

about two years, and had had no children and no miscarriages.

About eight years ago the patient noticed for the first time and quite by accident a swelling in the left iliac region. It was about the size of a hen's egg when she first felt it. For a month or two it increased in size slightly, then ceased growing and remained stationary until she became pregnant at the end of February. On February 19th she menstruated for the last time. Three or four weeks after she began to be troubled with morning sickness, and about the middle of June she felt foetal movements for the first time. She was quite satisfied that she was pregnant; but what troubled her was the fact that her abdomen became so rapidly distended. It was, however, during the six or seven weeks previous to her admission into hospital that the distension seemed to increase most rapidly.

Her general condition on admission was not very satisfactory. There was great oedema of the legs and thighs but apparently no ascites. There was some dyspnoea. The mucous membranes were of a good colour. She had no difficulty in passing urine but her bowels had been very constipated. There was nothing abnormal in the lungs and heart; milk could be expressed from both breasts. The abdomen was much distended, presenting the appearance of a pregnancy at full time. It measured 37 inches at the level of the umbilicus. On palpating the abdominal tumours, a large smooth, round, hard swelling was found to occupy the left side. It crossed the middle line, and was continuous with a swelling on the right side, from which it was separated, however, by a sulcus. This swelling on the right side was elastic in consistence, but two or three hard rounded nodules could be distinctly made out upon its anterior surface. The uterine *souffle* could be heard over it, but no foetal heart sounds could be recognised.

On vaginal examination, the whole cavity of the pelvis was filled up with a hard mass firmly impacted into it, and continuous with the tumour above. So completely did this tumour block up the pelvic cavity that the forefinger could with difficulty be passed up the vagina. The uterus appeared to be very much drawn up, as the examining finger could not reach the os externum.

On July 19th, the patient was examined under chloroform, but nothing further was made out.

On July 22nd abdominal section was performed. On opening into the abdomen a large irregular tumour was met with, the left portion consisting of an interstitial myoma, the right of the distended uterus. In addition, implanted on the upper and posterior uterine walls, were several subserous myomata, varying in size from a walnut to an orange. Having made an incision through the anterior wall, a foetus of 5 months was removed. It was perfectly formed, and had evidently only quite recently died. The placenta was well developed, and was easily detached. An elastic ligature was passed round the uterus and tumours as close as possible to the cervix and secured, after which the uterus with the tumours were cut away. The uterine and ovarian arteries could now be more easily reached and were ligatured. The ovaries and tubes were also removed. The tumour blocking up the pelvis was with some difficulty drawn up on account of impaction and adhesions. Having enucleated this mass of tumour nothing remained but the cervix, which was also separated from its connections. The peritoneum was stitched round and round with catgut ligatures to the mucous membrane of the vagina. These ligatures were then drawn down into the vaginal canal by means of a pair of long forceps passed up into the abdomen through the vagina. The abdominal wound was then closed with silkworm sutures; no drainage tube was used. The parts removed weighed 27 lbs.

The patient made a good recovery. She had a little sickness on the third and fourth day, when the temperature thrice registered 100.2° F. After that it never rose above 100°, and fell to normal after the ligatures were discharged from the vagina on the tenth to the twelfth days. She left the hospital in the seventh week after the operation perfectly well.

A POST GRADUATE School of Medicine has recently been founded in Washington, where it is said to be much needed, as there is no school of the kind south of New York and Philadelphia.

THE TREATMENT OF MALIGNANT TUMOURS BY THE TOXINS OF THE STREPTOCOCCUS ERYSIPELATIS AND BACILLUS PRODIGIOSUS.

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THE treatment of inoperable malignant disease has hitherto proved so hopeless that it is not to be wondered at that we have been slow to believe that any remedy can do good in such cases, and that therefore the method indicated by the title of this paper has scarcely received the attention it deserves, although in proportion to the hopelessness of the case we should be glad to welcome any gleam of hope.

Malignant tumours have been known to disappear occasionally after the patient affected had suffered from an intercurrent attack of erysipelas, and when Fehleisen¹ made the important discovery that he was able to produce a factitious erysipelas by inoculating pure cultures of the streptococcus erysipelatis, he applied this knowledge to the treatment of malignant disease. Although only 1 of the 6 cases which he inoculated was reported as being well six months after inoculation, other inquirers were stimulated to work in the same direction, and Bruns,² Kleebblatt,³ Coley,⁴ and others have published cases in which an accidental or factitious erysipelas has exerted a beneficial or curative effect in cases of malignant disease. Sarcoma has generally been more amenable than carcinoma, and Bruns, in his record of 14 cases of malignant disease associated with erysipelas, found that of 5 cases of sarcoma in which the diagnosis was confirmed microscopically 3 were permanently cured.

Coley⁵ has collected 38 cases (including his own) of malignant disease, in which erysipelas occurred either accidentally or intentionally. "Of these 38 cases the erysipelas occurred accidentally in 23 cases, and was the result of inoculation in 15 cases." Seventeen cases were carcinomatous, of which 3 (17.6 per cent.) were cured, and 1 (5.9 per cent) died; 17 were sarcomatous, of which 7 (41 per cent.) were cured, and 1 (5.9 per cent.) died; 4 were either carcinomatous or sarcomatous, of which 2 were cured. "Grouping by themselves then the cases where the erysipelas was artificially produced, we find 7 cases of carcinoma, 1 cure or 14.3 per cent., and 8 cases of sarcoma, 2 cures, 25 per cent." From these figures it appears that a factitious erysipelas has not been attended with such good results as regards disappearance of the tumours as an accidental erysipelas.

The reaction following inoculations (for Coley repeated them in the same patient) usually subsided in 36 to 48 hours, unless a definite attack of erysipelas was produced; but as the effect on the patient and the tumour was much the same in either case, Coley argued that the effects must be due to the toxic products of the streptococci rather than to the active development of the organisms themselves, and he therefore determined to experiment with filtered cultures, "the germs having been removed by means of a Kitasato filter, without subjecting the filtrate to heat."

Roger's⁶ researches pointed in the same direction, but he further found in experiments upon rabbits that the bacillus prodigiosus has the power of intensifying the action of the streptococcus erysipelatis, and therefore the toxins of the two germs were mixed—the filtrate in each case being obtained by means of a Kitasato filter as already explained. The advantage of using these filtrates, if successful, lay in the fact that the danger of an attack of erysipelas would be removed, and that isolation of the patient would not be necessary.

This was a great advance, and Coley⁷ confirmed the fact that the mixed toxins had a more beneficial effect than when used singly, and also found that in a certain proportion of cases (*vide infra*) the tumours disappeared. He subsequently thought that the filtration method failed to utilise anything of value in the bodies of the organisms themselves, and he therefore prepared the toxins "by subjecting the cultures to the lowest temperature (58° C) that would suffice to destroy the germs." In this way Coley⁸ has treated 13 sarcomata, with 3 cures, and 11 carcinomata with improvement only; or,

counting all cases of sarcomata in which the mixed toxins have been used, we find 38 cases with 9 cures.

The toxins prepared in the way last stated represent the present method of dealing with these cases. I am aware that Coley⁹ has treated several cases with blood serum obtained from animals inoculated with the two organisms under discussion, but I am informed by my friend Dr. Parker (Clifton) that Dr. Coley has told him that the results are unsatisfactory.

The following is a brief record of a case which I treated unsuccessfully in this way, the toxins being obtained from America, where they had been prepared according to Coley's directions.

G. K., aged 48, had the right upper jaw removed on April 10th, 1894, for malignant disease. Microscopical examination of the growth showed it to be round-celled sarcoma. On December 3rd, 1894 he again came under my care with a recurrence, and the remainder of the malar bone and part of the zygoma were removed.

On June 2nd, 1895, he was admitted to the Bristol Royal Infirmary for the third time. There was then a large recurrent sarcomatous growth occupying the whole of the right cheek, and extending into the orbit and towards the base of the skull. There were enlarged lymphatic glands in front of the right ear, in the right submaxillary region, and at the angle of the jaw. There was also a secondary subperiosteal deposit in the frontal region immediately above the root of the nose.

On June 3rd, injections with the toxins were commenced and continued until July 9th. In all the patient had twenty-eight injections, which at first were given daily. The quantity of injection used was gradually increased from πj up to $\pi xviii$, according to the effect produced. The first eleven injections were given either under the healthy skin, or into the affected cheek or glands. πij into the cheek was the smallest dose which produced a rise in temperature, but as no temperature reaction followed the injection of πvij under the healthy skin, all the later injections were given either into the affected cheek or lymphatic glands. The maximum temperature recorded was 103.8° F. Rigors frequently followed the injections. The details are as follows:

June 4th. πj injected into affected cheek. One hour afterwards complained of feeling cold but there was no rise of temperature.

June 8th. πij injected into gland in front of ear, followed by rigor, and temperature rose to 100°. Complained of severe burning pain in throat, and was very restless.

June 10th. πiv injected into gland in front of ear, followed by rigor and temperature of 101.8°. Centre of affected cheek had become softer and more prominent, and on the following day the skin "broke," and pus was discharged.

June 12th. πv injected into cheek. There was a slight rigor but no rise of temperature occurred. Complained that it "made him feel ill." The gland in front of the ear was found to be fluctuating.

June 15th. πvj injected into cheek. Two hours afterwards had headache (which was an usual result), followed by muscular pains in limbs. Vomited twice.

June 20th. πxj injected into cheek. No rigor had occurred since June 12th. The discharge from the cheek still continuing. Several other parts of the growth where injections had been given were softening, and some appeared less in size. Patient had lost 2 lbs. in weight since admission.

June 27th. πxiv injected into gland at angle of jaw. Temperature rose to 101.8°.

June 28th. πxv injected into gland in front of ear, followed by rigor and temperature of 103°. Patient had lost another 1½ lb. in weight. Feels weak and ill. Gland at angle of jaw rather larger, but softer. Gland in front of ear and secondary deposit on forehead both smaller and softer.

June 30th. Gland at angle of jaw breaking down rapidly.

July 1st. Portion of growth near right side of nose into which the last two injections had been given getting softer. πxvj injected into gland at angle of jaw, followed by rigor and temperature of 100.2°.

July 2nd. $\pi xvij$ into gland at angle of jaw, followed by rigor and temperature of 103.8°. Although the parts into which the toxins have been injected appear to rapidly soften, the general infiltration of the growth is over a more extensive area.

July 5th. $\pi xvij$ injected into portion of cheek adjacent to the upper lip. Rigor and temperature of 101.4°.

July 6th. The soft area at the angle of the jaw almost "bursting."

July 7th. The portion of growth injected on 5th has now "broken down." Patient has lost another ¾ lbs. in weight.

July 9th. The area injected on 5th has now "burst," and is discharging pus freely. The patient, who was much weaker and very depressed, decided to have no more injections.

The patient ultimately died at the end of September, 1895.

This case was doubtless an unfavourable one for injection with the toxins, but the rapid necrobiosis which occurred in the neighbourhood of the injections gave some hope for the future. Moreover, it is desirable that unsuccessful cases should be reported, so that we may form a proper estimate of

the value of this method of treatment. McBurney¹ has also recorded three unsuccessful cases.

It is, perhaps, interesting to speculate how the toxins act in these cases. Although tumours have been known to disappear in the course of infectious fevers other than erysipelas, I cannot think that temperature alone is the cause of the rapid destruction of the sarcomatous tissue, for in the case above-recorded the temperature was at no time very high and never continued much more than twenty-four hours after injection. From the marked difference in action between the injections placed under the healthy skin and those into the growth itself it appears as if the toxins exerted some direct influence on the sarcomatous tissue, but whether of a specific or non-specific character it is difficult to determine.

Can it be that the lowly-vitalised cells of a malignant growth are more easily destroyed than the stable and resistant cells of normal tissue, by such baneful influences as toxins and febrile conditions acting in a non-specific manner? Whether this is so or not, I am unable to admit that there is necessarily any specific action of the toxins, or that the results support the theory of a bacterial origin of sarcoma and carcinoma upon which the streptococcus erysipelatis has a directly antagonistic effect. Bruns seems unable to account satisfactorily for their action.

That all cases should be equally affected by the toxins is not to be expected. According to Coley, the osteo-sarcomata are least benefited, and from the fact that in the case reported above the effect was greater and more rapid when the injections took place into the growth itself, it seems that the more superficial forms of sarcoma would be more hopeful than those in which the growth has extended very deeply.

It is scarcely necessary to point out that this method of treatment should not be thought of except in cases that are unfit for operative interference. My chief object is to draw attention to a therapeutic measure which may have some good in it, and in such deplorably hopeless cases as inoperable malignant disease we may surely give it a fair trial; but in order that we may not arrive at false conclusions it is necessary that the diagnosis should in all cases be supported by microscopical examination.

REFERENCES.

- ¹ *Die Etiolog. des Erysipel.*, Berlin, 1883. ² *Beitr. f. klinisch. Chirurg.*, 1888. ³ Quoted by Coley, *v. infra*. ⁴ *Annals of Surg.*, September, 1891. ⁵ *Amer. Journ. Med. Sci.*, vol. cv., 1893, p. 487. ⁶ *Rev. de Méd.*, December, 1892. ⁷ *Amer. Journ. Med. Sci.*, vol. cviii., 1894, p. 50. ⁸ *Med. Rec.*, New York, January 19th, 1895, p. 65. ⁹ *Ibid.*, May 18th, 1895. ¹⁰ *Ibid.*, January 19th, 1895, p. 871.

A CASE OF CELLULITIS TREATED WITH MARMOREK'S ANTISTREPTOCOCCIC SERUM.

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ON July 2nd I was asked to see J. P. B., aged 15 years, an engineering student, previously healthy except for an attack of acute rheumatism two years ago. He had a suppurating boil below the right angle of his mouth, which had been coming some days, and was making him feel ill. The temperature was 103° F. The boil was incised and some thick creamy pus let out. The patient felt faint. No enlarged glands were to be felt. During the next few days the swelling gradually spread over the right side of his face, becoming red and brawny, and being surrounded by an advancing zone of oedema; points of slough also appeared on the mucous membrane of the lower lip. The swelling was attended with very little pain, but the patient rapidly became weaker and was restless at night. The ordinary treatment of cellulitis, including incisions, was carried out, but apparently without benefit; the tissues, when incised, cut like potato, and bled slightly.

On July 6th nearly all his joints were painful and tender, but not enlarged nor red. He complained also of pain in the left side of his chest, and a pleuritic rub was heard in the axillary line. The surface of the brawny swelling was mottled in colour, and there was no fluctuation; the right half of his upper lip and the adjoining part of the cheek were 1 inch in thickness; there was tenderness over the region of the liver; there was no albuminuria.