

THE INFLUENCE OF LEUKÆMIA UPON PREGNANCY
AND LABOR.

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OUR knowledge of leukæmia is at best fragmentary and incomplete; for its etiology is uncertain, its course and symptoms variable, and its treatment unsatisfactory. It occurs more frequently in men than women (at least 2:1, according to Osler¹); but even in the few recorded cases of leukæmia in women the effect of the disease upon the reproductive functions is barely mentioned. We find it stated that sometimes menstrual and sexual disturbances are among its early prodromata; that it is most frequent at the climacteric; that in a few cases it has developed during pregnancy or after several miscarriages or difficult labors; that it has occasionally followed the sudden suppression of the menses from cold; that in non-pregnant leukæmic women amenorrhœa is the rule, though occasionally menorrhagia has been observed. Uterine hemorrhage seems to be rare, for Mosler² says that in 81 cases of leukæmia observed by himself and Ehrlich, hemorrhage occurred in 64, and that in only 3 was there hemorrhage from the uterus. In 21 cases of leukæmia in women observed by Mosler, disorders of the reproductive system occurred in 16.³ M. Vidal⁴ says that in four cases out of ten, pregnancy is the commencement of the disease in women. I have been able to find the reports of only four cases in which leukæmia was said to have occurred in the course of pregnancy; I have found none where a woman already leukæmic has been known to become pregnant.

A case was reported by Dr. Ingle to the Cambridge Medical Society

¹ Pepper's System, vol. iii. p. 909.

² Ziemssen's Cyclopædia, vol. viii. p. 385.

³ *Ibid.* vol. viii. p. 506.

⁴ Dictionnaire Encyclopédique des Sciences Médicales. Leucocythémie.

in 1880.¹ The patient, æt. thirty-three, when near her confinement showed extreme pallor and weakness. On examination the blood showed none of the characteristic changes found in pernicious anæmia, but there was a marked increase in the number of white corpuscles, so that white to red = 1:20. After a natural labor with very little bleeding, the symptoms persisted and fainting fits began; but she recovered completely under a course of iron. She had suffered in a similar way toward the end of her last confinement, but regained her health in the interval.

In May, 1870, Dr. Robert Paterson² read a paper before the Edinburgh Medico-Chirurgical Society on "Acute Leucocythæmia in connection with Pregnancy," in which he reported three cases, two of them fatal upon the eleventh and fourteenth days respectively after delivery. These cases, though interesting, are not very satisfactory, because no blood counts were made, the relation of the white to the red being roughly estimated during an ordinary microscopic examination, and no autopsy was held upon the fatal cases. The first fatal case reads very like one of acute puerperal septicæmia, and even in the second sepsis was probably an important factor. Dr. Paterson attributed death in both cases to the more or less rapid enlargement of the lymphatics of the throat, neck, and upper part of the chest. He says that he has carefully watched a number of cases during the latter months of pregnancy, and has always found that where there was marked sallowness of skin with general languor and tendency to faint, the blood was always crowded with leucocytes, even though spleen, liver, and glands were not enlarged; and that whenever these symptoms were absent, leucocytes were not abnormally abundant. I have been unable to find any other cases at all bearing upon the relations between leukæmia and pregnancy.

The following case, which I have still under observation, is unique and has some points of peculiar interest:

Mrs. S., æt. thirty-six, VII-para, was first brought under my notice in October, 1886, by Dr. George Ross, Professor of Clinical Medicine in McGill University. She was then seven months pregnant. During the autumn of 1885 she had been under treatment for leukæmia in Dr. R. L. MacDonnell's clinical wards in the Montreal General Hospital, and to him I am indebted for the earliest reliable report we have of her condition. Briefly her history then was as follows:

September 15, 1885. Mrs. S. entered Montreal General Hospital complaining of vomiting and a tumor in the left hypochondrium. Has been married fourteen years, has had six children (the youngest three months old), all living, and all subject to attacks of jaundice more or less severe. One attack of rheumatism at the age of thirteen. Never had malaria, though she lived in a malarious district in England until

¹ *Lancet* (London), 1880, vol. i. pp. 334, 335.

² *Edinburgh Medical Journal*, vol. xv. pp. 1073-1078.

the age of fifteen. Three years ago she came from England to Montreal, a city free from malaria. Since marriage has had occasional attacks of jaundice, ushered in by chills, vomiting, and slight abdominal pain. Occasional attacks of epistaxis ever since childhood. Diarrhœa a common symptom. Syphilis, alcoholism, and injury negative. Menstruation began at the age of thirteen—always scanty—intervals sometimes prolonged to six weeks. No pain until the last three years, since which time she has suffered pain in back, pelvis, and groins. Splenic tumor was first noticed by her about a year ago, at the beginning of her sixth pregnancy. She has been losing flesh for three years, but in the intervals of her icteroid attacks she is fairly well, though weak. The present attack began ten days ago with a severe rigor and fever; then followed anorexia, nausea, vomiting, constipation, sleeplessness, slight cough, and increasing feeling of weakness. She nursed her baby until the milk ceased, a few days ago.

Physical examination. Appears weak, pale, and anæmic—conjunctivæ pearly—a sallow tinge of skin, but no jaundice. Muscles soft and flabby. Temp. 103°; pulse 104, regular and of good volume; resp. 28. Tongue coated and moist; attacks of vomiting occur three or four times daily; skin harsh; no œdema, ascites, or enlarged veins. Splenic tumor extends from sixth left rib obliquely downward toward the umbilicus, and backward to the post-axillary line—oblique measurement 23 cm. (9 inches)—feels firm and smooth, and is notched on anterior edge. Liver dulness begins at the fifth rib and extends 5 cm. (2 inches) below costal border—measures 16.5 cm. (6½ inches) in mammary line; border sharp and well defined, surface smooth and firm. There is moderate tenderness over liver and spleen, and moderate tympanites, though the abdominal walls are flaccid. Lymphatic glands not enlarged. Heart: apex beat between fifth and sixth ribs, 11 cm. (4½ inches) from mid-sternum. The area of dulness considerably increased, beginning above at third rib and transversely about mid-sternum. A systolic murmur soft and blowing, maximum at apex, transmitted up to pulmonary cartilage, but not around to the left. Second sound normal at pulmonary cartilage, but very feeble at the aortic. Lungs clear throughout. Urine: heavy deposit of lithates. Retina unchanged.

17th. Red corpuscles per c. mm. 2,400,000. W : R = 1 : 40.

25th. Red corpuscles per c. mm. 2,900,000. W : R = 1 : 17. White cells all of large size.

October 31. Red corpuscles per c. mm. 2,480,000. W : R = 1 : 12½. White cells nearly all small and more the shape of red cells.

November 2. She left hospital and gradually regained health so as to be able to do housework without much fatigue.

January 28, 1886, her menses reappeared and lasted one week, varying in amount from day to day, very little at times, and again at times so profuse as to compel her to lie down from sheer weakness.

March 28. Menses appeared again, but were very scanty. Soon afterward morning sickness began, and during the next few weeks there were several attacks of epistaxis and melæna. The urine became high colored and scalding, and over the hepatic region dragging pains were felt, increased by overwork.

April 28. She again entered hospital. The spleen was found to be somewhat sensitive, and the liver so tender that she could not bear the slightest pressure. There was slight dyspnœa, but no œdema of feet.

or legs. Lips and gums pale; no fever or thirst; tongue clean, moist, and indented; appetite failing; abdominal walls flaccid. Temperature 98.4°, pulse 74. Lower edge of spleen extended downward to within 7.5 cm. (3 inches) of the left anterior superior spinous process. The vertical line of dulness in midaxillary line measured 15 cm. (6 inches), the oblique line 24 cm. (9½ inches). Liver dulness extended from sixth rib to costal margin. Blood: red corpuscles per c. mm. 3,400,000. W : R = 1 : 50. She was put upon a course of arsenic and iron and left hospital on May 3d, when a blood count showed, red corpuscles per c. mm. 2,900,000. W : R = 1 : 45.

October 8. She again entered hospital and for the first time came under my care. Her health was fairly good all summer, till about a week ago, when she had a sudden attack of vertigo while ironing. She fell to the floor and remained unconscious for about half an hour. Ever since she has suffered from headache. The next day she felt soreness over the epigastrium, aggravated by movement. Temp. 98.6°, pulse 108, resp. 20. Œdema has appeared in face, feet, and legs, varying in amount according to position. Thirst, anorexia, vomiting, dyspnoea on the slightest exertion, occasional attacks of epistaxis are now the chief symptoms. The dyspnoea is growing worse; there is no diarrhoea. The urine is orange-yellow in color, acid, sp. gr. 1015, contains 10 per cent. of albumen, but no sugar or casts. Splenic dulness 28 cm. (11 inches) in the oblique measurement. Hepatic dulness 15 cm. (6 inches). Blood, pale and watery-looking, hæmoglobin very pale, red corpuscles small. Red corpuscles per c. mm. 1,070,000. W : R = 1 : 10. After this she had repeated attacks of epistaxis and diarrhoea; the dyspnoea and œdema became rapidly worse, till at last she could not lie down at all and could get a few snatches of sleep only when in the knee-elbow position or propped up in a chair. During the two days immediately preceding labor, the attacks of epistaxis were frequent and uncontrollable, continuing for a couple of hours and then suddenly stopping. She grew so weak and faint that her condition became alarming, and it was with great difficulty that she was removed to the University Maternity Hospital. Soon after her arrival there slight labor pains began; in about three hours the liquor amnii came away and with it came the child (Oct. 29th). Not a drop of blood was to be seen. Frictions were applied to the fundus and after an hour and a half the placenta was carefully pressed off. Not a drop of blood was lost either then or afterward. Involution was excellent; the lochia were scant and slimy, without a tinge of blood, and ceased in a couple of days. Some hard scybalous masses gave her trouble for a few days. Her appetite was ravenous and could scarcely be controlled. A thin, watery fluid could be squeezed from the breasts, but there was never any tension or flow of milk. She convalesced rapidly and was discharged from hospital on the twelfth day.

Child. A female, born on the 214th day from the cessation of menstruation; weight, 4½ pounds; length, 18½ inches; length of cord, 20 inches. Apparently strong, slept well, nursed vigorously from a healthy breast, and thrived nicely for the first day. The following morning, however, the mother clandestinely put the child to her own breast. It sickened at once; in a few hours a purpuric rash appeared on its face and spread slowly over its back and chest; it vomited and purged and in spite of every care died on the fourth day.

Blood two hours after birth of the child. *Mother*, red corpuscles per c. mm. 990,000; W:R = 1:4. *Child*, red corpuscles per c. mm. 5,210,000; W:R = 1:175. At the end of the third day another count was made. *Mother*, red corpuscles per c. mm. 1,100,000; W:R = 1:20. *Child*, red corpuscles per c. mm. 5,000,000; W:R = 1:150.

On the day of her discharge from the hospital the count showed, red corpuscles per c. mm. 1,900,000; W:R = 1:35.

The *placenta* was sent for examination to Dr. W. G. Johnston, Demonstrator of Pathology in McGill University; the following is his report:

Placenta, eighteen hours after delivery, was of normal size. Nothing special in its appearance. Blood in sinuses looked thin, pale, and watery; that in placental vessels only slightly clotted, in most places quite fluid and of a dark rich color. With the hæmatocytometer (Zeiss-Thoma), *placental vein: trunk*, red corpuscles per c. mm. 4,610,000, white 26,000; W:R = 1:173. *Branch*, red corpuscles, per c. mm. 4,600,000, white 36,000; W:R = 1:128. *Placental artery*, red corpuscles per c. mm. 5,410,000, white 20,000; W:R = 1:270. *Placental sinuses*, red corpuscles per c. mm. 950,000, white 263,000; W:R = 1:3.6 nearly.

NOTE.—The average of three counts was taken—the maximum and minimum were very near the average—no marked difference in any count; difference was under five per cent., which is the error allowed by this method. Hæmoglobin not estimated.

Microscopical examination of blood showed some nucleated red cells in samples from the *artery and vein*, but not in abnormal number. Nothing especial in the white cells on examination by Ehrlich's method of fixing and staining. In the *sinuses* a large number of small pale cells were found, highly refracting and difficult to distinguish from leucocytes. They were over one-tenth the number of red cells. In estimating the number of white cells, only those were counted which were obviously of that nature—doubtful cells were not included in either count—nucleated cells were not specially numerous in the blood.

Autopsy upon the infant, ten hours after death. Body fairly well nourished, numerous petechial spots about face, thighs, and neck, otherwise nothing of note externally. Thymus and thyroid normal, organs all normal, spleen not enlarged, Malpighian corpuscles distinct, but not enlarged. Blood was fluid and dark colored—nothing abnormal on microscopical examination. Bone-marrow red and abundant everywhere, also normal microscopically. Further careful microscopical examination of the organs showed that no collections of leucocytes existed, and that the thymus, thyroid, and spleen were normal.

After her discharge from the Maternity Hospital, Mrs. S. enjoyed tolerably good health, her color improved, the dyspnœa and œdema disappeared, and she gradually resumed her household duties. The menses appeared in December and returned regularly for a few months; and for the first time in her life the flow was profuse and bright red. They last appeared on April 28, 1887, shortly after which she again became pregnant. A little blood was occasionally vomited when the morning sickness was specially severe. The *splenic tumor* began at once to enlarge, just as it did when she was last pregnant.

July 12. Oblique line of splenic dulness 20.5 cm. (8 inches), and edge of spleen within 9 cm. (3½ inches) of the umbilicus. Downward in the axillary line, the dulness extends 20 cm. (8 inches) reaching the

crest of the ilium. No increase in hepatic dulness. *Blood*, red corpuscles per c. mm. 1,406,000; W : R = 1 : 20.

August 18. Looks more pale and puffy, splenic dulness about the same. *Blood*: red corpuscles per c. mm. 1,373,000; W : R = 1 : 3. Since the last count the red cells have not diminished very much, but the white cells have enormously increased.

Family of Mrs. S.: Grandmother, mother, and brother have suffered from symptoms pointing probably to leukæmia.

Walter, æt. fifteen, clerk in an office, is in poor health, feels languid and dull, and is losing flesh; slight splenic enlargement. July 13, 1887, red corpuscles per c. mm. 3,355,000; W : R = 1 : 200. August 18th, red corpuscles per c. mm. 3,240,000; W : R = 1 : 275.

Arthur, æt. fourteen, July 13, 1887, red corpuscles per c. mm. 4,725,000; W : R = 1 : 350.

Lydia, æt. eleven, July 13, 1887, red corpuscles per c. mm. 4,795,000; W : R = 1 : 350.

Louisa, æt. eight, was treated for leukæmia in Montreal General Hospital from October 5, to December 12, 1885. Splenic dulness then extended two inches below the costal margin, and stretched over toward the umbilicus. She is now in poor health, very puffy in cheeks and eyes, with spleen considerably enlarged, both laterally and vertically. October 12, 1885, red corpuscles per c. mm. 1,912,000; W : R = 1 : 15. December 2, red corpuscles per c. mm. 3,576,000; W : R = 1 : 16. July 13, 1887, red corpuscles per c. mm. 4,220,000; W : R = 1 : 300. August 18, 1887, red corpuscles per c. mm. 3,183,000; W : R = 1 : 240.

Charles, æt. six, July 13, 1887, red corpuscles per c. mm. 4,525,000; W : R = 1 : 350.

Freddy died December 26, 1885, æt. six months; was apparently pretty well until the mother's milk failed, a few days before her admission to the Montreal General Hospital (September 15, 1885). On examination at the hospital he was found to be leukæmic, with enlarged spleen, diminution in red and increase in white corpuscles. Unfortunately, the record of his blood count has been mislaid. He died three months afterward from abscess. No autopsy was held.

The chief points of interest in this case seem to be

1. The *family history*: Grandmother, mother, and brother of the patient have suffered from symptoms probably pointing to leukæmia. Two of her own children have had well-marked leukæmia, another is now in ill health with diminished red cells and enlarged spleen. None of her children reaches the standard of 5,000,000 per c. mm. All have had attacks of jaundice. Does heredity play any part in this case?

2. *Splenic enlargement* was first noticed by the patient at the *beginning* of her sixth pregnancy.

3. *Splenic and hepatic enlargement* always occur during pregnancy, and are generally accompanied by tenderness.

4. The *blood*: the progressively enormous increase of white cells with a decrease of red as pregnancy advances.

5. *Absence of uterine hemorrhage* during labor and the puerperal period; labor was dry and bloodless and the lochia untinged with red.

6. Rapid subsidence of œdema and dyspnœa after the termination of labor, together with the rapid increase in the number of red, and decrease in the number of white corpuscles.

7. The *extent* of recovery, so as to be able to resume household duties, and the remarkably chronic course of the disease in this case.

8. The *recurrence of pregnancy*—now the third time since splenic enlargement was first noticed.

9. Remarkable difference between the blood of the mother and child, and in the placental vessels and sinuses.

10. The disastrous effect upon the child of nursing from its own mother's breast—purpura, vomiting, purging, and death.