course the patient is thoroughly immunised to it and doses of as much as 10,000 millions produce practically nothing in the way of reaction.

The patients' urine was examined for the presence of haziness or threads by means of the two glass test. If threads were found, they were examined under the microscope for pus cells or gonococci.

All tests proving negative, the patient was instructed to report again in one weeks time and a suction smear was then taken. This process was repeated on three occasions after which the patient was discharged as cured with instructions to report immediately should there be any return of symptoms.

The Silver Nitrate or Stout Tests were not employed as both are inferior to the provocative vaccine. The former on account of its action in cauterizing a mucous surface which one is doing ones' best to heal; the latter, if disease still be present, it will, by causing oedema of the urethral lining, bring about conditions favourable to a relapse.

The foregoing "Test of Cure," with suitable modifications, was employed throughout this research.

(6) Posterior Urethritis.

This condition was divided, for purposes of classification, into:-

- (a) Acute Posterior Urethritis.
- (b) Sub acute Posterior Urethritis.
- (c) Chronic or relapsing Urethritis.

Acute Posterior Urethritis

Twelve cases were treated by vaccines.

Series 1. Treated by Thomson's Vaccine. (6 cases)

Series 2. Treated by fat free vaccine. (6 cases)

These cases presented the following features:-

- i. All contained gonococci, both intra and extra cellular in the urethral smear.
- ii. A small amount of muco-purulent discharge from the meatus.
- iii. All four glasses, in the four glass test, were hazy.

- iv. The prostate gland usually shewed a moderate degree of firm, diffuse enlargement, both lobes being equal. If this gland was greatly enlarged, nodular or boggy, one assumed that it had actually become implicated in the disease.
- v. Frequency and pain on micturation were present.
- vi. An ~~in~~varying amount of systemic disturbance. In one case Haematuria was present.

The local and dietetic treatment was the same save for the following differences:-

- i. Irrigation was carried right into the bladder. After the acute symptoms had subsided altogether, Hydrarg Oxycyanide in a solution of 1/5000 was substituted for Potassium Permanganate.
- ii. Prostatic massage was instituted after the acute stages had subsided.
- iii. The necessity for rest was more strongly advocated.

"Test of Cure" was the same as previously stated with the exception that:-

- i. Smears were taken after Prostatic massage.
- ii. Posterior urethroscopy was resorted to.

Dosage was the same as in Anterior Urethritis

Synopsis of Results.Series 1.

Suction Smear No gonococci or  
pus cells 33 days.

Urine Clear of threads 40 "

Discharge entirely disappeared 38 "

Reaction as before almost entirely  
absent.

Complications entirely absent.

In one case gonococci had disappeared  
in 11 days and all symptoms had cleared up in  
21 days.

In four cases no gonococci were found  
in 28 days and all symptoms had cleared up in  
34 days.

The following case which I will quote  
at length is typical of this series.

Case 1.Age 23.Painter.

1st day. Reported complaining of pain and  
frequency of micturation following  
coitus 7 days ago.

On examination

- i. A thin muco-purulent discharge was  
present which contained gonococci,  
both intra and extra cellular
- ii. Urine hazy in all four glasses.

Treatment . Irrigation daily with  
1/8000 Pot Permang.

Case 1. contd.

	<u>Detox. Vaccine.</u>
<u>1st day contd.</u>	2500 mill.
<u>4th Day.</u> Slight local reaction after vaccine.	2500 mill.
<u>8th Day.</u> No reaction, pain diminished.	3000 mill.
<u>12th Day.</u> No reaction. Discharge now clear. Urine hazy in 1st glass only.	5000 mill.
<u>16th Day.</u> Discharge only seen in morning. Urine shows a few threads in 1st glass.	6000 mill.
<u>20th Day.</u> General condition much improved. Smear shows pus cells only.	7500 mill.
<u>24th Day.</u> Slight muco purulent discharge after Prostatic massage. Irrigation with Hydrarg Oxycyanide 1/5000.	7500 mill.
<u>30th Day.</u> Suction smear shows epithelial cells only. Urine after Prostatic Massage quite clear.	
<u>35th Day.</u> Prostatic normal. Stop local treatment.	
<u>42nd. Day.</u> <u>Provocative Vaccine Polyvalent 100 mill.</u>	
<u>43rd. Day.</u> Posterior Urethroscopy reveals a healthy mucous membrane. Urine clear after Prostatic Massage. Prostate not enlarged. Suction smear shows epithelium only.	
<u>DISCHARGED.</u> with instructions to return in one month for examination.	

Series 2.

The fat free vaccine was slightly more successful in this condition, the following being the percentage results arrived at:-

Suction Smear No gonococci 35 days.

Urine Clear of threads. 44 "

Discharge entirely disappeared 44.2 days.

Reaction. was again well marked, both general and focal manifestations were frequently produced.

Complications One case developed Epididymitis, but cleared up with remarkable rapidity, all signs of Gonorrhoea having disappeared in 32 days.

Three cases showed a return of symptoms after provocative injection; one of these showed gonococci in the discharge which had been restarted. All three cases cleared up, however, after three further injections of fat free Vaccine.

To sum up the results of these cases is almost to repeat what one has already said of Anterior Urethritis, save that fat free vaccine was a little more successful. Thomson's vaccine undoubtedly cut short the duration of the disease and also diminished the incidence of complications. It again shewed a remarkably analgesic effect. Fat free vaccine also, although somewhat toxic, diminished the incidence of complications as

as compared to cases not treated by Vaccine.

Both vaccines, I consider, were useful in improving the general mental and bodily condition of the patient and also in stimulating regular attendance.

The actual statistics, I am quite aware, are not impressive and indeed are inferior to those of some observers who did not use Vaccine at all. I should like to point out, however, that patients continued their work to a great extent throughout treatment in spite of a great deal of systemic disturbance almost invariably present in this condition.

### Sub-acute Urethritis.

No less than thirty two of my cases fell into this category. They largely consisted of men who had neglected treatment in the first few weeks of the disease with the result that the disease had been thoroughly disseminated throughout the submucous tissues well beyond the reach of any local treatment.

Urethroscopy of a case of this sort revealed a patchy granular condition of the mucous membrane with, usually, numerous infected follicles, on the roof and sides of the urethra, shining through the epithelial lining in a manner strongly reminiscent of Koplik's spots.

The discharge was usually scanty and muco-purulent and the urine, as a rule, showed small white threads in both glasses.

Treatment was along the same lines as in the acute stage save that prostatic massage was resorted to from the onset and the mercury salt employed for the irrigation.

Kollman's dilator and also penile and suction bougies were employed.

"Test of Cure" was as previously stated. Every case was urethroscoped before final discharge.

With regard to dosage, the same course was given as in the acute condition, but it was



was found necessary to repeat the course twice or even thrice in the more obstinate cases.

I will now give the results of treatment and will afterwards discuss a few individual cases; these latter varied so greatly that bare statistics are apt to be misleading.

Sixteen cases treated by Thomson's Vaccine.

Prostatic Smear contained no  
Gonococci or Pus 56 days

Urine clear of threads 58 "

Urethra bone dry 62 "

Prostate normal 52 "

Reaction trifling or absent altogether.

Complications (during treatment)  
Arthralgia one case

Epididymitis one case.

Sixteen cases treated by fat-free Vaccine.

Prostatic Smear contained no  
Gonococci or pus 54 days

Urine clear of threads 70 "

Urethra dry 77 "

Prostate normal 77.3 "

Reaction Always marked and in some cases severe. Two cases were confined to bed for 48 hours after first and third dose respectively.

Complications (during treatment)

Toxic conjunctivitis one case.

Epididymitis one case.

Prostatitis two cases.

As I have pointed out comparison of these cases is unfair as individual cases varied widely in their clinical manifestations. Thomson's vaccine was again proved to be less toxic and also to control the incidence of complications more effectively.

The effect of both vaccines upon the patients' outlook was very satisfactory; their general condition, also, seemed to be improved by them.

Two cases of this series reported each with a large fluctuating swelling in the perineum due to an infection of Cowpers' gland. These swellings were incised, and fat-free vaccine was administered after gonococci had been demonstrated in the pus which was evacuated. Both cases did extremely well and were able to leave Hospital in ten days. A third case also appeared with a peri-urethral abscess about the size of a marble, this was incised and gonorrhoeal pus evacuated. Pus continued to discharge from the abscess cavity for a period of fourteen days after which fat-free vaccine was administered. The discharge then rapidly diminished and the condition had entirely cleared up after three injections.

These conditions show very clearly the advantage of combining the two forms of therapy.

It is quite obvious, that a large infected follicle or an abcess of Cowpers' gland cannot be cured by Vaccines alone; on the other hand, after incision, vaccines assist these cases to clear up in a remarkable manner. Fat-free Vaccine was found particularly useful for this purpose.

The case which developed Arthralgia was, doubtless, a case which would have developed a definite joint condition without vaccine treatment.

One has noticed frequently, that in the early stages of joint affections, this flitting pain, known as Arthralgia, is present before the disease becomes localised to one joint. In the case referred to above, this patient had received in all 5000 millions of the detoxicated organisms before the condition developed. Vaccine was then pushed and after the patient had received 15,000 millions in all, pain had vanished entirely and did not recur.

Exactly the same thing may be said of the case, treated by fat-free vaccine, which developed toxic-conjunctivitis, after three doses of 125 millions each no gonococci were present in the eye discharge and the condition was cured in ten days by two further injections of 250 millions each.

I should like to point out here the

the futility of attempting to treat such conditions, as the last two mentioned, in any way save by vaccine therapy. It should be obvious, even to the most confirmed disciple of Kidd, that no form of local treatment can anticipate the disease and actually cure it before it occurs, to use an Irishism, as was undoubtedly done in the above two cases.

Another point I should like to bring forward in this connection is this:-

Roughly about 7% of all cases suffering from sub-acute Urethritis, who were not treated by vaccine, returned suffering from relapse within two months of discharge.

I arrived at these figures by consulting the ward files over a period of six months when vaccines were not being used in this condition.

On comparing the above with cases on Vaccine treatment, I find, I have not a single case of relapse in the foregoing series of cases despite the fact that they have all been discharged for the last ten weeks and have been carefully instructed to report should there be any return of symptoms. While admitting that local treatment in these wards has improved greatly in the last six months, yet I feel I can justly draw the conclusion that both vaccines have the effect of

of decreasing the likelihood of relapse almost to a vanishing point.

To conclude, I consider there is a good case for both vaccines in this condition if combined with efficient local treatment.

Of the two Vaccines I should again prefer to use that prepared by Thomson.

#### Chronic or Relapsing Urethritis.

To deal at length with this condition would be to repeat a great deal of what has already been said. I propose, therefore, briefly to give a summary of the results arrived at.

The great majority of these cases had been treated in various Naval and Military Hospitals during the War and had been discharged when treatment was incomplete, either owing to exigences of service, or, perhaps, because an efficient standard of cure was not maintained.

Relapse usually occurred after a drinking bout or sexual excess. Patients usually gave a history of a slight clear discharge since leaving hospital which became yellow and turbid

turbid shortly after excess of some sort. I observed fifteen such cases.

Urethroscopy usually revealed submucous infiltration, Litttritis, etc.

Both vaccines did well in combination with local treatment. Symptoms had usually entirely cleared up in 28--30 days. There was really very little to choose between the two in this condition save that, as always, Thomson's Vaccine provoked less reaction.

With regard to complications, one case on Thomson's vaccine developed a slight synovitis of the left knee; a second under fat-free vaccine developed an acute prostatitis which took nine weeks to clear up. The joint condition rapidly disappeared with further dosage by Thomson's Vaccine.

Two cases whose film showed mixed infection were treated by a Vaccine prepared from detoxicated secondary organisms. I shall have occasion, however, to refer to these cases subsequently.

(7) Prostatitis.Acute Prostatitis.

Four cases appeared with this condition presenting, briefly, the following characteristics:-

- i. A history of Gonorrhoea for six weeks or more.
- ii. Sudden cessation of urethral discharge together with pain and difficulty of micturation.
- iii. Great pain in the rectum and loins, rendered worse on going to stool.
- iv. On rectal examination, a boggy swelling, usually about the size of a walnut, could be palpated in the position of one or the other lobe of the prostate.
- v. Always a considerable degree of systemic disturbance - fever, constipation, thirst, etc.

Treatment:- All cases were admitted to the ward and kept in bed for the first fourteen days or thereabouts.

- i. Sitz baths were given daily and hot applications in the intervals between them.
- ii. During the more acute stage, Atropin Suppositories  $\frac{1}{10}$  gr. were introduced into the rectum each evening.
- iii. Irrigation was not proceeded with until the acute symptoms had subsided and was then carried out cautiously.

- iv. Prostatic massage was carried out gingerly when the pain and tenderness associated with that organ had to some extent diminished.
- v. The bowels were carefully regulated.

Vaccines were not exhibited until, by the increased amount of discharge or the appearance of blood in the urine coupled with a sudden diminution in the size of the prostate, as felt from the rectum, one had concluded that the pus had found an outlet.

In the later stage, when the condition showed signs of becoming chronic, Kollman's dilator was resorted to. Its use being controlled by Urethroscopy.

"Test of Cure" was much the same as already described. Patients were not discharged until three successive smears, taken after dilatation and prostatic massage, had proved negative to pus and gonococci.

Two cases were treated by Fat-free Vaccine, dosage being as previously stated.

One case was treated by Thomson's Vaccine.

The fourth, the only case the smear of which did not show a pure culture of gonococci,



received concurrently Thomson's Gonococcal Vaccine and also a Vaccine prepared from detoxicated Secondary Organisms; this latter contained chiefly - Staphylococci, Diphtheroids and gram positive cocco-bacilli. Dosage was commenced immediately pus had found an outlet, and the following were the results obtained from the two on Fat-free Vaccine:-

Able to attend as Out Patient 21 days

Prostatic Smear Free from pus  
or gonococci 60.5 "

Urine clear of Haze and Threads 70 "

Prostate normal 70 "

Reaction always sharp. In one case  
3rd injection was followed  
by severe haematuria.

Complications One case developed  
Arthralgia and myositis  
of the lumbar muscles,  
which, however, cleared  
up in a short time.

It is interesting to note that the case which developed Haematuria had a history of a previous attack while in Egypt. The Urine, consequently, was examined for Bilhartzia haematobium. The Ova were found, thereby clinching the matter. There is no doubt, however, that he also had a prostatic abscess of gonorrhoeal origin.

The two remaining cases cleared up much more rapidly results being as follows:-

Able to attend as Out Patient 26 days.

Prostatic Smear Clear of pus 48 "  
and gonococci

Urine clear of haze and threads 57 "

Prostate normal 60 "

Reaction Slight general disturbance  
as a rule. Rise of temperature  
1 - 2 degrees.

Complications none.

As can readily be perceived from the foregoing statistics Thomson's vaccine was more effective in this condition. As I have noticed throughout the whole of this work fat-free vaccine is to be avoided in acute conditions.

Neither vaccine should be administered on the same days as the patient undergoes prostatic massage if it can be conveniently avoided. The reason for this is as follows:-

Massage has the effect temporarily of increasing the blood supply of the gland, also of breaking down and disseminating areas of pus formation. It is thus quite clear that there is a great increase in the amount of toxic material absorbed from this gland into the systemic circulation. Now if one administers vaccine, however atoxic, synchronously with prostatic massage, one runs the risk of provoking a severe general reaction. This, I may say, actually does occur.

The auto-vaccination produced in the foregoing manner by prostatic massage is, to my mind, a factor in the cure of this condition which has been insufficiently recognised in the past.

Chronic Prostatitis  
with gleet.

I originally had sixteen cases under observation in this category. Four of these were transferred to another centre before completion of treatment with the result that instead of there being an equal number of patients on each vaccine I was left with seven on Thomson's vaccine and five on the fat-free variety.

The chief points in the history of these cases are as follows:-

- i. An attack of acute urethritis at a time varying from three months to ten years ago.
- ii. Patient had usually received some form of treatment elsewhere which usually had the effect of clearing up acute symptoms but had left a legacy of gleet.

On examination these cases usually showed a slight stickiness at the meatus or a slight discharge of clear fluid. The prostate was enlarged, uneven and often hard and nodular.

In five of these cases one vesicle was palpable and, in one case, both of these organs were enlarged.

Examination of a smear after prostatic and vesicular massage usually revealed a mixed infection of pneumococci, diphtheroids, cocco-bacilli, etc.

In four cases only were gonococci demonstrated.

The urine after prostatic massage usually showed pus and threads in the first two glasses.

All cases received the following routine treatment:-

- i. Alcohol and coitus were forbidden, but otherwise patient was advised to live his ordinary life and take plenty of exercise.
- ii. Posterior irrigation with Hydrarg Oxycyanate 1/5000 at a temperature of 110° F.
- iii. Prostatic and Vesicular massage bi-weekly.
- iv. Posterior dilatation by means of Kollman's dilator, its use being controlled by the Urethroscope.

"Test of Cure" Particular attention was paid to the state of the urine as regards threads after prostatic and vesicular massage and also the disappearance of pus from the prostatic fluid. The presence of organisms of secondary infection were

not regarded as evidence of morbidity. In doubtful cases a culture was made of the urine after provocative injection to detect the presence of gonococci.

With regard to dos-age, those on Thomson's vaccine received detoxicated secondary organisms starting with 2500 millions and working up to 10,000 at the 7th dose.

Two cases, included in the above, and in whom gonococci were demonstrated, received in addition an equal amount of Thomson's Gonococcal Vaccine.

Results in this series were as follows:-

No pus in Urine threads or prostatic smear.	10 days.
No discharge from meatus.	14 "
Prostate and Vesicles normal.	22 "
Reaction usually slight focal manifestations of about 24 hours duration.	
Complications - None.	

One case on this Vaccine is not cured yet so he is not included in the above table. Up to date he has been under treatment for three months and has received three courses of detoxicated secondary organisms. His urine still shows heavy threads laden with pus cells but no gonococci can be produced by provocative injections.

The figures for those treated by fat-free Vaccine were very similar:-

No pus in urine threads or  
prostatic smear. 9 days

No discharge from Meatus. 17 "

Prostate and Vesicles normal. 19 "

Reaction slight, as a rule. One case, however, was incapacitated from work for one day after his fourth dose of 500 millions.

Complications - Epididymitis one case which cleared up quite satisfactory.

The weak point about this series is the fact that gonococci were not demonstrated in the majority of cases so one could not say that the condition was due to that organism. Still gonococcal vaccine was administered as an experiment.

\* I am inclined to attribute the rapidity of cure to the careful local treatment rather than to any virtue possessed by the Vaccine in this condition.

The Vaccine prepared from the detoxicated mixed organisms gave me the impression of being quite inert. Probably these mixed organisms are not the cause of the trouble at all but are merely saprophytic, discharge being kept up by the unhealthy catarrhal condition of the glandular elements of the prostate.

To conclude, I think both gonococcal vaccines are probably useful in those cases in which

Gonococci have actually been demonstrated, as they apparently lower the incidence of complications. They are also worth using if only for their effect on the mentality of the patient. He is invariably depressed and neurotic, in some cases even suicidal. He has usually tried every form of treatment and is convinced that he is incurable; hence the desirability of impressing him by the use of Vaccine.

(8) Epididymitis.

This is an extremely common complication of Gonorrhoea. Of the 150 cases which I had under observation no fewer than 17 were suffering from this condition and 5 developed it in the course of treatment. These latter five I have referred to previously.

Chronic constipation was a very constant feature in the history of these cases and is, to my mind, an important factor in the causation of epididymitis. Constant straining at stool accompanied by the passage of hard faecal material

over an acutely inflamed prostate causes infective material to be forced into the mouths of the ejaculatory ducts, extension to the epididymitis is then almost a foregone conclusion. The administration of Sulphur or Liquid Paraffin, as a routine measure in all cases of posterior urethritis to regulate the bowels, is therefore advisable and will be found a valuable adjunct to vaccines in the prevention of this complication.

Of the 22 cases under treatment 17 were acute conditions and presented the following run of symptoms:-

- i. A varying amount of acute hydrocele was almost invariably present.
- ii. One or both epididymi were enlarged and tender.
- iii. Usually a slight muco-purulent discharge from the urethra.
- iv. A varying amount of systemic disturbance.
- v. The prostate and corresponding vesicle were somewhat enlarged.
- vi. The cord showed no marked degree of thickening.

In addition to vaccines they received the following routine treatment:-

- i. Irrigation daily with 1/8000 Pot. Permang from a height of three feet if the condition were not too acute.
- ii. Locally an Icthyol fomentation was applied to the testicle until the acute stage was over, after which Scott's dressing was substituted.
- iii. After patient was able to leave his bed a suspensory bandage was



recommended to be worn for some months.

iv. Diet and general hygiene as in acute urethritis.

Ten cases received Thomson's

Vaccine with the following results:-

Gonococci and Pus absent  
from Urethral discharge. 30 days

Testicle, cord and  
epididymitis normal. 38 "

Prostate normal. 40 "

Reaction - occasionally a slight rise of temperature after injection (see chart) Occasionally, also, there was a slight local reaction characterised by pain and swelling in the testicle. More often, however, pain was relieved after injection to quite a remarkable extent.

Complications - Other testicle became slightly swollen in one case only.

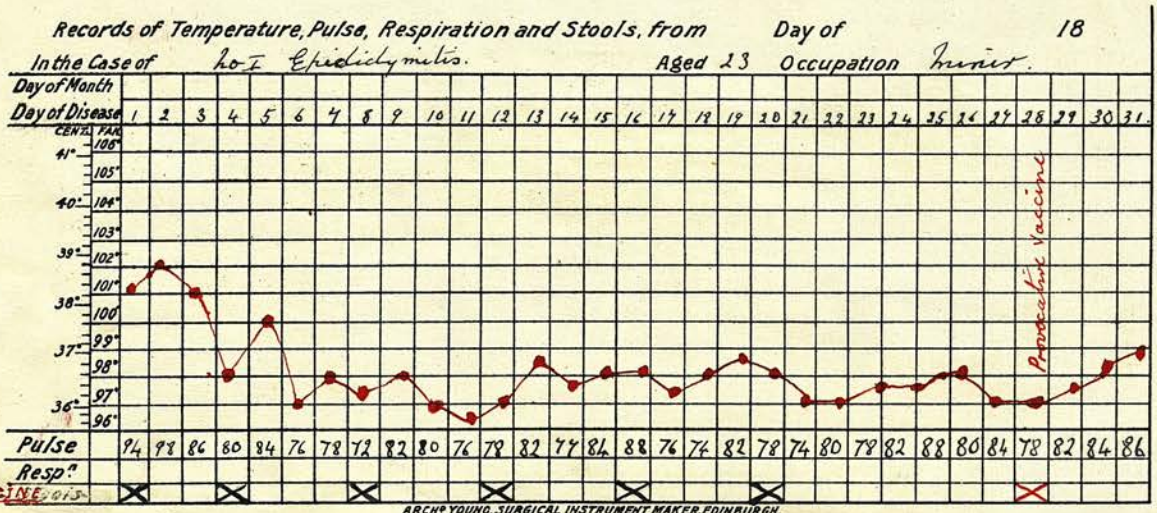
The urethral discharge behaved in much the same way as in acute urethritis save that agglutination was more marked and gonococci disappeared more rapidly.

I will quote the following case in full with temperature chart to give some indication of the typical course of a case of this series treated by Thomson's Vaccine.

recommended to be worn for some months  
 iv. Diet and general hygiene as in acute epididymitis  
 Ten cases received Thomson's

Vaccine with the following results:-

Gonococci and Pils absent



Vaccine 2013

The vaccine was prepared in the following manner...  
 I will quote the following case in full with temperature chart to give some indication of the typical course of a case of this variety treated by Thomson's Vaccine.

Case 1.

Age 23.

Miner.

History.

Urethral discharge for three months.  
Pain and swelling in the left testicle  
since playing football seven days ago.

Examination.

Temperature 101° F.  
Moderate muco-purulent discharge  
containing gonococci chiefly intra-  
cellular.  
Left Epididymis swollen and hard.  
A little free fluid present in left  
Tunica. Cord was not thickened.

Treatment.

Patient was put to bed and Icthyol  
applied locally in the form of a hot  
fomentation. Purgative administered.

1st. Day.

Discharge muco-purulent.  
Urine haze in both glasses.  
Reaction general, slight.  
Local - pain diminished.

Detox.Vaccine.

2500 mil.

4th. Day.

Discharge muco-purulent.  
Urine haze both glasses.  
Reaction slight local.

3000 "

8th Day.

Discharge, clear fluid.  
Urine haze in both glasses.  
Epididymis slightly reduced.

5000 "

12th Day.

Discharge, slight gleet.  
No fluid in Tunica now.  
Urine, 2nd glass clear.  
Reaction none.  
Scotts' dressing applied  
to testicle.

5000 "

16th Day.

Discharge, nil.  
Urine:- 1st Glass threads  
2nd. " clear.  
Discharged from Ward to  
attend as out-patient.

7500 "

20th Day.

Discharge, slight gleet.  
Urine clear both glasses.  
Epididymis, still slight  
thickening in tail.

10,000 "

Case 1 contd.

<u>24th Day.</u>	Discharge, nil. Urine clear. Epididymis almost normal.	<u>Vaccine</u>  --
<u>28th Day.</u>	Polyvalent Toxic Vaccine 100 millions.	
<u>29th Day.</u>	No reaction. Urine clear after prostatic massage. Testicle normal. Prostatic Smear shows:-	
	Epithelial cells. A few polymorphs. A few sperms. No organisms.	
	Prostate both lobes slightly enlarged. To irrigate with Hydrarg Oxycyanate 1/5000.	
<u>32nd. Day.</u>	No signs of Gonorrhoea. To be placed on "Test of Cure".	
<u>40th Day.</u>	Discharged with instructions to appear for examination in one month.	

---

Case 1 contd.

40th Day. Discharged with instructions to appear for examination in one month.

39th Day. No signs of gonorrhoea. To be placed on "Test of Cure".

38th Day. Prostate both lobes slightly enlarged. To irrigate with 10% Boric Oxycerate 1:5000.

37th Day. No organisms. A few squames. A few polymorphs. Epithelial cells.

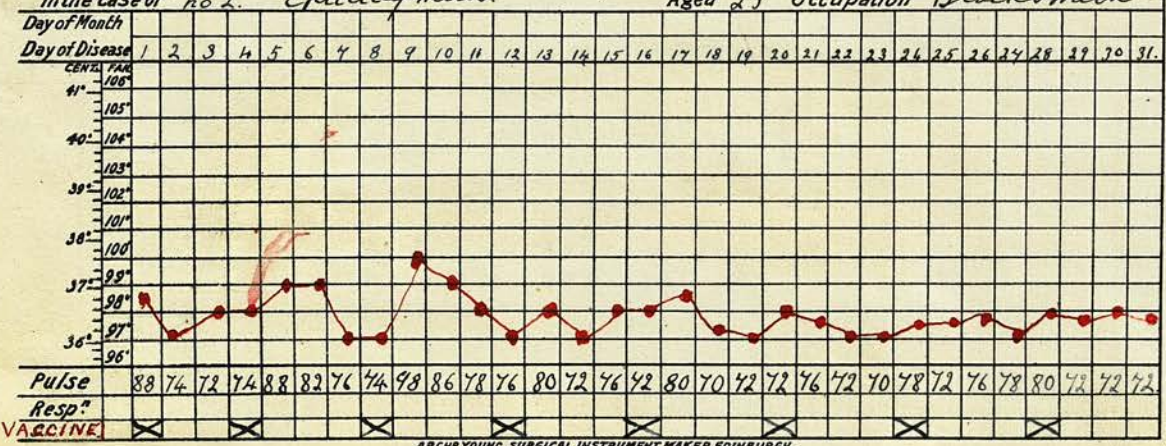
36th Day. Prostatic smear shows: Testicle normal. Urethra clear after prostatic massage. No reaction.

35th Day. Polysplend Toxic Vaccine 100 millions.

34th Day. Discharge, nil. Urethra clear. Testicles almost normal.

Vaccine

Records of Temperature, Pulse, Respiration and Stools, from Day of 18  
 In the Case of No. 2. Epididymitis. Aged 23 Occupation Blacksmith



The seven cases treated by fat-free vaccine also did well, indeed the actual time under treatment was shorter.

Gonococci and pus absent from discharge. 27 days.

Epididymis normal. 38 "

No discharge from meatus. 29.5 "

Prostate normal. 42 "

Reaction usually and increase in the swelling after the initial dose, together with rise of temperature and feeling of malaise. Always more marked than in detoxicated series.

Complications - none.

The following is a case, given in full, treated by fat-free Vaccine.

### Case 2.

Age 23.

Blacksmith.

#### History.

Contracted Gonorrhoea five weeks before reporting for treatment. Left testicle began to swell seven days before he reported.

#### Examination.

Purulent discharge from urethra containing gonococci both intra and extra cellular. Left epididymis greatly swollen and tender. Skin over scrotum slightly red and oedematous. Slight thickening of the left Vas.

Case 2. contd.

<u>Day.</u>		<u>Fat-free Vaccine.</u>
<u>1st. Day.</u>	Discharge, M.P. Reaction, Temp 97. Testicle more painful. Urine both glasses hazy	125 mill.
<u>4th. Day.</u>	Discharge decreases. Epididymis slightly diminished.	125 "
<u>8th. Day.</u>	Discharge: Slight muco- purulent. Epididymis much improved. Reaction: Slight general.	250 "
<u>12th Day.</u>	Discharge slight gleet. Urine haze in 1st glass only. Epididymis: some induration but pain entirely gone.	250 "
<u>16th Day.</u>	Discharge clear fluid. Urine threads in 1st glass. Scotts' dressing applied to testicle. To attend as out-patient.	300 "
<u>20th Day.</u>	Discharge slight muco-purulent. Urine haze in 1st glass only. Testicle practically normal.	350 "
<u>24th Day.</u>	No discharge. Urine threads in 1st glass. Testicle normal. Prostatic Smear shows:-  Epithelium. Pus cells. No Organisms.	400 "
<u>28th Day.</u>	Discharge nil. Urine threads in 1st glass. Urethroscopy reveals an infected follicle near meatus. This was emptied of its contents by massage on a penile bougie.	500 "
<u>36th Day.</u>	Provocative Injection of 100 millions polyvalent Vaccine. Reaction: slight pain in testicle. Smear shows - Epithelial cells only.	
<u>40th Day.</u>	Urine clear in both glasses. Testicle normal. Prostate normal. Urethroscopy shows normal mucosa. No follicles seen. To return in one month for examination.	

To compare these two vaccines as regards:-

i. Toxicity.

Thomson's vaccine is undoubtedly preferable, there being practically no reaction set up beyond a slight stiffness locally and a rise of temperature of one to two degrees. On the other hand the fat-free vaccine occasionally gave rise to pain in the affected testicle which radiated up the cord; this pain often persisted for 48 hours.

ii. Therapeutically.

The fat-free vaccine appeared to have a more specific effect but requires careful handling. If the dose is regulated to the effect produced accidents will be avoided but it was found inadvisable to adhere to any fixed scheme dos-age.

Both Vaccines had the effect of modifying the course of the disease to an appreciable extent. Thomson's vaccine had a remarkable effect in relieving pain.

The aim in treating epididymitis is, obviously, to restore that organ to its normal state and thus to preserve its function. I feel that this ideal can be brought nearer by early and energetic Vaccine therapy which will shorten the duration of the inflammatory process in this very delicate and



highly specialised organ and thus reduce the danger of fibrosis to a minimum. By these means the most fruitful cause of sterility in the male may be to a large extent avoided.

#### Chronic Epididymitis.

The remaining five cases fell into this category.

- i. All these cases had suffered from the condition for at least three months with a history of one or more relapses.
- ii. Usually both testicles were affected to a certain extent.
- iii. All showed a definite thickening of the cord on the affected side, also usually some chronic enlargement of the corresponding testicle.

They were treated similarly to the acute cases and showed even more rapid response to Vaccines.

It could not be reasonably be expected that the end results would be so good in view of the fact that a good deal of fibrosis had already occurred. Yet in two cases with a history of relapsing epididymitis for over six months I was able to demonstrate sperms in the seminal fluid after repeated massage of the Vesicles.

(9) Arthritis.

While Arthralgia was relatively common among these cases, actual involvement of a joint with the production of visible clinical signs was comparatively rare. In fact I can only produce four cases in which definite morbid signs could be demonstrated.

I find that most writers give the average of joint complications at 2%; my figures, four out of 150, correspond roughly to this.

Two cases were treated by each vaccine and all showed a well marked response. One can speak confidently of the value of both Vaccines in this complication, as all these cases had received various forms of treatment previously without gaining any permanent benefit.

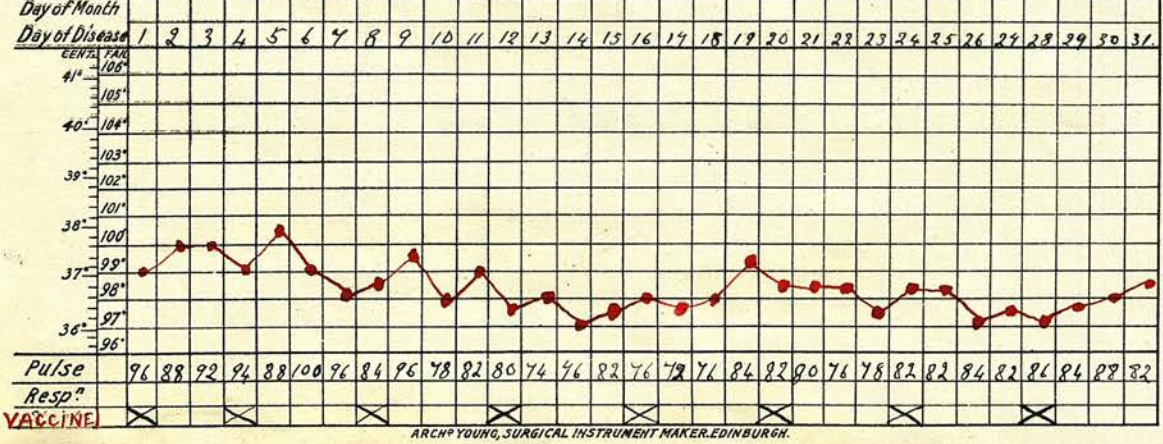
Figures are of no value here as the clinical condition of the cases varied widely. I propose, therefore, simply to give a short history of the progress and treatment of each case.

## Case 1.

While Arthritis was relatively common among these cases actual involvement of a joint with the production of definite clinical signs was comparatively rare. In fact I saw only

Records of Temperature, Pulse, Respiration and Stools, from Day of 18.

In the Case of No. I Arthritis Aged 20 Occupation Sailor.



## Case 1.

Age 20½

Sailor.

History of urethral discharge for three months.

Two months ago a large fluctuating swelling developed over the left tarsus. This had been incised and fluid evacuated.

On appearance.

- i. Thick white muco purulent discharge from meatus.
- ii. Pain and limitation of movement of left mid-tarsal joint.
- iii. Large fluctuating swelling on dorsum of foot.
- iv. Slight pain and stiffness right wrist.
- v. Smear from discharge shows:-  
 "Numerous Gonococci placed both intra and extra cellularly"
- vi. Rectal examination showed definite enlargement of both lobes of the prostate and both vesicles.

Treatment. Was the same as previously described.

Locally. Hot Icthyol fomentations were applied to the wrist and foot.

After a total of 30,500 million detoxicated gonococci given over a period of 25 days:-

- i. The wrist was quite normal.
- ii. The ankle still showed slight stiffness, but the swelling had entirely subsided.
- iii. The patient, who had previously been

Case I. contd.

- iii. been confined to bed, was allowed to get up and use his foot for a short time each day.
- iv. The urethral smear now showed Pus and a few gram + cocci but no typical gonococci.
- v. The prostate and vesicles, which had been massaged regularly twice per week, were now approximately normal.

Liniment was now substituted for Icthyol fomentations and patient received a further 35,000 million detoxicated organisms over a further period of forty days.

Examination after this period showed:-

- i. A perfectly normal joint.
- ii. Urine after prostatic massage quite clear.
- iii. No discharge from urethra.
- iv. Urethroscopy revealed a perfectly healthy mucous membrane.

The patient having survived the "Test of Cure" was discharged.

Reaction:- In this case was at first quite marked. It took the form of a definite increase in size of the joint. This usually persisted for two or three days. The patient himself stated that he was quite convinced that he saw a definite improvement after each injection which usually became evident about three days afterwards.

iii. been confined to bed was allowed to get up and see his foot for a short time each day.

iv. The medical man now advised 1/2 oz and a few grains of cod oil but no typical gonorrhoea.

v. The prostate and vesicles which had been enlarged regularly twice per week were now approximately normal.

Treatment was now substituted for local formations and patient received a further 25,000 million tubercled organisms over a further period of forty days.

Examination at the end of this period showed:-

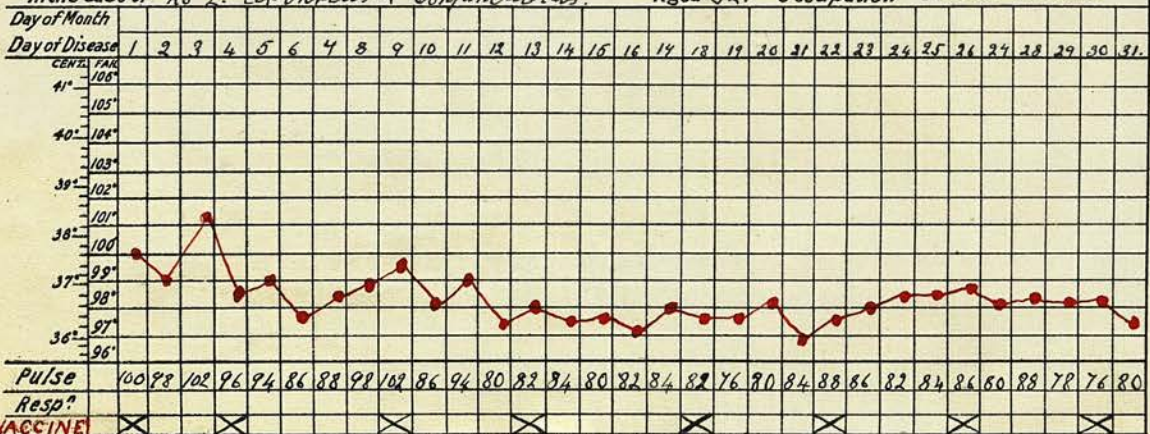
i. A perfectly normal joint.

ii. Urine after prostate massage quite clear.

iii. No discharge from urethra.

iv. Urethroscope revealed a healthy mucous membrane.

Records of Temperature, Pulse, Respiration and Stools, from Day of 18  
 In the Case of No. 2. Arthritis & Conjunctivitis. Aged 32. Occupation Farm Hand.



To epitomise this case:- Here is a man, with a gonorrhoeal hydrops of two months duration, who came into Hospital hobbling on two sticks, discharged completely cured in 61 days.

His treatment, other than vaccines, had been exactly the same as he had received before admission without permanent benefit. One can justly claim therefore that he owed his rapid improvement to the Vaccines.

Case 2.

Age 32.

Ploughman.

Was extremely interesting.

History:-

- i. Gonorrhoea of four days duration.
- ii. Stoutly denied any previous infection.

Examination, revealed:-

- i. Purulent discharge from the urethra containing gonococci.
- ii. Frequency of micturation.
- iii. Eyes. Inflammation of both conjunctivae with a thin discharge of muco-pus from the palpebral fissure on both sides - no gonococci were found in this discharge.
- iv. Right knee was greatly swollen and tense, movements were restricted and painful but no creaking was elicited.
- v. The prostate showed a moderate degree of enlargement but the vesicles were not palpable.

Case 2 contd.

Treatment:- The eye condition was treated locally by :-

- i. A 5% solution of Argyrol to which atropin had been added.
- ii. Boric eye baths.
- iii. An eye shade.

Otherwise treatment was as in

Case 1. Improvement was really remarkable.

Three days after the first injection he was able to remove the shade from his eye, and the fluid in the knee was visibly reduced.

After 16,5000 millions of detoxicated organisms he was able to leave hospital and attend bi-weekly as an out-patient, the knee being entirely free from fluid.

After a further 30,000 millions he was put upon the "Test of Cure" which he successfully survived.

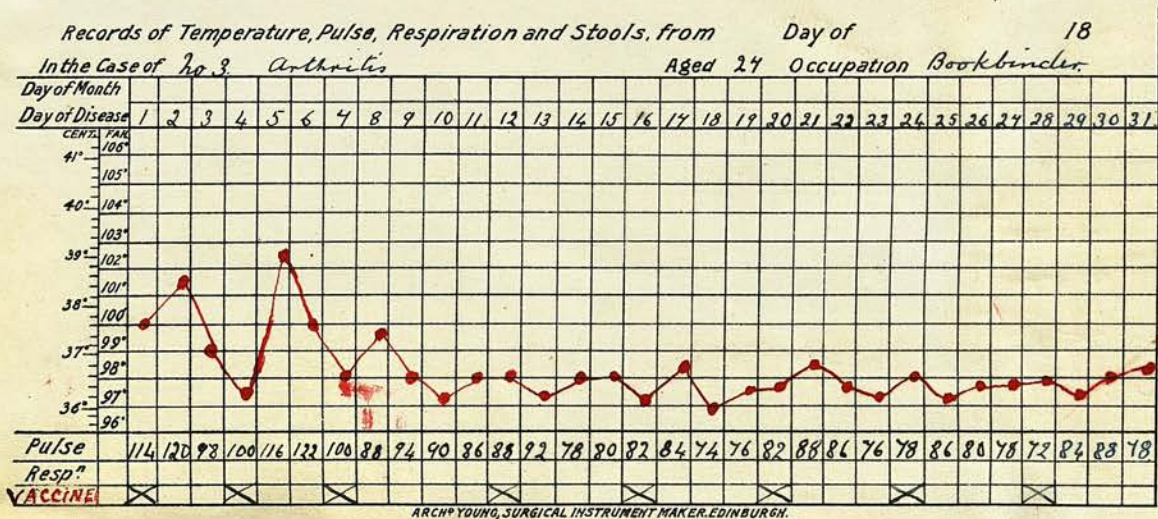
This man was obviously suffering from a toxic conjunctivitis; the premonitory inflammation set up by the gonococcal toxin, circulating in the blood, before the organisms themselves settle down in the focus.

Treatment extended over a period of five weeks at the end of which both the knee and the eye condition were completely cured and no sign of gonorrhoea remained.



Case 2

The eye condition was treated  
 locally by  
 A 5% solution of Atropin 1/2 which  
 atropin was then added.  
 For eye baths  
 An eye shade  
 Otherwise treatment was as in  
 Case 1.  
 Improvement was readily perceptible.  
 Three days after the first injection  
 he was able to remove the shade from the eye and the  
 fluid in the eye was visibly reduced.  
 After 10,500 million of desiccated  
 organisms he was able to leave hospital and attend  
 to his work as an out-patient, the same being entirely



Case 2 contd.

Reaction in this case was less marked and improvement seemed to set in from the very first.

The following cases treated by fat-free vaccine also showed a gratifying response.

Case 3.

Age 27.

Bookbinder.

History:- Contracted gonorrhoea six months ago. Has had rheumatism in the left knee and left metatarsals for the past five months.

Examination:-

- i. Left knee swollen and tense.
- ii. Left elbow painful on movement and also slightly swollen.
- iii. Slight gleet from the meatus in which gonococci could be found.
- iv. Left lobe of the prostate and left vesicle were moderately enlarged.

Treatment:- The same as in previous cases.

Course:- Improvement was not so steady but patient was completely cured in six weeks after a total number of 20,000 millions of fat-free gonococci had been administered.

Case 3 contd.

Reaction:- Reaction was sharp and painful after each of the first three injections. Latterly there was nothing beyond the usual local disturbance.

This case had been under treatment in the Lock Department for one month before receiving vaccine. During that time he had shown practically no improvement and, indeed, the muscles associated with those joints affected were already beginning to show signs of wasting. Progress after vaccine was administered was by fits and starts. One occasionally thought that the patient was going back as he developed Lumbago about half way through treatment; this quickly cleared up, however, and the patient left hospital in a perfectly sound and healthy condition.

Case 4.

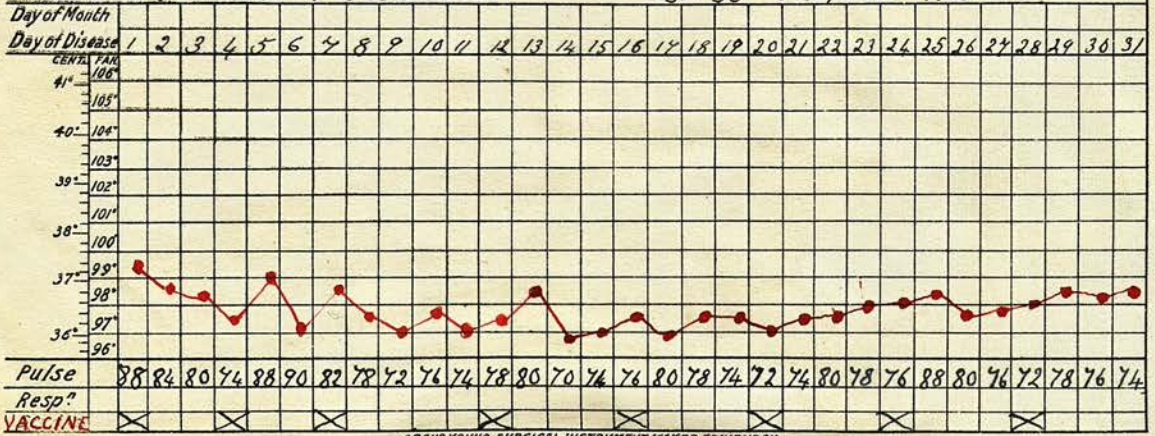
Age 33.

Miner.

History.

- i. Gonorrhoea three years ago which was apparently cured.
- ii. Coitus seven days ago after which discharged restarted.
- iii. Pain in buttocks, shooting down both legs, started one week ago.

Records of Temperature, Pulse, Respiration and Stools, from Day of 18  
 In the Case of 4. Arthritis & Sciatica Aged 33 Occupation Miner



ARCHER YOUNG, SURGICAL INSTRUMENT MAKER, EDINBURGH.

...the ...  
 ...improvement ...  
 ...associated with ...  
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 Case A  
 Miner  
 History  
 1. ...  
 2. ...  
 3. ...

Case 4. contd.Examination:-

- i. Slight muco-purulent discharge from meatus.
- ii. Pain and hydrops of left shoulder joint. Some limitation of movement.
- iii. Tenderness on pressure over course of each sciatic nerve.
- iv. Prostate moderately enlarged. Vesicles not palpable.
- v. Smear showed:-  
"Epithelial cells, pus cells, and a few gonococci."

Treatment:- As before.

Patient received a full course of fat-free vaccine totalling 19,000 millions. At the end of this the gonorrhoeal sciatica had entirely disappeared and the shoulder was quite normal. Treatment extended over a total period of 36 days after which the patient successfully negotiated the "Test of Cure",

A feature of this case was the rapid disappearance of the Sciatica. One wonders how many of these obstinate cases of Sciatica, one so often meets with in a Medical Out-Patient Department, are due to Gonorrhoea.

To weigh up the results of these cases one comes to the following conclusions:-

- i. Vaccine is undoubtedly the specific treatment of joint conditions.
- ii. Both vaccines are approximately equal in their therapeutic effect, but as that of Thomson causes less disturbance, I should prefer to use it.
- iii. Fat-free Vaccine is useful and in some instances appeared to have a more powerful effect.
- iv. One occasionally noticed pain in a fresh joint shortly after vaccine administration but one never saw actual involvement.

(10) The Phenomenon of Agglutination.

I was, at first, inclined to be somewhat sceptical of this as one could observe extracellular clumps of gonococci in the film of quite acute cases. These are simply due to active division of the cocci and the colonies thus formed are, therefore, direct evidence of an active process rather than of cure. Further investigation, however, on cases treated by Vaccines convinced me that agglutination does actually take place.

Torry in 1907 injected rabbits with gonococcal vaccine. He then tested the serum of the rabbits so treated for the presence of

bactericidal substances against living gonococci with most convincing results. He was able to prove that both agglutinins and precipitins were produced. From this one is led to presume that the defence mechanism of the body against the gonococci lies in the production of Agglutinins, precipitins and, perhaps, bacterolysins.

Oponins evidently are not an important factor in the curative process as I have never observed an increased phagocytosis as the condition trends towards cure. The presence of intracellular gonococci is looked upon rather as a feature of an acute process. McDonagh<sup>b</sup> goes so far as to say that the gonococci are really the aggressors and actually invade the polymorphs.

Agglutinogen, the substance said to stimulate the production of agglutinin in the body, is probably contained in the stroma of the germ rather than in the endotoxin. It can be seen, therefore, that Thomson's vaccine, which is said to contain capsule+stroma, should stimulate the production of agglutinin. This actually does occur, photographs 4 and 5 are from the smears of two cases of posterior Urethritis after they had received doses of 20,000 million and 18,000 million Detoxicated Organisms respectively. Photographs 3 and 6 are from two cases of approximately the same duration who received no vaccines.

All four cases received the same local treatment.

I have observed this phenomenon in many dozens of films and am convinced of its truth. It was these very cases which showed agglutination most definitely that did best clinically.

I look upon this phenomenon as a most valuable guide to dosage and progress in this condition. It should form a useful substitute for the opsonic index which, according to Cole and Mekins, is useless in this disease.

The best means of observing agglutination is to take a slide upon which a small drop of saline has been placed; then allow a drop of the urethral discharge to fall on the saline, and the mixture thus formed to spread itself. It can then be examined under a high power.

To obtain the above photographs, I was compelled to spread the film mechanically and to dry it. In this process probably some of the larger clumps would become broken up and diffused throughout the slide. The films themselves were stained by Gram's method, neutral red being utilised as the counter stain.

Agglutination was not usually evident until the 2nd. dose of Vaccine had been administered, after which it quickly became well marked. The phenomenon was best shown in the



the discharge of those cases suffering from one or other of the complications of gonorrhoea, more particularly epididymitis. I attribute this to the large amount of bacterial substance absorbed from these foci with a consequent large out-pouring of agglutinins.

Bacterolytic action was evidenced by the fact that the gonococci became less sharply defined and lost their characteristic bean shape, many becoming hemispherical, as the tissues began to gain the upper hand. Their staining character also seemed to alter until one was led to suspect that the gram positive diplococcus, so often observed in the later stages of Gonorrhoea, was really an involution form of gonococcus.

Photographs 1 and 2 show typical films of urethral discharge in the acute stage. It will be noticed that the organisms are almost entirely intracellular.

Photographs 7 and 8 are films taken after prostatic massage in a sub-acute stage of the disease. They also show a moderate degree of clumping but probably again the larger clumps have been broken up.

(11) Concluding Remarks.

Throughout this work I have aimed at a permanent rather than a speedy cure.

I had a great advantage over those who worked in Military Hospitals, in that any case of relapse would probably return to the same clinic for further treatment. It is gratifying to know therefore that, up to the time of writing, not a single case of relapse has so reported.

Conclusions.

- i. With regard to toxicity. Thomson's Vaccine is practically non toxic.  
 Fat-free Vaccine on the other hand is very little less toxic than ordinary polyvalent vaccine.
- ii. With regard to therapeutic effect. Thomson's Vaccine is the only vaccine of any value in uncomplicated urethritis; it, however, takes second place to local treatment in this condition.
- iii. In Epididymitis and the metastatic complications of Gonorrhoea both vaccines are of the greatest value. They, indeed, form the only specific remedy in the treatment and prophylaxis of these sequae.
- iv. None of the more recent vaccines produced experimentally by Thomson are so satisfactory from a therapeutic point of view as his original preparation.

- v. The Vaccine prepared from detoxicated secondary organisms is of no proved value in mixed infection of the urethral tract.
  
- vi. Vaccine treatment is particularly useful in the present system of Venereal Clinic as it impresses the patient and stimulates regular attendance.
  
- vii. Agglutination as seen in smears from the urethral discharge is a useful guide to the effect of vaccine treatment.

I am greatly indebted to Mr. David Lees, F.R.C.S.E. for his kindness in affording me every facility to carry out this work.

Photograph 1.



Photograph 2.



Photograph 3.



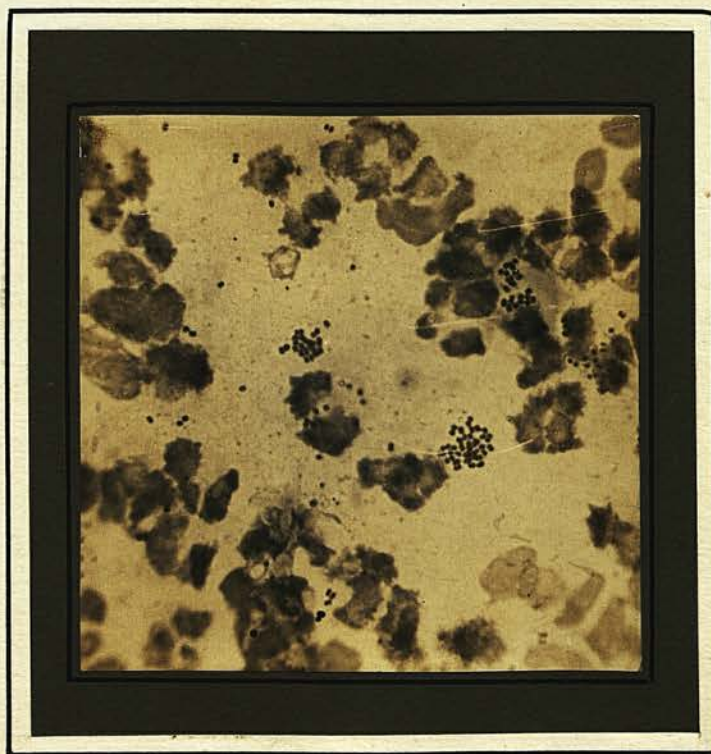
\* Photograph 4.



Photograph 5.



Photograph 6.



Photograph 7.



Photograph 8.

