of the treatment. The low mortality rate and the high percentage of cure attending surgical operations on the thyroid has made surgical treatment popular. Yet, although good surgical technique is the chief reason for the low mortality rate among our cases, it may also be due partly to the previous improvement in some severe cases under x -ray therapy, and partly to the fact that most of the patients on whom thyroidectomy was performed gave an excellent response to iodine when administered pre-operatively. Many of our cases were operated on from the medical side of the hospital and returned to it from the theatre. It is possible that some who were sent for operation might eventually have improved considerably had x -ray therapy been continued, but many of them might in the end have presented a serious surgical risk to life. Our x -ray cases were drawn from the working classes, and therefore it is the aim to try and produce satisfactory results in one year; this wish, coupled with our low surgical mortality rate, no doubt accounts for the fact that a greater number were operated on than Dr. Murray found necessary in his cases.

None the less, I believe that by sending cases which are not showing progress at an early date for operation a hospital as a whole is able to show a better percentage of improvement in all cases attending, and a lower surgical mortality rate. X -ray therapy should be given a trial in the large majority of cases, the results considered at three-monthly intervals, and those cases which do not show adequate improvement should be sent for surgical treatment. In the case of patients who, for financial or other reasons, cannot face more than a short absence from active life, an operation seems to be the treatment of choice.

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TREATMENT OF ACUTE GONORRHOEA BY MEANS OF A NEW GONOCOCCAL VACCINE OF LOW TOXICITY

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The treatment of gonorrhoea is generally acknowledged to be unsatisfactory, and the multiplicity of therapeutic methods which have been used may be regarded as an indication of their inefficiency. Unfortunately, we still lack a specific antidote. The local application of antiseptics has only a limited effect because certain areas of infection are frequently inaccessible. Drugs, whether given by mouth or by injection, are of uncertain value. Specific antisera, which raised such high hopes, have failed to fulfil their promise.

The various types of vaccine which have been used and recommended for years do not appear to have maintained a high standard of effectiveness. Despite many attempts to use vaccines in the acute stages of the disease, the effects have often been disconcerting, and accompanied by a high proportion of complications. Hence their use is generally restricted to chronic cases; but here again, owing to lack of antigenic power, results have often been indifferent.

Nevertheless, it was felt that if a vaccine of low toxicity could be prepared which, when administered to patients with acute gonorrhoea, would evoke a rapid and substantial antibody response, it should at least prove useful in the treatment of the disease. Such a vaccine has been prepared by one of us (I. N. O. P.), and this paper has been written to show:

1. The low toxicity of this vaccine.
2. The rapid and substantial response of the antibody-forming mechanism of the body (as measured by the complement-fixation test for gonorrhoea) following the administration of this vaccine.
3. The effect of the presence in the blood of specific gonococcal antibodies as a result of this vaccine administration in: (a) curtailing the duration of the infection; (b) the prevention of complications; (c) curing the disease.

SUMMARY OF PREVIOUS WORK

It is stated by Thomson¹ that the first investigations of vaccine therapy in the treatment of gonorrhoea were made in 1907, when Wollstein, following the researches of Flexner on the meningococcus, showed that injections into animals of dead gonococci produced specific agglutinins and complement-deviating substances. In the same year Cole and Meakins² reported encouraging results in cases of gonococcal arthritis from the subcutaneous injections of large doses of gonococcal vaccine. Since these initial observations the subject has accumulated an enormous literature. Numerous observers have assessed results on widely different standards of cure, and a great variety of conclusions have been reached concerning the best method of preparation of the vaccine, the dosage, the type of case most suitable, and the stage of the infection at which the best results may be obtained. Autogenous vaccines and stock vaccines, recent strains and old subcultured strains, polyvalent strains and single strains—all have been recommended with varying results. These earlier workers relied mainly upon emulsions of killed gonococci injected subcutaneously or intramuscularly. Most of the vaccines so prepared were found to have the great disadvantage of marked toxicity. The general and local reactions which followed a dosage that was considered adequate were found to be distressing, and in weakly patients sometimes dangerous.

In 1913 Cruveilhier,³ following the researches of Besredka (1911), prepared a gonococcal vaccine which was "sensitized" by the addition of serum from goats that had been immunized previously by the intravenous injection of dead gonococci. He reported good results in complicated cases and the absence of any severe general reaction following the use of this vaccine; but a slight rise of temperature with some transitory pain and redness of skin round the injection site sometimes occurred. He also recorded some good results with sensitized vaccines made from living gonococci. In the same year Broughton-Alcock,⁴ working with a vaccine similarly prepared, confirmed Cruveilhier's observations as to the therapeutic benefit derived from its administration in cases where complications had occurred. In a further series of cases (twenty-six) of acute gonococcal urethritis without complications he was not convinced of any curative effect.

Subsequently, numerous workers have concentrated upon the attempt to produce a non-toxic vaccine, and brief mention of the more important of these may be made. In 1913 Nicolle and Blaizot⁵ produced "Dmagon," a vaccine which was claimed to have been rendered non-toxic by culturing gonococci on a special medium and by their subsequent treatment with a solution of sodium fluoride. They then added to the vaccine a proportion of "syncocci"—Gram-negative cocci, which these authors believed to be frequently associated with the gonococcus. In 1913 Hirschfelder⁶ used an extract of gonococci. This was obtained by dissolving them in pan-

creatin and sodium bicarbonate solutions, and then acidulating with weak hydrochloric acid. Large doses of this solution were injected intravenously, but pyrexial reactions with malaise were apt to occur. Thomson (1919,⁷ 1920,⁸ 1922⁹) stated that he was convinced that the disappointing results from vaccine treatment were due to inadequate dosage—the dosage being, of course, restricted by the marked toxicity of vaccines in general use. By patient research he elaborated a complicated chemical method of removing the "endotoxins" from gonococci. After detoxication by his method initial subcutaneous injections of 5,000 millions to 10,000 millions of organisms could be given without ill effects, and the dosage by this route could be increased at short intervals up to a very large amount. Also, after a small preliminary sensitizing dose, large doses of this vaccine were given intravenously, again without unpleasant reactions. This preparation is still used and rightly esteemed, but the results obtained from it are admitted to have fallen short of early expectations. More favourable results are obtained from its employment in the treatment of chronic and complicated cases than in acute urethritis.

Lambkin and Dimond (1927¹⁰ and 1928) supplemented the routine treatment of gonorrhoea by intradermal and intramuscular injections, together with the intraurethral instillation of an "exotoxin" derived from cultures of gonococci grown on a medium containing animal nucleo-protein. Briefly, they observed that gonococci grown in cultures of this kind produced "polar bodies" histologically similar to those associated with the diphtheria bacillus. They washed off gonococci plus their polar bodies from the culture with 2 per cent. saline solution, and allowed the wash to stand for three or four days. This was found to separate into three distinct layers. The bottom layer contained heavy gonococci; the intermediate layer was a lighter white, powdery material termed "alpha nucleo-protein"; and the supernatant clear fluid contained a substance termed "beta nucleo-histone." The two upper layers were believed to result from the splitting by the saline solution of the polar bodies into their main constituents. The beta nucleo-histone, which was separated in this way from the poisonous endotoxins resulting from autolysis of the gonococci, was employed as the vaccine. This was found to have marked antigenic properties, and could be tolerated in doses which were large when compared with the equivalent in ordinary vaccine. The method of preparation is, however, a complicated one, and accurate standardization is difficult. Some excellent results have, nevertheless, been reported, and investigation is still proceeding along these lines. Clements and Oliver,¹¹ using a modification of this preparation, have recently reported some good results in chronic cases.

THE VACCINE DESCRIBED

Many attempts have been made to utilize the various vaccines described above during the acute stage of gonorrhoea, but the results have generally been unsatisfactory and accompanied by a high proportion of complications, which seem to "flare up" suddenly after the administration of the vaccine. Consequently, gonococcal vaccine therapy is not generally favoured for acute gonorrhoeal cases. The ideal vaccine is one which combines ease of preparation and powerful antigenic qualities with the absence of marked toxic effects following its administration.

The vaccine described below is not claimed to be ideal, but it would appear to combine these cardinal merits to a greater extent than any vaccine with which we are acquainted.

Technique of Preparation

Gonococci, grown on hydrocele agar (pH 7.5) in a triangular Roux bottle at 37.5° C. for forty-eight hours, were washed off into a cylinder with 100 c.cm. of physiological saline; this yielded a suspension of about 180 millions of organisms per c.cm.; 1 c.cm. of N/1 NaOH was added, and the cylinder placed in the 37.5° C. water-bath for two hours, when most of the organisms were found to be in solution. The fluid was filtered through sterile lint, 1.5 c.cm. of N/1 HCl added, and the cylinder returned to the bath. After fifteen to twenty minutes white flocculi appeared, and these were centri-

fuged out of solution (3,000 revolutions per minute) and then suspended in 9 c.cm. of sterile saline. N/1 NaOH was added to the suspension drop by drop until a pH of 7.5 was reached, when the precipitate appeared to go into solution. To this 1 c.cm. of formo-saline (1 per cent.) was added. This colloidal suspension of gonococcal protein constituted the vaccine, 1 c.cm. of which contained the protein content of approximately 1,800 million gonococci.

CLINICAL APPLICATION

This preparation was employed in the treatment of forty-six men who were suffering from acute gonococcal urethritis. The occupations of the men are of interest, and may be analysed as follows: twenty-four manual workers, eighteen sedentary workers, and four unemployed. Their ages varied from 19 to 42 years, the average being 26½ years. The incubation period varied from one day to twenty-four days, but in the majority of cases evidence of infection was present within a week. When first examined at the L.C.C. (Whitechapel) Clinic the infection was apparently limited to the anterior urethra in thirty (65 per cent.) of these patients, but the remaining sixteen (35 per cent.) were suffering from both an anterior and a posterior urethritis. In most cases the patient presented himself for treatment, and the first dose of vaccine was administered within six days of the onset of the symptoms.

Dosage and Method of Administration

As already stated, the vaccine was made up so that 1 c.cm. was equivalent to the protein content of 1,800 million gonococci. All injections were given subcutaneously over the gluteal muscles, the right and left sides being injected alternately. The initial dose in each case was 1/4 c.cm. (450 million organisms), and this was increased to a maximum dose of 1.5 c.cm. if no untoward manifestations occurred. The actual amounts of vaccine received by the patient are shown in the table below.

Number of Patients	Consecutive Days									Total Amount of Vaccine Received per Patient
	1	2	3	4	5	6	7	8	9	
5	½	½								½ c.cm.
3	½	½	½							¾ "
10	½	½	½	½						1 "
9	½	½	½	½	½					1½ "
3	½	½	½	½	½	½				1½ "
5	½	½	½	½	½	½		½		1½ "
1	½	½	½	½	½	½		½	½	2 "
2	½	½								½ c.cm.
2	½	½	½	½						1½ "
1	½	½	½							1½ "
2	½	½	½	½						1½ "
1	½	½	1	1						2½ "
1	½	½	½	½	1					2½ "
1	½	½	½	1	1	½		1½		5½ "

This shows that the period during which vaccine was administered varied from two to nine days, whilst the total amount injected in any one case ranged from 0.5 c.cm. (the protein equivalent from 900 million gonococci) to 5.25 c.cm. (the protein equivalent from 9,450 million gonococci). Two groups of patients are represented in the table. Group 1 represents the earlier patients, none of whom received more than 0.25 c.cm. per diem. With the experience gained from the reactions of the patients in this group we were able, in most of our later cases,

to advance the dosage more rapidly. This is shown in Group 2. The injections were given each day where possible, but the daily and the total dosage were modified according to the individual reaction.

Immediate Results

A local reaction occurred in every case. The mildest reaction consisted of a tender, slightly indurated, circumscribed area of approximately $1\frac{1}{2}$ inches in diameter at the site of injection, with a slight enlargement of the nearest inguinal glands. This was accompanied by mild subjective discomfort. A good reaction was indicated by a painful indurated area 5 inches in diameter, with enlarged painful inguinal glands. In such cases as these the site of injection was covered by an area of vivid scarlet erythema, from which a well-marked red band of lymphangitis extended across the buttock and round the flank to the inguinal glands on the same side. The skin overlying the glands became red and tender. The acute local signs and symptoms following injection produced their maximum effect within twenty-four hours of the administration of the vaccine and took two to three days to subside, while the subcutaneous induration remained for a day or two longer. The local reaction in twenty of the forty-six patients injected was moderate, and confined to the immediate site of the injection. In twenty-six patients, in addition to the tenderness and enlargement of the corresponding inguinal glands, a well-marked induration developed at the point where the vaccine was injected. In seven of these a well-marked band of lymphangitis was present. This tracked from the area of induration at the site of injection to the enlarged tender inguinal glands on the same side.

The general reaction consisted of symptoms which ranged from a slight headache and malaise to a severe rigor with vertigo, nausea, retching, and vomiting in some cases. Occasionally insomnia and restlessness were well marked, but in most cases the only result was a headache of moderate severity and some feverishness. These symptoms, which did not invariably follow the first injection, were alleviated by mild analgesics such as aspirin or pyramidon. A general reaction was absent in ten (21.7 per cent.) of the forty-six patients injected. In thirty-four (73.9 per cent.) some general reaction developed in from one to five hours after injection. In only two patients (4.4 per cent.) was the general reaction so severe that the vaccine treatment was stopped after the second dose had been administered.

CLINICAL RESULTS

The clinical results following injection of the vaccine may be classified into two groups:

Group 1.—Those in which the signs and symptoms of the infection remained absent after a definite period of time. These may be subdivided as follows:

(a) Absence of signs and symptoms within ten days from beginning of treatment. In five (10.8 per cent.) cases the absence of urethral discharge or other symptoms, and the absence of haziness and threads from both specimens of urine, were noted after ten days' treatment or less. One of these cases, which will be mentioned later as the most rapid cure in the series, remained entirely without symptoms or signs after only three days' treatment.

(b) Absence of signs and symptoms within two to four weeks from beginning of treatment. These consisted of nineteen cases (41.3 per cent.).

(c) Absence of signs and symptoms within one to three months from beginning of treatment. This group contained sixteen cases (34.8 per cent.); in a proportion of these patients this clinical improvement occurred in

spite of irregular attendance and neglect of routine treatment.

In this whole group of forty (86.9 per cent.) cases the results may be said to be satisfactory.

Group 2.—Those cases which developed acute complications of gonorrhoea. There were only six cases (13.1 per cent.) in this group. Two of them developed a unilateral acute epididymo-orchitis; two had periurethral abscess of the penile type; one suffered from an acute prostatitis and vesiculitis, which was accompanied by gonorrhoeal rheumatism. The sixth case was transferred to another department as a suspected case of chronic pyelitis. No complications occurred during the period of vaccine administration. The shortest time between the cessation of the injections and the onset of a complication was two days.

The above results may be compared with those obtained by ordinary routine treatment. In order to do this the records of 100 unselected patients, who originally attended this clinic suffering from acute gonorrhoea, were examined, and the proportion of these cases which developed acute complications of the disease during their early treatment was noted. Of the 100 unselected patients, twenty-four developed acute complications, an analysis of which is shown below.

Acute epididymo-orchitis	...	...	...	12 per cent.
Acute prostatitis	...	...	...	5 " "
Periurethral abscesses	...	...	...	4 " "
Acute arthritis	...	...	...	1 " "
Gonorrhoeal rheumatism	...	...	...	1 " "
Gonorrhoeal teno-synovitis	...	...	...	1 " "
				24 " "

SEROLOGICAL RESULTS

These may be divided into three groups:

Group A.—Those in which the complement-fixation test for gonorrhoea (Price's former technique¹²) was negative in the blood serum at the onset of treatment, but became positive within ten days. This group contained thirty-four (73.9 per cent.) cases, and the results are tabulated below.

G.F.T. at Onset of Treatment	G.F.T. within Ten Days or Less	Number of Cases
Negative	++ (40) strongest positive	1
"	++ (20) very strongly positive	2
"	++ (5 to 10) strongly positive	14
"	+ positive	12
"	± weakly positive	5
	Total	34

The bracketed figures show dilutions of the serum—for example, (40) indicates that the serum was diluted 1 in 40. It should be remembered that without treatment a positive gonorrhoeal complement-fixation test, as recorded by the above technique, is not usually obtained in acute cases until fourteen to twenty-one days after the onset of symptoms. These cases, however, had been treated by routine methods (irrigations, etc.), and therefore positive serum reactions were not to be expected until later in the course of the disease.

Group B.—Those in which the complement-fixation test was positive at the beginning of treatment, but showed a definite increase in the strength of the reaction at the end of the period of vaccine administration. This group included four (8.7 per cent.) patients whose sera behaved as shown:

Patient	Complement-fixation Test	
	First Day	Tenth Day
First	±	++ (20)
Second	+±	++ (40)
Third	+±	++ (40)
Fourth	±	++

Group C.—Those in which the complement-fixation test was negative at the outset, and in spite of vaccine treatment remained negative at the end of ten days. This group consisted of seven (15.2 per cent.) cases. Later in the course of the disease a weakly positive (±) reaction developed in three of these cases, but evidently this was not due to the effect of the vaccine. The remaining four failed to record a positive reaction at any time. Five of these seven cases were the least satisfactory of all the cases in the series from the point of view of clinical results. The two remaining patients showed a remarkable and unexpectedly rapid recovery: the reason is not apparent. One case, not included in this classification, was a patient who refused to allow more than one venepuncture, and subsequently defaulted.

END-RESULTS

In view of the widely divergent views held as to the standard of cure on which results of treatment should be assessed, the test of cure employed in all these cases is set out below.

1. **Urethral Discharge.**—Absent.
2. **Urine: "Two-glass" Test.**—Both specimens were free from haziness and threads on repeated examination.
3. **Rectal Examination.**—Clinical evidence of infection of the prostate or seminal vesicles was absent on digital examination.
4. **Microscopical Tests.**—Three successive smears of the contents of the prostate and the seminal vesicles taken at intervals of one week or more showed less than five leucocytes per 1/12 microscopic field.
5. **Instrumental Examination.**—(a) A metal sound of average size (16/20 Clutton) was passed into the bladder without difficulty. (b) *Urethroscope*: No lesion could be detected in the anterior urethra.
6. **Complement-fixation Test for Gonorrhoea.**—This had to be completely negative. The complement-fixation test employed as a test for cure in all but one case in the series was Price's improved method.¹³ This more sensitive technique considerably enhances the value of the test as a criterion of cure.
7. **Provocative Diet.**—A negative complement-fixation test for gonorrhoea and no excess of leucocytes in the prostatic and vesicular smears after a provocative diet, including alcohol and spices, for a period of from two to four weeks.

At this stage it would be well to emphasize the importance of the complement-fixation reaction for gonorrhoea in the test for cure of patients, even in those who have undergone vaccine treatment. Many authorities believe that the results of the complement-fixation test for gonorrhoea are valueless when applied to the sera of patients who have received gonococcal vaccines. It was definitely established in the course of this investigation that the injection of vaccine stimulates the production of antibodies (as demonstrated by the complement-deviation test for gonorrhoea) only so long as the administration is continued. In cases in which we were able to establish a rapid cure the reaction became negative in approximately six weeks from the cessation of vaccine treatment. But it was also established that if the

complement-deviation test for gonorrhoea remained positive more than six weeks after the vaccine had ceased to be injected it was invariably possible to demonstrate a persistent focus of infection.

On reviewing the end-results of any treatment for gonorrhoea one is always confronted with the difficulty of patients who default when they become symptomless, although they may not necessarily be cured. In this category were fifteen (32.6 per cent.) in the series of forty-six patients who failed to pursue their treatment upon the cessation of symptoms. Of these, ten did not return, and so no assessment of the curative value of the vaccine treatment could be made in these cases; three defaulted whilst undergoing their final tests, so that a cure could not be established; two defaulted but returned later with symptoms.

The final tests of cure were passed by twenty of the remaining thirty-one patients. The varying periods of treatment before cure of these twenty patients are set out in the table below.

Number of Patients		Period of Treatment before Cure	
1	...	...	7 days
3	...	...	6 weeks
1	...	...	8 "
2	...	...	12 "
1	...	...	16 "
2	...	...	18 "
2	...	...	20 "
3	...	...	28 "
1	...	...	32 "
2	...	...	36 "
2	...	...	40 "
20			

From this it will be seen that of the twenty patients who remained under observation throughout the clinical course of the disease and were cured seven were discharged within three months, eight within six months, and five within ten months.

The following table shows the results obtained in twenty unselected cases treated by routine methods, *without vaccine*, during the same period. The same standard of cure was, of course, adopted.

Number of Patients		Period of Treatment before Cure	
1	...	...	8 weeks
3	...	...	12 "
6	...	...	20 "
4	...	...	24 "
3	...	...	28 "
2	...	...	32 "
1	...	...	40 "
20			

Comparison of the two tables shows that a somewhat larger proportion of rapid cures was obtained in the patients treated with the vaccine.

Apparently, cure of the disease was not hastened by vaccine in the remaining eleven patients. Two reached the test of cure stage after twelve and fifteen months respectively. Nine still remain under treatment after periods varying from ten to eighteen months. It must be remembered that these cases were all treated as out-patients, and most of them continued their daily work, so that adequate control of their actions and habits during this period was impossible.

CONCLUSIONS

1. This vaccine is a powerful and prompt stimulant to the production of gonococcal antibodies as demonstrated by the complement-fixation test for gonorrhoea. When employed in the acute stage of the disease in the manner already described—that is, daily injections—thirty-eight (82.6 per cent.) patients out of forty-six showed a marked increase in the strength of their serum

tests within ten days—namely, during that period of the disease when such a result is not to be anticipated.

2. In view of the protein equivalent of the number of gonococci (1,800 million per c.cm.) contained in this vaccine, it may well be described as a detoxicated vaccine. Furthermore, it can easily be prepared and standardized.

3. No fixed method of dosage of the vaccine is possible. The maximum dose which a patient will tolerate can only be found by the individual response of the patient to gradually increasing doses.

4. In those patients who responded serologically to the vaccine a definite clinical improvement almost invariably followed within a short time, but the percentage of cases which subsequently presented symptoms of chronic infection was not lessened.

5. Where serological response to the vaccine was not forthcoming the results were disappointing in all but two cases.

6. Two cases which showed no serological response made a rapid recovery. The explanation of this is not apparent.

7. No acute complications occurred as a result of the vaccine, although it was administered during the acute stage of the disease. The number of acute complications—six (13.1 per cent.)—occurring later in the course of the disease in patients treated by this method is definitely lower when compared with patients treated by ordinary routine methods alone (24 per cent.).

8. The time taken to effect a cure is somewhat shortened in some cases when the routine methods of treatment are supplemented by the administration of this vaccine, but on the whole *the results are disappointing*.

9. It would appear that the type of gonococcal infection most likely to be benefited by treatment with this vaccine is that in which the patient is suffering from a *chronic* gonococcal complication such as arthritis, and the blood, when tested by the complement-fixation reaction, reveals a low ($\pm$) specific gonococcal antibody content. This point is at present under investigation (A. J. K.). Of the forty-six cases treated with vaccine, thirty-eight showed an increase in the antibody content of the blood (as evidenced by the complement-fixation test), and a definite decrease in the severity of the clinical symptoms within ten days of the first vaccine injection. It would be natural to anticipate that the time taken to cure these patients would be definitely shorter than when the ordinary routine methods of treatment are employed. This, however, was not the case, and, whilst admitting the danger of drawing conclusions from such a small number of cases, it would appear that specific gonococcal antibodies tend to prevent the occurrence of severe *acute* complications and to shorten the acute stage of the disease, but seem to have *little effect in eradicating the infection from its localized sites in the genital system*. This would account for the disappointing results from the use of gonococcal vaccines, prepared in all manner of ways, in the routine treatment of gonorrhoea.

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NOTES ON A SMALL OUTBREAK OF GLANDULAR FEVER

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Glandular fever in epidemic form is not an uncommon disease. The literature¹ on the subject has grown during the last few years; but some of the cases occurring in the outbreak now to be described showed certain unusual symptoms, which are the main reason for these notes.

The cases arose in a preparatory school in October, 1933. Out of eighty-four boys eleven developed the disease; two cases were of alarming severity, three others were severe in type, the remainder were moderate or mild in character. All boys in the school occupy separate bedrooms or cubicles, but it is of interest that a direct relationship could be traced among the infected boys in friendship, or proximity in work and play. Further, a case of chicken-pox arose early in October, and although there were over sixty vulnerable boys, no other contracted this disease, so that the methods of isolation and prophylaxis, valid in the latter disease, were of no avail in glandular fever. The cases occurred within the space of twelve days. The school was disbanded on the fifteenth day after the onset of the epidemic and reassembled on the thirty-second day. Of the boys sent home two only developed the disease, and those in mild and attenuated form. Six of the adults in attendance on the boys fell ill, five with frank follicular tonsillitis and one with a doubtful attack of glandular fever. Nine out of eleven boys had had their tonsils removed; the illness of the two who retained them was mild in type.

As the cause of the disease is unknown, search was made among the domestic staff for a possible carrier of throat infection, but without any definite result. Analysis of the milk and water supply proved negative, and the drainage system of the school, tested regularly, was beyond reproach. Sporadic cases of glandular fever had arisen in the district during the previous two months, which had been prolific in producing other throat infections, and notably scarlet fever.

SYMPTOMS AND SIGNS

Before describing any case in detail the following general statement of symptoms and physical signs is given.

Onset.—The first complaint, in the majority of cases, was of the collar being too tight. This was followed by pain or stiffness of the neck. Slight fever occurred in the beginning, and the groups of glands under the sternomastoid muscles or in the submaxillary triangles were found to be tender and enlarged. There was vomiting at onset in five cases; headache was not noted.

Development.—Fever increased quickly and the glands became more swollen. Usually both sides of the neck were affected, but not equally. Glands in the posterior triangles of the neck were quickly and commonly affected; the axillary and inguinal groups of glands enlarged definitely in only four cases. Peradenitis developed in the severe cases, the cervical swellings becoming diffuse and very tender. Dysphagia occurred as a sequel of this, produced in two cases by oedema of the palate and fauces. An enlarged spleen was noted twice, enlargement of the liver once. Epistaxis gave some relief to the congestive symptoms early in the disease. A rash was observed in two cases only, once urticarial and once macular in type. All severe cases showed a typical feature, which came to be regarded as almost diagnostic. When asked to sit up in bed a hand was placed behind