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.

3. *Ulcerative Endocarditis*.—Boy, aged 16. (Pneumococcal.) Sequela of pneumonia and empyema. The boy was almost moribund when treated, and two doses of 10 c.cm. had no effect.

4. *Sleeping Sickness*.—Man, aged 30. This case has been published *in extenso* by Professor Ronald Ross and Dr. D. Thomson. It may be stated here that very interesting and remarkable results were obtained.

5. *Hip Disease*.—Woman, aged 45. A large offensive, discharging sinus, which had some internal connexion, and which resisted all antiseptic treatment. The patient received three injections of 10 c.cm. leucocytic extract in fifteen days. The discharge became greatly diminished and lost its offensive smell. The patient left hospital still discharging freely.

(○) 10 c.cm. leucocytic extract.

6. *Acute Osteomyelitis of Tibia*.—A boy, aged 14. A diagnosis of acute rheumatism had been made, and the boy entered hospital on the third day of illness. A blood culture gave 750 colonies of *Staphylococcus aureus* in each 1 c.cm. of blood. When the first dose (10 c.cm.) was given symptoms of pneumonia and pericarditis had appeared. The boy was delirious and semicomatose. The immediate effect of the leucocytic extract was to send the temperature up, but next day the patient was conscious, sensible, and his toxæmia had disappeared. Three injections of 10 c.cm. were given, with the effect seen in the chart. Death occurred four hours after the last injection. At the *post-mortem* examination there was found pericarditis, right pleurisy going on to empyema, and small abscesses in the liver and left lung. A pure culture of *Staphylococcus aureus* was recovered from all these lesions.

7. *Acute Osteomyelitis of Left Ilium*.—Boy, aged 15. Blood culture gave one colony of *Staphylococcus aureus* in each 1 c.cm. of blood. The leucocytic extract was administered in small doses of 4 to 6 c.cm. repeated frequently. The effect upon the temperature was temporary, and upon the discharge nil.

8. *Streptococcal Septicæmia*.—Man, aged 45. Blood poisoning through accidentally cutting his hand with a dirty cheese-knife. A blood culture was negative. The patient suffered from frequent rigors. Antistreptococcal serum, though well pushed, produced no effect. Leucocytic extract was injected in doses of 10 c.cm. on three successive days, and the rigors stopped. The patient died two days later. No *post-mortem* examination was permitted.

9. *Anthrax*.—Man, aged 30. Treated with Solavo's serum and leucocytic extract. The patient recovered.

10. *Chronic Furunculosis*.—Man, aged 36. A year's duration; repeated crops of boils on arms, legs, body, and neck. Two injections of 8 and 10 c.cm. were given at an interval of three days. In a week after the second injection no fresh boils had appeared and the older boils had almost entirely disappeared. This case is still under observation.

These cases do not present any striking successes at first sight. Two factors have militated against more encouraging results:

1. Several of the cases have been handed over for treatment in a hopeless condition; thus any treatment which will give a measure of relief in such a case as No. 6, for example, is worthy of trial.
2. It is difficult to obtain permission to persevere with the treatment.

In some cases it is absolutely necessary to push the administration of the leucocytic extract, and the patient occasionally rebels although the temperature chart and the general condition witness an improvement. Thus cases which began to improve were lost.

The injections were given into the flank or into the buttock. No attempt was made to approximate the site of injection to the infected part.

MODE OF ACTION OF LEUCOCYTIC EXTRACT.

Pettersson, Hiss, and Zinsser have demonstrated bactericidal and bacteriolytic properties in leucocytic extracts

in vitro. They agree that the power is not great and quite inadequate to account for the destruction of large doses of the bacillus of anthrax, which were administered in the guinea-pig experiments.

They at first considered that the leucocytes supplied complement to the infected organism; for Metchnikoff has claimed that the cytases (complement) are not normally free in the plasma, but are contained in the leucocytes and only given up by them under stress of death or injury. But they have not been able to prove the presence of complement in their extracts. Kling, however, has recently published experiments which may ultimately show that leucocytic extracts possess the power of reactivating serum, even leucocytic extract itself which has been inactivated by heat. The body which has this power is not identical with the complement of the serum, since it withstands heat at 70–75° C., whereas the serum alexine is readily destroyed at 56° C.

Pettersson, Hiss, and Zinsser finally agree in the theory of endolysins. Hiss and Zinsser say that the beneficial effects obtained by the administration of leucocyte extracts are due to

the action of digestive substances usually not liberated from the leucocytes . . . to poison-neutralizing or destroying bodies, which act on the endotoxins and thus relieve the leucocytes of the animal from fatal poisoning and protect the higher cells of the animal so that their functions are not deranged.

Whether these theories be correct, I found that a marked leucocytosis followed an injection—a phenomenon not mentioned by other workers. Hiss and Zinsser give figures of blood counts in some of their cases of pneumonia, but these are in relation to the crisis and not to the injections. Floyd and Lucas state that:

A study of the white count has frequently shown a steady diminution in the number of leucocytes present in the peripheral circulation following the beginning of inoculation until the termination of the disease . . . possibly suggesting a diminished demand upon their reproduction with the addition of the extract.

This has not been my experience, and below will be found a table of results. For this table I am greatly indebted to Dr. D. Thomson, who is engaged in research upon malaria at the Royal Southern Hospital for the Liverpool School of Tropical Medicine under the Colonial Office, and who first discovered that the leucocytic extract produced a leucocytosis.

Count Before.	Amount Injected.	Hours After.	Count After.
6,800	8 c.cm.	12	50,000
		18	10,000
5,280	3 c.cm.	19	17,000
3,000	10 c.cm.	24	20,000
P. 41 %			P. 58 %
M. 59 %			M. 42 %
11,000	6 c.cm.	17	4,500
P. 41 %			P. 60 %
M. 59 %			M. 40 %
4,500	4 c.cm.	19	20,000

P. = Polymorphonuclear. M. = Mononuclear.

These figures were obtained from Case iv (sleeping sickness). Dr. Thomson proceeded with these counts throughout the course of the case, but remarks that:

The later effects of injections were complicated by an abscess forming, and by the onset of bronchopneumonia. But after all injections there was invariably a marked leucocytosis within twenty-four hours. The whole case was complicated by variations in the number of leucocytes which is characteristic of the disease. Also the differential count varies in the disease, but it seemed that this leucocytic extract tended to affect the polymorphonuclear cells slightly more than the mononuclears, though both were markedly increased.

Dr. Thomson tried the effect upon himself on one occasion of 15 minims of leucocytic extract subcutaneously into the forearm. His leucocytes before injection were 5,500 per c.mm.—polymorphs, 63 per cent.; mononuclears, 37 per cent. Twenty-four hours later the count was 9,800 per c.mm.—polymorphs, 64 per cent.; mononuclears, 36 per cent. It appears from these counts that a new view may be taken of the action of these extracts. They may in themselves be bactericidal and bacteriolytic to

some slight degree, and they may contain natural anti-endotoxins. But they seem to act chiefly as leucocytic stimulants, inducing a huge outflow of cells, whose function is to protect the body from infection.

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ELECTRICITY IN NEURASTHENIA.*

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I wish to bring before you the uses of some forms of electrical applications in the treatment of neurasthenia. But before doing so it is necessary to consider for a few minutes what is generally meant by neurasthenia. It is difficult in a few terse sentences to define this disease. The term has been applied so widely and to such various and varied symptoms that it would be impossible to discuss it exhaustively in the time at my disposal. But I will take the main symptoms as they have exhibited themselves in the cases I have had to treat. These may be general, or local, or a combination of both. The patients are usually irritable or depressed. They are very anxious and consider their condition as extremely dangerous to life. They frequently are in dread of becoming insane. Sometimes the brain appears to be too active, and they are constantly pestered by all kinds of possible and impossible problems presenting themselves to their imagination day and night. They dread meeting people; they fear they are victims to some imaginary disease. They are frequently worried and are annoyed by the veriest trifles. Everything is a cause of complaint. They are great egoists and feel compelled to discuss their troubles with every patient listener. Many of them sleep badly—in fact, insomnia is one of the most trying symptoms of the disease. They suffer from flushes and fullness in the head and sometimes severe headaches. Frequently there is a sense of oppression in the chest and difficulty of breathing. Tachycardia is common, and the patient believes he or she is suffering from severe heart disease. Many suffer from gastro-intestinal neurasthenia. Feelings of distension, noisy eructations, borborygmi, and gurgling are complained of. Anorexia is usual. There is often aching in the eyes and neuralgic pains in the head. Spinal symptoms are common—localized pains in the back, disturbances of sensation, and intercostal pains. In some cases there are pains in the extremities. The word that probably sums up the condition of the patient more than any other is—emotional.

The conditions which might be confused with neurasthenia are melancholia in which there are actual delusions, and hysteria in which there are marked hysterical paroxysms. Of course, tabes and general paralysis might also exhibit some of the symptoms mentioned—in their early stages, at any rate.

There is apparently no discoverable morbid anatomy in these cases, but there is undoubtedly a pathology. Hypertension appears to be a frequent concomitant, or perhaps a cause of the disease. According to Gay, the presence in the blood of alimentary toxins, generally acid and with a vaso-constrictor effect, and the retention of extractive substances of the xantho-uric series will cause hypertension. I believe, too, that a rigidity of the walls of the vessels set up by some central irritation of the nervous system is often present, and is a cause of a large number of the subjective symptoms. I have noticed, too, that this hypertension is not so readily observed by examination of the pulse as one would have thought. On examining the pulse of several neurasthenic patients the impression gained was that the pulses

were not high tension, but the sphygmomanometer usually revealed a considerable amount of hypertension. The point I am anxious to show is this: That the symptoms declined *pari passu* with a decrease in the sphygmomanometric readings until, if the latter could be reduced to nearly normal, the patient became well.

I am not now concerned with the usual methods of treating neurasthenia. The cases I have had in hand have all received skilful medical treatment before they were sent to me. One or two had had Weir Mitchell treatment, in which, of course, a certain amount of electrical energy is used. The currents I have treated these cases with have been those known as high frequency, or d'Arsonvalization; or, as an alternative, static electricity produced by a Wimshurst machine. I may say, as a rule, that where the neurasthenia has been associated with marked metabolic deficiency, or of the gastro-intestinal type, I have found high frequency currents the most effective; but if the symptoms pointed more to a condition of a pure neurosis, I have observed that static electricity produces the best results. (Here followed a description, with illustrations, of the high frequency and static machines used.)

I wish to draw attention to a few cases treated by these methods during the last few years. I will not record a large number, because they give, to a great extent, a mere recapitulation of the same class of disease. I think I may say that in most cases the results of treatment have been permanent:

1. Unmarried woman, aged 46. Gastro-intestinal neurasthenia, flatulency, tachycardia, panophobia; ill six months. Received auto-condensation high frequency on the couch thrice weekly from April 7th, 1904, to May 13th. Cured.
2. Lady, aged 36. Insomnia, restlessness, depressed; great fear of railway travelling (sidero-dromophobia); pains in limbs and in breasts; ill many months. Twelve applications of general static electricity. Cured.
3. Gentleman, aged 38. Depression, insomnia, distension of stomach, flatulency; ill for more than twelve months. Had been treated, in addition to ordinary methods, previously by light baths and Weir Mitchell treatment. Received 300 to 500 milliamperes of auto-condensation for half an hour at a time and a few minutes' application of a glass vacuum electrode over stomach. Attended eighteen times between June 14th, 1907, and July 31st. Cured, and has remained so.
4. Mr. P., aged 35. Remarkable case. Began with nervous symptoms in 190; always frightened, dreading what he could not describe; constantly thinking in bed; pain in head, with fullness mostly at back of head; always burning pains in stomach and sense of distension; bowels somewhat loose; terrible insomnia, had never slept more than an hour or so consecutively for years. Had nineteen applications of auto-condensation, 400 to 800 milliamperes of current, for half an hour at a time, and local glass electrodes to stomach, head, and spine. Blood tension, according to the Riva-Rocci, on first treatment, 190; at end of treatment only 120 to 130. Cured, and has remained perfectly well for over two years.
5. Miss S., aged 25. Nervous, depressed, insomnia, etc., many months. Twelve applications static electricity. Cured.
6. Mr. W., aged 39. Twelve months before treatment began to lose appetite, could not sleep, and always tired; gets horribly depressed, sometimes feeling almost suicidal; bowels sometimes constipated, sometimes loose; very irritable. Treated by high frequency auto-condensation and glass vacuum electrode to stomach and head. Remained cured over two years.
7. Gentleman, aged 59. More or less insomnia four or five years. Aching pains and fullness in the head; some distension and flatulency; insomnia now constant; arterial tension 180. Had twelve and a half hours' applications of auto-condensation and local electrodes to head and stomach. Now sleeps soundly, and arterial tension 120 to 130, and feels quite well.
8. Lady, aged 33. Very neurotic; complains of her head, difficulty of breathing, and sobbing respiration; ovarian neuralgia; constant insomnia; blood tension 160. After twelve applications of static bath slept perfectly, and difficulty of breathing, etc., disappeared. Blood tension reduced to 120.

I do not wish it to appear that every case of neurasthenia treated electrically is cured, nor do I suggest that every case of neurasthenia should receive this form of treatment. A large number of cases treated by rest, fresh air, drugs, and other methods, recover. But the cases I have quoted had been treated by the usual methods by the practitioners who referred them to me. They have been obstinate, obdurate—conditions not amenable to the usual remedies. Neurasthenia is a condition frequently seen by every general practitioner, and the anxiety this class of case gives him appears out of all proportion to the seriousness of the disease. I think it well to remember that when all other methods fail there is still a possibility of effecting a cure.

*A paper read before the Bradford Medico-Chirurgical Society, January 17th, 1911.