

CONTRIBUTION TO THE KNOWLEDGE OF
SARCOMA.¹

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OF NEW YORK.

- I. A CASE OF PERIOSTEAL ROUND-CELLED SARCOMA OF THE METACARPAL BONE; AMPUTATION OF THE FOREARM; GENERAL DISSEMINATION IN FOUR WEEKS; DEATH SIX WEEKS LATER.
- II. THE GENERAL COURSE AND PROGNOSIS OF SARCOMA, BASED UPON AN ANALYSIS OF NINETY UNPUBLISHED CASES.
- III. THE TREATMENT OF SARCOMA BY INOCULATION WITH ERYSIPELAS, WITH A REPORT OF THREE RECENT (ORIGINAL) CASES.

I. THE patient a young lady, æt. 18, had been in perfect health from earliest childhood. The family history was likewise good with the exception of a remote tubercular tendency, and the fact that an ancestor, three generations before, had died of "cancer" of the lip, presumably epithelioma.

In the early part of July, 1890, she received a slight blow upon the back of the right hand. The hand became a little swollen and somewhat painful the first night. The next few days the pain became a trifle less and the swelling subsided, but did not entirely disappear. About a week later the swelling again began to increase very slowly, and the pain became more severe. She consulted a physician at the time of the injury, but there being no evidence of anything more than an ordinary bruise the usual local applications were applied.

August 12. The pain and swelling continuing, she again sought

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medical advice and as motion seemed to aggravate the pain, the hand and wrist were immobilized with a straight palmar splint.

This gave patient but only temporary relief. During September the swelling and pain both gradually increased. The pain was constant, usually dull, but sharp and shooting at times, and much worse at night, generally keeping the patient awake from one to two hours every night. It was always much relieved by letting the hand hang down as low as possible.

On October 1 the patient came to New York for further surgical advice and was referred to me. A careful examination at that time showed a small fusiform swelling about the size of half an olive upon the dorsum of the right hand, and situated just over the middle of the fifth metacarpal bone. The skin over this was perfectly normal.

There was an indistinct sense of fluctuation on deep pressure, but as pressure was so painful this fact could not be clearly made out. The base of the swelling was not distinctly outlined, there being a gradual shading off into the surrounding tissues.

There was a slight local increase in temperature. The ring and little fingers were held in an extended position and any attempt to flex them at the metacarpo-phalangeal joint caused pain. On the palmar side there was a slight induration corresponding in position to the swelling on the dorsum. There were no enlarged glands in the axilla.

As local applications had been very thoroughly tried, and as a second and more careful examination on October 3 made me inclined to regard the nature of the trouble as probably a subacute periostitis, I decided to make an incision. Under cocaine I cut down to the bone through the center of the swelling. On reaching the vicinity of the periosteum a small amount (few drops) of what appeared to be thin pus mixed with blood escaped, but no collection could be found. The tissues cut seemed abnormally hard and more of a grayish color than normal.

The wound was packed with iodoform gauze and a small wet antiseptic dressing applied, the hand being kept at rest on a long splint. When the packing was removed there was scarcely any discharge. The pain had not been relieved by the incision. The hand was dressed daily with wet carbolic compresses (1-60)

The following week as the pain and swelling were slowly increasing I thought it better to seek further advice and accordingly consulted Dr. William T. Bull.

He was inclined to regard the trouble as a periostitis, probably of tubercular nature, and advised waiting for further developments.

As the symptoms continued to increase in severity, I decided to make a more thorough exploration and on October 14 I gave her ether and enlarged the wound.

The metacarpal bone was bared a distance of three-fourths of an inch. The bone itself showed no evidence of disease, but the periosteum was thickened. No collection of pus could be found.

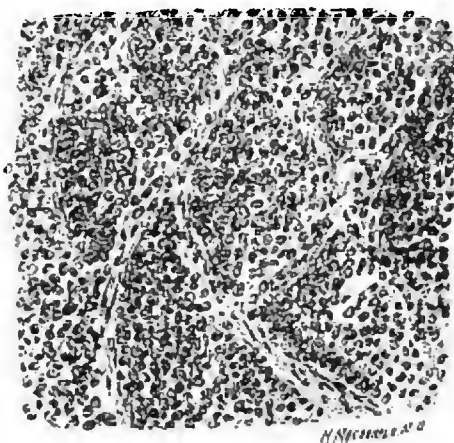


FIG. I.—MICROSCOPICAL APPEARANCE PRESENTED BY SARCOMA OF METACARPAL BONE (CASE I.)

The grayish granulations were scraped away and the wound was dressed with iodoform gauze. The pain was somewhat relieved for a day or two and then returned as severe as before. Although there was no suppuration the redness and swelling increased. The base of the swelling showed no line of demarcation but slowly extended in all directions, and movements of the fingers became more and more painful. The induration upon the palmar side, which at first was very slight, had now become well marked and over a small area, one-half an inch in diameter, the skin was reddened and showed signs of softening.

There was also a gradual loss of sensation in the ring and little

fingers. The pain soon became so severe that I was obliged to give morphine to secure relief. The increase of pain, the gradual impairment of motion, the increasing loss of sensation, together with the general appearance of the swelling and the absence of the usual signs, characteristics of an inflammatory trouble, led me to suspect the possibility of malignant disease, probably sarcoma.

I again had a consultation with Dr. Bull, and as the nature of the trouble was still very obscure it was thought best, at his suggestion, to seek additional advice, and accordingly Dr. Robert F. Weir was called in. The suspicion of malignant trouble was considered sufficient to warrant the removal of a small portion of the tissues for microscopical examination. Two days later the patient was given nitrous oxide gas and a small wedge-shaped piece removed from the edge of the old incision. This was very carefully examined by Dr. Walter B. James, Assistant Pathologist of the New York Hospital. As so much depended upon a thorough examination and an accurate diagnosis, several days were required before the result could be known.

On November 6, Dr. James reported the portion examined to be from an alveolar, round celled sarcoma. (Fig. 1).

On the following day after a consultation, with Drs. Bull, Weir and McBurney, it was decided that amputation at the middle of the forearm offered the best chance of saving the patient's life.

The next day, November 8, I amputated at the forearm at about the middle. No enlarged glands could be detected in the axilla. The patient suffered very little from the shock of the operation and the stump healed satisfactorily. The appetite remained very poor and she did not regain strength as rapidly as I had hoped.

There was no appreciable loss of flesh and no fever, but the pulse continued abnormally high (100-110), as it had been previous to the operation. Three weeks following the operation she had an attack of severe abdominal pain, localized in the epigastrium, and lasting two or three days. There was no indiscretion in diet that could account for it. There was a small area of resistance in the region mentioned, which was quite tender on pressure. After a few days the pain ceased, and the abdomen was apparently normal.

On December 11, four and a half weeks after the amputation, a small nodule was discovered in the upper portion of the right breast. It was about the size of a small almond and was very tender on pressure. It was quite painful, the pain being sharp and shooting, but not constant. The other breast, as well as both axillæ, were carefully examined and nothing found.

The following day the nodule had perceptibly increased in size, and two similar but smaller nodules had appeared on the left breast.

Dr. Bull again saw the patient and the nodules were considered undoubted evidence of a recurrence, but as it had been so rapid and at the same time general, we thought it best not to attempt removal of the tumors in the breast unless very rapid increase in size and the severity of the pain should demand it as a means of affording temporary relief. About the same time she began to have severe neuralgic pains in the left thigh. The strength began to fail and there was almost complete anorexia.

One week after the recurrence in the breasts the glands in the axillæ became enlarged and painful. The nodules in the breasts increased in size and became more numerous. The pain was so severe that the patient had to be kept under the influence of opiates. She was able to go out walking and driving until December 25, and then she became too weak.

At this time a slight induration appeared in the epigastrium. It was tender on pressure and the seat of a dull pain.

December 28. A small area of anæsthesia appeared on the lower lip and chin, and patient also complained of numbness in lower incisor teeth. This zone of anæsthesia slowly increased in size and remained until death.

January 1. Slight icterus was noticed in the conjunctivæ, and a little later in the skin. This rapidly increased and a week later marked jaundice was present and the urine contained a large amount of bile.

Small nodules about the size of a split pea now began to appear in the skin of the chest and abdomen, and the lymphatic glands just above the inner condyle of the right arm became enlarged and painful.

From this time the loss of flesh and strength was very rapid. She could take almost no nourishment, even liquids causing severe pain in the abdomen.

The induration in the abdomen increased in size and January 9, on deep palpation, a well-defined tumor could be felt occupying the whole of the epigastrium. It was firmly fixed and was lost at the edge of the ribs.

The liver was enlarged and its lower edge fell below the free border of the ribs.

The heart's action, which, up to this time, had been good, now began to fail, and became very weak and irregular. It responded well to digitalis, which was given in fairly large doses. Brandy was also

given for two or three days, but could be no longer borne by stomach.

The urine January 11 was high colored, very small in quantity, contained a large amount of bile pigment, and a trace of albumin. Microscopical examination showed hyaline, epithelial and granular casts, and renal cells. Examination of the chest showed slight dulness over upper portion of the right lung with expiratory murmur roughened. A little later crepitant râles appeared in subclavicular region in front. The heart sounds were all abnormally loud, and there was a soft systolic murmur at the base.

January 20. She began to vomit and this continued once or twice a day. The vomitus consisted of only mucus or liquids that had been taken into the stomach.

January 21. Vomiting increased in frequency and vomitus contained blood in quite large amounts. The attacks occurred almost hourly, and were very exhausting to the patient in her extremely weak condition.

January 22. The blood was no longer seen but the vomiting continued, and the matter ejected was a thin, dark liquid, evidently biliary in character.

She was conscious up to a few minutes previous to death, which occurred on Friday, January 23, at 7 A. M.

She had taken practically no food for two weeks. The bowels had not moved for twelve days, and no urine had been passed in forty-eight hours, and the bladder was empty.

At the time of death the tumors in the right breast had reached the size of a goose egg, and were made up of several hard nodular masses slightly attached to pectoral muscle and firmly adherent to the overlying skin. The glands in both axillæ were enlarged and hard. The left breast was almost as extensively involved as the right, but the mass was less protuberant and the skin less adherent. The whole epigastrium was occupied by a tumor (intra-abdominal) about the size of a child's head, hard, coarsely nodular and almost absolutely fixed. The lower boundary only could be made out by palpation, its upper being loose at the free border of the ribs. This was undoubtedly connected with the stomach, and the liver and omentum were also probably involved.

The skin over the entire body was infiltrated with small, shot-like bodies varying in size from a No. 4 shot to a split pea. These were far more numerous over the chest, abdomen and back than the extremities, and during the last few days of life they began to be pigmented. There was no autopsy.

The rapid course of the primary disease, the extensive general dissemination that followed so quickly the attempt at removal, show the intensely malignant character of this growth.

A disease that, starting from an insignificant injury, can attack a person in perfect health, in the full vigor of early maturity, and in some insidious, mysterious way, within a few months, destroy life, is surely a subject important enough to demand our best thought and continued study.

II. In the hope that some little light might be thrown upon this obscure subject, that some aid might be given toward making an earlier diagnosis and, consequently, a more hopeful prognosis, I have been led, not only to report this case in detail, but also to add a few remarks upon sarcoma in general, based upon a careful analysis of 90 unpublished cases. These cases embrace nearly all that have been treated at the New York Hospital during the last 15 years, and, in addition, a very valuable series of private cases which I owe to the courtesy of Dr. Weir and Dr. Bull.

Of these 90 cases, 68 had their origin in the soft parts, while the remaining 22 started in the bone or periosteum.

The subsequent history, which is so very important and at the same time so difficult to obtain, I succeeded in getting in 44.

Of these 26 were followed by fatal recurrence while 9 were living at the end of periods ranging from 3 to 10 years after last operation, and 4 others were alive, free from recurrence, 12 to 18 months after the operation.

Sex.—37 were female and 53 male.

Although I have gone over the literature of sarcoma very thoroughly, this is the only case of subperiosteal sarcoma of the metacarpal bone that I have been able to find reported.

Butlin, in his well-known work on "Operative Surgery of Malignant Disease," says, subperiosteal sarcomas may effect most of the bones of the body, but they are *very rare* in the short and irregular bones, and the only bones he mentions are the bones of the thigh, arm, forearm, clavicle, scapula and jaw.

Moulin, of London, in *Treatise on Surgery* that has just been published, says: "Periosteal sarcomas are more common in the femur than elsewhere, shaft or epiphysis, but there is no bone in the body that is exempt. They are *all* of them of the most intensely malignant character, so that if amputation is performed as soon as the diagnosis is made, the stump may remain healthy to the last, but secondary growths are almost sure to appear within the twelvemonth."

The classical paper of Dr. Samuel W. Gross, on "Sarcoma of the Long Bones," with an analysis of 165 cases, published in the *American Journal of Medical Sciences*, July, 1879, still remains the basis of our knowledge. Yet in the entire collection there is not a single case of sarcoma, either central or periosteal, of the metacarpal bones.

7	occurred in the femur.
46	" " tibia.
21	" " humerus.
13	" " fibula.
7	" " ulna.
6	" " radius.
1	" " ulna and radius.

Of these cases 13 only were periosteal, of which but 4 were of the alveolar type. Of these 13 cases

4	were found in the humerus.
2	" " femur.
1	was found in the ulna.
1	" " tibia.

Ten occurred in males and 3 in females.

The average age of the patients in Dr. Gross' collection was 22½ years, 5 years less than the average in central sarcoma.

The malignancy was much more marked, being 47% greater than in central sarcoma.

There seem to be little tendency to invade the joints or the bone itself, though in some instances the bone has been eroded, and the medullary cavity invaded.

While no single symptom or physical sign is pathognomonic, still there may be such a grouping of them as to form a clinical picture, highly suggestive of periosteal sarcoma.

The chief characteristic of subperiosteal sarcoma, derived

from a study of the cases of Gross and those collected by myself, may be summarized as follows:

1. *A history of traumatism.* This was found in 7 of the 13 cases of Gross, and in 3 of the 5 in my collection.

2. *Early pain.* This precedes the tumor in over one-half of the cases, and usually remains throughout the course of the disease.

Both pain and traumatism are much more frequently found in the round-celled type than in the spindle-celled.

3. *Form of the tumor.* Usually fusiform and seldom encapsulated, there being a strong tendency to early infiltrating the surrounding tissues.

4. Rapid increase in size, and discoloration of skin in later stages.

5. Slight elevation of temperature and pulse abnormally high.

6. Very little tendency to ulceration.

SUBSEQUENT HISTORY.

Gross was able to give the after history of 8 of the 13 cases.

Of these 2 died from the operation, 3 died of general dissemination at the end of 7, 8 and 9 months after operation; 1 lived 32 months after operation and then died of metastasis, while a fifth had local recurrence at the end of 3 weeks. Of the remaining two, one was lost sight of at the end of 4 months, so only one of the eight was known to have been free from recurrence.

Of my 5 cases of round-celled sarcoma (periosteal), one of the femur is alive and well at present, 3 years after the operation. A second of the femur is alive, 2 years after the operation. A third of the scapula died of pyæmia, following operation. A fourth, of the metacarpal bone (which I have just reported) had general recurrence in 4½ weeks, which proved fatal 6 weeks later, while the fifth I was unable to trace.

The spindle-celled type give a more favorable showing.

One of these, a periosteal sarcoma of the clavicle, is of such great interest, that it deserves more than a passing notice.

Butlin says the "disease appears to be very rare. Still more rare are the cases in which an attempt has been made to remove it." He reports two cases. Resection was performed in both. The patients were both young, and to this fact he ascribes the success of the operation. One was lost sight of and the other died shortly afterward from recurrence. Central sarcoma of the clavicle is almost as rare, as he was able to find but 3 cases reported. Resection was practiced in all of the cases. One patient was lost sight of; the second had a recurrence in 2 months. The third was the famous case of Dr. Valentine Mott, and the operation was performed in the year 1828. The clavicle was resected for a rapidly growing central tumor of 4 months' duration, in a patient, æt. 19. Although no microscopical examination was made, Butlin thinks there can be no reasonable doubt as to its sarcomatous nature. The patient died in 1883 at the age of 73.

The case in my collection was operated upon by Dr. Bull, in January, 1883, for sub-periosteal sarcoma of the clavicle. The patient was 33 years old, male, and both clavicles had been fractured in childhood. Six weeks previous to operation he began to have slight pain in the sternal end of left clavicle, followed two weeks later by a tumor. At the time of operation the tumor was one and a half inches in diameter, slightly nodular and firmly attached to the bone. The skin was not adherent and the tumor was not tender. There were no enlarged glands. The clavicle was sawn through at the middle point and the sternal half removed. The patient made a good recovery, and is alive now, 1891, 8 years after the operation. (He has been confined in an asylum for a number of years for an obscure brain trouble.) The growth was a subperiosteal spindle-celled sarcoma.

Scapula. I have collected 3 cases of sarcoma of the scapula with excision of the entire bone. In one (referred to above) death resulted from pyæmia. The second died of shock, while the third, a periosteal spindle-celled sarcoma the size of an egg, which was operated upon by Dr. Bull, 1883, was alive and free from recurrence in January, 1891, 9 years after the operation. The entire scapula and an enlarged axillary gland were removed.

Poinsot's¹ table, published in 1885, contains the largest number of complete removals of the scapula. Of the 45 cases, 25 were for tumors, the malignant nature of which was either certain or probable. The mortality from the operation was 10%. Although 6 of the cases were tabulated as "cures," the time of observation is not stated, and Butlin considers it doubtful if more than one case can be claimed as actually cured. This case was alive and well 6 years after the operation.

SARCOMA OF THE MUSCLES.

Butlin, in the work already referred to, says that he has been able to collect from all sources over 20 cases of tumors of the muscles (sarcoma), and in every case recurrence followed operation, so that he regards the prognosis as bad as it well can be.

In my collection I have 8 cases of tumors of sarcoma of the muscles, and of these 4 were found in the triceps, one in the gastrocnemius and the others in the adductor muscles of the thigh. In one case, the sarcoma of the belly of the gastrocnemius, the tumor was the size of a small orange, and was supposed to be an aneurism until the operation. The growth was removed over 2 years ago, and the patient is free from recurrence at the present time. As recurrence in Butlin's cases was nearly always within the first year there is a good chance of this case proving a cure.

Breast. Seven of the cases were sarcoma of the breast, of which 2 occurred in the male. There was a history of injury in 2 cases, and 2 are now living, 2¹/₂ and 2 years after operation.

Heredity. No clear evidence of heredity was found in any case.

In one case, a sarcoma of the neck in a woman, æt. 25, the growth recurred 4 times within 3 years, the last recurrence proving fatal. It is interesting to note that a child of this woman's died of sarcoma of the brain at the age of 3 years. Death occurred one year previous to death of mother.

¹Rev. de Chirurg., v. 5, 201.

TREATMENT OF SARCOMA.

While early operation gives a possibility of complete cure in a certain number of cases, the large proportion of cases in which fatal and often speedy recurrence follows operation, is sufficient to make the surgeon almost lose faith in his art in the treatment of this dread disease.

There are certain types of sarcoma that seem almost hopeless from the start, and when surgical skill, if called upon, only proves how utterly powerless it is. Is there nothing else that can be done to stay the progress of this disease? This is a question that has long occupied the attention of many of the best minds in the medical world, and at no time has it received as much thought as it does to-day.

Nature often gives us hints to her profoundest secrets, and it is possible that she has given us a hint which, if we will but follow, may lead us on to the solution of this difficult problem.

III. THE CURATIVE EFFECT OF ERYSIPELAS UPON MALIGNANT DISEASE.

That erysipelas has an influence upon malignant disease has long been recognized in a general way, but only recently has there been any scientific attempt to determine the nature and limits of that relation. The cases that could throw light upon this question until of late have been few and isolated, and, consequently, it has been impossible to draw absolute or far-reaching conclusions, but the evidence has been steadily accumulating.

Fehleisen's famous paper upon the etiology of erysipelas was published in 1883. His experiments upon dogs, and later upon a few cases in man, showed that it was possible to produce erysipelas by inoculating with pure cultures of the streptococcus erysipelatis. Fehleisen inoculated 7 patients with inoperable malignant disease, and of these 6 reacted. The seventh had suffered from erysipelas a short time before, and did not react. One was inoculated 3 times at intervals of two weeks, but reacted only after the first inoculation.

One case was a fibro-sarcoma of the cheek, with enlarged glands.

The superficial nodules disappeared and the enlarged glands diminished one-half.

The remaining cases were of carcinoma. One was a cancer of the breast which had recurred twice within two years. The patient was inoculated with erysipelas, and within one week the tumor had disappeared. There had been no recurrence at the date of publication of the article, six months later.

A third case was a cancer of the breast, the size of two fists and ulcerated. The axillary glands were enlarged. The enlarged glands disappeared and the main tumor was reduced in size one-half.

The remaining three cases showed but little change.

Bruns, in the *Beitrag f. klinische Chirurgie*, 1888, p. 443, has written an exhaustive article upon the subject, and his paper contains a detailed account of most of the cases up to that date. He discusses the effect of erysipelas, not only upon sarcoma and carcinoma, but also upon lupus, keloid and specific lesions. What chiefly concerns us are the cases of malignant disease. He has collected 14 cases of undoubted malignant disease, in which erysipelas occurred, either accidentally in the course of the disease, or was produced by inoculation. Of these 5 were sarcoma (diagnosis confirmed by the microscope) 3 were epithelioma, while 6 cases were either carcinoma or sarcoma.

Of the 5 cases of sarcoma 3 cases were *fully and permanently* cured.

The *first* was the case of (Busch) a multiple sarcoma of the head.

Second (Bruns) a *melanotic sarcoma* of the breast.

Of the two remaining cases (lympho-sarcoma of the neck) one was temporarily reduced in size, and the other had decreased one-half when the patient died in collapse.

To these 5 cases collected by Bruns I have been able to add 9 others (three recently inoculated by myself).

CASE I.—(Bull²). "*Round celled sarcoma of the neck, with 5*

²Unpublished.

recurrences within 3 years. Erysipelas, Recovery. The last operation was performed by Dr. W. T. Bull, Sept., 1884. The growth was found to be too extensive for complete removal. A large open wound, 5 inches long by 2 wide, remained and was soon filled by flabby sarcomatous granulations. Two weeks after the operation the patient had a severe attack of facial erysipelas, and shortly after the first a second attack. The granulations quickly disappeared, the wound rapidly cicatrized and the patient has been well and free from recurrences up to the present time, June, 1891. He was seen both by Dr. Bull and myself 7 years after the attack of erysipelas.

CASE 2.—(Winslow³). A middle-aged sailor with sarcoma of the neck, while being treated with injections of chloride of zinc developed erysipelas. The tumor *entirely* disappeared. One year later a sarcomatous growth appeared in the left breast.

CASE 3.—(Stein⁴). A woman, æt. 48, had a painful tumor of the breast. It was irregular, nodular, fixed to the chest wall, fluctuating in parts and not accompanied by enlarged glands. Clinical diagnosis, sarcoma. A severe attack of erysipelas accidentally followed a hypodermic puncture in the *dorsal* region. The attack lasted 12 days and at the end of that time the tumor in the breast had disappeared. No recurrence.

CASE 4.—(Kleeblatt⁵). Primary lympho-sarcoma of tonsil. Removal (by Czerny) was followed, a few months later, by recurrence in the neck. An accidental attack of erysipelas caused some improvement. Three months later an inoculation with Fehleisen's erysipelas cocci was made. At the end of 2 days a marked outbreak occurred. *Decided* temporary improvement followed, but death occurred 3 months later.

CASE 5.—(Kleeblatt). Lympho-sarcoma of the neck. Inoculation, pure culture. Erysipelas occurred 2 days later, followed by entire disappearance of the growth. No recurrence followed.

³London Medical Recorder, 1884, ii.

⁴Vratch, 1882, No. 16. London Medical Recorder, 1883.

⁵Munchener Med. Woch., No. 7, 1890.

CASE 6.—(Fehleisen). Fibro-sarcoma of the face, with enlarged glands. Erysipelas was produced by inoculation. Marked temporary improvement followed and the tumor was reduced in size one-half.

CASE 7.—(Coley). Sarcoma of the neck (spindle-celled). Male, æt. 40, born in Italy. He was operated upon by Prof. Durante, of Rome, 3 years before. Recurrence took place 2 years later, and in April, 1891, a second operation was performed by Dr. Bull. The growth was too extensive for removal and early in May he consented to inoculation. At the time of inoculation the wound in the neck had not entirely healed, and the cicatrix as well as the tissues along the upper portion of right sterno-mastoid muscle were markedly indurated. There was marked dullness at the apex of right lung and the patient was troubled with a continual hacking cough. There was a tumor in the right tonsil, the size of a small hen's egg, and almost blocking up the pharynx. He could swallow only liquids and these with great difficulty and they often regurgitated through the nose.

In the presence of Dr. Attinelli and Dr. B. M. Bolton I inoculated him, May 3, with two different cultures, which had been kindly furnished me, one by Dr. Harold Ernst, of the Harvard Laboratory, and the other by Dr. Bolton, of the Hoagland Laboratory of Brooklyn. One was a gelatin culture which I used by scarifying and rubbing in the virus, and the other, a beef tea culture which I introduced by means of a hypodermic needle. I watched the patient very carefully, seeing him 2 or 3 times a day for several days following the operation.

Twenty-three hours⁶ after the inoculation he had chilly sensations, nausea, but no vomiting, headache and general malaise. The temperature rose to $100\frac{1}{2}^{\circ}$ and pulse to 100. There was slight local redness. These local and constitutional signs gradually disappeared, and at the end of 3 days his condition was normal. I repeated the inoculation at intervals of 3 or 4 days, but got no very decided reaction until the fifth inoculation. I then used a larger amount of a fresh culture in

⁶In the German cases the reaction occurred at periods ranging from 16 to 61 hours, following inoculation.

beef tea prepared by Dr. Prudden and Dr. Cheeseman, of the College of Physicians and Surgeons, from material just obtained from Europe. The reaction was very well marked and appeared within 8 hours after the inoculation. He had a severe chill, intense pain in the head and vomited several times. The temperature rose to $101\frac{1}{2}^{\circ}$ and pulse to 101. The larger portion of the fluid had been injected into the unhealed portion of the wound, but a few minims had been injected in several places in the normal skin and adjacent to the old cicatrix. There was intense local redness about each puncture, extending through a radius of one-half an inch.

The symptoms remained two or three days and then, together with the redness, slowly disappeared.

Five days later I did a sixth inoculation, using about the same amount of virus.

The reaction was again well marked, and the same signs and symptoms appeared and ran the same course.

June 2. One month following the first inoculation the tumor in the right tonsil had appreciably diminished in size. (It was growing very rapidly at the time of inoculation). His cough had entirely disappeared and he swallowed food with very much less difficulty, and there was no longer any regurgitation. His general condition was excellent. From June 2 to June 24 the treatment was continued by Dr. E. T. Doubleday. Only one injection was made. His condition was then about the same.

CASE VIII.—(Coley). *Round-celled sarcoma of the lower end of the femur (periosteal); Inoculation with erysipelas (pure culture); Marked temporary improvement.* M. B., æt. 16, female. Six months ago, without apparent cause, the knee began to swell and became slightly painful. The swelling gradually increased and motion became somewhat limited.

She was examined at several dispensaries and the nature of the disease was thought to be tubercular. She was sent to the New York Hospital for excision of the knee.

An exploratory incision was made by Dr. Weir and a portion of tissue was removed and examined by the pathologist. It was found to be a round-celled sarcoma. The whole lower end of the femur was enlarged, but the enlargement was con-

ined chiefly to the outer condyle. It had apparently started in the periosteum, but had invaded the medullary cavity. It was too extensive for removal, and as the patient's general condition was bad (temperature 99° - 102° , pulse 120), it was thought doubtful if she could stand the shock of an amputation.

The middle of May, two weeks after the operation, she was taken to her home and put under my care in order to have the erysipelas inoculation tried.

At the first inoculation I used a small quantity of virus. I tried three different methods, scarification, injection and putting a little of the fluid culture upon the granulating surface.

A slight reaction followed, beginning eighteen hours after the inoculation. The temperature rose to 103° and pulse to 120, but there was no distinct chill. There was slight nausea, but no vomiting.

Three days later the reaction had entirely subsided, and I did a second inoculation. I injected the fluid culture into the tumor substance. I used a larger amount. Severe reaction followed. Nausea and vomiting with a severe chill began about fourteen hours after the injection. The temperature rose to 104.5° and the pulse to 140. The reaction took somewhat longer to subside than the previous one, but in four or five days it had entirely disappeared. The sloughing granulations where I had first put the virus had begun to rapidly clear off leaving a bright granulating surface.

The third inoculation I did June 1 into the tumor substance. This time I used π xx of beef tea culture, about the same quantity that I had used at the last inoculation. The reaction, instead of being less severe, was very much more marked. Within one-half hour after the inoculation she had a severe chill and violent vomiting, and the pulse became very rapid and weak. She was given brandy and water. Her temperature rose to nearly 105° . The reaction subsided in the same way as it had done before. The granulations continued to clear up and become more healthy, and her general condition remained about the same.

At the time the inoculations were begun the lower end of the right femur was about the size of a child's head. The old incision, six inches long, was widely gaping and a long sarco-



FIG. II.—DR. COLEY'S CASE OF SARCOMA OF LOWER END OF FEMUR.
PORTION SHOWING GRANULATING SURFACES PRODUCED BY
THE Erysipelas Culture.

matous mass the size of two fists projected from the wound. There was a sinus large enough to admit the finger extending into the interior of the bone. There were no enlarged glands in groin. (Fig. 2).

During the first three weeks of June the treatment was continued (in my absence) by Dr. Samuel J. Milliken. Two more inoculations were made with smaller amounts. A good reaction followed in each case. The improvement in the lower portion of the tumor was marked, but her condition was so weak that she could stand only a small amount of the virus, and as the tumor was apparently increasing in size in the central and deeper portion, I decided to suspend further inoculations.

In both cases the antagonistic effect was well marked, and improvement, even if temporary, was sufficient to make me believe that, had the cases been less far advanced when the treatment was begun, it would not have been too much to have looked for a permanent cure. The fact that in one of the reported cases when two attacks of erysipelas had accidentally occurred, the first diminishing the size of the tumor, and the second causing it to disappear, led me to try *repeated* inoculations. I think that the *danger* which is by some urged against inoculation, can almost entirely be eliminated by beginning with small doses and repeating them. The amount to be used, of course, depends upon the condition and strength of the patient. What produced but a moderate amount of reaction in one case would doubtless have caused a fatal result in the other.

Just how this influence is exerted is at present undetermined. The theories that have the greatest support are (1), that the erysipelas coccus has a *direct destructive* action upon the cell elements of the new growth; (2), that the *high temperature* alone is sufficient to destroy the cells of lower vitality causing a fatty degeneration followed by subsequent re-absorption; (3), that sarcoma and carcinoma are both of bacterial origin and the erysipelas germ has a direct antagonistic effect upon the cancer bacillus.

Bruns does not think that any one of these theories is sufficient to account for the phenomena in the different cases, and

it seems in the light of the present knowledge not improbable that all of the three theories may contain an element of truth, and that a larger theory combining all these elements is necessary to explain the curative action of erysipelas.

That high temperature alone is a factor, and by no means an insignificant factor, numerous observations are cited where tumors both malignant and benign have shown marked diminution in size during an attack of the various infectious diseases, *e. g.*, scarlet fever, typhus, cholera, etc., and the same is true of pyæmia. It is possible to attribute the result even here to antagonistic bacterial action, and in every one of these examples the high temperature is due to bacterial infection, it seems to me much more rational to suppose that the curative effect on the new growth is dependent upon the same infection than upon what apparently is only a coincident, but unimportant result of the same cause.

In the cases which I have collected, there is one which bears upon this question. The patient, a male, *æt.* 35, was operated upon by Dr. W. T. Bull, in 1888, for large periosteal, round-celled sarcoma of the lower third of the femur, with secondary deposits in the center of the bone. Amputation of the thigh at middle and upper thirds was performed.

The second week after operation the patient had a very severe attack of pyæmia (possibly phlegmonous erysipelas) with multiple abscesses in various parts of the body. The temperature ranged from 104°-105°.

The patient has had no recurrence and is now living, nearly three years after the operation. Of course this is not to be regarded as absolute evidence that the attack of pyæmia had any influence in preventing a recurrence, but when we consider the highly malignant nature of the tumor and remember how few do not recur, there still remains a reasonable degree of probability that such influence existed.

APPENDIX, AUGUST 7, 1891.

While the above was in the hands of the publishers, the inoculations were kept up at short intervals in my cases of sarcoma of the neck and tonsils. The result has been very

marked, with continued improvement. The tonsil tumor is much smaller, and the nodules in the neck have nearly disappeared. His voice has very much improved, and his general condition is decidedly better. He has now had sixteen inoculations; reaction still takes place, though less marked than at first.

I will add a few brief notes of a third case which I have inoculated during the past two weeks:

The patient, a woman (young adult), received a slight injury to the back one and a half years ago. A short time afterward she began to have pains in the breast. Later, a small swelling appeared over the spine in the upper dorsal region; this grew slowly, and was slightly painful. The tumor was removed by Dr. Bull the latter part of April, 1891. It was so closely attached to the spinous process of two of the upper dorsal vertebræ, that the processes were removed at the operation. Examination showed the growth to be a round-celled sarcoma. Recurrence followed one month later, and in June a second operation was performed.

A second recurrence quickly followed, and the last of July I began inoculations with a pure culture of erysipelas, prepared by Dr. B. M. Bolton. The first two injections were subcutaneous, and only a small amount (m_{xv}) was used. There were no constitutional signs, and only very slight redness of the skin. The third inoculation I used m_{xlv}, and injected deep into the tumor-substance in two places. In two hours she had a severe chill, and the temperature rose to 103°. She also had several attacks of vomiting, with headache and general malaise.

At the end of two days her condition was normal. There was scarcely any local redness at any time. The tumor was much more movable and perceptibly smaller. The following week two more injections were given, but the reaction was slight, and there was no apparent effect on the tumor. The last injection (m_l) caused a slight chill, and temperature of 101°. The tumor was evidently again increasing in size; inoculation was discontinued, and a third operation performed two days after last inoculation. The tumor is now undergoing a careful microscopic examination by Dr. Bolton.

These last two are the only cases of periosteal origin in which erysipelas has been tried, and apparently this variety is less susceptible to its influence.

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