

**Original Articles**

**THE TREATMENT OF ERYSIPELAS BY INOCULATION WITH A SPECIFIC VACCINE\***

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In January of this year we undertook the study of erysipelas with the special consideration of the production of an artificial immunity by inoculation with a vaccine prepared from the *Streptococcus erysipelatis* of Fehleisen. "True" erysipelas, as you know, is due to an infection of the lymph spaces of the skin by the micro-organism just referred to, with or without involvement of subjacent cellular tissue; and the majority of investigators believe that the streptococcus of erysipelas is the sole or specific cause of the disease. Moreover, many believe that it is identical with the streptococcus causing puerperal septicemia, pyemia, etc. The work of Dean and Petruschky would seem to confirm this view.

From the standpoint of immune therapy it is a matter of some importance to discover whether the disease is one in which the bacteria are localized to the affected part or whether they commonly escape into the blood stream and produce a bacteriemia.

Experiments on animals and also blood cultures taken in severe cases would seem to establish the rarity with which it becomes a general infection. Furthermore, Manfredi and Traversa have succeeded in producing the severe constitutional symptoms of erysipelas in animals by inoculation of the toxins of the specific streptococcus. It would thus seem probable that the general symptoms of malaise, pyrexia, acceleration of the heart-beat, and mental apathy or irritability are all due to the absorption of the specific toxin of the streptococcus, while, on the other hand, the local signs and symptoms are consequent on the local multiplication of the micro-organisms in the lymph spaces of the skin and the local production of toxins; moreover, that a remedial measure which is capable of inhibiting the reproduction of the streptococcus would be likely to control the clinical manifestations of the disease quickly.

Our investigations of the opsonic content of the blood of 16 patients before inoculation was undertaken revealed the interesting and important fact that in 14 of these the streptococco-opsonic index ranged from 0.65 to 0.9; in the remaining 2 cases it was in one 1.1 and in the other 1.3. It is worthy of note that these last 2 patients were proceeding to recovery, presumably owing to the natural production of specific antibacterial substances as the result of autoinoculation, by which term is meant the escape of bacteria or their products into the adjacent lymph or blood streams and the consequent stimulation of the machinery of immunization to the production of antibacterial substances.

Perhaps this consideration will be more intelligible if we mention certain well-known phenomena of such localized infections as boils. In these the opsonic index to the specific micro-organism—that is, the *Staphylococcus pyogenes aureus*—is less than normal—for example, 0.7, 0.8, etc.—normal being taken as 1. The chronicity of furunculosis and the low opsonic indices

observed have been shown to be due to the absence of autoinoculation. Similarly in the case of certain localized infections due to the tubercle bacillus the opsonic index is less than 0.8. Tuberculosis of lymphatic glands, the bladder, etc., are characteristic instances of this. It is unnecessary for us to multiply examples of localized infections due to other micro-organisms; suffice it to say that continuance of these infections is associated with a lowered opsonic power while progress to cure is associated with a rise of the opsonic power above normal.

The sixteen cases referred to were studied with respect to their opsonic power to the *Streptococcus erysipelatis*, not only before active treatment by the streptococcus vaccine was undertaken, but also afterward. In the 2 patients proceeding to recovery a high opsonic power was observed before inoculation, so these must be omitted. In 13 cases a subsidence of the signs and symptoms of the erysipelas was definitely associated with a rise in the opsonic power. The remaining patient died; and it is of interest to note this patient particularly, since her case is the only fatal one of our series of 50 cases. The patient was a very fat woman, 61 years

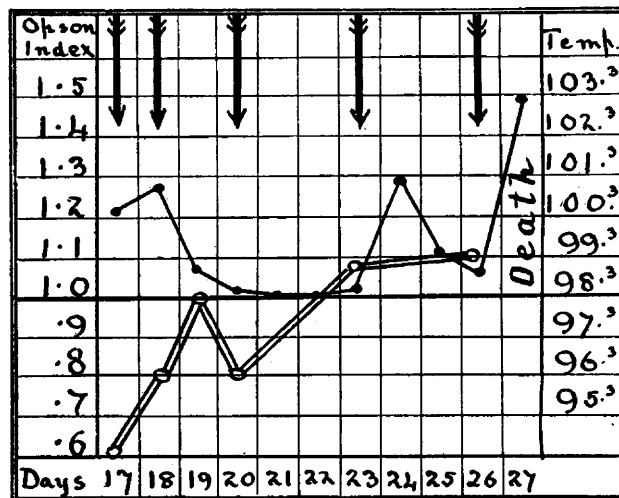


Chart 1.—Almost continued pyrexia with feeble response of opsonic immunity to inoculation with from 10 to 20 million devitalized streptococci. Double line is opsonic tracing; single line, temperature tracing; arrows represent inoculation. This chart represents the only fatal case in a series of 50.

old, comatose on admission to the hospital. Her leucocytes were not increased in number and her opsonic index to the streptococcus was 0.6. Just as she responded feebly to such general stimulants as alcohol and strychnin, so also was her response weak to the specific stimulation of our vaccine. It was with difficulty that we increased the opsonic power of her blood to 1.1 by inoculation. She died shortly after admission from the progress of her disease without regaining consciousness. This patient's case is graphically shown in Chart 1.

**STUDY OF PATIENTS TREATED BY INOCULATION**

Charts 2 and 3 represent fairly well the opsonic and temperature curves of 13 out of the 16 patients whose blood was fully and frequently investigated. It will be observed that in both the opsonic power was low before treatment and that it rose subsequent to one or two inoculations of the streptococcus vaccine; furthermore, that the fall of the temperature was shortly subsequent to the rise of the opsonic power. We may add that the rise of the opsonic power coincided more par-

\* From the Department for Therapeutic Inoculation, the Toronto General Hospital; an address given before the Medical Society of the County of New York, Oct. 26, 1908.

ticularly with marked diminution of toxemia and definite evidence of localization of the inflammatory area.

These observations on the course of immunity in erysipelas before and after inoculation with the vaccine appear to us important; but, after all, the final judgment on the value of an alleged specific remedy must rest on the comparison of the clinical results obtained by its use with those due to the administration of other alleged remedies. Erysipelas is so varied in its clinical manifestations that there are serious difficulties to an absolute comparison, but such a comparison is not impossible and we shall proceed with it.

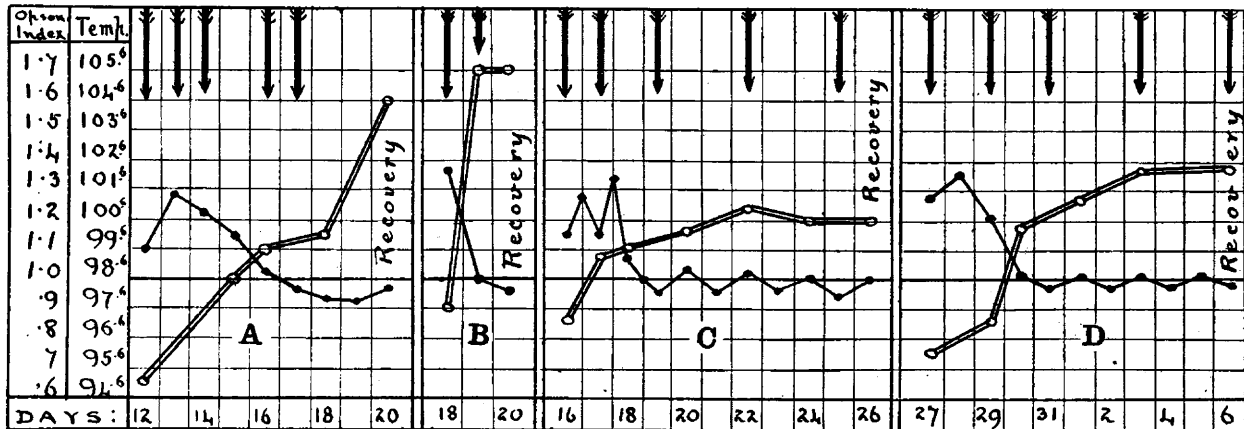
The first stage of the comparison is somewhat illogical, for we shall refer to our clinical observations of the course of the disease in our whole series of 50 cases and only then make certain detailed comparisons of a series of 19 cases treated without vaccination and a similar number treated by our specific vaccine.

Of the 50 cases 18 were very severe, 20 were severe, and 12 were mild cases. The chief criteria of severity were pronounced pyrexia (103 F. or more), tachycardia, mental dulness or delirium, and a considerable inflammatory area, with signs of rapid spread.

for the year 1907. Of these 19 are recorded, most of which were treated by some such external application as ichthyol or lead lotion or internally by ferric perchlorid. I realize the objection to accepting this series as parallel to our own, but probably the comparison is not an unfair one, as perhaps those who have had years of experience of hospital erysipelas will be able to testify. I think it will be agreed that the cases of one year closely resemble in average severity those of another. The salient features of this comparison are set forth in the accompanying table:

TABLE SHOWING THE RESULTS OF TREATMENT OF A SERIES OF 19 CASES OF ERYSIPELAS BY INTERNAL AND EXTERNAL MEDICATION AS COMPARED WITH A SERIES OF 19 CASES TREATED SOLELY BY INOCULATION WITH A SPECIFIC VACCINE

Method of treatment.	Pyrexia completed in 24 hrs.	Pyrexia completed in 48 hrs.	Pyrexia completed after 48 hrs.	Average duration of pyrexia.	Complications.	Average duration of illness.	Average stay in hospital.
<i>Non-specific.</i> Series 1907, 19 cases..	3	3	13	8.9	6	25.0	18.0
<i>Specific Vaccine.</i> Series 1908, 19 cases..	7	7	5	3.1	1	12.8	11.2



Charts 2-5.—Rise of opsonic immunity and fall of temperature in four patients, A, B, C and D. Double line is opsonic tracing; single line, temperature tracing; arrows represent inoculation with from 10 to 20 million devitalized streptococci.

Time will not permit us to detail cases, so we are forced to sum up our observations in a general way. Perhaps the most striking change in our patients was a rapid subsidence of such symptoms of toxemia as mental unrest or even delirium and of that profound malaise so usual in this disease. Even the patients in acutely severe cases almost invariably felt quite different—we might almost say infinitely better—in twenty-four to thirty-six hours after the first inoculation with our vaccine. Locally some spread of the process usually occurred until after the second inoculation, which was administered on the second day, and occasionally until after the third; but whatever the extension observed, it was remarkable in certain respects.

1. The color was of a brownish-red rather than the angry red of the acute process.
2. The swelling of the skin was less.
3. The tenderness over the area of extension was less acute or absent.
4. The patient complained of little pain in it.
5. The margin of the erythema was rarely raised but faded imperceptibly into the adjoining tissues.

For purposes of comparison of our own results of cases treated solely by inoculation with our streptococcal vaccine, we have had recourse to the records of all the cases in the case-books of the Toronto General Hospital

In the 1907 series the pyrexia lasted in 13 cases from four to thirty days.

In our own series of 19 only 5 lasted after forty-eight hours; that is, 1 for three days, 1 for four days, 1 for six days, 1 for nine days, and 1 patient died.

The cases of the 1907 series manifested the following complications:

- Recurrences, 2 on the fourteenth day.
- Synovitis, 1.
- Conjunctivitis, 1.
- Multiple abscess about face, 1.
- Pneumonia and cervical abscess, 1.
- In all, 6.

In our own series there are no complications to report, except an abscess over the parotid, which was due to a staphylococcus infection, probably the result of an incision previous to admission to the hospital.

We are unable to make any satisfactory comparison as to the rapidity or extent of the spread of the primary area involved in the two series. The data available on this point are insufficient.

We realize fully that a prolonged trial of the vaccine will be necessary before any final judgment can be reached by the medical profession as to its therapeutic value. Nevertheless our own belief is firm from the study of 50 cases that a vaccine prepared from the

*Streptococcus erysipelatis*, properly administered, exercises a specific and controlling influence on the course of the disease—preventing its spread, lessening its severity and hastening recovery.

The reason for our faith may be briefly summarized under two main heads:

1. From the standpoint of immunity: The opsonic power of the blood is low during the acute process of the disease and whenever more or less rapid spread is manifest; again, the subsidence of such symptoms as malaise, mental unrest or apathy, pain and tenderness and the localization of the inflammatory area are closely associated with an increased immunity as evidenced by a rise of opsonic power. We are inclined to attach great importance to these considerations of immunity because we have so frequently observed parallel series of events in therapeutic inoculations with bacterial vaccines in many cases of boils, septic hands, tuberculosis of the glands, bladder, etc., and in many other cases of localized bacterial infections.

2. From the standpoint of clinical observation of the course of the disease as apparently influenced by inoculation with our vaccine: Whatever surface becomes involved subsequent to inoculation manifests a less severe form of inflammatory process; mental unrest and physical discomfort are rapidly controlled; pyrexia seems to subside more rapidly and long-continued pyrexia has not been encountered; complications and sequelæ seem to be much less common.

We, therefore, submit that the evidence adduced in this communication is sufficient to justify the use of a vaccine prepared from the *Streptococcus erysipelatis* in the treatment of erysipelas, particularly as there is no recognized remedy for this disease.

#### TREATMENT

In our series of 50, only the first 16 patients were treated according to the opsonic principles of vaccine therapy, but these revealed such a uniformly satisfactory immunizing response and clinical result that we felt justified in attempting the administration of the erysipelas vaccine without the usual blood examinations; and it seems reasonably certain that in the vast majority of cases of erysipelas it will be unnecessary to be guided by estimations of the opsonic content of the blood to determine either the amount of the vaccine indicated or the appropriate time for reinoculation. We are led to this belief because, having once determined a satisfactory method of administration of the vaccine by the close study of the blood in 16 cases we achieved equally successful results in a series of 34 cases of erysipelas, many of which were severe, without having had recourse to the opsonic index in any case. We are, however, appreciative of the fact that in certain severe cases the usual thorough blood investigation may be required.

If we are right, therefore, in our conclusions that erysipelas vaccine when properly administered is a specific remedy for erysipelas, then the importance of being able to omit the laborious opsonic investigations becomes exceedingly great, for it puts into the hand of every practitioner of medicine a new specific for an exceedingly troublesome affection for which as yet only a multitude of remedies of alleged efficacy is available.

It is entirely unnecessary to prepare a vaccine for each case. It is, however, advisable to have a composite stock vaccine derived from several different strains, from as many different cases. It is probable that the

more virulent the case of erysipelas the more valuable will its streptococcus be as a vaccine.

Our method of treatment has been, in almost every case, to inoculate with 10,000,000 of the devitalized streptococci on the first visit if the case is a severe one, and with 20,000,000 if it is less severe. On the second day in the severe case the patient gets 10,000,000 more if there be signs of improvement. The most important of these signs is a certain clearing of the intellect, and the others are a lessened intensity of the local condition—less tenderness and pain. The temperature is not so satisfactory a guide, although a fall of 2 or 3 degrees on the morning following the injection is a valuable indication for a second inoculation. If, however, no evidence of improvement obtains in the very severe case and it is impossible to determine the opsonic power of the blood, then 5,000,000 only should be administered on the second day. In less severe cases improvement is almost invariably manifest on the day succeeding inoculation and the patient should receive half the first dose: that is, 10,000,000. We then inoculate with 5,000,000, 10,000,000 or 20,000,000 of streptococci on every second day until a week after the temperature has reached normal and the erythema has subsided. We are guided as to the amount of our dose in each case (when opsonic investigations are impossible or unnecessary) by its severity and the satisfactory results as shown by clinical observation. Our rule is: "The more severe the case and the less satisfactory the clinical response the smaller the dose."

The site of inoculation chosen has always been away from the area involved. Our results have been so successful by this method that we have not felt justified in attempting other measures, such as inoculation near the site of infection.

#### A MILK-BORNE OUTBREAK OF TYPHOID FEVER TRACED TO A BACILLUS-CARRIER

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The city of Washington and the District of Columbia are one. There is but one government, and there are no "city" boundaries except such as prior to 1871 marked the limits of the then existing corporation of Washington. To the westward of the city, across Rock Creek, there was at that time located a smaller, though older, community known as Georgetown. This, like the city of Washington, has long since ceased to exist as a separate corporation and now forms an integral part of the District of Columbia. Officially it is known as West Washington, but in the ordinary speech of either community it is still commonly referred to as Georgetown. For convenience it will be so designated in this paper. The water supply, the sewerage system, the food supply and the laws and sanitary administration of Georgetown are in no way different from those of the rest of the district. The annual police census of 1907, the latest returns available, gave to Georgetown a population of 17,168 and to the remainder of the District of Columbia 312,423, making the population of the whole district 329,591.