same dressing was repeated on the following day, but generally in twenty-four hours the cavity was found to be free of pus, its surface dry or secreting only a watery fluid, and further antiseptic dressing was usually unnecessary; the wound could be treated as aseptic and healed quickly.

Latterly, Peiser of Breslau and Kolaczek of Tübingen have employed aspiration and injection of serum instead of incision.^{5,7} In suitable cases the method has yielded good results, and it has the special advantage of producing good cosmetic effects.

Subjoined are notes, drawn up by my house-surgeon, Dr. Cunningham, of a series of cases which I have treated by leucofermantin kindly supplied to me by Merck of Darmstadt. With two exceptions, they were dealt with by aspiration and injection. I used a fairly large needle, and, after evacuating the abscess, I injected and withdrew a small quantity of serum, so as to clean out the cavity as thoroughly as possible before making the final injection, which was allowed to remain; a moist aseptic dressing was then applied. If the aspiration had to be repeated, the needle was inserted through the old puncture, so as to save pain. The quantity of serum left in varied, according to the size of the abscess, from 2 c.cm. to 15 c.cm.

CASE I.—Mrs. M., aged 38. September 14th: Axillary abscess of fourteen days' duration. Aspirated; 2 oz. of pus withdrawn, and $\frac{1}{2}$ oz. leucofermantin injected. September 15th: Pain and tenderness very much diminished. Aspirated; 4 oz. reddish-brown fluid removed, and 2 drachms of leucofermantin injected. September 20th: Aspirated; some reddish-brown fluid removed. September 23rd: Abscess cavity obliterated.

CASE II.—M. R., aged 40. October 16th: Large, intensely red, tender and fluctuating swelling in left side of neck. Incised under ethyl chloride spray; large quantity of pus. Cavity irrigated with leucofermantin and lightly tamponed with gauze soaked in leucofermantin; aseptic dressing. Dressed in same way for next two days; only slight serous discharge, redness and tenderness gone; healed rapidly.

CASE III.—J. M., aged 18. November 3rd: Abscess of mamma. Aspirated; 1 oz. pus removed and 3 drachms leucofermantin injected. Slight serous discharge took place from the puncture for the next two days. November 11th: Recovery complete.

CASE IV.—J. M., aged 11. November 19th: Acute abscess in front of upper part of thigh, 3 in. in diameter. Skin over fluctuating area very thin. Aspirated; 1 oz. of pus withdrawn and 2 drachms of leucofermantin injected. Sterile gauze dressing. On the next two days some leucofermantin was injected through a small opening that had formed in the thinned skin. November 25th: Abscess quite healed.

CASE V.—J. W., aged 19. August 3rd: Axillary abscess. Aspirated; a considerable amount of pus drawn off, and 2 drachms of leucofermantin injected. August 6th: Diminution of swelling and redness; some fluctuation. August 9th: Quite recovered.

CASE VI.—Mrs. W., aged 33. November 23rd: Mammary abscess swelling 2 in. in diameter; 1 oz. of pus drawn off by aspiration and 2 drachms of leucofermantin injected. November 25th: Aspiration repeated; serous discharge; 1 drachm of leucofermantin injected. November 30th: Quite recovered.

CASE VII.—R. O., aged 14 years. September 16th: Mammary abscess; swelling, 2 in. in diameter; aspirated, a quantity of thick pus removed, and 2 drachms leucofermantin injected. September 17th: Swelling and redness diminished; syringed out through puncture with leucofermantin. September 20th: Recovered.

CASE VIII.—G. S., aged 37 years. December 15th: Cellulitis of front of upper part of forearm; area 4 in. in diameter; fluctuation; incision made 2 in. long and $\frac{1}{2}$ oz. pus evacuated; plugged with gauze soaked in leucofermantin. December 16th: Swelling and redness diminished; still some pus; washed out with leucofermantin and plugged with gauze soaked in the same. December 17th: Two small abscesses incised and treated in same way. Dressed with leucofermantin daily till December 22nd; there was then no discharge, and wounds were looking dry and granulating.

CASE IX.—T. E., aged 14. December 21st: Abscess of forearm 2 in. in diameter; skin very red and considerable surrounding infiltration; incision; irrigated and tamponed with gauze soaked in leucofermantin. December 22nd: Looking clean and dry; redness and pain gone. December 27th: Granulating wound nearly healed.

CASE X.—F. T., aged 2. November 26th: Acute abscess under chin. Aspirated; 1 oz. pus withdrawn; washed out with leucofermantin, then 2 drachms injected and allowed to remain; injection repeated four times at intervals. December 9th: Quite recovered.

CASE XI.—L. M., aged 5. December 11th: Abscess of arm. Aspirated; 2 drachms of pus drawn off; washed out with leucofermantin and $\frac{1}{2}$ drachm injected. December 16th: Quite recovered.

CASE XII.—A. W., aged 14. December 9th: Abscess on back of neck size of walnut. Aspirated, and $\frac{1}{2}$ oz. pus withdrawn; washed out with leucofermantin and 1 drachm injected.

December 13th: Swelling has nearly disappeared. December 16th: Quite gone.

CASE XIII.—B. W., aged 22. December 17th: Abscess of mamma, size of apple; $\frac{1}{2}$ oz. of pus removed by aspiration; leucofermantin injected, repeated twice. December 25th: Recovered.

CASE XIV.—M. F., aged 18. October 12th: Infiltrating supuration of mamma. Aspirated, and injected several times without improvement; Bier's suction treatment was then adopted with success.

CASE XV.—Mr. W., aged 25. December 18th. Large, red, tender, fluctuating swelling on right side of neck; aspirated and injected, 2 oz. of pus; repeated four times. December 30th: Nearly closed, small sinus with slight serous discharge; examination of pus showed a pure streptococcal infection, probably accounting for the resistance to treatment.

With the exception of Cases XIV and XV the results were highly satisfactory. Recovery took place sooner than it would have done under the ordinary treatment, and, in the aspirated cases, without any visible scarring—an important matter in abscesses occurring on the face and neck. In Case XV, even although the progress was slower, probably owing to the purely streptococcal character of the infection, recovery took place comparatively early.

In the two cases treated by incision the rapid drying up of the purulent discharge and cleaning of the wound were very noticeable.

I feel convinced, from my experience of the method, that the principle on which it is based is sound, and that it opens up a new pathway in the physiological treatment of suppurative inflammation.

The serum employed probably possesses bactericidal and other defensive properties besides its antiproteolytic power.

One of the many explanations of the beneficial effects of Bier's congestion hyperaemia in suppurative inflammation is that they are due to the flushing of the focus with transudation fluid from the distended vessels. Both methods therefore appear to attain the same object in different ways—in the one through the action of serum produced by physiological processes and reaching the part from within; in the other by direct application from without.

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OBSERVATIONS ON

THE VACCINE TREATMENT OF A SERIES OF CASES OF STAPHYLOCOCCIC INFECTIONS.*

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DURING the last few years I have taken special interest in the vaccine treatment of bacterial diseases, and have had the opportunity of treating a large number of cases of this kind. I have also had the opportunity of working in Sir A. E. Wright's laboratory and attending his clinics, and would like to take this opportunity of acknowledging the courtesy and kindness both of himself and his staff at St. Mary's.

In order to avoid confusion, I think it best to take a definite series of some one infection. At first I had intended to bring forward a series of some of the less common infections, such as local tuberculous lesions, chronic catarrhal conditions, streptococcal infections, or infections by *Bacillus coli*, but I decided to take staphylococcal cases only—first, because of their frequency; and, secondly, because several articles have recently appeared in the medical press tending to throw doubt on the efficacy of vaccine treatment in this condition.

The following cases are selected as illustrating different types, and are a fair sample of those treated.

CASE I.

Male, aged 19, complained of a very painful boil on his chin. Has had slight acne for some years but there is very little now. General health good. Boil incised; bacteriological examination

* Read before the Swansea Division of the British Medical Association.

of pus gave a pure culture of *Staphylococcus pyogenes aureus*. Opsonic index to his own organism, 0.75. Injected stock vaccine containing 250 million *Staphylococcus pyogenes aureus*.

Seven Days Later.—No subjective effects after injection. Boil on chin healed, but has another smaller one on brow. Injected vaccine containing 250 million *Staphylococcus pyogenes aureus* made from his own organism.

Seven Days Later.—Boil on brow healed. Has had one very small one on neck. Opsonic index to own organism, 1.1. Injected 400 million *Staphylococcus pyogenes aureus* (own organism).

Six Months Later.—He has had no recurrence.

CASE II.

Male, aged 45, has had boils on neck for last three weeks, becoming progressively larger and more painful. Has now a very large one on neck; health otherwise good. Incised boil, grew culture from pus (pure culture of *Staphylococcus pyogenes aureus*), and from this made a vaccine. Opsonic index to own organism, 0.82.

Two Days Later.—Boil much better, but another is beginning. Injected 400 million *Staphylococcus pyogenes aureus* (own organism).

Five Days Later.—No subjective effects from the injection. The incised boil has quite healed and the later one aborted. Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Seven Days Later.—Slight malaise the day after last injection. Neck clear, and great diminution in size of indurated bases of all previous boils. Opsonic index to own organism, 0.95. Injected 400 million *Staphylococcus pyogenes aureus* (own organism).

Three Months Later.—He has had no more boils.

CASE III.

Male, aged 39, complained of boil on back of neck. Has been having boils off and on for three years. Incised boil; examination of pus showed pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.72. Injected 250 million *Staphylococcus pyogenes aureus* (stock vaccine).

Seven Days Later.—Another boil on neck. Injected 400 million *Staphylococcus pyogenes aureus* (stock vaccine).

Seven Days Later.—Two more boils on neck. Opsonic index to own organism, 0.84. Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—No more boils; old ones healed. Opsonic index to own organism, 1.15.

Nine Months Later.—No recurrence.

CASE IV.

Male, aged 23, complained of large boil in right axilla. Has been having boils very frequently during the last four years. When younger had acne. Incised boil; from pus obtained pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.68.

Four Days Later.—Injected 250 million *Staphylococcus pyogenes aureus* (own organism).

Seven Days Later.—No subjective effects from injection. Has had two small boils since which aborted. Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Eight Days Later.—No fresh boils. Opsonic index to own organism, 1.27. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—Skin quite clear. Feels much better in health. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Seven Months Later.—He has left the town, but I have heard that he has kept quite well and free of boils.

CASE V.

Male, aged 46, has been troubled with boils for many years. They come on different parts of the body, and he is seldom more than two or three weeks free of them. At present there is one boil on the neck, which is healing. Health otherwise good. Opsonic index to *Staphylococcus pyogenes aureus*, 0.65. Injected 350 million *Staphylococcus pyogenes aureus* (stock vaccine).

Fourteen Days Later.—No subjective effects from injection. One boil since which aborted. Injected 500 million *Staphylococcus pyogenes aureus* (stock vaccine).

Fourteen Days Later.—Has had one other abortive boil. Opsonic index, 0.9. Injected 650 million *Staphylococcus pyogenes aureus* (stock vaccine).

Eighteen Months Later.—I wanted to continue treatment longer, but did not see patient for eighteen months, when he told me that he had had no return of the trouble.

CASE VI.

Male, aged 27, had been troubled for about four years with small boils and pustules about the face and neck. At present has two small painful ones in the line of the collar. Bacteriological examination of pus, pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.5. Injected 250 million *Staphylococcus pyogenes aureus* (stock vaccine).

Ten Days Later.—No subjective effects. Neck better; one fresh pustule on cheek. Injected 500 million *Staphylococcus pyogenes aureus* (stock vaccine).

Fourteen Days Later.—Another fresh boil on neck. Injected 500 million *Staphylococcus pyogenes aureus* (stock vaccine).

Twelve Days Later.—Neck well, but fresh pustule on forehead. Opsonic index, 0.7. Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Fourteen Days Later.—No fresh pustules. Opsonic index, 1.1. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Sixteen Days Later.—No recurrence. Injected 1,000 million *Staphylococcus pyogenes aureus* (own organism).

Two more injections were given after this at intervals of eighteen days of 1,500 million *Staphylococcus pyogenes aureus* (own organism). Opsonic index, 1. Six months have since elapsed, and the patient keeps quite well.

CASE VII.

Male, aged 37, had a crop of boils nine years ago, and since then has never been free for more than a week or two at a time. At the beginning of the trouble they were typical large boils; in later years more commonly pustules, with a small root, but occasionally reverting to the earlier type. Has always treated them antiseptically, and has used various antiseptic lotions, baths, etc. Internally has taken endless tonics, calcium sulphide, yeast, and so on, without benefit. Health otherwise good. At present has two small boils on neck. Bacteriological examination of pus, pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.74.

Three Days Later.—Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Twenty-eight Days Later.—As he was living at a distance, I arranged with his own doctor that he should see the patient in ten days, send me a sample of blood for the index, and I would then forward a suitable dose of the vaccine. I heard nothing more for a month, when the doctor sent the blood, and said that as the patient was quite free of boils, he thought he would wait to see if any more came before having any more injections. Opsonic index to own organism, 1.4.

Six Months Later.—There has been no recurrence.

CASE VIII.

Male, aged 17, complained of large superficial abscess in left axilla. Has been having a succession of boils for the last six months. He is a miserable-looking, weedy, nervous lad. Would not allow me to incise abscess. Came back next day, as abscess had burst. Bacteriological examination of pus, pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.56.

Two Days Later.—Still a good deal of discharge from abscess. Injected 300 million *Staphylococcus pyogenes aureus* (own organism).

Six Days Later.—Abscess healed; has one pustule on left arm. Injected 600 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—Skin clear; looks a different boy, healthy and strong. His mother says that she has not seen him looking so well for years. Opsonic index to own organism, 1.3. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Eighteen Months Later.—Keeping in excellent health and free of boils.

CASE IX.

Male, aged 23. Three years ago a cut on the index finger of the right hand apparently became septic, for abscess formed, which, after opening, healed satisfactorily. A fortnight later, however, he had a boil on his neck, and since then has had boils and pustules frequently; hardly ever quite clear of them. Has now got two small ones on face. Health otherwise fair. Six months ago he had a course of vaccine treatment for his condition—apparently stock vaccine—but derived no benefit. Bacteriological examination, pure *Staphylococcus pyogenes aureus*; opsonic index to own organism, 0.66.

Three Days Later.—Injected 250 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—Felt seedy day after last injection. Has one small boil on neck. Injected 250 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—No subjective effects from last injection. Skin now clear. Opsonic index to own organism, 1.3. Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Eighteen Days Later.—Still clear. Feels much better in health. Opsonic index to own organism, 1.24. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Twelve Months Later.—Has kept quite well and skin clear.

CASE X.

Male, aged 20, complains of psoriasis and boils. Ten years ago had psoriasis on head, which under treatment disappeared for a year, and then returned. Was confined to bed till six months ago, when it spread to body, arms, and legs, all of which are now covered. The last few weeks he has had a number of boils. Father and sister have psoriasis. I explained that vaccine treatment would cure the boils, but could not say whether it would have any effect on psoriasis. Opsonic index to *Staphylococcus pyogenes aureus*, 0.88. Injected 500 million *Staphylococcus pyogenes aureus* (stock vaccine).

Ten Days Later.—No subjective effects from injection. The psoriasis spots are more painful. One fresh boil. Injected 500 million *Staphylococcus pyogenes aureus* (stock vaccine).

Seven Days Later.—Boil has gone; otherwise no effect. Opsonic index to *Staphylococcus pyogenes aureus*, 1.1. Injected 750 million mixed staphylococci (stock vaccine).

Seven Days Later.—No effect on psoriasis. Injected 1,000 million mixed staphylococci (stock vaccine).

Ten Days Later.—Psoriasis spots decidedly more painful, and patient gave up treatment.

CASE XI.

Male, aged 29, complained of pustules on neck, face, and scalp, going on for over two months in spite of treatment—tonics internally, antiseptics, etc., externally. Was supposed to have had syphilis eighteen months ago, and went on with treatment for a year. As treatment had been begun before secondary symptoms had developed—and none did develop—patient thought that a wrong diagnosis had been made. I thought that diagnosis had probably been correct, but decided to try vaccine treatment first. Bacteriological examinations, pure *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.78.

Three Days Later.—Injected 250 million *Staphylococcus pyogenes aureus* (own organism).

Seven Days Later.—No effect. Injected 500 million of the same.

Ten Days Later.—No new spots. Face and nose drying up. Crusts on places on scalp. Opsonic index to own organism, 0.88. Injected 750 million of the same.

Eight Days Later.—Nose and face well. Removed crusts on head, and found a few drops of pus below each. Ordered cyllin lotion. Injected 750 million of the same vaccine.

Seven Days Later.—Patient has got bad cold. Face keeps well; head much better. Gave no injection.

Nine Days Later.—Feels better, gained weight, and skin clear. Opsonic index, 1.12. Injected 1,000 million of the same.

He kept all right for six weeks, when ulceration appeared on the nose, obviously syphilitic, which cleared up under ordinary specific treatment.

CASE XII.

Male, aged 26. Had for six weeks suffered intolerable itching (worse at night) over arms, legs, and slightly on body. A few days later crops of vesicles appeared, which soon became pustular, and after some days gradually dried up, only to be succeeded by fresh crops. Has had a variety of treatment—sulphur baths, hydrarg. ammon. and tar ointments, various lotions, baths of cyllin, etc.—but the condition has got worse. Arms and legs practically covered with superficial pustules ranging in size from a mere point up to a diameter of an inch. Flexor and extensor surfaces alike affected. Only a few on body. No sign of scabies burrows between the fingers. He feels "seedy." Bacteriological examination of pus, almost pure culture of streptococcus; a few *Staphylococcus pyogenes aureus* (probably secondary). Opsonic index to his own streptococcus, 0.6.

Three Days Later.—Injected 15 million streptococci (own organism). Local treatment, continued cyllin baths.

Eight Days Later.—All spots dry; no fresh ones. Injected 25 million streptococci (own organism).

Ten Days Later.—Skin quite clear. Feels better in health than he has done for months. Opsonic index to own streptococcus, 1.34. Injected 25 million of the same vaccine.

Ten Months Later.—He has remained quite well.

CASE XIII.

Male, aged 18. Acne. Had scarlet fever when 3 years old, and this was followed by "running" right ear which has persisted. Three years ago a polypus was removed from this ear; adenoids were removed from the naso-pharynx at the same time. The acne commenced about fifteen months ago, first on the cheeks, then on the body. The back is now covered to such an extent that there was difficulty in finding a clear spot to make an injection. The face is covered with "black-heads" and pustules—the latter predominating. There is still a slight discharge from the right ear. Bacteriological examination of pus, pure *Staphylococcus pyogenes albus*. Opsonic index to own organism, 0.84.

Three Days Later.—Injected 250 million *Staphylococcus pyogenes albus* (own organism).

Ten Days Later.—No effect from injection. Opsonic index, 0.82. Injected 500 million of the same vaccine.

Ten Days Later.—Back very much better; face a little better, especially as regards the pustules. Opsonic index, 0.95. Injected 500 million of the same vaccine.

Twelve Days Later.—Back almost clear; face slightly improved. Discharge from ear has ceased. Injected 750 million of the same vaccine. Made another culture and found the acne bacillus in addition to *Staphylococcus pyogenes albus*.

Twelve Days Later.—Back keeps well; face about the same. Injected 750 million *Staphylococcus pyogenes albus* and 10 million acne bacillus (both from own organism).

Twelve Days Later.—Face much better; no pustules, but still a good many "black-heads." Ordered compound sulphur soap; also the occasional use of a sand soap. Injected 750 million *Staphylococcus pyogenes albus* and 10 million acne bacilli.

Fourteen Days Later.—Face better; back keeps well. Opsonic index to *Staphylococcus pyogenes albus*, 1.05. Injected 1,000 million *Staphylococcus pyogenes albus* and 15 million acne bacilli (both from own organism). Treatment had to be discontinued, as the patient left Swansea; and, although he promised to report progress, I have heard nothing further. In this case there was very great improvement, but not complete cure.

CASE XIV.

Female, aged 2 years 3 months. Since 3 months old spots began to appear on the body. The usual course of these was to appear as a papule the first day, becoming pustular on the second, then gradually disappearing, only to be succeeded by a fresh crop. At first her health did not appear to suffer, but the last six months she has been peevish, has little appetite, and is

generally out of health. About a fortnight ago she had an abscess the size of a hen's egg over the left great trochanter. This had no connexion with bone, and after incision and drainage healed up well. Since then, however, there has been no improvement in health, and the other pustules are coming as badly, if not worse than before. Bacteriological examination of pus, *Staphylococcus pyogenes aureus* and *Staphylococcus pyogenes albus*, in the proportion of four of the former to one of the latter. Opsonic index to *Staphylococcus pyogenes aureus*, 0.72.

Five Days Later.—Injected 50 million *Staphylococcus pyogenes aureus* and *Staphylococcus pyogenes albus*, mixed in the proportion of four to one, both prepared from her own organisms.

Seven Days Later.—Mother reports that from the day after the injection the child's appetite improved; from being listless and peevish she became bright and playful. Her colour and general appearance is much better. She has now two pustules, one on the left leg and another on the right ear. Injected 75 million organisms (same vaccine).

Three Days Later.—Abundant fresh crop of pustules came out the day after last injection, and general health not nearly so good. Opsonic index to *Staphylococcus pyogenes aureus*, 0.53.

Fourteen Days Later.—Only one pustule, on right cheek. Opsonic index to *Staphylococcus pyogenes aureus*, 0.9. Injected 25 million organisms (same vaccine).

Eight Days Later.—No spots; gained 2 lb. in weight; looks a different child. Injected 40 million organisms (same vaccine).

Seven Days Later.—Still no spots. Opsonic index to *Staphylococcus pyogenes aureus*, 1.1. Injected 50 million organisms (same vaccine).

Fourteen Days Later.—Skin quite clear; put on 1½ lb. more; is in excellent health. Opsonic index to *Staphylococcus pyogenes aureus*, 1.56. Injected 50 million organisms (same vaccine).

This is a recent case, so I cannot say whether the cure is permanent.

CASE XV.

Female, aged 39. Three and a half months ago had cellulitis of left leg caused by an abrasion on the heel. The leg was much swollen; she had a high temperature, and two very free incisions were made under an anaesthetic. Recovery was slow, and at the end of three weeks after the operation the wounds were still open, and there was much swelling of the leg and foot. At the end of six weeks one incision had healed firmly, but the other was still unclosed and was discharging a small quantity of pus. From then till the present time, although the patient has had change of air and the general health is good, this incision has skinned over several times but always broken down again. The swelling of the leg has persisted, and very little walking makes this very marked. The lower half of leg, ankle, and dorsum of foot are swollen. A little above and outside the external malleolus is a small opening in the scar of one of the incisions, and from this a drop of thin pus was expressed. There is a good deal of induration round this opening. Bacteriological examination of pus, pure culture *Staphylococcus pyogenes aureus*. Opsonic index to own organism, 0.6.

Two Days Later.—Injected 500 million *Staphylococcus pyogenes aureus* (own organism).

Three Days Later.—Wound healed; induration and swelling much less. Patient says that the leg is much more comfortable and "natural" than it has been since trouble commenced.

Three Days Later.—Improvement maintained. Opsonic index to own organism, 1.5. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Ten Days Later.—Wound firmly healed; induration gone and practically no swelling of leg, although patient has been walking much more than before. Injected 750 million *Staphylococcus pyogenes aureus* (own organism).

Two Months Later.—The leg has kept quite well.

This is a successful result, but much the most interesting feature is to follow. The patient from infancy has had chronic bronchial catarrh; constant cough, accompanied by profuse muco-purulent expectoration. Very liable to exacerbations on taking the least cold, but present the whole time, sometimes better, sometimes worse. It naturally interfered very seriously with her comfort, especially from a social point of view. When the vaccine treatment for the leg was begun she asked if I thought that a similar line of treatment would be at all likely to benefit the cough. Seeing that the complaint was of nearly forty years' standing, I did not hold out very much hope.

When she came to report after the first injection of the staphylococcic vaccine, she said that, "strange to say, my cough has not been nearly so troublesome." I did not pay very much attention, but when, after the next injection, she said that she had never been so free of cough and expectoration, I made a thorough bacteriological examination of the sputum. I found that there was a great deal of *Staphylococcus pyogenes aureus* in it; also *Micrococcus catarrhalis* and Friedländer's bacillus. After the leg was cured I made up a mixed vaccine of these organisms, and she has just been started on a course of this. Even now, however, the cough and expectoration are very much less than they have been all her life.

My experience bears out the almost universal conclusion that the treatment of acute recent cases of boils is very successful. As antiseptic treatment of this class of

case, however, is often quite satisfactory, or indeed no treatment at all, too much stress must not be laid on the good results obtained by vaccines. On theoretical grounds one would expect this treatment to do good, as the opsonic index to staphylococcus is low; and this depression of the index probably precedes the infection. By comparing the results in some cases treated by vaccines with other cases, which so far as we can judge are similar, treated without vaccines, I think that acute cases of boils are benefited by vaccine treatment. The course of the disease is shortened, the boil ripens sooner, and after the discharge of pus it heals up more quickly and leaves less induration.

It is with regard to the chronic cases that there appears to be most divergence of opinion. In these cases, however, we can get much more evidence as to the value or otherwise of the treatment, than in the acute cases. It is, of course, possible that an old-standing complaint might, by a mere coincidence, clear up after the commencement of vaccine treatment; but when, time after time, conditions that have been constantly present, in spite of all other kinds of treatment, for one, two, five, or even nine years, disappear under the use of vaccines, it is a fair inference that we are dealing with a case of *propter hoc*, and not merely *post hoc*. Some cases react with extraordinary rapidity, others take longer; but I have not seen a failure in a pure staphylococcic lesion, however long the duration, provided that the patient will give it a fair trial. Of course, as in Case XI, where there was an underlying syphilitic condition, this could not be expected to be cured by any increase of immunity to staphylococcus; but even there it is noteworthy how the syphilitic manifestation was kept in check for a time.

I have treated a considerable number of cases of acne with varying results. Some did quite satisfactorily, others only did well up to a certain point. Case XIII is fairly typical of a severe case. Preponderance of the pustular element is favourable. The disease is not always a pure staphylococcic infection, but probably due in part to the acne bacillus, and the addition of some of those to the vaccine usually improves the results. Case XV is a good example of the benefit derived from vaccine treatment in cases of cellulitis, which, after incision, are slow to heal.

What has struck me very much is the improvement in the general health of the patients under treatment. They seem to experience an increased sense of well-being as immunization advances.

With regard to dosage in children, Case XIV illustrates the necessity of beginning with a very small quantity, in order to avoid the production of a negative phase.

Value of the Opsonic Index in Diagnosis and Treatment.

It is not necessary to enter into what the opsonic index is, or how it is estimated, but I would like to say in passing that the difficulties of the process have been unduly emphasized. To any one who has been accustomed to carry out bacteriological and general laboratory work the technique presents no special difficulties. There are, of course, many details that require some practice to carry out quickly and neatly. Accurate and conscientious working is also a necessity if the margin of error is to be kept down. The use of a special spreader, with a concave end, for making the films (first suggested, I believe, by Dr. Fleming of St. Mary's Hospital) is of great importance. The leucocytes are nearly all drawn to the free edge of the film and deposited in a row, thus greatly facilitating the work of counting their contents. Sir A. E. Wright's method of estimating the opsonic index has been much criticized, and various other procedures have been suggested. I am rather favourably impressed with a modification of Leishman's original method. This approaches more closely the actual conditions in the body, as the patient's own leucocytes are used with his own serum, and the leucocytes do not get nearly so much handling before being set to work.

Method.

An equal volume of the patient's blood and a suspension of the organism (in 1 per cent. sodium citrate, with 0.85 per cent. sodium chloride) is drawn into a warmed pipette, expressed on to a warm slide, thoroughly mixed, drawn into the pipette again; the pipette is then sealed, and placed in the incubator. A sample of normal blood is treated in the same way. After

fifteen minutes' incubation the tubes are withdrawn, and films are made and counted in the usual way. It is important to use no pressure in obtaining the blood, otherwise there will not be the same proportion of leucocytes in the two mixtures, and this will vitiate the result.

Whatever method of obtaining the index is employed, it is very desirable to use a culture of the patient's own organism for making the bacterial emulsion.

There is one other point that has received too little attention—namely, leucocytosis. It does not seem reasonable to think that if a patient has, say, twice the usual number of leucocytes, the opsonic index of his serum is, *per se*, quite a fair criterion of the real state of his resistance.

In skin lesions the diagnosis is usually obvious from the appearance of the case, and from a bacteriological examination of the pus. But where we find a mixed infection, as Case XII, the question arises, which is the primary cause? The opsonic index helps here, as we may find the index normal to one of them, subnormal to the other, indicating that the latter is probably the culprit. In more obscure cases, where the patient's organism cannot be obtained, a wide departure from the normal in the index to the suspected organism would confirm the belief that it was the causative one.

There has been much discussion as to the necessity of knowing the opsonic index in order to regulate the dose of vaccine, and also to decide what intervals to allow between the doses. The effect on the index of a medium dose of vaccine is, first, a slight fall (negative phase); secondly, a rise (positive phase); thirdly, usually a more or less gradual fall. If the dose be too small, there is no negative, only a small and badly sustained positive, phase. If the dose be too large, there is a prolonged negative phase with a slow recovery. To get the best results the second injection should be given about the time that the positive phase reaches its height. The danger to be guarded against is that of injecting during a negative phase, which would cause a further, and perhaps dangerous, fall. I do not think that in ordinary cases of staphylococcic skin infections the estimation of the index is necessary; a negative phase being sufficiently clearly shown by a fresh crop of boils, pustules, etc., as in Case XIV. In the deeper seated and more serious acute infections, where there is nothing external to guide one, and where autoinoculation is probably going on, it is imperative to estimate the index and regulate the doses accordingly. Even in the skin infections it is very interesting to follow its course; at the beginning of treatment the index is low; when cure has taken place, it is usually high or at least about normal, but it does not always quite follow the clinical symptoms. When this happens I prefer to be guided by the clinical symptoms, for, as some one has remarked, it is the patient's disease and not his opsonic index that is under treatment.

The Relative Efficiency of Stock Vaccines, and Those Prepared from the Patient's Own Organism.

A vaccine is a suspension of dead bacteria in normal saline, to which a little antiseptic has been added. In order to make it we must have a pure culture of the organism. In many cases of staphylococcic lesions we can get this direct from the patient's pus. If there is a mixed infection we must separate the organisms by the ordinary laboratory methods. Having isolated the organism, an agar tube is inseminated, incubated for eighteen to twenty-four hours, and from this young culture the vaccine is prepared. Probably no two workers follow exactly the same method, but the essentials are—an even emulsion, of known strength, and absolute sterility. An important practical point which I have not seen mentioned, is to make the vaccine of such a strength that only a fraction of 1 c.cm. is required for a dose. I have found that patients object much more to the injection of the fluid than to the prick of the needle, and if the quantity injected is small they suffer much less pain. I usually make up staphylococcic vaccines so that 1 c.cm. contains 2,000 million organisms, and it is seldom necessary to inject more than one-third of a c.cm.

For certain infections Sir A. E. Wright insists that the vaccine should always be prepared from the patient's own organism; but in the case of staphylococcus he countenances the use of a stock vaccine, unless any difficulty is encountered. In his own clinic stock vaccines

are largely used. While this may be necessary in a large hospital clinic, I feel sure that it is not, especially in chronic cases, the ideal treatment. In acute cases one has to fall back on a stock vaccine for at least the first injection, but I am certain that all, or nearly all, the unsatisfactory results in cases of chronic staphylococcal skin infections are due to not using a vaccine prepared from the patient's own organism. The vaccine should if possible consist of the exact race and strain of the organism to which immunity is desired. There are several well marked varieties of staphylococci—*Staphylococcus pyogenes aureus*, *Staphylococcus pyogenes albus*, etc.; but I think it is certain that among, say, the *aureus* variety there are many subvarieties. Our methods of examination and classification, although apparently elaborate, are really, considering the minute size of a coccus, exceedingly crude. Their morphological characters, staining reactions, cultural properties, etc., may be apparently similar, and yet there may be minute though important differences which we cannot detect. Every one who has worked with *Staphylococcus pyogenes aureus* must have noticed that, even under identical conditions, there is considerable variation in the amount and shade of pigmentation, the rate of growth, and the reaction to various stains. The difficulty in accurately placing bacteria is increased by the fact that, even in a twenty-four-hour old culture we are probably looking at twenty or thirty generations. Again, it is not long since there were only two kinds of streptococci described; now one can hardly pick up a bacteriological journal without finding mention of new varieties. Taking all these points into consideration, I am sure that whenever possible it is important to use the identical organism which has caused the infection.

When we turn to practical results we find this conclusion confirmed. In Case IX treatment by a stock vaccine had been previously tried without benefit; the condition rapidly cleared up when an autogenous vaccine was used. In several of the other cases the patient did not make much progress until a special vaccine was employed. I feel confident that if autogenous vaccines were used in, at least, all the chronic cases, we would hear little more of unsatisfactory results. Some cases, even chronic ones, undoubtedly do well on stock vaccines. Case V is an example, but it seems to me that it is a case of hit or miss. The difficulty is only partially obviated by using several strains in making up the stock vaccine. It is still quite possible that the one required is not included; and, even if it be, the effective dose is only a fraction of the nominal one. True, one can begin with a stock vaccine, and if that fails go on to an autogenous; but, in case of failure, one is apt to lose the confidence of the patient, and so bring undeserved discredit on the whole treatment.

CONCLUSIONS.

Briefly summarized, my conclusions are as follows:

1. That vaccine treatment is of great service in most staphylococcal infections.
2. That staphylococcal skin lesions, however chronic, are curable by its means.
3. That in many cases estimation of the opsonic index is unnecessary.
4. That the best results are only obtained by the use of autogenous vaccines.

ULCERATION OF THE FACE AND FAUCES TREATED BY BACTERIAL VACCINES.

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THE following case seems worth recording as a testimony to the efficacy of vaccine treatment. The writer has failed to find in any textbook the description of any similar case.

The patient, a pale-looking man, aged 34, presented himself on April 26th, 1909, complaining of ulceration of the face, of a sore throat, and a discharge from the ear.

Previous History.

In September, 1908, his wife died from phthisis, and he, having done much of the nursing for the last few weeks of her illness, became "run down." He fumigated the death-chamber by boiling crude carbolic acid, which caught fire, and this

necessitated his being in the room for about half an hour. The next and following days his face was too sore to shave, and about a week later he noticed small sores on his lips, cheek, nose, and leg. They ran a very chronic course, those on the neck and leg eventually getting well. Soreness of the throat began about the same time, and was followed some weeks later by a discharge from the left ear. His sister, who entered the room at the time of disinfection, also developed similar ulcers on the face, and these, though milder in their course, were said to have made no improvement till recently.

Course.

The patient had applied all usual remedies in accordance with medical advice, but he stated that nothing had given him any marked relief, and that for the preceding six months the large sore on his lip had steadily increased. He did not suffer much pain, but experienced great inconvenience, both on account of difficulty in talking and eating, and owing to the copiousness of the aural discharge, which necessitated his plugging the ear with absorbent wool four or five times a day, to prevent the discharge from running down his neck.

Condition when First Seen.

The sore on the lip was a soft, fungating, spongy, cauliflower-like growth, infiltrating the right half of the lower lip; it was about $\frac{3}{4}$ in. long and $\frac{1}{2}$ in. broad, presenting numerous openings discharging a thin, watery, bloodstained pus, which had dried, forming a brown scab. There was no line of demarcation between the ulcer and the healthy skin; there was no deep infiltration round it, and it was not tender. The buccal aspect of the lip was involved, appearing sodden and white, the approximating gum and corresponding surface of the upper lip were infected, and similar ulceration was commencing. The soft granulation tissue could be easily broken down with a probe. There was a newly formed superficial ulcer on the side of the chin, which had a moist red surface.

Over the mucous membrane of the soft palate, uvula, anterior pillars of the fauces and the pharynx, were scattered about 100 white ulcerated patches, 1 to 3 mm. in diameter, and when these were rubbed with a swab a few points of blood appeared. The fauces were covered with glairy mucus, and appeared as if brushed over with milk, which had left scattered drops.

The meatus of the ear was plugged with absorbent wool quite sodden with a thin pus, which the patient stated had only taken three hours to accumulate. There was a perforation of the membrana tympani. On the neck and leg the healed scars, about the size of a sixpenny piece, were pigmented.

Bacteriological Examination.

Staphylococci, streptococci, and the pseudo-diphtheria bacillus were found in the ulcer on the lip. In the throat and the discharge from the ear staphylococci and these bacilli were found, while streptococci were absent, and staphylococci only were present in the newly formed ulcer on the side of the chin. Difficulty in isolating the streptococcus owing to its being overgrown by accompanying organisms led me to postpone immediate preparation of a vaccine from this organism, and to be satisfied for the time by making autogenous vaccines of the staphylococci and bacilli.

Vaccine Treatment.

Opsonic Estimate.—The opsonic index to staphylococci was 0.80, to the bacilli 0.76. I could not determine the streptococcal index till later for the reason mentioned above.

On May 3rd the first dose of mixed autogenous vaccine was given, 200,000,000 staphylococci and 7,000,000 bacilli, and on May 6th a marked improvement was manifest in all lesions.

On May 10th the small ulcer on the side of the chin had quite healed. A similar dose was given, with the result that four days later the ulcers in the throat quite cleared up; the aural discharge, which had greatly diminished after the first dose, had quite ceased. The ulcer on the lip had definitely improved.

On May 17th the patient's condition seemed at a standstill; definite improvement had taken place, but for a week no further improvement occurred. The ulcer on the lip, now the sole remaining lesion, during the preceding week had not improved. A larger dose of each vaccine—250,000,000 staphylococci and 10,000,000 bacilli—was therefore given, and was followed by slight improvement.

The pus now yielded a pure culture of streptococci, and from this a vaccine was prepared, and on May 24th of this 12,500,000 were given. This slightly large initial dose, which was warranted by the fact that the patient's opsonic index to this organism was only lowered to 0.81, was followed in eighteen hours by a marked negative phase, the lip becoming markedly painful and swollen. After another twelve to eighteen hours this condition passed off and the sore rapidly improved, till by the end of a week the ulcer had quite healed.

On June 1st the patient wrote to say he was practically cured. There was still a little scurfiness round the site of the big ulcer but no discharge, and he felt better than for the previous six months.

On June 5th he was seen. The ulcer on the lip had quite healed, slight redness and a little desquamation being all there was to show where the ulceration had been. The ear and throat were both healthy, he was able to shave comfortably. He seemed quite well, and had regained his colour and healthy appearance.

His opsonic index to streptococci was 1.20, to staphylococci 0.98, and to the bacilli 1.12.