THE
BOSTON MEDICAL AND SURGICAL JOURNAL.

VOL. LXII.

THURSDAY, FEBRUARY 23, 1860.

No. 4.

LEUCOCYTHÆMIA.

[Translated for the Boston Medical and Surgical Journal from No. 29 of the *Allgemeine Wiener Zeitung* for 1858.]

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Enlargement of the Spleen and Liver; Increase of the number of White Corpuscles during Life.

ELIZABETH HALLWACHS, æt. 45, Catholic, midwife, from Grinsing, mother of five children (the youngest being now 18 months old), had always been healthy. In August of last year she was for the first time attacked with chills, without being able to recollect any exciting cause. Two days later, at about the same hour, she had a similar attack. Fourteen days afterwards, there was a recurrence of the chills for eight days, in daily returning paroxysms.

The patient first noticed at this time, in the left hypochondriac region, a tumor which was not painful, and of considerable size (according to her statement about that of the fist). It was therefore of some size before discovered by her.

Since January of this year the patient had had pain in this tumor, which had become as large as an infant's head, and had lost, as she thought, its mobility.

During February and March, she was quite comfortable for six weeks. But after this the chills returned with greater frequency, and the pain in the tumor became more severe, particularly after the fever turns; so that, March 22d, she appeared as an out-door patient on Prof. Oppolzer's clinic. There was at this time a tumor that reached inwards as far as the navel, and downwards to within three inches of the symphysis pubis. It evidently belonged to the spleen, and the patient was ordered quinine.

Since then, however, the chills and fever returned daily, and were increasing in intensity and duration. The attacks that at first only appeared once, now came thrice, and even four times during the day, and began to lose their typical character. The patient had, at the same time, constant diarrhœa, with pain at stool.

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She also lost her appetite, and had a "bronchial catarrh," with purulent sputa.

She accordingly entered the Hospital April 1st, when her condition was as follows:

Body of medium height; muscular system feebly developed; skin of a pale brown color; eyes sunken, sclerotica not yellow, the vessels moderately injected; forehead had the so-called "chloasma uterinum"; tongue dry, white coat on its edges. The jugular veins strongly dilated with blood, and plainly undulating even during the intermissions of fever; no murmur in them. Carotids strongly pulsating. Glands of the throat and neck slightly enlarged. Formation of the chest normal; the breasts still swollen and hard (the patient had only a short time previously weaned her child).

Examination of the chest gave the following physical signs.

In the right axillary line, dulness from the eighth rib downwards; in the mammillary line, from the sixth rib, and in the parasternal line the same to the ensiform cartilage of the sternum. In the *left* parasternal line, dulness from the upper edge of the third down to the sixth rib, and from here downwards tympanitic. In the mammillary and axillary lines, dulness from the under edge of the seventh rib downwards. Impulse of the heart between the fifth and sixth ribs—plainest in the parasternal line. Heart's sounds normal; second sound over the pulmonary artery, not much accentuated; first sound over the aorta, dull; second, loud. Dulness over the liver reaches in the mammillary line from the sixth rib to an inch and a half below the edge of the ribs; in the axillary line, it begins at the eighth rib. In the median line, the left lobe of the liver reaches from the sixth rib to an inch below the xiphoid cartilage. Enlargement of the liver is therefore evident. Its right lobe extends lower than the left. On the left, the dulness over the liver is separated from that of the region under the ribs by a small intervening tympanitic space. Percussion in the right inguinal region, clear and full. Dulness from fecal masses, to a slight extent, over the crest of the ileum. Liver not sensitive to pressure.

As was said above, the dulness begins on the left side at the under edge of the seventh rib. This is also the upper edge of the tumor now to be described. This tumor extends furthest towards the right side below the navel, i. e., to the outer edge of the right recti muscles. At the navel it projects an inch beyond the median line; above the navel, to the median line; five inches under the navel, one inch over the median line. So that the tumor has a periphery convex towards the right side. Posteriorly, it reaches to within two inches of the vertebral column. Its inferior edge is bounded in the iliac region by the crest of the ileum; further forwards by Poupart's ligament. In the median line, it reaches to within an inch of the symphysis pubis. The superior border of the tumor can only be determined by percussion; its other limits by palpation also. Over the tumor percussion is flat; on its edges,

slightly resonant and tympanitic; in the neighborhood clear and tympanitic. The tumor is therefore surrounded with organs holding air. The surface of the tumor is even, and its consistence hard and uniform. The lower edge is blunt; the right edge has six perceptible notches, the deepest one (which is two inches) lying under the navel. No perceptible fluctuation over the tumor. Its elasticity but slight. The tumor can be moved within certain limits from one side to the other, and also upwards and downwards. Its position changes with that of the patient. During inspiration, it falls somewhat lower. In the region of the tumor, and especially towards its posterior border, the patient has continuous, severe, burning, and lancinating pains, even when she is quiet and has no fever. Lying on the right side decidedly increases this pain. The attacks of fever commence with coldness of the lower extremities, creeping upwards as far as the arms, and then changing to heat and burning thirst. These now (at the time of her reception) come on three or four times during the day. At these times the pain greatly increases, especially during the cold stage.

The inguinal glands are somewhat swollen. The pulse, during the fever, 128; between times 84, soft and full. Dejections, since a few days, normal. Secretion of urine not altered. Urine of normal specific gravity, rich in uric acid, and holding a trace of albumen. The digestion, during the intermissions of the fever, not much disturbed.

An examination of the blood, taken by a local venesection (ordered by Prof. Oppolzer on account of the enlargement of spleen and the fever), showed a relative increase of the white corpuscles. On coagulating, the blood formed a large white clot, under which were white granules the size of a millet or hemp seed, round, and streaked in appearance, composed, under the microscope, of white blood corpuscles rolled together. There was, in addition, also a large red clot. We had, therefore, blood, leukæmic to a small degree.

The following comprise the data from Prof. Oppolzer for the diagnosis of the case.

1. As regards the tumor in the left hypochondrium of the patient, it answers to the greatly enlarged and hardened spleen, which is shown by its position, its surroundings, the percussion, its movement during inspiration, absence of fluctuation, and the peculiar notches on its inner (anterior) edge.

We have here, therefore, a splenic tumor, and, moreover, that form which occurs with leukæmic blood.

The enlargement of the spleen in our case is a chronic one, as shown by the duration of the disease, the great increase of size of the spleen, and, finally, the absence of any injury, pyæmia, or inflammation in the heart, as primary lesions.

Of chronic splenic tumors are to be excluded the lardaceous

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(*speckig*) and colloid forms, such as accompany constitutional syphilis, the mercurial cachexia, rachitis, scrofula, &c., and which are generally associated with colloid degeneration of the liver and kidneys or albuminuria.

The "pigment spleen," after intermittent, has as little connection with a decided increase of the white corpuscles as the lardaceous degeneration. This leukæmic condition of the blood corresponds more to Virchow's so called chronic splenitis. Anatomically a "flesh spleen" (*Fleischmilz*), as a result of Virchow's "parenchymatous inflammation," where the capsule is thickened, the trabecular tissue hypertrophied, the intervening pulp hard, the parenchyma-cells in large numbers, and in many cases yellowish or reddish-brown formations. In all probability we have such a tumor as this in our case.

The question whether the leukæmic splenitis is in fact very different from the splenic tumor of intermittent (since the clinical course of the two diseases are in many respects similar), may be so answered. An increase of the white corpuscles of the blood occurs in intermittent, and also in typhus, pneumonia, during pregnancy, in the puerperal state, in tuberculosis, with cancer, in anæmia and inanition. But in these diseases the leukæmia is only small in amount, disappears again, and the patients convalesce. If leukæmia was identical with intermittent, patients with the latter, living in the malarious regions, and having enormous enlargement of the spleen, would exhibit a decided increase of leukæmic blood and all the peculiar lenteric symptoms of the disease.

Enlargement of the liver is very often associated with chronic splenitis, and Virchow mentions having found white corpuscles in the liver, which appeared precisely similar to the corpuscles of the spleen. In our case, also, there is enlargement of the liver.

2. The presence of leukæmic blood must be proved, in order to confirm the diagnosis.

In the first place it is to be remembered that leukæmic blood may be confounded with that of lipæmia, and, moreover, the character of the blood corpuscles may be altered by an increase of their coloring matter—*melanæmia*.

As regards lipæmia, the milk-white color of the serum of the blood is here occasioned by its richness in fat. If we shake up the serum with ether, the fat will be freed, which will not, therefore, be the case when the white color is dependent upon the presence of white corpuscles. Lipæmic blood occurs especially in hard drinkers, in pregnant women, and those in the puerperal state.

Our patient's blood was not lipæmic, but leukæmic. Its redness was caused by there still being a large number of red corpuscles present. (Their decrease is the principal characteristic of leukæmia.) Purely white blood has only been seen at *post mortems*; during life its color is generally only somewhat brighter, like raspberry syrup, and in the severest forms grayish red.

The diagnosis founded on the two points above mentioned was confirmed by the further progress of the disease, as will be seen further on.

As regards the character and form of the disease, it must be first said that the leukæmia is only to be considered a symptom. In the beginning of chronic inflammation of the spleen it is but slight, as was very markedly the case with our patient. Virchow records several cases in which, in spite of the size of the splenic tumor, there was at first no leukæmia, and where it did not appear till after several months.

Leukæmia is therefore a secondary appearance, that occurs with splenic tumors, and (which was not previously mentioned) with diseases of the lymphatic glands.

In the four cases that Prof. Oppolzer has seen up to this time, the lymphatic glandular system was but once the starting point of the disease, in which case all the glands of the body were considerably swollen, but also elastic, having the feel of lipoma, particularly on the neck. These tumors developed by sudden enlargements, without any particular pain, and whilst the other functions of the body were normal, notwithstanding the paleness and emaciation. The symptoms of leukæmia afterwards showed themselves in their fullest extent, and the patient succumbed to the disease.

Lately some cases have been seen, where cancer was mentioned as the cause of leukæmia. In one of Heschl's there was degeneration of the lymphatic glands, and in some other cases of English observers neither the spleen nor the glands are said to have been affected.

Before Virchow introduced the leukæmia into science, similar cases were explained as pyæmia. Nevertheless, Bennett, who introduced the name of *leukocythæmia* (which has now, and, in fact, with better right, spread abroad as *polyleukocythæmia*), has endeavored to defend his right of priority.

No satisfactory explanation of leukæmia exists as yet, because the formation and degeneration of the blood corpuscles, and the part which the spleen and lymphatic glands play in this, is not at all settled.

If we lay stress only on the increase of the white corpuscles, all attempts to explain the difficulty of breathing, the loss of muscular power, in short the chlorotic appearances, are useless. The diminution of the red corpuscles must also be explained, which has not yet been done by the vaguest hypothesis, although the increase of the white corpuscles has been said to be caused by those in the spleen passing into the stream of the blood.

The distinction that has been made between the white corpuscles and pus corpuscles amounts to nothing, when we remember that the size of cells suspended in a fluid depends upon the density of that fluid, and that the (larger) pus cells are floating in a thin-

ner medium than the white blood corpuscles; and, moreover, that we have *different* formative cells before us, which would naturally in some measure differ from each other in appearance.

The same applies to the corpuscles in the lymphatic glands when compared with those in the spleen.

The viscid character of the corpuscles, and their rolling and sticking together so easily, would explain why in leukæmia the capillaries are so readily plugged up and metastases follow in the later stages of the disease.

There is no ground here, however, for the theory of those who would assume a plugging up of the capillaries of the lungs with pus in pyæmia.

As to the causes of leukæmia, there is but one thing yet ascertained, namely, that in the cases that have occurred with women there was derangement of the menstruation, and that the disease was developed during the puerperal state; as was also the case with our patient.

One of Prof. Oppolzer's cases was a day laborer, who worked as a digger in a marshy place. Without having had any intermittent, he suffered from a splenic tumor, dropsy, and nasal hæmorrhage, of which latter trouble he finally died through anæmia. The other cases were of no particular ætiological interest.

Leukæmia has been seen at different periods of life, in both sexes, and with various constitutions. Intermittent fever is rarely a cause of the chronic splenitis in Virchow's acceptation.

The appearances in the disease are not yet sufficiently classified to establish its symptomatology. A variety of symptoms have been ascribed, which in fact are really not peculiar to it.

The color of the skin in most of the cases was pale, with a shade of yellow, as there was generally enlargement of the liver.

In all cases Prof. Oppolzer observed pain in the spleen, with the exception of the leukæmia above spoken of, which was accompanied by affections of the lymphatic glands. The pain came on at intervals, accompanying an increase of the fever, as in our case.

The *principal* symptom is the fever, which has a typical course, is accompanied with heat and chill, irregular in its duration and times of returning, appears on an increase of the pain, and is not generally much improved by quinine. There is generally emaciation during the later stages. The debility which is so constantly present, just as in chlorosis, may depend, like the difficulty of breathing and the mental depression, upon the diminution of the red corpuscles.

The augmented accumulation of white corpuscles may cause in the later stages great difficulties in the circulation, inflammation and metastases. Hence came the idea of regarding the disease as pyæmia. In this view the most common occurrences are thrombus in the vessels, with phlegmasia, bleeding from various mucous membranes; particularly of the nose, even to complete exhaustion, pe-

ritonitis, pneumonia (in one case of Prof. Oppolzer), formation of abscesses in the skin, furuncles, carbuncles, &c. Dropsy occasionally occurs, but it seems generally to be produced by the splenic tumor. It is by no means constant. Alterations in the digestive tract are not very marked, or at least do not seem to be immediately connected with the disease in the blood. For example, when our patient was troubled with diarrhœa, the leukæmia was certainly still very inconsiderable. The urine held a good deal of the urates, and afterwards free uric acid, which is especially connected with the disease of the spleen, for this formation of uric acid occurs also in intermittent fever.

The "key-stone," however, is generally the hectic fever, with a fatal termination, or death is caused by one of the above-mentioned secondary appearances.

The prognosis is most unfavorable. At least no case of lentic leukæmia has as yet been seen that was not fatal. The other form has not been often enough observed to decide this point as respects it, still the termination has always been fatal. Our treatment can therefore only be directed to the symptoms, since we do not know the nature or exciting cause of the disease.

The few therapeutical deductions from the previous cases which are applicable to leukæmia, will be spoken of in their application to our case.

The following was the course of the disease with our patient.

When she entered the hospital, a few leeches were applied over the spleen, without relieving the pain in the slightest. Sulphate of quinine was ordered at the same time, also without much effect, for on the 4th of April, when the patient had already taken forty-two grains of quinine, the attacks of fever were still very severe, and one that begun at 3 o'clock, P.M., lasted till the next morning. The condition of the patient, aside from the fever turns and pain in the spleen, was satisfactory. The bronchial catarrh that had for a long time troubled her, entirely disappeared, the diarrhœa had yielded to treatment, and the appetite was pretty good. The fever paroxysms and severe pain lasted in spite of the quinine. The leeches and warm applications were repeated, and continued up to the 9th.

Examination of the blood during this time, showed a continued increase of the white corpuscles.

On the 8th and 9th, the patient, under the use of quinine, had no chills, but they returned on the 10th, and lasted an hour and a half. On this day Fowler's solution was given, in order to allay the feverish symptoms.

A physical examination, on the 19th, showed a new enlargement of the spleen. The digestion still good, dejections somewhat loose. Urine held urates, but not so much as at the commencement. A trace of albumen was present. On the 20th, the patient again had fever, from which she had been free for two days. Re-

sort was therefore again had to quinine, and large doses of it finally prevented the paroxysms of fever from returning so often, and the pain was *entirely* relieved for a time.

This relatively favorable condition lasted till the beginning of May, when, without any apparent cause, the paroxysms of fever returned with still severer pain. At the same time the patient had oppression at the chest, diarrhœa, and the dejections were mixed with mucus and epithelium. The salicin, of which she took two scruples, had no effect. On the 9th of May, leeches and quinine were again ordered.

On the 18th, after four days' relief, the patient was again attacked with high fever and severe pain in the hypochondrium, and with this, headache, diarrhœa and strangury. In the intermissions, pulse 100. Frictions of *spiritus saponatus* were used, and extract of colombo, with tannin, given to check the diarrhœa.

The patient went on in this way, her condition sometimes made worse by the fever and pain in the spleen, the diarrhœa and loss of appetite, and sometimes better by the remission of the fever, especially after the use of Peruvian bark, which often was effectual for some time together.

On the 7th of July, the patient complained for the first time of pain in the thighs. Coagulation of blood was discovered partly in the deep and partly in the superficial veins, especially on the left leg. A hard cord was felt on the inner side of the left thigh, and a reddened streak over it. The same sort of cord was felt under Poupert's ligament.

There was œdema in the neighborhood, and the skin was red. These coagula corresponded to the saphena vein, but as that alone would not explain the interruption to the circulation, the crural vein must also have been affected. The patient felt very weak, complained continually of severe pain in the foot; the pulse was quick (120) and small; and the appetite quite gone. Cold applications of Goulard's lotion were made to the foot, strong doses of morphia given internally, and the leg raised.

On the 8th and 9th (July) this condition continued, the œdema having somewhat decreased, however. No metastases to be found. Lately the urine has held a great deal of the urates. The blood has been comparatively richer in white corpuscles. The sleep bad—the pain insupportable. The cold applications were continued, and also morphia, in stronger doses ($\frac{1}{4}$ gr.). This condition lasted, with slight intermissions, till the 13th.

On the 13th, the patient looked cadaverous, was very emaciated and extremely weak. Splenic tumor not very sensitive. No chills. Less pain in foot. Less œdema. The corded feeling of the vessels still perceptible. Pulse frequent (100), intermitting, small. Metastases or bleeding have not occurred. Urine rich in urates, thick, cloudy, pale brown. Lactucarium was given as a narcotic. After a short agony, death followed on the evening of the 14th.

As regards the therapy, we may gather from the course and progress of the disease, that of all the remedies used to allay the fever and relieve the pain in the spleen, quinine and cortex Peruvianus alone were of service, and only in a certain degree. Narcotics, bleeding, &c., were in this case almost of no service. Whether the use of the Carls baths, Marien baths or the waters of Kissing would be advantageous in the beginning of leukæmia, is doubtful. Hardly any other opinion could be held respecting the effects of moxæ, acupuncture and similar procedures in use among the natives of the East.

(To be continued.)

ATTEMPT TO PROCURE VACCINE MATTER FROM THE ORIGINAL SOURCE—PRODUCTION OF TRUE VARIOLA.

[Communicated for the Boston Medical and Surgical Journal.]

IN the year 1836, Dr. John C. Martin, then a practitioner of medicine in Attleborough, Mass., conceiving that the sometimes imperfect protection afforded by the vaccine disease, arose from a deterioration in the matter used, inserted into the udder of a cow lymph taken from a pock upon the body of a man who died of variola. Subsequently matter derived from the cow was inserted into the arm of about fifty persons. This was at the middle of October. Presently, one Babbitt, being among the first vaccinated, began to exhibit unlooked-for symptoms which alarmed his family. Physicians were summoned, and after examination and comparison of opinions, the patient was declared to have the true smallpox. Then all those who had been vaccinated from the same source inquired anxiously what was to be their fate. The vaccinations (the sequel will show that inoculation was the more proper term) had been made on successive days up to Babbitt's illness, and others soon began to be affected. The physicians in the neighborhood again assembled, and recommended that due precautions should be taken against the spread of smallpox, as probably all who had received the virus from Martin must suffer unmodified variola. Dr. M. became at once the most unpopular of men, although, as I learn from cotemporary informants, one of whom was himself a sufferer, the experiment had not been entered upon without consultation, which relieved him from undivided responsibility. Excitement and consternation prevailed, sustained by the consecutive occurrence of new cases. Business was suspended; the panic of fear magnified the danger, and no man could see where it would end. Dr. M. stoutly contended that the phenomena were merely the manifestations of genuine kine-pox in its pristine force; but we have the testimony of Dr. Sylvester Fuller, that the disease was variolous. Dr. Fuller was an accomplished physician; had served in the army, where he had seen much smallpox, and his evidence, in concurrence with other physicians of the time, is conclusive.