THE CLINICAL SYMPTOMS AND TREATMENT OF CHRONIC SUBCUTANEOUS FIBROSIS.

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WITH the exception of a short article bearing the title "De la Panniculite," by A. Kjellberg,¹ of Stockholm, which appeared in the *Journal des praticiens* for 1900, and in which reference is made to a previous description by Professor Salin, also of Stockholm, I have been unable to find any systematic account of this condition. Cases illustrating one clinical aspect of it have often been reported as "symmetrical diffuse lipoma," "symmetrical fatty tumours," or "diffuse fibro-fatty tumours"; and Dercum,² in 1892, in an article entitled, "Three cases of a hitherto unclassified affection resembling in its grosser aspects obesity, but associated with special nervous symptoms—Adiposis dolorosa," described a fatty condition, more generalized than these, which he regarded as a special and previously unnoticed disease. The cases on which he based his description all occurred in women past middle life, who had gradually developed masses of fat in the subcutaneous areolar tissue, these masses being irregular in their position and distribution, and very painful on pressure. Spontaneous pain of a constant dull aching character, or sharp and stabbing, was present in some of the swellings. Occasionally very severe paroxysms of pain occurred, and these were coincident with temporary swelling and hardening of the fat masses. The fat was not evenly deposited, but felt lumpy, lobulated, or like bundles of worms. Certain nervous symptoms were also described as characteristic, these being chiefly diminution of cutaneous sensibility in patches, motor weakness, a tendency to herpetic eruptions, and anidrosis. He distinguished the condition from ordinary obesity in that (1) the fat occurs in masses and is first deposited at one part, other parts being involved gradually; (2) the fatty masses are extremely painful on pressure, and (3) well-marked nervous symptoms are present. On these last he lays great stress. Subsequently Dercum³ published an account of the *post-mortem* examination of his first case. She weighed 300 lb., and there was an excessive deposit of fat in the subcutaneous tissue of the arms, shoulders, and back, rather less in the abdomen and thighs. The fat is described as normal, but containing numerous independent encapsuled lipomata. The peripheral nerves lying in it showed interstitial neuritis with proliferation of the connective tissue and diminution in the number of nerve fibres.

Burr,⁴ in another case, describes the fat as peculiarly fibrous and firm, with its peripheral nerves in a condition of interstitial neuritis, while Price⁵ gives a practically

similar description of the morbid anatomy, and expresses the opinion that the condition is due to changes in the pituitary body.

Dercum, on the other hand, had attributed its causation to an alteration in the function of the thyroid, and seemed to regard it as allied to myxoedema. A description of "adiposis dolorosa" (Dercum's disease) is now included in most of the recent textbooks, where it is variously classified under nervous diseases, constitutional diseases, obesity, and so forth. I am very doubtful, however, if it can be rightly ranked as a special disease. The condition was well known to me clinically for some years before I became acquainted with Dercum's original description of it, and I had come to conclusions different from his regarding its nature and etiology and the significance of the symptoms. These conclusions, stated shortly, are that the morbid condition is a very common one, and consists essentially in chronic subcutaneous fibrosis; and that the cases which Dercum has described under the name "adiposis dolorosa" are merely those occurring in people with a large amount of subcutaneous fat.

The excessive development of the subcutaneous fat is not an essential part of the morbid process, but only an accidental addition to it. The essential morbid condition is, as before said, a very common one, and occurs quite independently of bodily thinness or stoutness. It consists in an irregularly spread, patchy, chronic inflammation of the subcutaneous connective tissue, which involves also the small peripheral nerves and blood vessels.

Owing to the involvement of the nerves, the fibrous tissue at the affected parts is painful on pressure, and is subject to aching or pain from many kinds of influences, such as exercise, weather changes, indigestion, and others less obvious.

The condition is in fact one of so-called "chronic rheumatism," but which might be better designated as "chronic subcutaneous fibrosis." The former is a clinical, the latter a pathological, term, and neither indicates a disease, but rather a condition secondary to several antecedent diseases.

In two former papers⁶ I have described at length the pathology and symptoms of "chronic rheumatism," and I need only repeat here that, like the other fibrous tissues of the body, the subcutaneous connective tissue is very often the seat of chronic inflammatory changes as the result of acute rheumatism and influenza especially, but also after general gonococcal infection, mucous colitis, and other imperfectly recognized causes.

On microscopic examination of such a patch, the fibrous tissue is found to be thicker and denser than normal with numerous fibroblasts, the small nerve twigs running through it are in a condition of interstitial inflammation, and the small blood vessels show periarteritis and endoarteritis, the whole being evidently the result of a reaction to local irritation by microbic toxins. It is extremely common at all ages and in both sexes, and is quite independent of obesity.

Fig. 1.

Fig. 2.

The implication of the nerves gives rise to symptoms usually designated as "rheumatic"—aching, pain, stiffness, neuralgias, numbness, tingling, a feeling of chilliness, fatigue after exertion, muscular lassitude, and often a marked want of vigour and energy. These last symptoms are sometimes so prominent that the condition is very frequently, but erroneously, diagnosed as "neurasthenia." The thickenings can be readily felt and are usually very tender on pressure. When much subcutaneous fat is already present, or is afterwards deposited in persons suffering from subcutaneous fibrosis, the symptoms just mentioned tend to be of an aggravated character. Further, the hypertrophy of the connective tissue leads to certain peculiarities in the arrangement of the subcutaneous fat.

Normally fat is deposited evenly throughout the areolar tissue; it is not nodular or lumpy, and is not specially tender on pressure; but in persons with subcutaneous fibrosis it tends to form in more or less lumpy masses round the hypertrophied connective tissue, and to lie in rolls if very abundant (Fig. 1). In merely plump people the masses are pealike and very tender on pressure or pinching, while in the very stout they form veritable tumours of varying sizes (Fig. 2). These may be lobular and lumpy, or more diffuse and fibro-fatty in character.

Many stout patients have normal fat in some places and lobulated in others. The latter arrangement seems

interstitial inflammation; the fat cells are normal in appearance. Figs. 3 and 4 show such patches of inflamed fibrous tissue embedded in fat cells.

In some cases the fibrous tissue is much denser than in others. The condition is analogous to fibrosis of the lung, liver, kidney, or ligaments, and, as in these cases, is due to chronic local irritation from the toxins of germs or more definite chemical bodies.

The most suitable name to apply to the condition is probably the pathological one of "chronic subcutaneous fibrosis," but, as already mentioned, the term "panniculitis" has been previously employed.

I have never noticed any abnormality of the thyroid gland.

To sum up:

1. Chronic inflammation of the subcutaneous connective tissue is a very common affection.
2. It is secondary to various acute and chronic infections.
3. The implication of the small peripheral nerves in the chronic inflammatory process gives rise to sensations of aching, stiffness, numbness, fatigue, etc.
4. When persons already stout, or who afterwards become so, are affected as above, the fat tends to form larger or smaller masses round the hypertrophied connective tissue.
5. These masses are often very painful on pressure

Fig. 3.

Fig. 4.

to be determined by the preceding overgrowth of fibrous tissue, as is well illustrated in the condition of the middle part of the anterior abdominal wall often induced by previous pregnancy. During the pregnancy the fibrous tissue is hypertrophied in patches, and around these fatty nodules form which can be readily felt and are usually tender on pressure. If the person is very stout and the face is involved, there is a superficial resemblance to myxoedema, for which it is sometimes mistaken.

In middle-aged and elderly people Heberden's nodes and stiffness of joints are often found associated with the other symptoms. The association of fat with the fibrosis is certainly much more common in women than in men, probably because they have a larger amount of subcutaneous fat normally. One of my female patients weighed 20 st. 3 lb., another 18½ st., and a third 16 st. 12 lb., but many of them only weighed 9 or 10 st.

The abdomen, flanks, hips, thighs, shoulders, and upper arms are in general the parts most affected, but sometimes fat is also deposited in the face, forearms, hands, legs and feet, either diffusely through the hypertrophied fibrous tissue or in lobules.

Where there is a large amount of subcutaneous fat the secretion of sweat is interfered with, but in most cases the amount of perspiration is normal.

The morbid anatomy is very simple. When excised portions of subcutaneous tissue are examined microscopically, the fibrous tissue, the peripheral nerves, and the blood vessels are found to be in a condition of chronic

owing to the nerve twigs being in a condition of interstitial neuritis.

6. The fatty masses are deposited mostly in the ordinary situations of fat accumulation.

7. The condition described by Dercum as "adiposis dolorosa" cannot be ranked as a special disease.

Treatment.

Cases of subcutaneous fibrosis can be treated with a considerable degree of success if treatment is gone about in the proper way and is persevered in.

In thin people we have to rely on massage, daily exercises, directed to stretch the altered fibrous tissue and to accustom it to movement, along with an habitually active and as far as possible open-air life.

If all this is systematically carried out for some months the inflamed fibrous tissues gradually lose their extreme liability to become painful on exertion or exposure to cold and wet, and the patient is restored to comparatively good health. Some cases get practically well, many are improved, and in all considerable benefit is assured. An habitually active mode of life with plenty of outdoor exercise is necessary to maintain the improvement.

The massage must be given firmly and so as to reach the affected parts. It is always painful at first, and should be given only by those who have had experience of similar cases. What probably happens is that the massage lessens or gets rid of the local neuritis, and favourably affects the inflamed small blood vessels, so that exudation

is not so apt to occur from them. It is commonly said to act by improving the flow of blood and lymph locally, but there is no exact knowledge on these points.

In stout or plump people the principles of treatment are the same, but in them we have to deal with two distinct conditions—the fatness and the chronic fibrosis. The inflamed fibrous tissue is relatively in very small amount compared to the fat round about it, and, thus embedded, it is a hopeless business to try and reach it and its inflamed nerves and vessels by means of massage.

Massage under such conditions is quite ineffective, and often unbearably painful.

The first step in treatment is to get rid of the superabundant fat, and this is best accomplished by a more or less strict diabetic diet, and the administration of thyroid gland or liquid extract of *Fucus vesiculosus*. Exercises can be commenced at once and massage somewhat later, or the latter can be instituted gently from the beginning, and increased in vigour as it becomes less painful. Unless the obesity can be substantially reduced, the prospects of improvement are very slight.

The paroxysmal neuralgic pains, which are sometimes very severe, and accompanied by a palpable hardening and swelling of the fibro fatty tissue in the neighbourhood,

worked for three years, and was regarded as a case of incurable "neurasthenia." She has had rheumatic pains since she was 14 years of age, but they have become much worse of late. There is a thick layer of fat over the shoulders, backs of upper arms, abdomen, back, hips, and thighs. The fat is in lobulated masses, and these are very painful on pressure. In those regions there is continual dull pain, which at times becomes sharp and stabbing. Healthy otherwise.

Treatment.—A diabetic diet with a little brown bread, 5 grains thyroid daily, and massage. Before treatment was begun she weighed on December 15th, 1909, 10 st. 13 lb., and she measured, waist 30 in., abdomen 39½ in., and thighs 40 in. (Fig. 5). On April 20th, 1910, she weighed 8 st. 2 lb., and the measurements were 27, 32, and 34½ in. (Fig. 6). On October 5th she weighed 7 st. 9 lb., the fatty masses had disappeared, and there was no pain on pressure. She had lost 46 lb.—nearly one-third of her original weight. She had still rheumatic pain in the lumbar region, but felt well and was able to work.

CASE II.

Woman, aged 39. She began to get stout during pregnancy six years ago. The fat was not evenly distributed, but was in masses in the supraclavicular regions, across the abdominal wall in ridges, on the hips, along the inner sides of the thighs, and above the ankles. It was lobular, and very painful on pressure. The masses in the shoulders and thighs sometimes became hard and swollen, and then caused pain and a great feeling of fatigue. She scarcely perspires and often feels very chilly. Treatment consisted in dieting, along with 5 grains of

Fig. 5.

often disappear or greatly lessen as the fat becomes absorbed. This is explainable by diminution of pressure on the inflamed nerves.

So far as I have been able to judge, hot baths and hot air have no direct curative effects, but, given before the massage and exercises, they render them less painful and probably more effective.

In those cases in which the subcutaneous fibrous tissue is dense and widespread, with little fat, or the fat evenly diffused through it, treatment does much less good than in the other forms. Peat baths, very gentle massage, and soothing treatment generally are sometimes indicated, as the patient cannot stand the pain and fatigue of the more vigorous curative measures, but experience has led me in this class of case to expect very moderate betterment.

As regards drugs, I have made careful trial of iodine in various forms, many antirheumatic and antigouty remedies, fibrolysin (thiosinamin), so-called ionic medication, and counter-irritation with a considerable variety of substances, but, so far, I have not met with any drug which has the power of dispersing the denser kind of cirrhotic fibrous tissue.

CASE I.

Woman, aged 33, a cook. Complains of aching and shooting pains all over her body, and increasing stoutness. She has not

Fig. 6.

thyroid daily at intervals. She was practically well in a year. During that time she lost 30 lb. in weight—13 st. 3 lb. to 11 st. 1 lb. The abdominal measurement fell from 33 to 29½ in., and that of the thighs from 25½ to 22½ in. The chilly feeling has gone and she perspires more easily.

CASE III.

Girl, aged 22. In 1903 and 1908 she had attacks of acute rheumatism. In 1909 she complained of almost constant aching pain over the thorax, over both scapulae, and in both lower limbs. At times the pain became acute. She weighed 8 st. 3 lb., and was plump but not stout. Little pea-like masses of fibro-fatty tissue could be felt in the subcutaneous tissue, and these were extremely tender on pressure. Her condition improved under treatment, but only to a certain extent.

CASE IV.

Woman, aged 50. For two and a half years past has noticed that she was getting stouter, especially over the abdomen and hips, where there were fibro-fatty masses. The face had a swollen and puffy look, due to increase of subcutaneous fibrous tissue, and a similar condition was present over the chest and along the fascia lata. The legs, forearms, feet, and hands were thin and slender. Heberden's nodes were present, and there was a good deal of pain and stiffness in the knees and in some of the hand and foot joints, due to swelling of the periarticular fibrous tissue. She suffered from constant aching and tiredness, and often from very severe neuralgic pains in the chest and arms. The condition was one of widespread subcutaneous fibrosis with little development of fat in it, except over the abdomen. The hypertrophied fibrous tissue was very tender

on pressure. She was treated with massage, diet, thyroid, antigouty and antirheumatic remedies, hydrotherapy, and in other ways, without obtaining much benefit.

CASE V.

Man, aged 54. He has had mucous colitis of moderate severity for many years. About eight years ago he began to suffer from stiffness and neuralgic pains, which have gradually become worse. He is a tall, muscular man, with a very moderate amount of subcutaneous fat. Weight, 13½ st. Over the chest, abdomen, back, shoulders, and upper arms, the subcutaneous tissue is swollen at points and very tender on pressure, but no distinct fatty nodules can be felt. The colitis and stiffness and pain improve under treatment, but never wholly leave him, and he is apt to have relapses unless he lives in dry hill air.

The first and third of these cases are almost certainly attributable to preceding attacks of rheumatism, and the fifth to chronic poisoning from the colitis. The second, like other cases I have seen, began during pregnancy, while the fourth must be due to some unknown irritant which has affected very widely and insidiously the subcutaneous fibrous tissue and that of many of the joints.

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THE USE OF LEUCOCYTIC EXTRACT IN INFECTIVE PROCESSES.

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THE injections of living leucocytes or their extracts have produced such remarkable effects upon artificial microbic infections in animals by way of prevention and of cure, that within the last three years investigations have been made into the action of similar injections upon infective processes in man.

Petersson, who worked chiefly with living leucocytes obtained from the pleural or peritoneal cavities of rabbits or dogs, showed that an artificial anthrax infection in guinea-pigs was either overcome or the animals lived much longer than the controls, if a simultaneous injection of living leucocytes was made into the same area. The injection of living leucocytes into the blood stream had a certain influence, though not so well marked, upon a subcutaneous injection of anthrax. The leucocytes of an animal of a different species (dog or rabbit) injected into the peritoneum of a guinea-pig produced a great increase in the resistance of the animal against *B. typhosus*, *Vibrio metchnikovi*, and *V. cholera*. He performed many more experiments of this nature, and also made numerous investigations into the mode of action of these injections, as have also Korschun and Watabiki. Opie has also used living leucocytes and injected them into the pleural cavities of dogs previously infected with tubercle bacilli. The resulting tuberculous lesions were of "lessened extent and severity as compared with those controls," and "the animals did better, more often recovering."

Hiss and Zinsser pursued Petersson's lines of investigations, but apparently always with the object of finding a method that would prove applicable to human infections. They worked almost entirely with an extract of leucocytes induced in the pleural cavity of rabbits. Staphylococci, *B. typhosus*, pneumococci, streptococci, and meningococci were administered to various series of rabbits in lethal doses, usually by peritoneal injection. Many of the animals survived, and in every case they lived longer than the controls. They proceeded to treat several human beings with leucocytic extract, and have so far published 24 cases of epidemic cerebro-spinal meningitis, with 63.6 per cent. of recoveries; 7 cases of lobar pneumonia and empyema, all recovered; 8 cases of chronic and acute furunculosis, with excellent results; 2 cases of chronic acne and 1 case of chronic frontal sinusitis (*Staphylococcus pyogenes aureus*) with success.

Floyd and Lucas treated 41 cases of lobar pneumonia, of which 5 died and 36 recovered. They report that in a number of cases the disease was apparently shortened, and there was noticeable improvement in the comfort and symptoms after the injections. The toxæmia was strikingly lessened, and there was a lower mortality in cases so treated than in a similar series untreated by this method.

Lambert reports more fully several cases that are included in the series of Hiss and Zinsser. In addition, 2 cases of pneumococcal meningitis, both of which died; 3 cases of ulcerative endocarditis (pneumococcal), upon which the leucocytic extract had no effect; 1 case of tertian malaria, whose rigors were stopped for nine days by leucocytic extract; several cases of erysipelas, with the most excellent results; and 1 case of otitis media.

METHOD OF PROCURING THE LEUCOCYTIC EXTRACT.

The author has employed throughout the method of Hiss and Zinsser for procuring the leucocytic extract from the pleural cavity of rabbits. Since it has succeeded almost invariably in producing good results, no necessity was found for resorting to the perhaps more effective methods of Petersson and his followers, who use the more dangerous technique of abdominal injection.

A sterile 10 per cent. suspension of Mellin's food in distilled water was injected in amounts varying from 5 to 10 c.cm., according to the size of the animal, into each pleural cavity of a rabbit. The animal was killed twenty-four hours later, and the fluid exudate removed. Difficulty was experienced at first in obtaining this perfectly sterile until the following plan was adopted.

The skin is removed from the thorax and the ribs laid bare by cutting away the pectoral muscles. The surface of the ribs and intercostals is lightly scaped over the whole side of the thorax, a 10 c.cm. syringe with a large bore needle is thrust into the pleural cavity, through an intercostal space, usually the seventh or eighth, and the fluid removed by suction. If the nearer cavity be emptied, it is easy with practice to thrust the needle through into the opposite pleural cavity, and thus the fluid from both cavities may be drawn off through the one external opening. The fluid should be pale yellow with a flocculent haze of leucocytes. Any large masses of Mellin's food must be removed by a preliminary sedimentation. Ten to 20 c.cm. is the average amount of fluid obtained. The exudate is rapidly placed in sterile centrifuge tubes and centrifugalized until a thick grey deposit of leucocytes appears at the bottom of the tube. The supernatant fluid is carefully pipetted off. The leucocytes may be again centrifugalized several times with fresh amounts of normal saline to free them from the last traces of exudate fluid. This is not, however, in the writer's opinion, absolutely necessary, and is usually dispensed with unless some circumstance should arise, such as the presence of a trace of blood. Distilled sterile water is then added in equal volume to the deposited leucocytes, which are well broken up with a pipette or glass rod. The tubes are placed in the incubator at 37° C. for at least four hours. Each tube is then tested for sterility, and, if sterile, the contents of several tubes are mixed and distributed in 10 c.cm. ampoules, which are placed in the ice chest until required. Leucocytic extract so prepared will remain effective for at least three months.

RECORDS OF TEN CASES TREATED.

1. *Streptococcal Endocarditis*.—Male, aged 35. An autogenous vaccine had been administered without effect. The patient finally became unconscious with a continuous high temperature (102.5° to 103.8°). Two doses of 10 c.cm. of leucocytic extract were given. On each occasion the temperature fell to normal and the patient became conscious, recognizing relatives. He died two days after the second injection.

2. *Osteomyelitis of Tibia*.—Boy, aged 14. (*Staphylococcus aureus*.) Boy had received, when the condition became less acute, an autogenous vaccine, and reacted favourably for a time. A fresh collection of pus threatened, the vaccine was stopped, and 1 c.cm. of leucocytic extract administered on three successive days. The temperature, which had been running up to 102° at night, fell to normal by lysis, and remained at normal for nine days, when a small abscess appeared. This was the first case treated with leucocytic extract, hence the small dosage. After the opening of the abscess the boy's temperature fell again to normal, and he made an uneventful recovery. It cannot be contended that the boy's recovery was hastened, but the effect of such a small dose of the leucocytic extract was obvious.