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ON

IDIOPATHIC ANÆMIA.

A REPORT OF THREE CASES, WITH REMARKS;

AND

AN ANALYSIS OF THE CASES HITHERTO PUBLISHED IN AMERICA.

BY

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Chief of the Medical Dispensary, Hospital University of Pennsylvania
Pathologist to the Presbyterian Hospital, etc.

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THREE CASES OF IDIOPATHIC ANÆMIA, WITH REMARKS; AND AN ANALYSIS OF THE CASES HITHERTO PUBLISHED IN AMERICA.

Read before the Philadelphia County Medical Society, February 25, 1885.

BY J. H. MUSSER, M. D.

Chief of the Medical Dispensary, Hospital University of Penna.; Pathologist to the Presbyterian Hospital, etc

IN addition to placing on record the three cases of idiopathic anæmia which it was the writer's good fortune to be able to study, the object of this paper is to call attention to the work that has been done on this disease by the medical profession in this country and Canada, and to arrange this work in compact form for the purpose of analysis and of comparison with the series of cases that have been recorded in other countries. By this means it is hoped the character and nature of the disease, as seen among us, may be more broadly and clearly defined. Furthermore, it seems that the work that has been done has not been sufficiently appreciated in other countries to deem it worthy of the notice of their authors. For, save in but a few instances, have they at any time referred to our countrymen's labors. It is hoped this subjoined collection of cases, therefore, will show that we are perfectly familiar with the disease, and keenly appreciate its obscure pathology and difficult treatment.

By idiopathic anæmia, it is to be understood, we mean that form of profound anæmia which develops independently of any organic lesions; which is generally "progressive," and too often "pernicious;" which is characterized by diminution in the number and changes in the appearances of the red corpuscles; by retinal and other hemorrhages; by fever at times; by the absence of emaciation; and the occurrence of extreme fatty degeneration of the heart, and which yields no sufficient evidence after death to explain the cause of the disease. Some authors would have us believe it is only a grave form of chlorosis, or a pseudo-leukæmia of the myelogenic variety, or a grave anæmia not to be distinguished from the secondary anæmias.

We are wanting the time to show the differences between these affections, and will only say we believe that idiopathic anæmia is as capable of distinction, clinically, from other anæmias, as is one

form of Bright's disease from another, and that, in the absence of proof that the bone-marrow changes are not secondary, it cannot be called pseudo-leukæmia. It cannot be compared, as Quincke would have us do, with uræmia or jaundice. There is something back of these symptoms, which is the disease. And, so with idiopathic anæmia; although the blood-changes and the resulting tissue-changes are allied in all fatal anæmias, yet back of these are circumstances and conditions which go to make up the different diseases. The application of these remarks are only temporary, for sooner or later, as our knowledge of the blood increases, the fundamental cause of idiopathic anæmia will be determined, and the expression idiopathic will be improper and eradicated. The following cases illustrate well this form of anæmia:—

Case I.*—Idiopathic anæmia; no organic cause; no emaciation; retinal hemorrhages; reduction of r. c.; analysis of blood and urine; fatty heart.

K. McC., fem., white, æt. 42, was born in Cumberland Co., Pa. She resided in this county until 16 years old; since then she lived in Philadelphia until her death, with the exception of a few months spent in Harrisburg, Pa. Previous to her marriage, which took place at 17, she led a life of ease; since then, however, although her duties were those of housekeeper only, she worked very hard. Her first husband lived eight years after their marriage; he died of chronic Bright's disease. After an interval of six months she re-married and has since lived with her husband. She became pregnant once only, by her first husband, but lost her child by premature labor; she never conceived thereafter.

Mrs McC. never suffered on account of deprivation of food or life's ordinary comforts; her last husband kept a saloon and was of somewhat dissolute habits, so that this latter period of her life had been one of care and anxiety; her habits, as far as can be ascertained, were good.

The father of our patient died of an acute illness; the mother is living at seventy-two and quite active; her brother and two sisters are likewise in good health; there has been no hereditary tendency to disease.

A woman of considerable personal beauty and fine physique, she never had been sick until the development of the present illness. It is true, in childhood she had the specific fevers incident to that period, but the attacks were light and never followed by serious sequelæ. She never had malaria, and no knowledge of venereal disorder could be obtained. Menstruation had always been regular, though scanty and painful, and she believed the "change" had taken place one year previous to this note, attributing a parasthæsia to that cause. Within the year she menstruated twice, the first time seven months ago, the last time four months ago; the latter period was attended by a rather profuse flow.

The cause of the breakdown in Mrs. McC.'s health was attributed to

* Abstract in Case in Trans. Path. Soc. Phila., xi, p. 66.

shocks which occurred five years prior to her death. Her husband, while under the influence of liquor, abused her frequently, and once was about to kill her but for timely interference by friends. For many weeks afterwards she suffered the highest degree of mental excitement, so extreme at times, it was feared insanity would ensue. Thenceforth her health was poor, and gradually the anæmia developed.

The course of the disease can, it appears, be divided into three stages or periods. The first period continued from the time of the shock until about one year previous to the time she came under my care, or Jan., 1881; the second period continued from Jan., 1881, until about Dec., 1881; she then became so ill as to be unable to leave her bed, and came under my observation in Jan., 1882; this third period was of seven weeks duration, and terminated by her death, Jan. 19 of the latter year.

The first period was marked by ill-defined poor health. She knew that she was losing ground, but could not tell how. She did not emaciate, but weakened. She lost her hair, and it changed from a brown color to an iron-gray.

The symptoms of the second period were more defined. They were, change of color, of disposition, of strength, etc. The complexion—originally clear, with rosy cheeks—became sickly and dirty yellow. She became irritable, fretful and morose, contrasting with her previous good disposition. In the early part of this period, she had an attack of daily intermitting fever, with headache, lasting ten days. She lost her appetite; or if present, it was quite capricious. In February and March (1881), attacks of vertigo, faintness and vomiting occurred twice or thrice daily; consciousness was never lost in them; they occurred after exertion. Failure in strength became more and more pronounced towards the close of the year; inaptitude for exertion, either mental or physical, and a growing heedlessness of friends and surroundings, became marked. From the first of this period, numbness and tingling, and an increased sense of weight in the limbs, were noticeable and distressing.

The third period of the illness of our patient was marked by extreme exhaustion. On account of sheer prostration, of palpitation of the heart, and extreme dyspnœa on exertion, she was obliged to take her bed.

In addition to the preceding history, the following notes of her condition were gathered during the three weeks of my attendance:—

External Appearances.—Hair soft, thin, iron-gray. Eyelashes and eyes brown; eyelids puffy; conjunctiva pearl-white color; subconjunctival fat increased, especially in inner canthus, and quite icterode in hue—at first sight, considered to be due to bile pigment. Face not emaciated; appearance strikingly ghastly and wild; color, dirty yellow or earthy. Lips pale. Appearance of extreme bloodlessness of face and hands. The latter not pigmented. Finger-nails grew rapidly, but were brittle, and had white spots on them. Skin warm and oily; that of the hands wrinkled, and in the palms hard. Ankles and feet slightly œdematous. Body not emaci-

ated, though not as plump as in early years. Muscles flabby. Mammary glands well-developed.

General Symptoms.—Prostration; general aching, especially aching of the muscles of the neck; frequently said, "Feels if head were separated from body." Marked tenderness on pressure of ribs and lower part of sternum. At nights, a moderately profuse perspiration occured. Temperature recorded usually once daily, often morning and evening; the average was 98⅕° for the A. M., and 99⅘° for the P. M., temperature. Towards the end of life, coldness was complained of bitterly, and the extremities were quite cold. Extreme restlessness was observed the last days of patient's illness, especially tossing of arms and rolling of head.

Cerebro-spinal Symptoms and Alterations of Special Senses.—Mental faculties clear, but acts sluggish. Slow responses made to questions, and the recalling of events almost impossible. Towards the close of life, readily lost the thread of any discourse, and mind wandered. The delirium was low and muttering, and attended with emotional displays; at times crying, then laughing gaily. The delirium first developed acutely six days before death, preceded by an attack of semi-consciousness, and accompanied by thick, indistinct speech. The slight loss of consciousness was of four hours' duration, and was followed by headache. Three days preceding death, an attack of aphasia of a few hours' duration occurred. The last day of her illness, stupor was marked. Noises in the head, throbbing sensations, and ringing of the ears, were distressing for many weeks. She first complained of disturbed vision, January 2. Muscæ volitante were constant, feeble and double vision marked. An ophthalmoscopic examination, January 11, 1882, by Dr. G. A. Piersol, showed the following:—

Right Eye: Disc pale, its inner and lower margin indistinct; entire retina slightly clouded and hazy; vessels of eyeground abnormally pale; arteries on disc and throughout their course reduced in size; veins engorged, but of pale color; near disc, to inner and lower side, several small hemorrhagic spots, bright red. Refraction hypermetropic; media clear.

Left Eye: Disc pale, with some haziness, especially on nasal side; slight veil over entire fundus; vessels abnormally pale, arteries attenuated, veins congested; numerous hemorrhages in form of small streaks along course of vessels to nasal side of disc; large, yellowish white, irregular patch, with several small hemorrhagic patches about its margins. Refraction hypermetropic; media clear.

Gastro-Intestinal Symptoms.—Tongue generally furred, teeth good, mouth dry and sticky or pasty; a thick viscid saliva constantly discharged. No hemorrhages from gums, but during the three days preceding death sordes collected on teeth, tongue and lips. Mucous membrane of mouth pale; no bronze patches. Pain and tenderness in the epigastrium, with pulsation of abdominal aorta. No nausea or vomiting. Loss of appetite. Pain and some slight flatulency after tasting food. Bowels always constipated. Spleen and liver normal in size. Abdomen not scaphoid.

Pulmonary Symptoms.—Dyspnœa, which was an early symptom, became agonizing; at first on exertion, it became marked in the recumbent position also. Attacks of dyspnœa occurred frequently. Sighing was constant,

but Stokes-Chayne respiration never present. The respirations the first week were twenty-five to thirty per minute; the last two days they were forty, due to an œdema of the lungs, which gave the usual physical signs; otherwise the lungs were normal.

Circulatory Symptoms.—Cardiac palpitation on the slightest exertion or emotional disturbance, and attacks of syncope were frequently complained of. The pulsations of the large vessels were annoying. On physical examination, apex beat of heart in normal position, scarcely visible impulse, or impulse detected by palpation. Carotids throb visibly in neck; veins pulsate; aorta at sternal notch readily felt. No cardiac or vascular thrill. No increased area of cardiac dulness. At apex of heart, at pulmonary and aortic orifices, loud systolic murmurs. The murmurs at aortic cartilage heard also in carotids. Loud venous hum in jugulars. Pulse small and compressible, not over 80, until day preceding death. No hemorrhages were known to take place in any part of body save retina.

Examination of Blood.—Secured with difficulty by puncture, pale and liquid in color. On microscopical examination, red corpuscles diminished in number; no rouleaux formed; innumerable small corpuscles dark in color and appearing like oil globules (microcytes); most of the red cells are flat, some float on their edge; size varies from the microcyte to the normal red cell. No large or nucleated corpuscles seen. With Gower's hæmocytometer 715,000 red and 15,000 white cells were found per c. m. Color of cells paler than normal.

Genito-Urinary Symptoms.—None were noticed save the passage of an abundance of urine, and, the last four days, of its passage involuntarily. Urine of Jan. 4, analyzed by my friend, Dr. John Marshall:

Sp. gr., at 15° C., ...	1014.
Urea, ...	2·3 per cent.
Sodium Chloride, . . .	·12 per cent.
Phosphoric Acid, . . .	·13 per cent.
Uric Acid, ...	·087 per cent.
No Albumen or Sugar.	

Urine, Jan. 6, pale red color, normal odor, acid, sp. gr. 1010. Scarcely any sediment; on microscopical examination contained pus-corpuscles and granular matter.

AUTOPSY, 16 hours after death, assisted by W. E. Hughes, M. D.

Body of a large-framed woman. Not much, if any emaciation; panniculus adiposis well developed over abdomen. Skin extremely pale, with earthy hue of face. Petechiæ on back of hands and upper surface of feet. No postmortem staining. Rigor mortis well marked. No enlarged superficial glands; scar of an old suppurating one in groin. No cadaveric odor.

Brain.—Not examined.

On section, muscles normal color. Large layer of bright yellow fat over the abdomen. Abdominal organs occupied normal relations. The omentum covered and contained its usual amount of fat. The small intestines were much contracted; the colon filled with fæces. The stomach occupied its normal position and contained gas. The mesenteric glands were some-

what enlarged. The thoracic cartilages were not ossified, and on breaking the sternum a dark red grumous fluid exuded. The right lung was bound down at the apex by adhesions, while in the lower part of the pleural sac there was one-half pint of serum. A calcareous mass was felt in the apex of the left lung. Both lungs were œdematous.

Sympathetic System of Nerves.—On account of the bloodlessness of the organs and the small amount of discharges, the nerves were very distinctly seen—both filaments and ganglia. On microscopical section, the ganglia were normal, a slightly granular appearance of the nerve cells and some pigmentation of them and the nerve fibres alone, being found.

Heart and Blood-Vessels.—Pericardium healthy; sac contained usual amount of serum. Underneath parietal and visceral layer, small ecchymoses. In pulmonary vein, black clot; in aorta and pulmonary artery a soft yellow clot; in the venæ cavæ, soft red-brown clots with black specks or granules intermingled. The heart was pale, soft, flabby, extremely fatty. The degeneration was more marked on the right side; along the septa and the vessels there were areas of capillary injection. The right auricular wall was very thin, strands of muscular fibres being replaced by fat, while other strands seemed to be destroyed, so that parts of the wall were transparent, connective tissue forming the limiting membrane. The left side was similarly affected, but not in so intense a degree, there being only a diffuse yellowish discoloration. The papillary muscles of both sides were markedly changed; the fatty change was recognized by innumerable yellow dots. The right heart contained soft, semi-fluid, red-blood clots; the left, soft yellow clots. The aorta was a centimetre in width at the heart, and at the cœliac axis admitted the little finger only.

Organs of Abdomen.—Liver, enlarged in both lobes, with thickened edges; innumerable small ecchymoses underneath the capsule, especially along edges; fatty mottling of surface; on section, the organ was bloodless, the veins gaping and empty, markedly fatty to the naked eye—corroborated by microscopical examination.

Spleen, normal or but slightly enlarged; surface rough; on section, dark brown and hard. *Pancreas* apparently normal.

Stomach, slightly dilated, filled with mucus and liquid food; some mammillations and numerous submucous extravasations; pyloric orifice much contracted. *Supra-renal* capsules normal; on microscopical examination, a slight increase of interstitial tissue with lymphoid infiltration was seen; vessels engorged with blood; cells pigmented and slightly infiltrated with fat.

Diaphragm, very thin, and to the naked eye fatty; in parts, apparent streaks of fatty degenerated fasciculi were observed.

Genito-Urinary Organs.—Uterus and *ovaries* normal; left *kidney* enlarged, removed readily on account of the absence of fat around it; capsule adherent and on section cortical portion pale yellow or granular, and of narrow width; pyramidal portions very pale or yellow white; right kidney more congested than the left; otherwise appearance about the same; pelves of both kidneys filled with fat; bladder full; mucous membrane pale.

Bone Marrow.—Some removed from radius and sternum; the marrow of the radius was pale yellow in color, and on microscopical examination

revealed the appearances of healthy adult marrow ; the same may be said of the sternal marrow.

Blood.—Twenty-four hours standing in a beaker did not cause clotting ; in the bottom of the beaker a thin red film was seen, of coagulated matter ; microscopical examination revealed the same changes found during life. Chemical examination by Dr. John Marshall, Demonstrator of Chemistry, etc., University of Penna. With the record of the examination is added the results of the examination of the blood of healthy females for comparison. It will be seen there is a diminution of the amount of albumen in our case, there being 11 parts in the 1000 less than in health. Inorganic salts including iron exist to the amount of 7·15 parts in 1000 in health ; fatty matter, extractives and salts are represented by 9·01 parts per 1000 ; deducting the former from the latter figure, leaves 1·86 parts to represent the amount of fats and extractives. Our analysis shows an increase of these constituents to 2·18 parts. An increase is also seen in the inorganic salts ; salts and iron equal 7·15 parts, iron equal ·54 parts—the remainder, 6·60 parts, equals the amount of salts per 1000 in health ; an increase of ·64 parts is seen in these constituents, therefore (7·24 — 6·60 = ·64). As would be expected, the greatest change is in the amount of iron ; analyses show that ·54 parts in 1000 represents the amount of iron in the normal blood on an average. Dr. Marshall found but ·18+ parts in this case, or a reduction of two-thirds. The fibrin in our case was increased, a circumstance contrary to what would be expected or had been reported. A study of the many tables that Coupland presents in his admirable lecture shows that the amount of this constituent is an extremely variable factor.

ANALYSIS OF BLOOD.

Female, Idiopathic Anæmia. *Dr. John Marshall.* In 1000 parts.		Female, Healthy. *Becquerel and Rodier* (modified). In 1000 parts.	
Water,	800·1950	Water,	791·10
Fibrin,	4 9600	Fibrin,	2·20
Albumen.	59 7000	Albumen,	70·50
Inorganic Salts,	7·2410	Extractive Matter, Fatty Matter, Salts, including Iron,	9·01
Iron,	·1871		
Fats and Extractives,	2·1800		
Blood-Corpuscles,	125·5369	Blood-Corpuscles,	127·00

CASE II —Idiopathic anæmia; partial recovery; relapse; subsequent cure.*

Nov. 11, 1880. T. L., æt. 41, born in Pennsylvania, resides in Clearfield Co., Pa.; occupation, carpenter, past ten years; in winter engaged as lumberman; married; three healthy children; habits very good; has worked hard since a young man, through storm and in sunshine ; has had more than the average care and trouble falling to man ; never had venereal disease, and no venereal excess.

Mother died of cancer of the uterus ; father living and healthy ; patient one of ten children living ; the sisters, four in number, are in delicate health,

* Ward notes of writer as Med. Registrar; case under Prof. Pepper's care in Univ. Hospital.

others healthy; otherwise family history not definite, but believes there is no hereditary disease, either on the paternal or the maternal side.

When young was considered in delicate health, "having some kind of a scrofula." When twenty-one, and from then to twenty-five, was stout and hearty. Ever since then has been more or less delicate. Had measles. Twelve or fourteen years ago had an attack of dyspepsia; became debilitated and very miserable, remaining so the entire winter, during which he had an attack of pleurisy. For six or seven years was in fair health, when he had a similar dyspeptic attack; since then has been having more or less dyspepsia. The present trouble he dates from the harvest season of 1879. There was no exciting cause, but from that time became weaker and miserable, losing power to work and all ambition. Felt unable to work, yet continued at it until February; then he was taken ill, and confined to his house for two months. He lost his natural complexion, pain in the epigastrium and about the heart annoyed him, vomiting occurred at times, also diarrhœa with yellow stools with white curd in them. The diarrhœa and the epigastric pains were the first symptoms; in addition, lost flesh and strength—flesh rapidly. Appetite was lost. Throughout the summer and fall, until admission, suffered from pain at the heart, especially on exertion, with fluttering; at variable times, nauseâ or pain in the stomach, indigestion, a changeable, but generally poor appetite, and irregular bowels; debility also continued; had not gained flesh since the attack in February.

At present his condition is as follows:—

Considerably emaciated; skin muddy hue, soft and moist; conjunctiva pale; sclerotics not pearly white, but with a yellowish hue; hands pale, bloodless; mucous membrane of the mouth, the lips and the tongue very pale; hair and beard fully developed, black; eyes light brown; no tuberculous or scrofulous appearance.

Mental faculties normal; vision normal; when heart palpitates, a blowing sound is heard in the left ear, synchronous with the heart-beat; special senses otherwise normal.

Tongue pale, flabby, marked by the teeth, some papillæ prominent, no coating; in the morning, throat parched; appetite poor; no increased thirst; when hungry, or prior to meal-time, an empty sensation in the stomach, amounting at times to nausea. After eating, at times, weight and fulness in the epigastrium, flatulence, some slight regurgitation of food—not to mouth—but to a point behind notch of sternum, relieved by swallowing; this has been a constant and annoying symptom. Bowels now are regular and of a natural color. Suffers from pain in the middle of the sternum at the fourth rib, flatulence seems to increase it, exertion causing palpitation increases it; at times the pain radiates towards the axilla—more towards the left—extending on that side down the arm, not as a pain, but as a dumb-aching sensation; the left pectoral is sore to pressure at times.

The cardiac impulse is seen in the fourth interspace, at the nipple, and in the fifth, 1½ inches inside the nipple line. A distinct epigastric impulse is seen; area of cardiac dulness slightly increased. Full inspiration diminishes the area of dulness. Heart beating 120; pulse weak, compressible, not full. When admitted, at the first right rib, and in the first interspace, a

systolic murmur was heard, transmitted into the vessels; since the heart has been slowed by digitalis, a slight systolic low-pitched murmur is heard at the third rib, diminishing, yet heard at the apex, heard also louder at the aortic cartilage, louder and higher-pitched at the head of the first rib. It is also heard at the pulmonary valve, but less strong. The murmur is also transmitted in the vessels of the neck louder right than left, and in the abdominal aorta. On the right side a loud venous murmur is heard; on the left it is not so distinct. Similar murmurs are heard also in the iliac vein. Stomach dilated, apparently pressing upward. At the right edge of ribs, between median line and ribs, a small mass yielding dulness, noticed. Urine had a slight trace of albumen, otherwise normal.

Nov. 20.—Urine contained a trace of albumen when admitted, but now free from it. No abnormal sediments.

Blood is thin and pale; enumeration of blood-corpuscles shows 2,210,000 red cells to the cubic millimetre and 1 white to 147 red ones.

Improvement was marked under treatment by rest, careful diet and tonics. He left the hospital an improved, but not cured, patient.

Re-entered hospital March 3, 1881.

During interval, his condition as follows: First two months, he was weak and very tired; could not digest food; lost flesh.

He then began to improve, and ever since has been gaining strength slightly. Before the last admission, for some time had slight pain about heart, with palpitation, especially on exertion.

When admitted: Much paler and rather more sallow than when discharged, mucous membranes very pale, sclerotics pearly, conjunctivæ very pale, extremities bloodless. Does not complain of cold extremities. Fingers not clubbed. Slight puffiness of eyelids, and œdema of ankles at night. Appetite fair, tongue slightly coated, very pale; digestion very good; since discharge, looseness of bowels, but no diarrhœa. Stools thin, light clay-colored.

Murmurs in heart and veins very distinct; more so than when previously in house. Dyspnœa and palpitation on exertion; pulse 108, small, compressible.

Special senses good. Slight failure of memory. Loss of energy and of strength quite well-marked.

No hemorrhages. Examination of blood shows 1,000,000 red cells, and a proportion of 1 white to 40 red.

No enlarged lymphatics, or enlarged liver or spleen. Urine normal.

Soon after the above notes were taken, the patient left the hospital. It was learned by the writer, from reliable authority, that he had fully regained his health, and was able to engage in business. This was ascertained two years after the patient was under treatment.

Case III.—Idiopathic anæmia; improvement; relapse; subsequent course unknown.

Dennis French, æt. 44, saloon-keeper; miller in early days. Past fifteen

years addicted to free use of liquors. In the army for six months, and then discharged for so-called organic kidney-disease.

Since the war, complained of indefinite symptoms, which might be resolved into the term debility. He never had any special cause for mental strain or depression. Family history good. Aside from the above complaint, the patient's previous health was very good.

Among the symptoms of his later years that were especially noticeable, were a burning sensation in his tongue, amounting to a high degree of soreness the past two years, feeling as if it would drop off, and as if he had coals of fire in his mouth.

It was only about the holidays (1882) that the definite symptoms of anæmia developed. He noticed weakness and aching on the slightest exertion, with almost intolerable dyspnœa and palpitation. These symptoms increased, the latter becoming so pronounced as to prevent him going upstairs the past five weeks. Pallor of the countenance noticed at this time by wife.

Condition, April 2, 1883—occasion of first visit:—

General Appearance.—Emaciated (lost 30 pounds); extreme pallor, characteristic dirty yellow hue of skin; sclerotics dead-white; ears, fingers, and mucous membranes bloodless; hair abundant, soft and leaden gray; slight œdema of ankles and puffiness of eyelids; extremities cold, wrists especially; generally in recumbent posture.

Mental Symptoms.—None pronounced, save loss of memory and inability to concentrate his mind. Special senses about normal. Some dimness of vision; subjective noises in the ears, causing great distress, accompanied by pulsations in the head; the throbbing especially noticeable on the top of the head.

Digestive Symptoms.—Tongue pale, pointed, clean, very sore, without any appearance of irritation; appetite very poor; digestion slow; no vomiting; some flatulence, and uneasy sensations; obstinate constipation; no hemorrhoids. Liver and spleen normal size; abdomen normally distended.

Respiratory Organs.—Extreme dyspnœa on the slightest exertion and at times without apparent cause. Lungs normal. No cough. Nose-bleed was pronounced and profuse, occurring once or twice daily, causing extreme exhaustion. It had continued since December of the previous year (1882) or about the time of the development of the anæmia.

Circulatory Organs.—Palpitation distressing after exertion or excitement. Pulse small, feeble and rapid (100 to 120). First sound of heart moderately loud but quick, with muscular element not pronounced. Second sounds clear and ringing. At the base and the aortic cartilage very decided anæmic murmurs, influenced in loudness by pressure or change of position of patient, transmitted to the carotids, and generally soft and low in pitch. In the jugulars and the jugular sinus a loud continuous venous hum. Area of dulness of heart not increased, but square in shape. Apex in normal position, but found with difficulty. Impulse feeble. Aorta pulsated in epigastrium. Veins of neck appeared full. No murmurs over the head.

Urine clear in color, passes frequently O iij in twenty-four hours;

especially abundant at night; generally free from deposit. Sp. gr. 1017. Acid reaction. Quantitative analysis by Dr. Marshall. No albumen or sugar.

P_2O_5	= ·146 per cent.	=	2·46 grms.
Urea,	= 1·5 per cent.	=	25·28 grms.
Uric Acid,	= ·017 per cent.	=	28·645 grms.
NaCl,	= ·565 per cent.	=	9·52 grms.

Microscopically, nothing found.

Blood.—First examination, April 10, 1883, by Dr. W. E. Hughes. Very watery; 570,000 red cells per c. mm.; 2,000 white per c. mm.; 1 white to 285 red. Many of the red cells larger than normal; some at least twice the usual size and some smaller than normal. Many of them tailed and otherwise irregularly shaped. White corpuscles quite large, otherwise normal. Color of red fully up to normal.

Second examination, June 15, 1883, by Dr. Burgy,* 660,000 red; 170,000 white per c. mm. Many microcytes.

Third examination, February 17, 1884. Red corpuscles 1,600,000 per c. m.; white cells 20,000 per c. m. Microcytes in considerable quantity.

Treatment.—℞. Tr. Ferri Chlor., Tr. Digitalis, aa. ℥ss.; Hydrarg Bi-Chlor., ½ gr. M. Sig., 30 drops. T. D. in water. Regulated diet; laxative pill.

Under treatment improved rapidly, so that as far as strength was concerned, he was about all summer and the succeeding fall and winter, until December, being able to do light work, walk long distances and carry heavy packages, though with some inconvenience (dyspnœa).

In December had a relapse; debility and dyspnœa, with some loss of appetite, being most marked. He then passed from the writer's observation. It is to be regretted he never would permit an ophthalmoscopic examination. A note as to the temperature record was overlooked in the above history. For some time he had daily febrile exacerbations, rising to 102° or more. The exact record has been lost.

Remarks.—There was no difficulty whatsoever in recognizing the nature of the disease in the first and last cases reported. The profound anæmia, the cardiac and vascular murmurs, the preservation of adipose tissue in one, the absence of organic disease, together with the results of the blood examination, were sufficient points to establish the diagnosis. Case II was rather more obscure, the marked gastric symptoms, with the presence of a suspicious induration in the epigastrium, led us to consider the diagnosis of carcinoma of the pylorus. The anæmia was not as great on the first visit, and looked not unlike the anæmia of carcinoma. As is well known this is profound, and the reduction of the red cells may be as low as in our case. In one of the writer's cases, the red cells were reduced to 2,225,000 per c. mm., and 1

* Dr. Burgy was then engaged in blood examination at the writer's suggestion. His observations were recorded in a thesis presented to the Faculty of the University of Penna., and for which he received distinguished merit.

white to 225 red were counted. There was extensive carcinomatous disease of the pancreas, duodenum and lymphatic systems.

The return of our patient dispelled our thoughts of malignant disease, for the blood was much reduced in corpuscular richness without the advancement of organic disease; in fact, with the disappearance of dyspeptic symptoms almost entirely.

The following remarks are suggested by a study of the cases detailed, and the importance of the subject will warrant our trespassing on your time a few moments for bringing them to your notice.

1. *Ætiology.*—It is of interest to note in Case I, the possible relation of the development of the disease to shock, as observed by Dr. Curtin, whose views have been anticipated by others. The age and sex of our patients presented some variations from the usually accepted averages of the Germans on these questions. Two males beyond forty, and one female, mark them. The dyspeptic attacks possibly had some causal influence in Case II. But the cause of the third case is quite obscure. None of the cases were deprived of food or suffered any want.

2. *Appearances of the Blood.*—The blood examinations revealed the characteristic changes found in this form of anæmia. In our cases, nucleated red corpuscles were not seen, however. Changes in size and shape were marked in Cases I and III. Some cases of chlorosis and of puerperal anæmia have lately been under the writer's care. The examination of the blood will be subjoined for comparison. It will be observed that in the three varieties there was a reduction in the number of the red cells, but that in the cases of idiopathic anæmia changes in size were most marked, and the reduction in number was infinitely greater.

M. F., fem., æt. 19; *chlorosis;* red corpuscles, 2,600,000 per c. mm.; normal in appearance; no microcytosis; unusual number of collections of Max-Schultze's granules, large in size, with distinct nuclei.

Mrs. C., æt. 37; *anæmia of pregnancy and puerpurium;* red cells, 3,080,000; only slight variations in size; few Schultze's granules. Mrs. C.'s anæmia was most profound, reckoned by appearance and symptoms.

As has been noted by Prof. Osler, the Max-Schultze's granules are absent in idiopathic anæmia. The extreme reduction in red cells, the changes in size, shape and color, the adventitious cells (nucleated corpuscles), and the absence of Max-Schultze's granules, therefore, characterize the blood of this disease.

The extreme reduction in the case of French (III), with gradual increase in number, and subsequent recovery, is of extreme

interest. Yet cases are recorded by Quincke, and others, where the reduction was far greater and recovery followed.* If he is correct, one should scarcely despair, from the number of red cells alone, in giving a prognosis.

3. *The Urine.*—Urea is said to be lessened, uric acid relatively increased, and phosphoric acid and the chloride of sodium diminished in idiopathic anæmia.† The following table indicates the comparative analysis of urine in health, in idiopathic anæmia, in chlorosis and in puerperal or secondary anæmia. The analyses were made by the efficient Demonstrator of Chemistry in the University of Penna., Dr. John Marshall.

	Normal. per cent.	Secondary Anæmia. per cent.	Chlorosis. per cent.	Idiopathic Anæmia. Case I. per cent.	Idiopathic Anæmia. Case III. per cent.
Urea, . . .	2·8	0·9	1·00	2·3	1·5
Uric Acid, . .	0·06			0·087	0·017
Phosphoric Acid, .	0·20	0·056	0·134	0·13	0·146
Sodium Chlor., .	0·80			0·12	0·565

The degree of anæmia, if reckoned by the blood-examination, was more profound in the idiopathic variety. Yet the reduction in the percentage of certain constituents of the urine was greater in the secondary forms. One can conceive of an increased tissue-change, and the causes for it, in the more grave anæmia, especially in the fatal case, to explain the apparent discrepancy. In the instances above, we find a diminution in the amount of urea, phosphoric acid, and chloride of sodium, and, in one case, of the uric acid. The circumstances that influence the secretion of the various elements of the urine are so numerous, that it is almost impossible to reckon the value of analyses, unless definite circumstances are present, from which generalizations can be made.

The importance of the subject is sufficient apology for the following observations, which, though they appertain to, are not strictly of the subject. The reduction of the acid is possibly significant, in the cases of chlorosis. It has been held by a German observer that the conversion of the iron of the body into hæmoglobin, or rather the taking up of the iron by the corpuscles, is impossible without the presence of a certain amount of acid in the blood. He claims that a deficiency of this acid is the essential lesion, so to speak, of chlorosis. As a corollary to these facts, he demonstrates by a series of cases the value of hydrochloric acid in curing the disease.

* Quincke's case, 143,000 per c. m.; Worm Müller's case, 360,000. † See Müller, 'Die Prog. Pern. Anaem.," Zurich, 1877; Eichhorst, "Die Prog. Per. Anaem.," Leipsig, 1878.

4. *Sympathetic Nerves.*—The negative results of the examination of the sympathetic ganglion tallies with the observations of Wilks, Pye-Smith and others. It must be remembered that Queckett, in Addison's famous case, and Brigidi (Lond. Med. Rec., vi, 430) found marked anatomical changes. The evidence has not been sufficient to point to the sympathetic system as the primary organic affection in this disease.

5. *Bone-Marrow.*—In some cases (Pepper, Osler, Cohnheim, Scheby-Buch, Hughes, etc.) of so-called idiopathic anæmia, the marrow of the bones was seen to have reverted to its fœtal structure. In our cases, this reversion was notably absent, the yellow marrow not being replaced by red marrow.

6. *Blood Clots.*—Attention should be called to the black specks, or possibly pigment granules, in the blood-clots found in the heart. It is to be regretted their exact nature was not determined, and this remark is made in order that they may be looked for by future observers.

7. *The Chemical Examination of the Blood.*—The most striking feature is the reduction of iron in the blood, and this, taken with the deposition of iron in the tissues (siderosis), in the shape of granules (Quincke), and the increased amount of iron in the urine (Reynolds, in Purser's case*), would go to show a destruction of those elements in the blood which held this substance—the red cells. As this is the only analysis of the blood ever made that is known to the writer, more data will have to be collected in that direction, before conclusions can be drawn.

8. *Course and Termination.*—Finally, the course and termination of our last cases are worthy of attention. As is well known, relapses are extremely liable to recur in persons apparently cured of this affection. Caution should be used in pronouncing a cure. Case II was heard from, two years after dismissal from the hospital by the writer, and was pronounced by the informer a strong, healthy man. It is worthy of observation that this case improved under removal from his home in the mountains to a city hospital. On the other hand, one of Frerich's cases, recorded by Eichhorst, did not recover until he was sent to the country. Case III has been lost sight of. Although he improved very much, it cannot positively be said a cure took place.

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* Purser, *Dublin Quarterly Jour.*, 1877.

THE WORK OF OBSERVERS IN AMERICA ON IDIOPATHIC ANÆMIA.—AN HISTORICAL NOTE.

The English and Germans, most deservedly, have been accredited most of the honor for establishing this disease as a distinct clinical entity. It is almost beyond cavil that Addison was the first to distinctly impress on the profession the clinical and pathological nature of this affection as distinguished from like disorders. Others had described isolated cases, there is no doubt, but he had fixed it, so to speak, in nosology. At the same time the labors of our own countrymen, very early in the history of the disease, are worthy of serious attention and high honor. There is no doubt Channing * and his associates were perfectly familiar with fatal anæmias, independent of, or connected with, pregnancy and uterine disease. This was as early as 1842, or seven years prior to the publication of one of Addison's † cases. One of his observations was made in 1832. The publication of his series of cases were antedated only by the publication of the following isolated cases, which are referred to by Pepper,‡ and included by Pye-Smith § in a very exhaustive table of cases of idiopathic anæmia:—Combe, 1823; Andral, 1823; Marshall Hall, 1837; Piorry, 1840. There can be no doubt the observations of Channing were made independently of any other ones; the singular confessions of ignorance of the nature of the cases and of want of knowledge of any writings on similar ones, and the faithful and accurate description of them, coupled with the scanty dissemination of medical knowledge in that era, point irresistibly to the above conclusion. It is extremely bracing to moral medical courage to read this quaint article and feel the force of the honest expressions of ignorance of the obscure disease; it is a record of facts.

There is no doubt similar cases had been observed from this time to the publication of the next paper (1875); Osler tells us Prof. Howard taught to his classes, in 1869, the existence and symptoms of idiopathic anæmia. Flint, ‖ in his "Clinical Medicine," says that he had described, in 1871, cases of degeneration of the gastric tubules, which were no doubt cases of idiopathic

* Channing, *New Eng. Quart. Jour. Med. and Surgery*, 1842, No. 2, "Notes on Anhæmia, etc." Musser, J. H., *Medical News*, Oct. 7. 1882, "Historical Note on Progressive, Pernicious or Idiopathic Anæmia." † *Med. Times and Gaz.*, March, 1849.

‡ Pepper, *Am. Jour. Med. Sciences*, 1875.

§ Pye-Smith, Idiopathic Anæmia, Guy's Hosp. Rep., 1882. ‖ Flint, *N. Y. Med. Jour.*, 1871.

anæmia. The records of American medicine do not yield any observations, however.

Prof. Pepper,* in the latter part of 1875, published an exhaustive article. He considered the relations of this disease to other forms of anæmia, referred to the observations of previous contributors, discussed the clinical history, the course, the anatomical characters and the diagnosis. He suggested the name *anæmatosis* and was the first to suggest that the essential lesion was disease of the bone marrow, and that it was simply pseudo-leukæmia of the myelogenic variety. His observations were afterwards incorporated in a joint article by himself and Prof. Tyson and published in "Virchow's Archiv." The same year Dr. Chadwick,† of Boston, published a very interesting case.

The next contribution of any length was made to the International Medical Congress in 1876, by Prof. Howard.‡ Bradford had reported, however, another case in the "Boston Journal" a few months previously. Prof. Howard reported four cases, analyzed a large number and discussed the relations and pathology of the disorder. He concluded that all forms of anæmia may take on a progressive and pernicious character, and that, up to that time, we were not warranted in making a distinct variety of anæmia, called "progressive, pernicious."

Among the most important contributions to the study of idiopathic anæmia few are of greater value than those of Prof. Osler,§ formerly of Montreal, now of this city. Together with his colleagues, his contributions continue to the present time, beginning in 1877 with the report of a case, in conjunction with Prof. Gardner. Not only has he contributed to our knowledge of this disease, but he has made extensive researches into the changes the blood undergoes in health and disease. He confirmed the observations of Pepper, and regarded this variety of anæmia a myelogenic form of pseudo-leucocythæmia. His papers include careful observations of the size and shape of the blood-cells, and of the marrow-cells.

In 1879, Dr. Hutchinson, in a very complete clinical lecture,‖

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* Pepper, *Am. Jour. Med. Sci.*, 1875, Oct., "On Prog., Per. Anæmia or Anæmatosis."

† Chadwick, *Bost. Med. and Surg. Jour.*, 1875.

‡ Howard, *Trans. Internat. Med. Cong.*, Phila., 1876.

§ Osler and Gardner, *Canada Med. and Surg. Journal*, 1877; Osler and Bell, *Trans. Canada Med. Assos.*, 1877; Osler, *Centralbl. Med. Wissensch.*, 1877, No. 28; Osler and Gardner, *Centralbl. Med. Wissensch.*, 1877, No. 15; Osler, *Centralbl. Med. Wissensch.*, 1878, No. 26; Osler, *Canada Jour. Med. Sci.*, 1881.

‖ *Med. News*, 1879.

detailed one case, referred to several others, gave the result of his analysis of thirty-two cases, and a resumé of our knowledge up to that time. The four cases were males; one was 50 and another 25 years old. Hutchinson called attention to the influence of shock, worry, grief, etc., in the causation of the disease. In one, grief at the loss of his wife; in another, grief at the loss of his daughter; in a third, business worry, were powerful ætiological factors. One of his patients was a rich manufacturer. Cod-liver oil and iron seemed to be remedies that were of service in his cases. The one detailed in full will be found in the succeeding table.

The studies of F. P. Henry,* of Philadelphia, in blood diseases, are well known. For his efforts he received the Cartwright Prize of the College of Physicians, New York. In addition to this essay he has published numerous observations on the appearances of the blood in various diseases.

The remaining contributions to the study of idiopathic anæmia in America, are the reports of isolated cases with brief remarks on them. They will be included in the appendix table, in abstract, with the publication references to each one.

In our text-books on the practice of medicine, notice is given of this affection, by Flint,† Da Costa,‡ Bartholow,§ and Loomis.‖ Flint says, we know nothing of the primary morbid changes; the clinical characters are sufficiently distinct for its recognition as an individual affection; women are more liable to it than men, and middle-age more than any other period. He sketches very well the characters of the disease, in a concise chapter. Treatment is generally futile, he believes. Bartholow also gives to this form of anæmia a separate chapter, calling it prog. per., essential anæmia, or malignant anæmia. Causes: women, 15 to 40 years old, pregnancy, uterine hemorrhage, and bad hygienic surroundings. Fever, he thinks, is a constant symptom. "No cases of cure have been reported." Treatment, he believes, to be useless. Otherwise his account tallies with that of other observers; he does not lay sufficient stress on the blood changes, however.

Under the heading "Progressive Pernicious Anæmia," Loomis

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* F. P. Henry, Observations with the Hæmocytometer on the globular composition of the blood and milk; Cartwright Prize Essay, 1881 (Reprint); also, *Archiv. of M. d.*, New York, Seguin.

† Flint, *Clin. Med*, 1879. *Prac. of Med*, 1884.

‡ Da Costa, *Medical Diagnosis*, 1884.

§ Bartholow, *Prac. of Med.*, 1880.

‖ Loomis, *Practice of Med.*, 1884.

devotes a chapter to this affection. The disease occurs most frequently in women and between the ages of twenty and forty-five, according to this authority. He shows its entity apart from simple anæmia, leukæmia, pseudo-leukæmia and chlorosis, and believes the affection of the bone marrow is entirely secondary. The supervention of this form on a benign anæmia or on chlorosis, he believes to be uncertain. He does not lay stress on the use of any special drug in the treatment of the disease.

Da Costa, in his "Medical Diagnosis," treats of the affection under the head of anæmia, pointing out its symptoms, and referring to its possible near relation to pseudo-leukæmia.*

ANALYSIS OF THE CASES OF IDIOPATHIC ANÆMIA RECORDED IN AMERICA.

The following tables of cases are meant to show, in a compact form, the peculiarities of idiopathic anæmia as seen in America. It has been modeled after the admirably arranged table of Pye-Smith in the Guy's Hosp. Rep. (1882). An attempt has been made to separate the cases of myelogenic pseudo-leukæmia or so-called idiopathic anæmia, in which a change in the bone-marrow has been observed, from the true idiopathic cases. For, on the one hand, some teach that this change is secondary to the anæmia; others believe it to be a separate affection entirely, a cytogenetic anæmia, idiopathic anæmia likewise existing; while still others doubt entirely the existence of idiopathic anæmia, believing it to be a pseudo-leukæmia. The first table, therefore, will conform to the criteria of idiopathic anæmia, laid down by Pye-Smith, in order to supplement his collection. Cases of secondary anæmia, and of cytogenetic anæmia, will be excluded; the anæmias which developed in the puerperal period on account of hemorrhage, will also be excluded.

In the formation of the table, care has been taken to exclude all cases which might be considered doubtful. Those are included only, with a few glaring exceptions, which either had had a blood enumeration during life, or whose nature was determined by an autopsy. It is not to be presumed that all cases of this disease observed in America will be found in the table; only those cases which have been fully recorded:—

* See also American Edition of Reynold's "System of Medicine." Complete article, by Dr. Hartshorne.

TABLE A.—Cases of Idiopathic Anæmia in which there was an Absence of Changes in the Bone Marrow, or its Appearances were not Recorded.

No.	Physician, Date of Publication and Reference	Sex and Age.	Antecedent Conditions.	Symptoms.	Duration.	Results of Treatment or Autopsy.
1.	Channing, N. E Quart. J. of Med. and Surg., 1842.	M.	No causal antecedents.	Anæmia.		No lesions. Bloodlessness.
2.	Idem (ibid.).	F., 25.	Pregnancy. Healthy in pregnancy. Labor, third child, normal. No hemorrhage.	Robust appearance. Increasing pallor, surface like wax Nausea, vomiting, diarrhœa. Fever. Pulse 120–140. Cardiac palpitation; syncopal attacks. Dyspnœa. Delirium. No albumen.	16 days after confinement.	Autopsy—"Adipose membranes full of fat," serous effusions. Heart pale and flabby; no blood flowed on division of vessels. Blood small in quantity, pale liquid, uncoagulated. Spleen rather large.
3.	Idem (ibid.).	F., 29.	Pregnancy Three pregnancies previous. Healthy in pregnancy. Last confinement normal. No hemorrhage. Free secretion of milk, which disappeared in third week. Mammary abscess which discharged the third week.	Debility; pallor; constipation. "Sounds in the head like sawing wood."	7 weeks after confinement.	Autopsy—Whitish coagula in long sinus; ecchymoses of internal surface of dura mater. Heart moderately firm, some quite soft light-colored coagula in both sides Blood usually pale.
4.	Pepper. Am. Jour. Med. Sci., 1875.	F., 26.	Single Hard worker. No privation. Malaria (?)	Irregular fever; œdema; gastric disturbance; palpitation, hæmic murmurs, hemorrhages; somnolence, coma, death No enlargement of spleen or lymphatic glands. No albuminuria. Red cells reduced in number.	4 months under observation	No autopsy.
5.	Idem (ibid.).	M., 57.	Vague symptoms of failing health. Slight sunstroke; jaundice; temperate; good circumstances.	Rapid failure in strength, and progressive anæmia; dyspnœa; palpitation; nausea, vomiting; slight œdema; hæmic murmurs; very slight fever; slight emaciation; no albumen; delirium. Blood thin and dirty red; r. c. decreased.	14 months from first failure of health. Actual duration, 3½ mos.	Autopsy—No affection of lymphatic glands; slight enlargement of spleen; fatty degeneration of heart, liver and kidneys. Anæmia.

TABLE A.—Cases of Idiopathic Anæmia in which there was an Absence of Changes in the Bone Marrow, or its Appearances were not Recorded.—*Continued.*

No.	Physician, date of Publication and Reference	Sex and Age.	Antecedent Conditions.	Symptoms.	Duration.	Results of Treatment or Autopsy.
6.	Howard, Trans. Internat. Med. Cong., Philada., 1876. (Date 1st case, 1871).	M., 41.	Forward merchant; healthy until 2 years before; gradual loss of strength and color. Temperate.	Average nutrition; sallow white and then dull yellow color of face; no hemorrhages; distress after eating. Œdema of feet and scrotum; no albuminuria. Anæmic murmur. Pulsating jugulars. Suspected carcinoma of stomach. No excess of white corpuscles.	About 2 years and 2 months.	Autopsy—Spleen, liver, heart and kidneys normal. Slightly enlarged mesenteric glands. Blood not coagulated. Organs bloodless. Serous effusions.
7.	Idem (ibid.).	M., 37.	Wholesale fruit dealer. Ague 16 years previous. Change in color since residence in Montreal (8 years). Recurrence of former tendency to slight diarrhœa on simple cause.	Extreme pallor surface and mucous membranes. No emaciation. Venous and cardiac anæmic murmurs. Blood watery, pale red; no excess of white corpuscles. Slight fever. Œdema of legs. No albuminuria or organic disease.	Uncertain.	No autopsy.
8.	Idem (ibid.).	M., 53.	Bookkeeper; healthy; not robust. 1872, slight diarrhœa. April, 1874, indigestion which continued in a mild form all the year. Temperate.	Extreme anæmia; straw-colored skin. Dyspeptic symptoms. Cardiac anæmic murmurs. Œdema. No albumen. Delirium, fainting spells, dyspnœa; palpitation. Blood thin, watery, white not increased, red lessened After death, blood showed small red cells.	1 year from first consultation.	Fatty heart, normal liver. Atrophied, spleen and lymphatic glands. Serous effusions. Calcareous masses in lungs.
9.	Bradford, Boston Med. and Surg. Jour., July, 1876.	F., 11.	Health good; well fed; good family history.	No emaciation. Anæmia. Heart, liver, spleen and glands normal. 714,145 red cells per c. mm., 1 w. to 290 red. Much variation in size; all rather too small. White abnormally granular. Hemorrhage from lungs and mouth. Cerebral symptoms.	About 71 days.	No autopsy.
10.	Chadwick, Bost. M. and S. Jour., Jan., 1875.	F., 32.	Puerperal flooding.	Cardiac bruit. Slight fever; vomiting.	12 weeks.	Fatty heart, capillary hemorrhages in brain.

11.	Hutchinson, J. H., Philada. Med News and Lib., 1879, xxxvii	M., 50.	Miner. Grief at loss of wife. No antecedent causal disease. Family history good.	Anæmia. Dirty yellow complexion. Dyspepsia; nausea. Basic, cardiac and venous murmurs. No albumen. Spleen and lymphatics not enlarged Diminution of re t cells. No increase of white. No retinal hemorrhage.	Unknown.	Improved; relapse, subsequent death from anæmia (private communication).
12.	Cary, Buffalo M. and S. Jour., 1880–1881, p 259.	F., 22.	Suppression of menses by cold 5 months previous No syphilis.	No emaciation Profound anæmia Fever. Pulse 110. No organic disease. Rapid and extreme exhaustion.		Direct venous transfusion. Cure.
13.	Henry, Cartwright Prize Essay (Reprint, 1881, p. 36).	M., 40.	Carpenter. Intemperate in sexual intercourse and the use of stimulants. Family history good.	Pallor; emaciation Progressive weakness. Slight fever. Heart, lungs, liver and spleen normal. No albumen. Mental hebetude, slight delirium, coma. Retinal hemorrhages. No. r. c., 525,000 per c. mm., 1 w. to 105 r.	About 25 months	No autopsy.
14.	King, J. S., Can. Lancet, 1881–'82, xiv, 383-386.	F., 27.	Fever; dyspeptic symp.; hæmic murmurs. No alb. 625,000 r. c. per c. mm.	Liver and spleen normal. Blood pale and watery. Irregularity, in shape, and some in s ze, of red corp. 625,000 r. c per c mm. No giant corp., or Schultze's masses.	Uncertain. 26 weeks after confinement.	No autopsy.
15.	Edes, Bost. Med. and Sur. Jour., 1882, cvi, 457.	M., 25.	No previous debilitating or depressing influence.	Pallor mucous membranes; skin yellow No emaciation. Purpura, vertigo, noises in head, delirium. Diarrhœa. Dyspnœa. Vascular murmurs. Retinal hemorrhages. Blood pale and watery; r. c. 800,000 and 670,000 per c. mm. Not much deformed. A few microcytes. No albumen.	7 weeks.	Autopsy—Fatty heart. Ecchymoses under serous membranes and in brain. Fatty liver and kidneys. Marrow normal microscopically. Spleen normal.
16.	Bierwith and Alt., Am. Jour. Oph., St. Louis, 1884–5, i, 147–149.	F., 23.	Poor health; 4 years married; menses regular.	Blood pale and watery R. c. larger and paler than normal. No rouleaux. No increase in white. Retinal hemorrhages.		Improved under treatment.
17.	Graham, Canada Pract., 1884, ix, No. vii.	M., 30.	Farmer. Married.	Pallor. Emaciation Temporary paralysis lower extremities Gastralgia. Pale, greenish countenance. Fever. No organic disease. 1,560,000 r. c. per c. mm.	10 months.	No autopsy.

TABLE A.—Cases of Idiopathic Anæmia in which there was an Absence of Changes in the Bone Marrow, or its Appearances were not Recorded.—*Continued.*

No.	Physician, date of Publication and Reference	Sex and Age.	Antecedent Conditions.	Symptoms.	Duration.	Results of Treatment or Autopsy.
18.	Idem (ibid.).	M., 47.	Tannery business. Good family history.	Pale, yellow countenance. Slight emaciation. Debility. Dyspeptic symptoms. Cardiac bruit. Dyspnœa. Fever. Œdema. 1,500,000 r. c. per c. mm. Irregular caudate in shape.		Improved with Fe. and Quinia.
19.	Idem (ibid.).	M.	Attributed disease to catching cold, lying on grass in perspiration.	Pallor. Slight emaciation. Dyspnœa. Anæmic murmurs. Œdema. 1,580,000 r. c. per c. mm : irregular in outline, elongated and presenting projections.		Cured.
20.	Hamill, R. H., Phila. (private communication).	F., 31.	Married. 3 children. Anæmic symptoms noticed 6th month of gestation. Parents healthy.	Pallor extreme. Anæmic murmurs. Œdema. Copious menstrual flow. Vomiting and diarrhœa. No albumen. Progressive course. Liver and spleen normal.	Uncertain.	Fatty heart and kidney. Ecchymoses and serous effusions. Spleen slightly enlarged.
21.	Shattuck, G. B., Boston M. and S. Jour., Jan. 1885.	M., 38.	Farmer. Parents died of phthisis. Ague 2 years previously. Habits good. No depressing influences. No syphilis.	Debility. Physical signs, subacute pneumonia. Pallor extreme. Emaciation. Epistaxis. Retinal hemorrhages. Spleen enlarged slightly. Fever (97½° to 103°). 595,000 r. c. per c mm., 1st count; 1,180,000 r. c. per c. mm., 2d count; 3,025,000 r. c. per c. mm., 3d count.		Cured. Arsenic in increasing doses. Early diagnosis, phthisis. Cardiac bruit absent.
22.	Curtin, Philada. Co. Med Soc., Trans., 1885.	F., 38.	Great shock, 3½ years previous to anæmia.	Pallor. Debility. Emaciation. Palpitation. Dyspnœa. Vascular murmurs. No albumen. Occasional vomiting; constipation. No blood count. Suppression of menses.	Anæmia 1 year.	No autopsy.
23.	Idem (ibid.).	F.	Shock, 3½ years previous to anæmic manifestations.	Pallor. Debility. Anæmic murmurs. Dyspeptic symptoms. Indigestion. Slight diarrhœa. Palpitation. Dyspnœa. No albumen.	3½ mos.	No autopsy.

24.	Hinsdale (private communication). Case to be published in Am. Jour. Med. Sci., April, 1885, in full.	M., 22.	Bar-tender. Used stimulants freely. Previous health excellent. No syphilis.	Pallor. Yellow conjunctiva. No emaciation. Constipation. Anæmic murmurs. Retinal hemorrhages. Spleen enlarged in vertical line. No enlarged lymphatics. Fever. 985,000 r.c. per c. mm., 1st count; 890,000 r. c. per c. mm., 2d count; 4,500,000 r. c. per c. mm., 3d count.		Cured. Arsenic in increasing doses.
25.	Haven, H. C., Archiv. Pediatrics, Dec. 15, 1884.	F., 10.	No family history. At 4 years pertussis and measles. Illness began 6 weeks before admission.	Pallor. Debility. Vomiting. Diarrhœa. Œdema. Hemorrhage. Liver, spleen and lymphatics not enlarged. Heart normal. Venous hum, and arterial murmurs. Irregular fever.		Autopsy—Serous effusion. Cytogenitic organs normal. Fatty heart and kidneys.
26.	Musser (Case I, *supra*).	F., 42.	Shock, 5 years before death. Married. No children. Hard worker. No deprivations. Family and personal medical history good.	Pallor; sallow. Not emaciated. Œdema. Hemorrhages. Vascular bruit. Cerebral symptoms. Dyspepsia. Palpitation and dyspnœa. Reduction of red cells. No albumen.	Anæmic sympt's 1 year.	Autopsy—Fatty heart. Serous effusion. Ecchymoses. No lesion of marrow. Iron reduced in blood.
27.	Idem (Case II).	M., 41.	Hard worker. Moderate circumstances. No deprivations.	Anæmia pronounced. 1,000,000 red cells. Dyspnœa and palpitation. Slight albumen; no casts.	Over 2 yrs.	Cured. Iron, rest, food, etc. Relapse. Permanent cure.
28.	Idem (Case III).	M., 44.	Saloon-keeper. Use liquors freely. Not deprived of life's comforts. Good family history.	All usual anæmic symptoms rapidly develop, and pronounced. R. c., 570,000 per c. mm.; irregular in shape, increased in size.		Improvement. Relapse. Subsequently case lost sight of.
29.	Bruen, Medical News, Philada., 1884.	F., 47.	Metrorrhagia; malaria. Fast life.	Pallor; yellow tint; dyspeptic symptoms. Spleen enlarged. 600,000 r. c. per c. m. Change in shape of cells. Vascular bruit.		Improvement. Bichloride of mercury.
30.	Bellinge, F. A., Pacific M. and S. Jr., 1879, xxii, 504–509.	M., 65.	Retired plasterer. Yellow fever in early life. Good habits.	Pallor: œdema. No emaciation. Spleen, liver and glands normal. No alb. Hemorrhage once. Constipation; dyspeptic symptoms; coldness and numbness most marked symptoms. Mental hebetude to coma.	About 18 months.	No autopsy.

TABLE B.—Cases of Idiopathic Anæmia in which the Lesions of the Bone Marrow were found.

No	Physician, Date of Publication and Reference	Sex and Age.	Antecedent Conditions.	Symptoms.	Duration.	Results of Treatment or Autopsy.
1.	Pepper (*op. cit.*)	M. 50.	Chronic follicular catarrh. Attacks of hepatic colic Mental and bodily overstrain. Iron founder. Psoriasis 12 years. Loss of all his teeth 15 years.	Debility and anæmia apparently causeless; tendency to syncope; œdema transient; hæmic murmurs. Dyspnœa. Irregular fever. Somnolence. Hemorrhages. Delirium. Spleen slightly enlarged. Liver and lymphatics normal. No albuminuria. Extreme reduction of red corpuscles No rouleaux. Individual corpuscles pale and less biconcave.	3 months.	Fatty heart, liver and kidneys. Chronic suppuration of gall-bladder Lymphatics normal. Bone marrow made up of granular cells, large and small, some nucleated. The lymphoid elements replaced the fat.
2.	Gardner and Osler, Canada Med. and Surg. Jour., March, 1877.	M 52.	Laborer. Always subject to slight diarrhœa. Shock and grief 5 years previous.	Pallor; debility; waxy hue; diarrhœa; bruit in heart and vessels; palpitation; dyspnœa; syncopal attacks; fever; no albumen; liver, spleen and lymphatics normal. Alteration in size and shape of red corpuscles Microcytosis. No marked emaciation.	Over 2 years.	Fatty heart, liver and kidneys. Spleen normal. Medulla of bones 1. Colorless corpuscles, various size. 2 Red corpuscles; *a* normal as seen in blood of various shapes; *b*. microcytes. 3 Nucleated red corpuscles. 4 Cells containing r. c. 5. Myeloplaques. 6. Fat cells absent in some parts. 7. Charcot's crystals.
3.	Bell and Osler, Trans. Canada Med Assoc.,1877.	M. 47.	Shoe cutter. Married. Healthy. Good family history. Mental anxiety.	Pallor; debility; loss of appetite. Organs normal. Retinal hemorrhages. Hæmic murmurs. No albumen. Some emaciation. Blood thin and watery. Diminution in number and change in size of r. c. Microcytosis.	1 year and 2 months.	Failure of transfusion. Autopsy.—Ecchymoses and serous effusion. Fatty heart. Spleen enlarged, slightly soft. Bone marrow as in Case 2. Extreme bloodlessness of organs.
4.	Osler, Canadian Jour. of Med. Science, May, 1881.	M. 47.	Soldier. Baggage-man later. Healthy. No mental distress.	Dirty yellow hue of skin; slight emaciation; debility; dyspnœa; palpitation; poor digestion. Hæmic murmurs. Spleen slightly enlarged. Organs normal. No albumen. Hemorrhages, nasal and retinal. Œdema. 970,000 r. c. per c. mm. Hæmoglobin lessened. Change in form of r. c. Microcytosis and giant corpuscle.		

5.	Osler. Ueber die Entwickelung von Blutkörperchen im Knochenmark bei perniciösen Anamie; Centralbl. Med. Wissensch., 1878, No. 26.	F. 20.		Blood showed microcytes and large, irregular, non-nucleated cells. No Schultze's granules.		Autopsy.—Bone marrow not fatty, deep red color. The central marrow of radius was fatty. Marrow made up of large and small granular marrow-cells, colorless cells of large size and homogeneous structure Nucleated red blood-corpuscles, varying in size and shape, red corpuscles, large and small microcytes, cells containing red corpuscles and myeloplaques.
6.	Osler, Centralbl. Med. Wissensch., 1877, No. 28.	M. 54.		No full history detailed. Red cells pale, flat and irregular in shape. Microcytes. No change in white corpuscles. General anæmia.		Transfusion. Autopsy.—Bone marrow dark violet-red and without fat except that from fibula. Histological elements as described in the other case.
7.	Starr, Phil. Med. Times, 1881.	M. 40.	Diarrhœa in war, ague at same time. No syphilis. Worked in lead works at one time.	Early symptoms weakness and frequent urination Diarrhœa; pallor; dyspnœa; palpitation; œdema. Increased hepatic and splenic dulness. Fever. 745,000 r. c. per c. mm.; 5000 w. c. Hæmic murmurs.	2 years.	Transfusion. Death. Fatty heart. Spleen slightly enlarged and firm. Bone marrow red, soft, without fat or fibrous tissue. Lymphoid elements of various size, increased in number Nucleated red corpuscles and myeloplaques
8.	Hughes, W. E., Med. and Surg. Rep., 1884.	M. 45.	Clerk.	R. c. vary in size, many small and tailed. No retinal hemorrhages. No albumen.		Fatty heart. Normal spleen. Small pancreas. Marrow in tibia, humerus and sternum. Fat replaced by leucocytes and forms intermediate between red and white corpuscles. No blood clots.
9.	Ross, Canada Med. and Surg. Journal, August, 1884	M. 65.	Saddler. Drank to excess in early life. Good medical antecedents.	Pallor marked; dirty lemon hue; little emaciation; dyspnœa; palpitation; cardiac and vascular bruit; œdema. Retinal hemorrhage. R. c. 1,150,000 to 800,000 per c. mm. Microcytes. No nucleated red cells. Few Schultze's granules. Some large r. c. Irregularity of shape of r. c. Blood pale. No fever. Delirium.	2½ years.	Autopsy.—Bone marrow like fœtal marrow. Heart fatty.

Cases of pernicious anæmia have been reported from time to time, which, in the light of the recorded evidence, do not appear to be that affection. With all due deference to the judgment of the reporters, for the want of proof, we have not admitted them to our table. Thus in the admirable paper of Prof. Howard, he reports a case which he admits is doubtful, lacking the proof of blood-examination and autopsy. He places it on record on account of the interesting family tendency to anæmia. Four cases of Graham (*op. cit.*) were omitted from our table on account of the same lack of evidence. One (Case I of his list) presented such great changes in the supra-renal capsules as to make a doubtful case of Addison's disease without pigmentation; another did not want much evidence to prove it scurvy, rather than idiopathic anæmia. For similar reasons we have excluded the long list of cases Channing presented in his early memoir.

Westbrook* records a case of supposed pernicious anæmia. It does not stand the test of close scrutiny, however, and with Drs. Kretzschman and Armor, who discussed the case, we must consider its nature undetermined. We are forced to the same conclusion from a want of a blood count, the retina examination and autopsy, in the case reported by Kemper.†

In addition to the above-recorded examples, references have been made frequently to cases in discussions or papers, without giving detailed reports. Prof. Minot, in the discussion on Shattuck's case,‡ refers to four cases which he had seen; and Hutchinson, in his lecture, in addition to the carefully recorded case, makes allusion to three others he had under observation at various times. Prof. Walker, in a discussion in the Phila. Clin. Soc. (1884), alluded to a case of pernicious anæmia under his observation. So, doubtless, it may be in many more instances; hence our collection does not absolutely indicate the frequency of idiopathic anæmia in this country; it is claimed to be representative of the published records.§

A cursory analysis of the above tables yields some facts of interest. It is observed, that of the thirty-nine cases, comprised

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* Westbrook, *N. Y. Med. Rec.*, 1884, xl.

† Kemper, *Cin. Lancet and Clinic*, 1879, n. s., iii, 101.

‡ Shattuck, *op. cit.* (see table).

§ Rotch's article, *Bost. M. and S. Jour.*, 1876, xciv, is simply a report of two cases from Germany, included in a letter from that country.

in both tables, nine presented evidence of lesions of the bone marrow. Of the remaining thirty, two alone were examined for that change, with negative results, so that of eleven cases of idiopathic anæmia in America, in which the bone marrow was examined in two, the appearances were normal.

Believing that these changes are probably secondary, the following analysis is the result of the study of the combined tables. It embraces chiefly an examination of the ætiological factors, for the purpose of comparison with the results of similar cases in other countries. The symptomatology, the course, the duration, and the morbid anatomy vary so little, if at all, from the results of the elaborate analysis of Eichhorst, Müller, and Pye-Smith, that too much of your valuable time would be occupied by reaching a similar analysis.

Age.—Beginning, therefore, with the age of the cases of idiopathic anæmia, we find but little difference from the accepted dictum on this predisposing cause. Pye-Smith's collection embraces cases from all countries, including but two, however, from America. He excludes all cases in which the bone marrow was affected. The following table includes his series for comparison, and shows the relation of sex to age and also to marrow changes.

TABLE OF AGE AND SEX. IDIOPATHIC ANÆMIA.

	Pye-Smith.		*Musser.*				
			Marrow changed.		Marrow normal, or not examined.		
		MALE.*	FEM.	M.	F.	M.	F.
Under 15,	6	0	2	0	0	0	2
15–20,	4	0	1	0	1	0	0
21–30,	29	3	6	0	0	3	6
31–40,	26	4	3	1†	0	3	3
41–50,	21	9	2	4	0	5	2
51–60,	13	4	0	2	0	2	0
61–70,	4	2	0	1	0	1	0

It will be seen at once that the disease is most frequent in adult years prior to the age of fifty, and that the age in females is strikingly earlier than in males. Looking at each table separately, we find that with the exception of the one female, the age of the other cases in which the bone marrow was diseased, was forty or over. The ages in Table A correspond with the first statement in this paragraph.

* Age of three not reported. † Aet. 40.

Sex.—Here, too, our analysis does not coincide with similar ones of Pye-Smith and Coupland,* and differs radically from the Germans. Müller, of Zurich, observed nine men in forty-four patients, and Eichhorst's collection gives sixty-five women to thirty men. Coupland's ratio is fifty-six men to fifty-four women, and Pye-Smith's forty-eight of the former to fifty-nine of the latter sex. Our collection yields twenty-four men and fifteen women; or again deducting the marrow cases—which gave the very unusual ratio of the males to the females as nine to one—sixteen males and fourteen females.

Occupation, Habits, etc.—In our cases the occupation was so varied that conclusions would be almost valueless. It could not be said even that physical labor was paramount, as a causal factor, to mental strain, although when noted, the former exceeded the latter. Three were laborers, two mechanics, one a tanner, one a miner and two were farmers; on the other hand, business men and clerks were similarly affected. Pregnancy, usual considered a predisposing cause, was seen in four cases only. Five of our list were intemperate; four very temperate. One observer thought the free use of stimulants caused the disease in one instance. In four the family history of the patients was good; in one it was wretched. Privation is said to be a causal agency; not so in our cases; in five the circumstances were very good, in six moderate. Not one instance is recorded in the table of actual poverty. Peasants are said to be most frequently subjected to the disease; in our cases we find, though a large number were hospital cases, yet they deserved a higher grade socially, than what is given to the German patients. Malaria was not thought to have any connection with cause in any instance, save one. Shocks and mental strain were observed by some to antedate the disease. The cases of Curtin, of Pepper and of Osler indicated this cause. Diarrhœa seemed to be the only derangement of the system that influenced the development of the disease. It occurred, or was readily excited in three instances, in all of which the bone marrow was affected. So isolated are these apparent causal factors in an array of cases that one is almost forced to the conclusion, that their relation to the disease was simply as a coincidence, and that the analysis proves that the disease is a primary one, the cause being thus far unknown.

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* Coupland, "Lectures on Anæmia." *Lancet*, London, 1881.

For those who believe the " bone marrow " cases were cases of pseudo-leukæmia it is well to advert the remarkable features of late age and male sex and the fact that marked mental depression or physical exhaustion, shown by diarrhœa, were present (mental anxiety and shock three cases, diarrhœa three cases). Could not these depressing influences have had some bearing on the myelogenic changes?

Finally it is instructive to note the localities in which the disease was observed. It had been thought because in parts of Switzerland the inhabitants were so frequently affected with idiopathic anæmia, it was an endemic disease. It will be seen that three places in this country give nearly all the cases, and yet we believe, for reasons entirely apart from endemic influences. Thus fifteen of the cases were observed in Philadelphia, thirteen in Canada (Montreal and Toronto), eight in Boston, and the remainder in separate localities. This is to us curious, and yet readily explained. In each locality the great attention paid to blood diseases was apparently more influential in recognizing the disease. In Philadelphia, by the labors of Pepper and Henry, the profession has been kept on the lookout for cases. In Canada, Prof. Howard and Prof. Osler; and in Boston, Bradford and Cutter and others kept the profession alive to the possible presence of idiopathic anæmia. There is no doubt in other places in this country, similar people under similar conditions exist for the development of the disease.

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