

SELVA (J.)

A STUDY OF ERYSIPELAS :

*Its Infectious Nature ; the Depression upon
the Vital Powers ; Septicæmia as a
Complication ; the Curative In-
fluence upon granulating Sur-
faces and upon Sarcoma-
tous Growths.*

BY

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Late Interne to the Boston Children's Hospital.

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A STUDY OF ERYSIPELAS :

ITS INFECTIOUS NATURE; THE DEPRESSION UPON THE VITAL POWERS;
SEPTICÆMIA AS A COMPLICATION;
THE CURATIVE INFLUENCE UPON GRANULATING SURFACES
AND UPON SARCOMATOUS GROWTHS.

*WITH A REPORT OF ELEVEN CASES.**

BY JULIUS SELVA, M. D.,

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WHILE a surgical interne to the Boston City Hospital I have had the opportunity of observing many cases of erysipelas of unusual type, and from their character I have formed the opinion that the disease is more dangerous than it is usually supposed to be.

In looking up the literature on the subject I have been led to the belief that many writers consider this affection more from a local than from a general point of view; there is more attention paid to the local process than to the systemic disturbances, which are by far of capital importance, inasmuch as they may in many instances seriously endanger life or even cause death.

Some authors define erysipelas as "an acute and specific inflammation of the skin and subcutaneous tissue, charac-

* A thesis presented for graduation at the Medical School of Harvard University, June, 1894.

terized by diffuse, shining redness, pain, swelling, and elevated temperature of the affected part, terminating in desquamation and usually accompanied by fever."

Other writers go somewhat further and state at once that "erysipelas is, on the one hand, a *general intoxication*, and, on the other hand, an acute, progressing inflammation, with predominant serous infiltration of the tissues, associated with febrile movements, and produced as the result of local *infectious action*."

In the light of modern bacteriology it is a well recognized fact that erysipelas is an acute infectious disease, caused by the *Streptococcus erysipelatos*, the micro-organism always obtaining an entrance into the system through a wound or a small abrasion of the skin.

That there are mild forms of the affection with localized symptoms is unquestionable; that these forms are quite common is also true; but it is not less true that there is sufficient clinical and pathological evidence to show that the general infection often overshadows the local condition and plays a more important rôle in the course of the illness. Indeed, there are cases where erysipelas presents the picture of a general infectious disease with a local manifestation.

The symptoms which the disease produces vary in their nature and intensity, and in reporting the following cases I will classify them in two different groups.

1. *In the first group* I shall consider those cases of erysipelas where the local inflammation is subordinated to the general infection, as manifested by the presence of suppurative processes, by the marked prostration and lowering of the vital powers, by the typhoidal condition, and by the occurrence of septicæmia.

2. *In the second group* I shall dwell upon cases of erysipelas which bear relation to the curative effect upon granulating areas and upon sarcomatous growths,

GROUP I.

CASE I. *Erysipelas of the Face; Marked Pyrexia; Depression of the Vital Powers; Recovery.*—M. F., aged forty-two years, laborer, entered the City Hospital on March 1, 1894.

History.—On the afternoon of February 23d he was thrown from a sleigh, landing on his nose.

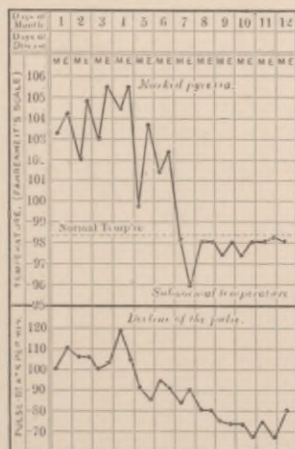
Physical Examination.—Well developed and fairly well nourished. Heart and lungs not abnormal. Liver and spleen: No enlargement made out.

Face: On the left side of the nose there is a superficial wound half an inch in length and nearly healed. The skin covering the anterior and lateral surfaces of the face, the ears, and both sides of the neck is swollen, red, and painful, with a smooth, glazed appearance. The edges of the swelling are well marked. No evidence of fracture present. The urine is negative, excepting the presence of the diazo reaction. The pulse is 100, of fair strength and volume. The temperature is 103°. The respiration, 26.

Subsequent History.—The case was treated by the judicious use of stimulants, careful diet, ice cap to the head, and lead wash to the inflamed skin.

On March 9th the swelling of the face had disappeared; desquamation was present, and resolution was thus being established.

The special feature of this case was the increased pyrexia for a period of six days (*vide* chart), corresponding to the height of the inflammation. The constitutional disturbances were well marked; headache and dizziness pres-

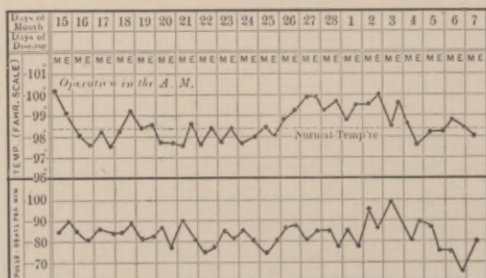


Group I, Case I.

ent. With the drop of the fever there was a similar decline of the pulse.

It will be noticed that toward the close of the disease the temperature became subnormal, as the result of the great prostration which the disease had produced. This depression of the vital powers is a feature of the affection which should always be borne in mind.

CASE II. *Erysipelas of the Right Leg; Necrosis of the Skin and Subcutaneous Tissue; Suppuration; Operation; Recovery.*—P. K., aged thirty-eight years, laborer, entered the City Hospital on February 14th.



Group I, Case II.

History.—Swelling and pain of the right leg. No apparent cause. These symptoms have steadily grown in severity, and patient has been confined to bed.

Physical Examination.—Heart action regular; no murmur. Liver and spleen not enlarged. Right leg: On the outer aspect of the thigh and extending downward to a little below the knee the skin is tense, red, and covered with vesicles of varying sizes. At places the skin is desquamating. There is fluctuation and boggy of the soft parts.

Urine, acid; no albumin or sugar. Diazo reaction present.

Subsequent History.—On February 15th Dr. Watson made an incision seven inches long over the seat of the swelling in the

right thigh. A large abscess cavity was opened between the skin and the fascia lata, involving the outer and posterior portions of the thigh. A pint or more of foul, acrid, thin pus was evacuated. Sloughs of the connective tissues were removed in masses by the curette. The skin appeared necrosed in places, and it was excised. Smaller counter-incisions were made for drainage.

Direct examination of the purulent fluid showed streptococci. Blood-serum cultures, at the end of twenty-four hours, showed pure cultures of the same micro-organisms.

There was a diminution of the temperature after the operation. The case made a steady recovery. A clean granulating area, fifteen inches in length and four inches wide, appeared in the course of two weeks. This ulcer healed slowly, and on May 8th, at the time of the patient's discharge from the hospital, it was almost entirely healed. Good general condition.

The treatment consisted of stimulants, nourishing food, and daily application of antiseptic dressing to the right thigh.

In the above-related case the virus did not confine itself to the superficial capillary lymphatics, but it spread to the subcutaneous connective tissue, thus bringing about supuration, which process is extremely rare in ordinary erysipelas. So I will classify this case as one of the variety known as "phlegmonous erysipelas."

CASE III. *Erysipelas of the Face and Scalp; Morphine Habit; Exhaustion; Death.*—R. K., a married woman, aged forty-eight years, entered the hospital on January 29th.

Family history negative.

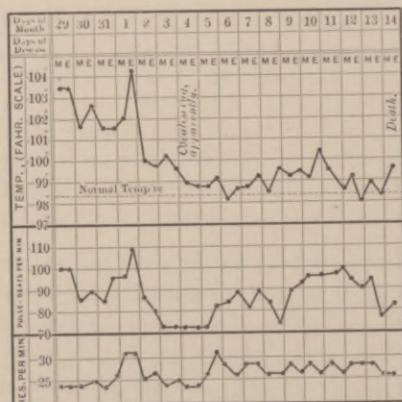
Past history: Patient has been addicted to the morphine habit in a marked degree for a number of years. Several ounces of the drug are said to be consumed in the period of four to five weeks.

Present illness: For a week has had swelling and redness of the nose, which swelling has now spread all over the face.

Physical Examination.—Body fairly well developed and greatly emaciated. Face: The *alæ nasi* and both sides of the face as far as the ears present a circumscribed swelling, of a

reddish color, fading on pressure and with shining, smooth appearance. Two small vesicles, a quarter of an inch in diameter, are seen on the left cheek. The scalp: That portion covering the forehead appears similarly affected.

There was no apparent cutaneous wound. The temperature, 103° ; pulse, 100, regular. Heart: No abnormal sound; action weak. Lungs: Occasional râles; no dullness. Liver and spleen not palpable. Urine: Diazo reaction present; otherwise negative.



Group I, Case III.

Subsequent History.—On January 30th the redness increased backward behind the ears. Alcoholic stimulants and nervous sedatives were given and lead-wash compresses applied on the face.

On February 4th the local process appeared to have subsided, desquamation ensued, and convalescence was apparently being established. This, however, was not the case. The patient's general condition became severely impaired; diarrhœa came on; she complained of pain in the posterior part of the legs; her heart became weak and irregular; and, in spite of nervous sedatives and active stimulation, death occurred on February 14th. There was no autopsy.

The clinical history of this case is interesting, because the disease, though apparently mild in its course and duration, was severe enough to bring on death in a subject who had been under the influence of morphine for a number of years—a subject who had become debilitated and of insufficient strength to counteract the prostration and toxic influence of the erysipelatos infection.

CASE IV. *Erysipelas of the Face; Fatty Degeneration of Muscles of the Right Thigh; Death from Septicæmia; Autopsy.*—M. G., a woman, fifty-two years of age, seamstress, entered the medical wards on February 7, 1894.

Family history and past history negative.

Present illness: Ten days previously had a fall, following which there was swelling, tenderness, and redness of the skin covering the forehead and eyelids. Patient is unable to walk on account of pain in the right thigh. Further history is not obtainable.

Physical Examination.—Body extremely fatty. Pulse regular, of fair strength and volume. Heart: Area of dullness not determined on account of the development of the breast. Auscultation of heart and lungs imperfect on account of the continual groaning of the patient. Liver and spleen not palpable. Abdomen prominent, tympanitic, not tender. Extremities: Marked swelling about the outside of the right hip joint, with a large discolored area of the size of the palm of the hand, the swelling and ecchymosis extending over the right buttock. There is pain at the right hip, greatly aggravated by motion or pressure. Inability to stand on her feet.

Face: The skin over the forehead, extending down into the bridge of the nose and to some extent into the cheeks, is reddened, œdematous, and tender to pressure, presenting a well-defined margin. Both eyelids are œdematous, obliterating all facial expression. Pus exudes from sinuses in both eyes. In the right inner canthus a probe passes into a cavity extending from half an inch to an inch in all directions. Urine: Traces of albumin, occasional granular casts.

Subsequent History.—The case was treated with alcoholic stimulants, careful diet, and the application of lead wash to the inflamed skin.

On February 8th patient became heavy and stupid. The pulse was feeble, rapid, and irregular. The swelling of the eyelids and forehead was more marked. The right leg was half an inch shorter than the left; there was pain at the right hip, increased on motion; and this fact led to the assumption that there might be a fracture. On this account the patient was transferred to the surgical wards. Crepitus and abnormal mobility were not detected, and final diagnosis as to the nature of the injury was not made.

On February 9th, at 3.30 A. M., patient entered into a deep collapse, with cold, clammy skin; cyanosis; intermittent, feeble pulse; and finally died at 6.20 A. M.

Autopsy on February 10th by Dr. Councilman.

Body large and extremely fatty.

The skin of the face is œdematous and congested. Eyes nearly closed from œdema. Over the right eye there is a superficial contused wound about three centimetres long. Over the right buttock there is a large contusion, circular in outline, and about ten centimetres in diameter. Over the contusions and the surrounding skin there are large blebs filled with clear, blood-stained fluid.

Lungs and pleura: The pleuræ smooth. There is a slight amount of fluid in the pleural cavity. There is also congestion and œdema in the posterior portions of the lungs.

Pericardium normal.

Heart very soft, pale, and flabby.

Peritonæum smooth. Several of the appendices epiploicæ hæmorrhagic.

Spleen somewhat enlarged, rather soft. Neither Malpighian bodies nor trabeculæ visible.

Kidneys of ordinary size. Cortex pale and cloudy.

Stomach and intestines normal.

Adrenal glands and pancreas normal.

Aorta: In the arch there are a number of calcified plates in the interior, the largest perhaps a centimetre in diameter.

Uterus somewhat enlarged and filled with mucoid material.

Muscles: The muscles of the right thigh in the neighborhood of the hip are pale and soft, almost diffluent.

There is no fracture.

Anatomical diagnosis: (1) Erysipelas of the face, (2) *Streptococcus septicæmiæ*. Fresh examination of the muscles about the right hip joint showed extreme fatty degeneration of the muscular fibers and enormous numbers of streptococci. Few pus cells were present.

Cultures on blood serum of the liver, spleen, kidneys, muscles of the right thigh, and blood showed a great number of streptococci.

CASE V. *Erysipelas of the Right Leg; Death from Septicæmia; Autopsy*.—O. C., a laboring man of about thirty-five years of age, entered the hospital on February 17th in an unconscious condition. The *history* was not obtained.

Physical Examination.—Body strongly built and well nourished. Heart: Strong impulse. No murmur or enlargement. Liver and spleen enlarged and palpable. Urine negative. Right lower extremity, from the foot to the upper part of the thigh, is much swollen, red, and hot. The swelling and redness present a sharply defined border at the upper part. On the posterior, the outer, and the inner aspects of the lower leg the skin is raised and necrosed, and purulent discharge appears from the ulcerating surface. The temperature, 104°. The pulse, 106, regular, full, and strong. The respiration, 25, shallow and rapid.

Subsequent History.—Stimulants were given and corrosive dressing (1 to 6,000) was applied to the right leg.

On the following day, February 18th, at 12.05 in the morning, patient suddenly collapsed and died, the pulse apparently of good tension until the last.

Autopsy by Dr. Councilman on February 19th.

Body large, tattooed on the anterior surface of both forearms.

Right lower extremity: On the posterior surface of the right leg there is a small ulcerating area. The entire lower leg, extending upward over the thigh, is deeply congested, injected, and œdematous.

The inguinal glands on the same side are swollen, reddened, and in places in the tissues adjacent to them there appear to be small purulent foci. Subcutaneous fat abundant. Muscles dark red. Lungs: Both lungs are adherent at their apices. Their posterior portions are intensely congested. In both lungs the anterior portions are emphysematous. Heart of medium size. Valves, normal. Liver, very large and pale. Spleen weighs six hundred grammes; $11 \times 9 \times 5$ centimetres. On section, rather soft, darkened. The capsule tense.

Kidneys: Both kidneys enlarged. No appearance of nephritis. Adrenal glands and pancreas normal. Peritonæum smooth. Intestines: Large intestine and sigmoid flexure distended. Testicles normal. Anatomical diagnosis: (1) Erysipelas of the lower leg with infection of the lymphatics and acute septicæmia. (2) Acute swelling of the spleen. Cultures from blood and organs contain numerous colonies of the *Streptococcus pyogenes*.

CASE VI. *Erysipelas of the Face and Scalp; Death from Septicæmia; Autopsy*.—A. B., laborer, forty-nine years of age, entered the City Hospital on January 12th. The patient was in a delirious condition and the history was not obtained.

Physical Examination.—Well developed and well nourished. Tongue, dry, brown-coated. Pulse regular and of good strength and volume. Heart negative. Lungs. Front aspects, negative; backs, not examined. Abdomen distended and tympanitic. Liver negative. Spleen obscured by tympany. Extremities negative. Face: The skin of the whole face is greatly swollen, red, and excoriated. There are blebs, and serous fluid oozes here and there. Eyes: Thick purulent discharge from conjunctiva. Urine not obtained.

January 13th.—Patient gradually became more and more delirious; the pulse became feebler and feebler, irregular and dicrotic; no response to stimulation, and death occurred at 4 A. M.

Autopsy by Dr. Councilman, January 15th: Body large, with marked posterior curvature of thorax. Marked rigor mortis. Subcutaneous fat abundant. Muscles red, somewhat infiltrated with fat. Thorax narrowed; very deep antero-posteriorly. Scalp thick, filled with yellowish serum and pus;

rigid, almost incapable of being bent. Skull thick and firm. Dura mater somewhat thickened. Meninges œdematous. Convulsions of brain well developed; brain normal. Diaphragm extremely high. Heart lay almost at cleft of sternum; valves normal. Lungs, both adherent, congested posteriorly. Liver large and extremely fat. Spleen large, rather soft. Pancreas infiltrated with fat. Adrenal glands normal. Intestines: Mucous membrane rather pale. Testicles: Left is small, almost entirely atrophied; right normal. Face swollen and œdematous. Both conjunctivæ filled with pus.

Anatomical diagnosis: (1) Erysipelas of the scalp and face. (2) Septicæmia.

Results of the Bacteriological Examination by Dr. J. H. Wright.—Tissue of the scalp: Colonies of the *Streptococcus yogenes*, a few colonies of the *Staphylococcus albus*, and a segmented bacillus resembling the *Bacillus diphtheriæ*. Lateral sinus: Numerous colonies of the *Staphylococcus albus* (?) and a moderate number of the segmented bacilli found in the scalp. Meninges: Sterile. Left lung: Colonies of the *Staphylococcus aureus* and a few colonies of the *Bacillus coli communis* (?) Kidney: Colonies of the *Bacillus coli communis*. Liver and spleen: Sterile. Heart blood: Colonies of an unknown bacillus and a few colonies of various other bacteria. The segmented bacillus resembling the *Bacillus diphtheriæ* was found to differ from the *Bacillus diphtheriæ* in its biology and in that it had no pathogenic effect on two guinea-pigs which were inoculated subcutaneously.

GROUP II.

Before entering into the second group of cases, where erysipelas has a curative influence upon granulating areas and upon sarcomatous growths, a few introductory remarks upon this important subject may not be out of place.

Dr. W. B. Coley, of the New York Hospital for the Ruptured and Crippled, has discovered a new treatment for malignant tumors. He began his investigations as early

as September, 1891, independently of similar experiments going on in Germany (Fehleisen's); and to him belongs the credit of having first introduced into America the inoculation with the streptococcus of erysipelas as a therapeutic agent. Dr. Coley professes to have obtained, in many cases, the complete disappearance of carcinoma and sarcoma under this new method of treatment.

Dr. J. H. Monks, of the Boston City Hospital, followed Dr. Coley's treatment in two cases of large inoperable sarcoma, but his results have not been favorable.

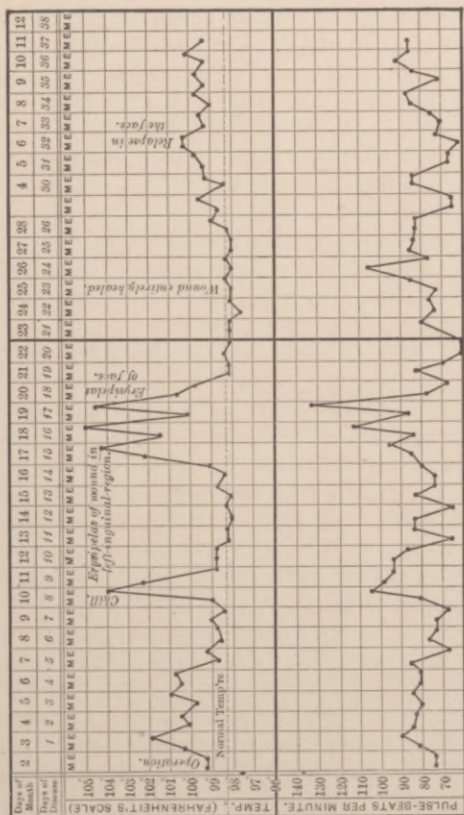
CASE I. *Operation for Left Inguinal Adenitis; Accidental Erysipelas of the Wound and of the Face; Curative Influence upon the Wound; Relapse at the Face; Recovery.*—P. C., stableman, twenty-two years of age, entered the hospital on February 1, 1894. He is a strong, healthy adult, who was admitted into the hospital for operation upon a left inguinal adenitis of six weeks' standing, due to gonorrhœal urethritis. Abdominal and thoracic viscera negative. Urine negative.

Operation by Dr. Watson on February 2d. The glands of the left inguinal region were dissected out and excised. Incision seven inches long. Enlarged lymphatics and bleeding vessels were tied. The wound, after having been scrubbed with iodoform gauze and peroxide of hydrogen, was closed with interrupted silk sutures, except at the ends, where drainage was established by means of a dozen heavy silk threads. There was slight purulent discharge from the wound, and the case followed a normal course under daily corrosive dressing.

On the eighth day after the operation, however, the patient had a sudden chill with marked constitutional disturbances. An examination of the wound at the time showed no perceptible change, and drainage was apparently perfect. The spleen was not enlarged and there was no malarial history. The temperature subsided and it remained within the normal limits for several days, and it was then supposed that the chill had no relation to the local condition.

On the fifteenth day after the operation (February 17th)

the morning temperature rose to above 104° and it became irregular, with morning remissions and evening exacerbations, for a period of four days. The pulse showed corresponding



Group II, Case I.

changes, as will be seen in the chart; it became feeble and rapid. There were constitutional disturbances.

During this febrile period the local condition of the wound showed striking changes; the discharge became purulent and

increased to about two ounces in the twenty-four hours. There appeared an area of redness for about two inches around the wound, with sharply defined outline; and there was also an increased tension of the parts accompanied by a burning sensation. The right side of the face became similarly involved, and the patient was isolated. It was evidently a case of erysipelatous infection occurring through two remote and different channels: (1) through the wound at the left inguinal region, and (2) through a small abrasion of the skin of the face probably.

Then it was interesting to observe the effect which such an infection had upon the suppurating surface. In the course of a few days the swelling, redness, and pain had disappeared; the amount of discharge gradually diminished, and on February 25th the whole inguinal wound appeared entirely healed. Desquamation ensued at the face and left inguinal region and resolution took place.

On March 6th slight redness of the face reappeared, apparently a relighting of the process. This relapse lasted only two days, and on March 12th desquamation had been completed and the patient was discharged well.

This case was treated as usual by the judicious use of stimulants, the application of lead-wash compresses to the face, and the dressing of the inguinal wound with corrosive gauze (1 to 6,000) daily.

CASE II. *Traumatic Periostitis of the Right Leg; "Erysipelas Ambulans"; Marked Pyrexia and Typhoidal Condition; Curative Effect upon the Granulating Area; Recovery.*—J. C., engineer, thirty-two years of age, entered the hospital on January 7, 1894, with the history of having struck his right shin against a barrel two weeks previously. Swelling of the leg and an ulcer resulted. Feverishness and constitutional disturbances for the last few days present. No venereal history obtained.

Physical Examination.—Well developed and well nourished. Examination of the heart, lungs, liver, and spleen negative. Urine, smoky, and sp. gr. 1.026; albumin $+\frac{1}{2}$ per cent. No sugar. Diazo reaction present. Sediment; excess of normal and few abnormal blood globules. Some round cells.

The further history, however, cleared up the diagnosis. There was no splenic enlargement made out at any time during the illness. The blush and swelling, with a smooth, shiny appearance and a well-defined margin, advanced steadily upward over the anterior surface of the thigh, and at each successive day the upper limit of the inflammation had reached a higher level. As the blush and swelling advanced upward, there was correspondingly disappearance in the lower regions. On January 23d the inflammation had involved the uppermost part of the thigh, extending over the outside of the hip joint; beyond this the process reached no farther. Resolution took place and desquamation made its appearance. The constitutional disturbances abated with the lowering of the temperature.

This was unquestionably a case belonging to the variety known as "erysipelas ambulans," the infection having taken place through the wound in the right leg. In this case we also have an illustration of the curative effect upon the wound. The swelling subsided; the discharge, which had increased during the height of the fever, gradually diminished from day to day; the bone became covered with periosteum, and the wound was completely healed on February 5th.

The treatment was symptomatic. The wound was dressed antiseptically. Flaxseed poultices were applied during the acute stage.

CASE III. *Large Inoperable Sarcoma of the Right Thigh. Five Inoculations with Cultures of the Streptococcus Erysipelatos; Partial Disappearance of the Growth; Death from Septicæmia; No Evidence of Retrograde Metamorphosis on Microscopical Examination; Autopsy.*—O. M. M., aged sixty-nine years, carpenter, entered the City Hospital on August 24, 1893.

Family and past histories negative. Present illness: About four years previously patient noticed pain and slight stiffness of the right thigh; these symptoms have steadily increased in frequency and severity. Last December he first noticed an indurated area upon the posterior upper surface of the same thigh.

Physical Examination.—Well developed and well nourished. Heart and lungs not abnormal. Right thigh considera-

bly enlarged. On the middle third of the posterior surface is a cicatrix of a former operation (?) and a bluish soft tumor the size of an orange projecting from the surface, to which it is attached by a small, short-necked pedicle. Its surface is uneven. There is considerable induration around and beneath the tumor. Urine negative. General condition fair.

Subsequent History.—An operation for the removal of the growth was not deemed advisable, and the question of an artificial streptococcus infection was judiciously considered. The nature of the disease and of the proposed inoculation having been explained to the patient, he made a request for such an inoculation, and this was performed by Dr. Monks on September 5th. The field of operation was shaved and covered with corrosive poultice; during the preceding night and just before inoculation it was scrubbed with boric-acid solution.

The skin about the tumor was scarified in five or six places, making slightly bleeding and oozing surfaces. Platinum wire, sterilized in a Bunsen burner, was inserted into colonies of the *Streptococcus erysipelatos* in agar-agar cultures (obtained from Dr. Coley, of New York), and the inoculations were made by applying the platinum wire to the scarified areas. A small portion of the tumor was removed for examination. One inoculation was made into the tumor itself. Sterilized gauze and a rubber dam were applied.

September 6th.—The temperature is slightly elevated, but no constitutional disturbances, such as chills or vomiting, have intervened. Right thigh: Scarified areas are reddened and oozing. Sterilized dressing applied.

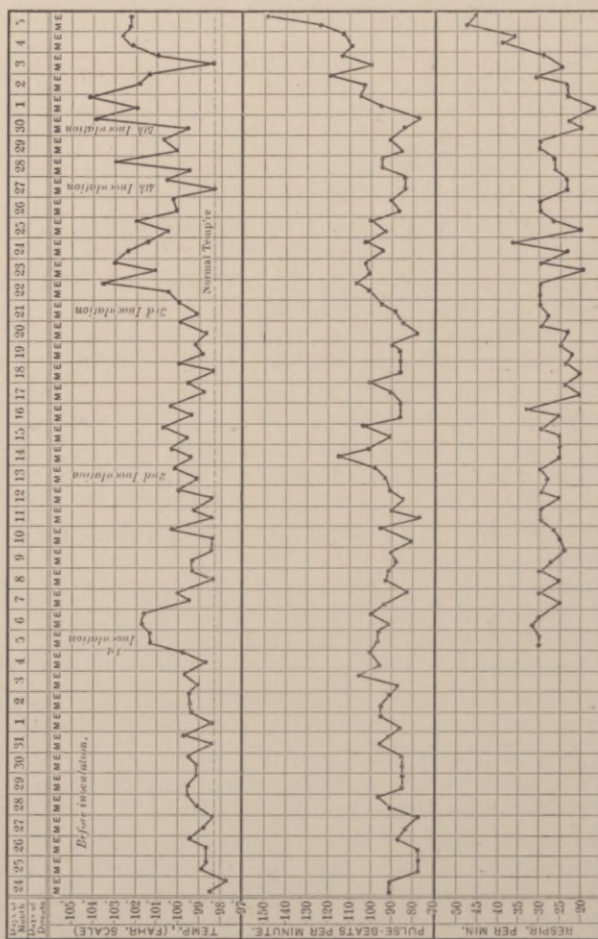
The temperature subsided, and on September 13th there was no apparent change to be noted in the tumor. Inoculations were made, in a similar way to that of September 5th, with a streptococcus culture obtained from a patient with erysipelas in the next bed. Sterilized gauze and rubber dam applied.

With the exception of shooting pains in the affected thigh and of slight rise of temperature, there were no changes to be noted, the signs of erysipelatos inflammation being absent.

21st.—The tumor of the right thigh was inoculated with the *Streptococcus erysipelatos* by two different methods:

(1) By scarification and the application of the platinum wire from agar cultures.

(2) By the injection with a Koch's syringe of two cubic



Group II, Case III.

centimetres and a half of bouillon culture of streptococcus. (Both cultures were obtained from Dr. Coley, of New York.)

22d.—Patient had a chill at 3.30 A. M. Nausea, vomiting, and general malaise appeared. There is a red swelling on the right thigh, completely surrounding the tumor for an area of twelve to fifteen inches in diameter, with irregular edges. Here and there red islands are seen. Sterilized dressing was applied three times a day. The tincture of chloride of iron, ℥ x ; quinine sulphate, gr. ij; and whisky, $\frac{3}{4}$ ss., were given every six hours.

25th.—Patient complained of nausea and vomiting. Pain in the lower abdominal region and darting pains in the right thigh were present. The area of redness is more extensive. A part of the tumor has apparently sloughed away, though no pieces have been found in the dressing, and a new area of ulceration on one side of the tumor has formed.

27th.—The inflammation has undergone resolution and the blush has faded. General condition improved. The tumor was then inoculated for the fourth time by the (1) scarification and by the (2) injection methods, five cubic centimetres of bouillon culture having been used (Dr. Coley's cultures of streptococcus). Sterilized dressing applied.

28th.—In the morning an area of redness 2×5 inches has appeared about the points of inoculation. In the evening there was a rise of temperature to 103° , and the patient suffered from general distress. Anorexia present.

29th.—The temperature lowered. The appetite was better. The red areas had scattered over the posterior aspect of the thigh, and the pedunculated portion of the tumor had sloughed off, leaving granulations beneath. No larger sloughs have been seen at any time. The whole size of the leg not apparently materially changed.

30th.—The temperature subsided and the patient was inoculated for the fifth time by injecting two cubic centimetres and a half of the bouillon culture subcutaneously, two cubic centimetres and a half in the deep layers of the skin, and one cubic centimetre in the substance of the tumor itself, beneath the granulations.

Five hours after inoculation the patient had a chill and the

right thigh increased in size, measuring twenty-five inches in circumference. Marked constitutional disturbances followed.

October 3d.—In the morning the temperature dropped, to rise upward again in the evening. The pulse became weak and rapid. Respiration superficial and frequent. Nausea and vomiting appeared.

4th.—Tenderness, swelling, redness, and heat present in the first phalangeal joint of the right forefinger.

5th.—Patient has been in a condition of stupor all day. The right thigh seems to have diminished in size; the tumor is softer, more flabby, and movable in the soft parts.

6th.—The patient continued unconscious, with high pulse respiration, and temperature. Stimulants had no effect, and death occurred at 4 A. M.

Autopsy by Professor Councilman, of the Harvard Medical School, at 2 P. M. Body large, strongly built, well nourished. Abdomen greatly distended. Dark fluid flowing from the mouth.

Right thigh.—On the posterior aspect of the right thigh, at about the junction of the upper and middle thirds, there is a large projecting tumor mass, eight centimetres in diameter. Below this, in the same line, is a smooth cicatrix extending five centimetres downward, and three centimetres broad at its upper margin. The skin in the neighborhood of the tumor, and for some distance over the thigh, is mottled. In the middle of the projecting mass is a large opening with extensive sloughing edges, which pass downward into a cavity. The entire projecting mass is to a large extent gangrenous and sloughing. This is more marked in the lower portion than in the upper. On section into the tumor, directly through the projection, the cavity is found to continue down into the tumor, making irregular projections into the surrounding tissue for a distance of seven centimetres. The edges of this cavity everywhere are black, sloughing, and necrotic. The slough extends from the edges of the cavity for some distance into the surrounding tissue. On the outer aspect of the tumor, beneath section and extending downward into the muscle, and connected by a passage with the central slough, are large cavities with gangrenous edges, filled with a black, stinking fluid.

The tumor proper is of irregular shape, with circumscribed and smaller masses more or less connected with the central tumor, extending into the tissues all about. The central mass measures in all directions eight centimetres. It is—except in the sloughing portions—of a grayish-red appearance, and contains one or more small cysts with gelatinous contents. Immediately at the bottom of the tumor is a small mass of the same consistence and three centimetres in diameter. At another place adjoining the tumor is a slightly yellowish translucent mass of tissue containing several hæmorrhages and presenting the appearance of fat. From the inner side of the tumor there is a large projecting mass, five centimetres in circumference, circumscribed in part and in part connected with the parent growth, but easily separable from the main tumor and surrounding tissues. This mass is opaque and whitish-gray in color, and of tolerably firm consistence, though not so consistent as the main tumor. There is slight infiltration into the muscular tissue. In the surrounding muscle there is considerable fibrous tissue.

The part of the autopsy relating to the tumor is here given in full. An examination of the other organs showed the general lesions of septicæmia. There were marked parenchymatous swelling and degeneration of the liver, spleen, and heart; also minute hæmorrhages in both the pleura and pericardium. Cultures were made at the autopsy from various parts of the tumor and from all the organs. The results of the cultures are as follows: 1. From the tumor and its neighborhood there were numerous colonies of streptococci, a few of the colon bacillus, and a few of the *Bacillus pyocyaneus*. 2. From the inguinal gland on the inside of the tumor, pure cultures of streptococci. 3. From the spleen, liver, and blood of heart, pure cultures of streptococci. The streptococcus in its growth conforms to the character of the *Streptococcus pyogenes*.

Careful microscopic examination of the tumor was made, both fresh and after hardening in various media. The tumor was found to be a large *mixed-cell sarcoma*, with a considerable formation of myxomatous tissue in various parts. The gelatinous-looking nodule in the remnants of the tumor had a typical myxomatous structure; throughout the tumor, especially in

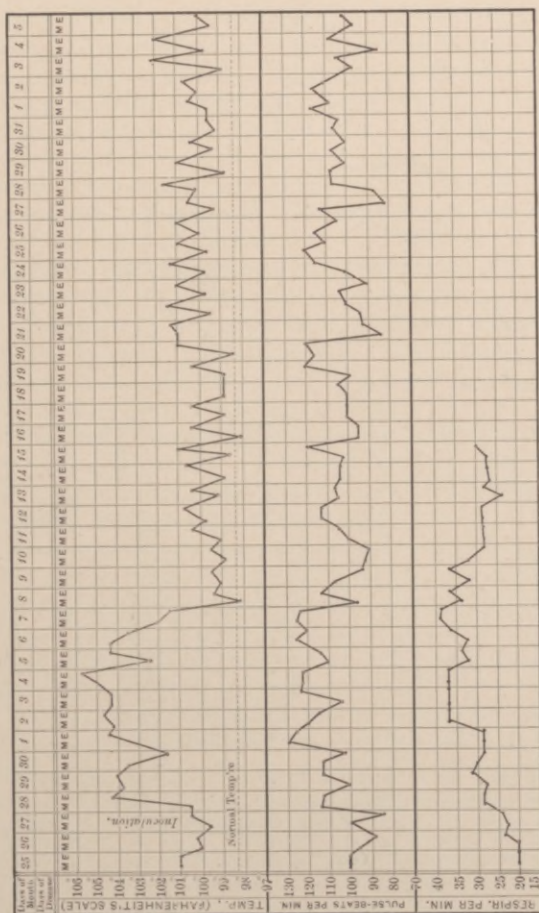
sections of portions adjoining the slough, numerous groups of streptococci were found. They were to a great extent in the blood-vessels and lymph spaces of the tumor, associated often with thrombi. These were the only bacteria found on microscopical examination. The cells of the tumor, except where the actual slough had taken place, were well preserved and contained numerous nuclear figures indicating rapid cell proliferation.

The results of the pathological examination show a general streptococcus septicæmia proceeding from the tumor; the extensive slough may have been due to interference with blood supply from the inflammation attending the injections, or may have been due to the direct effect of the streptococcus on the tissues. The microscopic examination failed to show any evidence of retrograde metamorphosis in the tumor at a distance from the slough, but, on the other hand, as far as could be judged from the evidence of the very numerous nuclear figures, an increased degree of cellular activity.

CASE IV. *Large Inoperable Sarcoma of the Neck; One Inoculation with the Streptococcus Erysipelatis; Recovery from the Inflammatory Reaction; Slight Influence upon the Growth; Death; no Autopsy.*—E. D., domestic, thirty-five years old, entered the Boston City Hospital on September 12, 1893. Family and past histories negative. Present illness: About three months ago she first noticed small lumps, of the size of a bean, non-painful, on the left side of the neck. They have gradually increased in size, and during the past few weeks the growth has become more rapid and a large mass has resulted. Pain has become a prominent symptom.

Physical Examination.—Well developed; somewhat emaciated. Heart and lungs negative. Liver and spleen not enlarged. Neck: On the left side of the neck (*vide* cut) is a swelling, about the size of the fist, extending from the mastoid process downward almost as far as the clavicle, and from the ramus of the jaw in front backward to within three quarters of an inch in the median line. This tumor is firmly adherent to the deeper structures, but is movable under the skin, except at its lower part, where there is a swelling about the size of a hen's egg, dis-

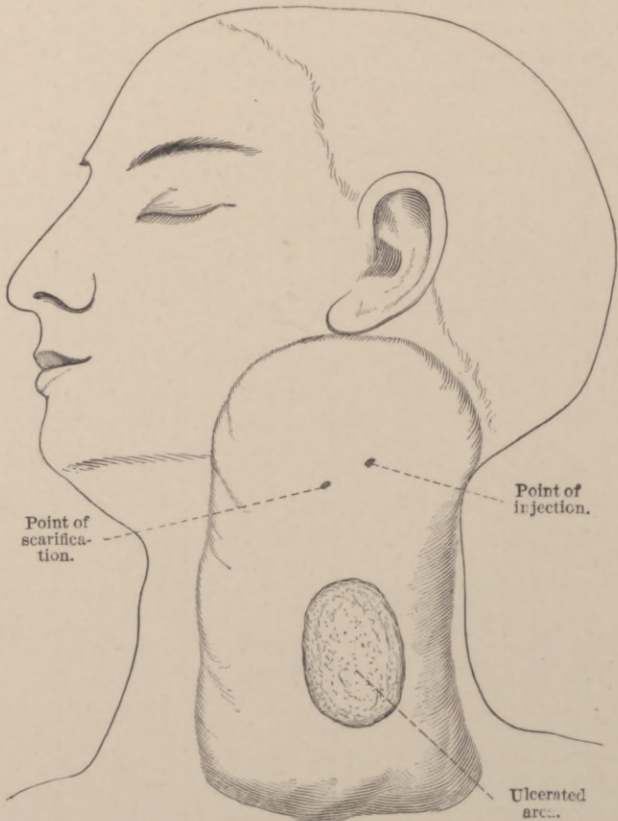
colored and fluctuant. The surface temperature is not increased.



Group II, Case IV.

Subsequent History.—The expectant treatment was used. The patient's general condition was failing. On September 20th

the growth had apparently increased considerably in size, and a bloody discharge appeared from an ulcerating area at its lower part. In this large inoperable sarcoma of the neck its removal



Group II, Case IV.

was contraindicated, and the case seemed to be suitable for the treatment with artificial streptococcus infection, at least as a last resource,

On September 27th, at the patient's request, Dr. Monks inoculated the tumor in the neck with cultures of the *Streptococcus erysipelatos* on the anterior and upper parts (*vide* cut) by the two methods of (1) scarification and (2) subcutaneous injection. In this case two cubic centimetres and a half of bouillon culture were injected. The cultures were taken from a case of erysipelas occurring in Dr. Post's service.

This inoculation was followed by a febrile period, which lasted ten days (*vide* chart), during which period marked constitutional disturbances were present. There was also a marked local reaction, manifested by a general swelling and redness around the points of inoculation. Examination of the throat showed enlarged tonsils and general redness of the pharynx.

October 20th.—The swelling and redness about the tumor have disappeared, leaving the tumor apparently of about the same size as at the time of entrance. The ulcerated area is about two inches by one inch, and bleeds at each dressing slightly. (Sterilized dressing was applied daily.)

On several occasions patient's general condition was somewhat improved, and she was allowed to sit up. The tumor, which before inoculation had shown signs of active growth, has reached apparently a state of quiescence.

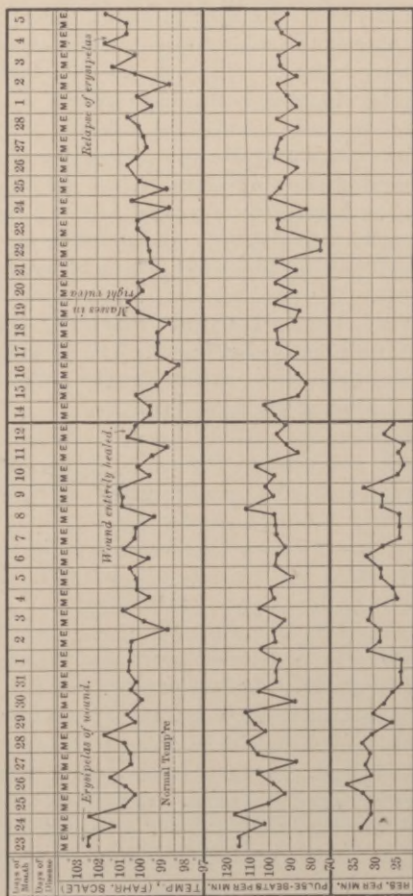
November 30th.—A hæmorrhage from one of the veins of the neck occurred, which was controlled by pressure. The tumor began once more to show signs of active growth.

December 6th.—The size of the tumor was considerably increased, especially at the posterior part; the ulcerating area has enlarged, and the discharge become profuse.

A glance at the chart shows that the temperature was constantly somewhat elevated, with morning remissions and evening exacerbations, even after the subsidence of the inflammatory reaction following the inoculation. The patient became more and more exhausted from day to day. She was unable to retain nourishment; stimulants had no effect; and finally, on December 11th, she became unconscious, and died at 6.30 P. M. No autopsy.

CASE V. *Sarcoma of the Right Thigh in a Woman Seventy Years of Age (Recurrent?); Operation; Accidental Erysipelas;*

Curative Effect upon the Wound; Two Relapses of the Erysipelatous Inflammation; Influence upon Tumors in Right Labia



Group II, Case V.

and Right Iliac Region; Recovery.—E. B., seventy years of age, widow, entered the City Hospital on December 8, 1893, in

Dr. Bolles's service. Family history negative. Past history: She was operated on for the removal of "hæmorrhoids" in England many years ago. Entered this hospital on January 22, 1892. At that time it is stated in the records that she had about the anus a tumor, an inch by a quarter of an inch thick, of fungoid appearance and purplish in color. The growth was removed, and it was reported to be an "intracanalicular papillary fibroma."

Present illness: Patient claims that two weeks after the last operation "lumps" appeared in the right groin, which increased slowly in size. For the last year the rapidity of the growth is more noticeable. Patient has been confined to bed for the last three months on account of shooting pains over the legs and general distress.

Physical Examination.—Body fatty and anæmic. Heart weak; no enlargement; sounds normal. Lungs, liver, and spleen negative. Urine acid; slight traces of albumin; specific gravity, 1.018; abnormal blood and occasional hyaline and fine granular casts. Inguinal glands enlarged on both sides, especially on the right. Right thigh: On the anterior aspect, just below Poupart's ligament, there is a tumor of the size of an orange and of semisolid consistence.

Subsequent History.—On December 12, 1893, Dr. Bolles removed the mass in the right thigh. The wound, five inches long, was allowed to heal by granulations. The growth was found to be a sarcoma.

January 23d.—The wound became swollen, red, and painful; the area of redness extended two inches around, with a zigzag margin. There were constitutional disturbances. The patient was transferred to Dr. Watson's service. Profuse discharge from wound.

This was a case of accidental erysipelatos infection, and it is reported as an illustration of the curative effect which the *Streptococcus erysipelatos* has upon the granulating surface. The discharge gradually diminished; the wound became covered with healthy granulations, and on February 12th it was entirely healed.

There were other features in this case which are worthy of note.

February 19th.—Small masses, of the size of a marble, appeared in the right side of the vulva, which became softened in a few days and discharged puslike fluid. Larger masses were felt in the right iliac fossa, apparently under the abdominal wall.

On March 4th and March 27th the patient had two successive fresh outbreaks of erysipelatous infection in the upper part of the right thigh. The patient remained in the hospital for several weeks, and convalescence was slow. Complained of pain in abdomen and legs.

May 15th.—She was much improved. The bowels have been kept open. No pain in the legs or abdomen. At the right iliac region the tumors have apparently diminished in size. The small masses over the right labia have increased considerably during the preceding two weeks; now they appear red and somewhat soft, as if ready to ulcerate. One of these masses is actually discharging a thin fluid. Good general condition. Patient was discharged, and has not been heard from since.

The curative influence of erysipelas has been shown by the rapid healing of purulent granulating surfaces, and Cases I, II, III, and V, of Group II, are obvious illustrations.

In Dr. Monks's two cases of sarcoma, although a cure was not obtained, there occurred changes of some significance. In the first case inoculated with cultures of the *Streptococcus erysipelatos*—a large inoperable sarcoma of the right thigh—there was a partial disappearance of the growth, yet there was no microscopical evidence of retrograde metamorphosis, as was shown at the autopsy. In the second case inoculated, the tumor at one time appeared to have reached a quiescent stage. The patient recovered from the inflammatory reaction, and died many days afterward. No autopsy was obtained.

And in the last case of my list there appeared to be also a certain influence upon the tumors in the right labia and right inguinal region, besides the healing of the wound.

In addition to ten original cases, Dr. Coley has tabu-

lated the reported cases of carcinoma and sarcoma in which erysipelas, either spontaneous or artificial, intervened, making up a total of thirty-eight cases. Of these cases, the erysipelas occurred accidentally in twenty-three cases, and was the result of inoculation in fifteen cases; seventeen cases were carcinoma; seventeen cases were sarcoma; four either sarcoma or carcinoma. The results were as follows: In carcinoma (seventeen cases), three cures, 17.6 per cent.; one death, 5.9 per cent. In sarcoma (seventeen cases), seven cures, 41 per cent.; one death, 5.9 per cent. Four carcinoma or sarcoma, two cured. From the figures it is evident that the curative action is more marked in sarcoma.

I will devote a brief consideration to the method of action of the *Streptococcus erysipelatos*.

According to Ernst, bacteria produce their effect upon the living tissue in three different ways:

1. By mechanical obstruction.
2. By abstracting from the tissues of the body the material necessary for their own growth, and by so much depriving the tissue cells of nutrition necessary for their own development.
3. By the production, during their growth, and either by direct exciting metabolism or as the result of the chemical affinities of the elements left in unstable equilibrium after those necessary for the bacteria have been abstracted, of new chemical compounds that are destructive to their own further activity or even to their further existence.

And now the question comes, In which way does the *Streptococcus erysipelatos* produce its curative action upon sarcomatous growths?

Dr. Coley, believing in the parasitic origin of cancer, explains the action of erysipelas as follows: If a small quantity of blood serum of an animal rendered immune to tetanus is capable of destroying or rendering inert the virulent

bacilli in a fresh case, it is quite as easy to understand that the toxic products of the erysipelas streptococci might bring about such changes in the blood serum as to destroy the parasite of cancer. The parasite having been destroyed, the irritation would consequently cease, and this would lessen the hyperæmia of the parts, upon which factor the life of the tumor cells of low vitality largely depends.

Dr. Coley believes also that the phagocytosis theory is insufficient to explain the action of erysipelas. According to this theory, after the introduction of bacteria into the living tissues, certain cells of the body act as actual phagocytes, destroying by absorption the bacteria. I would venture to say that perhaps phagocytosis can not be absolutely discarded in view of the fact that in many instances repeated injections of cultures of the *Streptococcus erysipelatos* have failed to produce the disease. Dr. Coley himself has reported eight of these classes of cases.

Was not this failure the result of the destruction of the streptococci by the phagocytes ?

And is not the phagocytosis theory another reason for preferring the use of the toxic products of erysipelas to that of the cultures ?

Conclusions.—1. The general infectious nature of erysipelas and its dangers should always be borne in mind. Marked prostration, cerebral symptoms, and septicæmia are not infrequent complications.

2. Accidental erysipelas has a curative influence upon granulating surfaces, but its use in the treatment of ulcers would be unjustifiable.

3. In the treatment of neoplasms by Dr. Coley's method of inoculation with the streptococcus of erysipelas we have a therapeutic agent which should not be employed indiscriminately.

4. There is a marked discrepancy between the clinical

and the pathological evidences; Dr. Coley's cases of disappearance of neoplasms under his treatment with streptococcus inoculation contrast with the results obtained by Dr. Councilman at the autopsy.

5. Further investigations, especially with the toxic products of erysipelas, are necessary for the resolution of this important problem.

Before concluding I wish to acknowledge my indebtedness to Dr. W. T. Councilman, Dr. W. P. Bolles, Dr. F. S. Watson, Dr. G. H. Monks, Dr. H. W. Cushing, Dr. A. M. Sumner, and Dr. V. Bowditch, of the Boston City Hospital, for their kindness in allowing me to use the hospital records of the cases which I have discussed.*

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* Since this paper was first written Dr. Coley has published, in the July number of the *American Journal of the Medical Sciences*, an article entitled, Treatment of Inoperable Malignant Tumors with the Toxine of Erysipelas and the *Bacillus prodigiosus*.

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