and second sounds; but it is noteworthy that in such cases this sound frequently occurs only at the commencement of inspiration, when the ventricles must feel the negative intrathoracic pressure and tend to become more distended than at other periods of respiration, and it is reasonable to suppose that their muscular tone has been lowered by the fever, rendering them unable to cope with the distending forces.

Of the importance of this cardiac physical sign as regards prognosis, only those who have observed it carefully during long periods are perhaps able to express a definite opinion. That importance must, of course, depend largely upon the nature of the heart-failure with which it is associated.

In cases of hypertrophy of the heart without valvular disease the writer has seen the *bruit de galop* appear and disappear with little apparent alteration of general condition. On the other hand, it has been persistent for weeks and months until death has occurred, and in one instance was the only abnormal sign present where sudden death took place in a patient who was not considered seriously ill.

The fact that the *bruit de galop* may be sometimes transitory and of no great serious import, at other times permanent and apparently as much to be feared as the diastolic aortic murmurs, should, I think, give it an interesting if not an important place among abnormal cardiac sounds.

THREE CASES OF ESSENTIAL ANÆMIA IN ONE FAMILY— FATHER AND TWO DAUGHTERS.

BY WHARTON SINKLER, M.D.,

AND

AUGUSTUS A. ESHNER, M.D.,
OF PHILADELPHIA.

THE occurrence of a profound degree of anæmia in three members of one family—father and two daughters—with the development of symptoms of posterior spinal sclerosis and a fatal termination in one of the cases, would seem to be sufficient justification for detailing at length the history of this interesting group.

J. S., sixteen years old, who had for a time been a salesgirl in a store, presented herself at the Infirmary for Nervous Diseases, in the service of Dr. Wharton Sinkler, on October 28, 1895, when the following history was obtained:

Her father had died of locomotor ataxia and pernicious anæmia at the age of forty-five years. His history is hereto appended. The mother was living, about forty-five years of age, and was said to be also pallid and weak. On examination at a subsequent time she was found to be

a young-looking woman, whose blood presented no abnormality. A younger brother was well. He proved to be a bright little fellow of five or six years of age, and his blood also showed no deviation from the normal. An older sister had had "weak spells," and had been under treatment at the Infirmary on account of pallor. A report of her illness is included in this paper. The patient herself had never been strong. She had had no attack of acute rheumatism when about five years old, and was at this time in bed for about two weeks. Menstruation first appeared at the age of fourteen years, but recurred with much irregularity, at intervals of four or five months. This function was attended with pain, but the discharge was pale—from its description almost serous—and scanty in amount. The last period had been five or six months previously. The girl had been accustomed to drinking two cups of tea and one cup of coffee daily. As a matter of fact, she admitted that she was unable to obtain an adequate amount, not only of nutritious food, but even of the bare necessities of life, and had been eating but little food.

According to the girl's statement, she had always been pale, although she had at no time observed an acute development or exacerbation. The degree of pallor, however, varied from time to time, somewhat in accordance with her nutritive supply. She improved upon a dietary of meat and milk, and grew worse when deprived of these. She had suffered considerable deprivation for a period of four or five years covering the illness, and the time subsequent to the death of her father. She complained of excessive palpitation of the heart on exertion or excitement, with presternal pain. A sense of pain, weakness, and soreness was referred to the lumbar region of the spine. The girl always felt tired and was easily fatigued. She had noted staggering in walking and also in greater degree in standing. At times the fingers felt numb, and painful cramps appeared in the calves of the legs. She suffered from recurrent attacks of what she called "biliousness," characterized by impairment of appetite, coating of tongue, disagreeable and bitter taste, nausea, and pyrosis. Vomiting occurred rarely. There was moderate cough, with considerable expectoration, and the sputum was from time to time admixed with dark, clotted blood. The patient had had an attack of diarrhoea two or three weeks before coming under observation, but this had not been repeated. There was no further history of hemorrhage or other abnormal discharge; and there had never been observed subcutaneous extravasations of blood. A pin-prick would be followed by scanty escape of pale blood, almost serous. There was at various times a good deal of abdominal colic. The bowels were, as a rule, obstinately constipated. There had been loss of flesh to the extent of nineteen pounds in a period of less than two months, although a gain of eleven pounds had been effected during the preceding summer in the course of a three weeks' stay in the country. There was shortness of breath on exertion and also frequent sighing. Chills occurred at irregular intervals—sometimes two or three in a night, at other times none at all—during a period of six months. These were often followed by a sense of overheating, with dyspnoea at times so intense as to cause a fear of death. There was no undue sweating. The feet did not swell. There was increased frequency of micturition both by day and by night, and the patient thought the amount of urine increased. For a long time there had been frontal headache, together with pain referred to the eyes.

Although the eyes were used but little, there was a feeling of weakness referred to them. Dr. A. G. Thomson examined the eyes and reported the absence of any lesion of the fundus. There was some vertigo. Sleep was poor, the patient being restless and wakeful. So far as the girl knew, she had always lived in dry, well-ventilated houses, and had resided in some six or seven different dwellings during the preceding seven years.

On inspection the girl appeared slender and rather small of stature, though not appreciably emaciated. Her complexion, however, was most striking and pronounced. The color was pale yellowish-brown, almost ashen, while the conjunctivæ were clear and white. The gait was fairly steady, withal a little debilitated. Stature was perfectly steady, both with open and with closed eyes. The knee-jerks were active, extensive, and ready; ankle-clonus could not be elicited. The muscle-jerks in the upper extremities were active and vigorous. The action of the heart was rhythmic; the first sound was rather dull and heavy; at the left base a blowing systolic murmur could be heard over a limited area; the second sound of the heart was distinct; a hum could be heard in the neck from the gentle pressure of the stethoscope. The thyroid gland was full, but scarcely enlarged.

The blood was examined by Dr. J. R. Hunt, who made the following report:

The red corpuscles present much variation in size. Both macrocytes and microcytes are to be seen. Some cells show marked distortion of shape—poikilocytosis. The color of the corpuscles generally is pale; some of the smaller forms are dark tinted. The blood macroscopically is watery in consistency and the drop presents pale and red areas. Amoeboid movement and a nucleated red corpuscle are observed (?). The erythrocytes number 3,000,000 to the cubic millimetre; the hæmoglobin-estimation is 20 per cent.

Tincture of ferric chloride, ten drops three times a day, was prescribed, and a few days later Bland's pill of iron sulphate and potassium carbonate, each two and a half grains, was given.

The patient was admitted to the Infirmary on November 9, 1895, and was ordered Fowler's solution of potassium arsenite, five drops three times a day, to be increased at the rate of one drop three times a day. Full diet, including milk, beef juice, and eggs, was also ordered. Besides, gentle massage daily and general faradization were directed. Examination of the blood on December 17, 1895, showed the number of red corpuscles to be 3,936,000 in the cubic millimetre and the hæmoglobin-estimation 39 per cent. The patient improved markedly in color and flesh, but complained often of abdominal pain. She was discharged on January 28, 1896, looking quite like a different person. Her weight had increased from 86 to 94 pounds, and her color was bright and good. Unfortunately the last blood-reports have been mislaid, so that they cannot be cited, but judging from the general appearance of the patient the state of the blood could not have been far from normal.

The sister of the patient whose history has just been detailed, M. S., presented herself at the Infirmary on February 18, 1891, in the service of Dr. Morris J. Lewis, complaining of vertigo, referred more particularly to one side—i. e., the right eye—together with a nervous sensation in the right ear. The erect posture induced nausea, with a feeling of weakness, so that the patient was unable to continue standing. The girl

ate very little—rarely any breakfast. She was constipated and suffered from shortness of breath.

The patient dated all her trouble from an attack of influenza from which she had suffered nearly two months earlier. Menstruation was regular; the color of the flow was thought to be good; the discharge was sometimes profuse; the function was always attended with much pain; and there existed leucorrhœa. The breath was noted to be peculiarly cool. The heart was rapid in action and feeble in force. A hum was heard in the neck, as well as in the cardiac region, with a loud systolic murmur at the apex. The knee-jerk was normal on both sides. The patient presented an appearance of marked anæmia. The mucous membranes were very pale; the ears were waxy. Some fullness of the thyroid gland was appreciable. The skin presented a somewhat sallow appearance. There was slight pretibial œdema. There was no tenderness over the superficial bones. The lips were purplish in hue. The nails were white and flat, without curve. A large, irregular bronzed spot was present on the left breast; and the areola was very dark. The patient was in the habit of eating a good deal of fried food, much bread, and little meat. She was given Fowler's solution, three drops, with tincture of ferric chloride, twenty drops, three times a day, and under this treatment improved greatly in color and general appearance.

S. S., the father of the two patients whose history has already been related, applied for treatment at the Infirmary for Nervous Diseases, in the service of Dr. Wharton Sinkler, on January 12, 1891. He was at the time forty-one years old, and a laborer in the pumping department of the Philadelphia Gas works. He stated that his mother had died after a third paralytic seizure, while his father was still living and well. Three sisters also were living and healthy; two brothers had died in childhood; and one sister had died, it was believed, in consequence of some digestive disorder. There were no other children than those already referred to in this report. The wife had miscarried thrice: once between the birth of the first and second children, and twice between the birth of the second and third. The man had had "typhoid pneumonia" at the age of sixteen years, and again when twenty-seven years old; and each time made a satisfactory recovery. Until two years before coming under observation, he had for eight years suffered from aggravated derangement of digestion, vomiting at least once and sometimes thrice daily, feeling well afterward, but suffering from pyrosis. In consequence he had learned to be careful in regard to food. He denied venereal infection; nor had he noted any cutaneous exanthem or suffered from sore throat or iritis. He smoked but seldom, although he chewed a good deal of tobacco. He used alcohol in moderation. About four years before presenting himself he had in wheeling a loaded barrow, which struck some object, felt as if something had given way in the small of the back. He had to be taken home and for a time was unable to straighten himself. He was put to bed and there remained for about two weeks, suffering no pain unless he moved his body, as in turning. The pain was distinctly localized to the small of the back. The patient seemed to recover perfectly and did harder work afterward than he had done previously.

The trouble for which the man presented himself had begun with a feeling of numbness in the legs about thirteen months before, in the sequence of mental depression due to loss of work; either coincidently

or shortly afterward, numbness appeared also in the finger tips. At about the same time he noticed that he staggered in walking, especially at night, and that he could not control the movements of his legs; but he had never fallen. After a while vertigo was noticed on stooping, with a feeling on the part of the patient as if he were about to pitch forward. At times there was difficulty in buttoning the clothes and in picking up small objects. Walking upstairs occasioned great weakness and exhaustion. The patient had a feeling as if a band were fastened around the waist and the knee. There were no gastric crises and no pain in any part of the body. For a short time the patient had a feeling as if he were walking upon cotton. His general health was good. Considerable complaint was made of frontal headache. The memory was retentive. The eyesight had been failing for a year or more, the greatest trouble in the use of the eyes being experienced in reading at night; there had never been diplopia. The patient had for a period of nearly two months been as pale as when he first presented himself. The appetite was good. There was occasional flatulence after eating. Vomiting occurred only infrequently. The bowels were very constive. The functions of the sphincters were underanged. The patient was easily made short of breath. There was no palpitation of the heart. The feet had not been swollen except for about a week before the patient entered the Infirmary, when they, together with the face, became noticeably swollen. He arose usually once at night to urinate, and had so arisen for some time before his immediate trouble had begun. Sleep was not otherwise disturbed. Sexual desire had been lost for six months, and sexual power was also diminished. There had never been lancinating pains.

The patient was pale, presenting a somewhat muddy tint and waxy aspect. The mucous membranes also were very pale. There appeared to be little blood beneath the finger nails. The pupils were equal and slightly contracted and reacted well to light and in accommodation. There was no appreciable ocular palsy. Both optic disks were exceedingly white; the arteries and veins were intensely pale, the latter pulsating actively. The eyes were hyperopic and astigmatic. The tongue was protruded straight; its papillæ were poorly developed. The spleen was not enlarged. The pulse was quiet and regular, and the tension slightly increased. The first sound of the heart was blurred at the apex, but no distinct murmur could be heard. The gait was somewhat ataxic. Station was good until the eyes were closed, when swaying became quite marked. The grasp of the hand was only fair, but equal upon the two sides. Biceps jerk, triceps-jerk, and muscular irritability were normal and equal in the two upper extremities. The points of the æsthesiometer were differentiated at a distance of half an inch on the dorsum of the hands. The sense of touch was not delayed. Tactile sensibility was impaired on the legs. A feeble cremasteric reflex could be elicited upon the right, but none upon the left. The abdominal reflex could not be developed. The plantar reflexes were diminished. The knee-jerks could not be elicited, even with reinforcement. On the dorsum of the foot the two points of the æsthesiometer could not be differentiated at a distance shorter than three inches. There was prompt response to the touch of the points. The spine was straight and free from tenderness on percussion. Pressure upon the bones occasioned no pain. The patient was directed to take twenty drops of tincture of ferric chloride and five drops of Fowler's solution thrice daily, and on February 11, 1891, he was

admitted to the hospital. The number of red corpuscles as determined at different counts by Dr. C. W. Burr was 2,350,000, 2,700,000, and 2,000,000 to the cubic millimetre, and the hæmoglobin-estimation 35 per cent., 27 per cent., and 30 per cent., respectively. The following additional observations of the state of the blood were made by Dr. Burr:

March 2, 1891. Red blood-corpuscles, 2,325,000; hæmoglobin, 35 per cent.

10th. Red blood-corpuscles, 4,125,000; hæmoglobin, 55 per cent.

17th. Red blood-corpuscles, 4,475,000; hæmoglobin, 60 per cent.

April 11th. Red blood corpuscles, 4,350,000; hæmoglobin, 80 per cent.

The note made on May 18, 1891, reads that the patient had returned to his heavy work in the gas works. He still had some girdle sense and tightness about the waist, but no shooting-pains. The numbness of the feet and soles persisted. The knee-jerks were absent. The station was good. There were no vesical or gastric symptoms. Strychnin sulphate, one thirtieth of a grain thrice daily, was now prescribed.

On September 30, 1891, the hæmoglobin-estimation was 80 per cent., the number of red blood-corpuscles 3,750,000. On January 28, 1892, the hæmoglobin-estimation had fallen to 30 per cent., and the number of red cells to 2,300,000, without poikilocytosis and without increase of colorless cells. It was noted that the red blood-corpuscles varied but little in size. No nucleated red cells were observed.

In February, 1892, the patient went to bed on account of his anæmia, and he remained there for four months. Then he resumed work for three weeks, after which he suffered from a dysenteric condition for three months. Then he worked for another month. For three weeks at this time he had been at home. His difficulty in walking had grown gradually and slowly worse. He had suffered pain in lying on the right side. He was unable to read without glasses, though he had at no time diplopia. Girdle-sense persisted. At times there was dyspnoea. There was almost total inability to button the clothing. Numbness was still present in hands and feet. There was no vertigo. Cramps in the legs were present every morning. The appetite was good, the bowels constipated. Sleep was good. At times the feet became swollen. The gait was very ataxic and the hands had now also become ataxic. There had never been tinnitus aurium. Knee-jerks, elbow-jerks, and chin-jerks could not be elicited. Common sensibility was normal in the hands and there was no wasting. At this time the appearance of the patient was less waxy than at earlier observations. A basic systolic murmur could be heard on auscultation of the heart. The pupils were equal and reactive to light and accommodation. Bland's pill, five grains, with Fowler's solution, three drops, was now given thrice daily. At the next examination of the blood the hæmoglobin-estimation was 55 per cent., and the red corpuscles had risen in number to 4,800,000 to the cubic millimetre.

The patient was readmitted to the hospital on November 4, 1892, in a markedly ataxic condition. His weight was 111½ pounds. There was no Argyll-Robertson pupil. The knee-jerks were still absent. The patient was put to bed and made a gradual gain in strength up to January 16, 1893, when he weighed 118½ pounds. On January 12th it was noted that the pupils reacted normally to light and in accommodation. There was now, however, partial atrophy of the optic disks, the more marked upon the left. The girdle-pain kept constantly ascending until

it reached about the level of the nipples. On January 17, 1893, the patient had a chill, the temperature rising to 102.8°, but coming down to normal in the course of three days. Suspension was being tried. Coincidentally it was found that the knee-jerks reappeared. The patient was discharged not improved on March 14, 1893, and died at his home on May 5th, in a "weak spell." An autopsy was held on May 8th, but the specimen of cord furnished for study was not in condition to permit of satisfactory histological examination.

The last case is of more than ordinary interest for several reasons. When the patient first came under observation he was regarded as a case of locomotor ataxia of somewhat irregular type. The absence of true fulgurating pains and of ocular symptoms showed, however, that it did not belong to the ordinary form of tabes. It seemed probable that the symptoms of disease of the posterior columns of the cord were due to the pernicious anæmia that was present, and this view was supported by the fact that when the patient's general condition markedly improved the tabetic symptoms all changed for the better. When the man was first treated in the hospital there was unusually rapid improvement in the state of the blood, and considerable increase in weight took place. At the same time the disorder of the muscular functions persisted. There were absence of the knee-jerks and unsteadiness in gait. The patient was, however, as stated in the notes, able to return to work and performed the duties of a laborer for several months. Another point of interest in the case is the fact that during the last period of hospital treatment after suspension, which was employed according to the method used in the treatment of locomotor ataxia, there was a return of the knee-jerks.

A number of cases presenting lesions of the spinal cord in conjunction with pernicious anæmia have been placed on record since Lichtheim¹ announced the results of his investigations upon this subject. Burr² has detailed seven cases, in only one of which was the cord found normal. He states that the only parts of the cord affected are the posterior columns, the lateral columns in and near the crossed pyramidal tracts, and occasionally the direct cerebellar tracts.

Many of the symptoms present in all three of the cases are suggestive of a gastro-intestinal origin for the anæmia, as the general condition, including the state of the blood, varied directly as the nutritive condition. Whether the spinal changes occasionally associated with profound degrees of anæmia—and symptoms of which were so prominent a feature of the fatal case detailed—are to be attributed directly to the anæmia or to some intoxicant perhaps equally responsible for the anæmia, has not yet been determined; yet it would appear that some such relationship must exist. It may reasonably be admitted, further, that so-called pernicious anæmia may result from a variety of causes in whose train blood destruction is in excess of blood regeneration.

¹ Congress für Innere Medicin, 1887.

² University Medical Magazine, April, 1895.