feine for the cardiac debility, four grains being given at a dose, thrice daily.

It is to be regretted that we are compelled to add that often, in spite of the most careful hygienic and medicinal treatment, our efforts are in vain, and the disease progresses to a fatal termination.

For bibliographies the reader is referred to the previous edition of this work, to Coupland's article in Allbutt's "System of Medicine," and to the article of Ehrlich and Lazarus in Nothnagel's "Specielle Pathologie und Therapie."

John H. Musser.
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ANÆMIA, SECONDARY.—Strictly, all anæmia must be considered secondary. It cannot be more than a symptom of some deeper cause, but there are certain types of anæmia in which we can form no idea of any underlying cause, and which, therefore, we designate as "primary anæmias." On the other hand, there are other cases of anæmia in which the symptom is clearly the result of some definite cause, such as hemorrhage, malaria, or tuberculosis. Such cases we designate as "secondary or symptomatic anæmia."

Anæmia, of whatever variety, consists in a deterioration of the blood with diminution either in the number of corpuscles per cubic millimetre, in the amount of hæmoglobin contained by individual corpuscles, or in a combination of both changes. The latter form is the commoner. Very possibly these changes in the number and quality of the corpuscles are all secondary to some change in the plasma, but this must be for the present largely a matter of hypothesis, as our knowledge of the changes in the plasma is still very limited.

Cases of secondary anæmia have been divided into the acute and the chronic.

Acute Anæmia.

The great majority of cases are, of course, due to hemorrhage, either through traumatism with obvious hemorrhage through the skin, or from rupture of the liver, spleen, or kidney. Among the other pathological conditions which are most apt to lead to severe spontaneous hemorrhage, we may mention the following list: (1) Abortion and the puerperium; (2) extra-uterine pregnancy; (3) tumors of the uterus; (4) the peptic ulcer, gastric or duodenal; (5) typhoid fever; (6) tuberculosis of the lungs; (7) epistaxis; (8) carcinoma of the stomach, intestine, or liver; (9) aneurism; (10) hemorrhagic pancreatitis.

It has been shown experimentally that the withdrawal of even 50 or 70 cm. of blood is enough to make an appreciable change in its quality. Hoffmann experimented upon a healthy man who had 5,219,000 red corpuscles per cubic millimetre, withdrawing 425 gm. of blood by venesection. Half an hour after, the red corpuscles were reduced to 4,762,000; one day later, they numbered 4,681,000. The amount of blood removed here was estimated to be about six per cent. of the total blood mass, supposing the weight of the blood to be one-thirteenth of that of the whole body. The fact that the blood shows more loss a day after a hemorrhage than half an hour after has been very often observed, and the difference is more marked the larger the amount of blood lost. This is undoubtedly due to the fact that the blood immediately after hemorrhage is unduly concentrated, whereas later on it is diluted again by fluid taken up from the surrounding tissues. As regards the amount of blood which an individual may lose without dying, observations differ a good deal. Behier records a case in which the red corpuscles were reduced to one-fifth their normal number after an attack of metrorrhagia, yet the patient recovered. Hayem describes the case of a woman who had, during six days following the puerperium, a number of severe hemorrhages. Fifteen hours after the second of these, the number of red corpuscles was reduced to 550,000, or eleven per cent. of the normal, yet the woman recovered. It has been repeatedly observed that women bear loss of blood better than men. It seems to be pretty well established that no animal can survive the loss of more than half its entire blood-mass at a single hemorrhage, but apparently men can stand a great deal more than this. [For the conditions obtaining during the regeneration after hemorrhage, see *Blood Formation*.]

Aside from cases due to hemorrhage we occasionally meet with what is practically an acute anæmia in cases of (1) Virulent septicæmia; (2) destruction of red corpuscles within the vessels as a result of poisons; for example, snake poison.

1. In cases of acute puerperal sepsis, I have known the red corpuscles to fall within a few days to 1,450,000 and the hæmoglobin twenty per cent. Grawitz* reports a case of acute puerperal sepsis in which the red cells were reduced to *300,000 within twenty-four hours!* This case seems almost incredible, but is related in great detail in Grawitz's recent text-book on "Diseases of the Blood."

2. Blood destruction as a result of poisons, such as chlorate of potash or nitrobenzol, may produce an acute anæmia, as happened in a case reported by Brandenburg: A woman who had taken two and one-half ounces of chlorate of potash the night before showed on the

First	day, red cells	4,300,000
Second	" "	2,500,000
Fourth	" "	2,300,000
Fifth	" "	2,100,000
Sixth	" "	1,900,000
Seventh	" "	1,600,000—death.

Symptomatology.—*The Blood.*—As regards the condition of the blood following hemorrhage, it has been already mentioned that the diminution in the number of corpuscles per cubic millimetre continues and increases for several days after the hemorrhage. After severe cases the lowest count is not reached until from five to seven days after the accident. While this process of deterioration is going on the hæmoglobin percentage always falls more rapidly than the count of red corpuscles, so that after the first twelve or twenty-four hours the color index is always low. Moreover, when regeneration begins, the hæmoglobin is always slower to reach the normal than the count of red corpuscles, so that the color index may even become lower, despite a distinct gain in both red corpuscles and hæmoglobin, because the latter gains so much more slowly. This is not in any way peculiar to acute anæmias, but is well exemplified in them.

In stained specimens normoblasts begin to be seen within from twenty-four to forty-eight hours of the time of the hemorrhage, or even sooner, and are continuously present in the peripheral circulation until blood regeneration is complete. As a rule they are scanty, and careful search is necessary to find them, unless the blood loss be very great and the regeneration very rapid. Occasionally they are so numerous as to appear in almost every field. Von Noorden was the first to observe that during the regeneration period a very large number of normoblasts may be suddenly discharged into the circulation within a few hours or days. This flood of normoblasts quickly ceases, and is then followed by marked increase in the total number of red cells. Such an appearance of large groups of normoblasts intermittently, and followed by a marked increase in the total count of red cells, has been named by Von Noorden a "blood crisis."

Atypical staining reactions in the red corpuscles (*polychromatophilia*) is often seen even within the first twenty-four hours after the hemorrhage. Careful measurements have shown that the red corpuscles undergo a *swelling* after hemorrhage, both their diameter and their thickness being increased. *Deformities* in size and shape are occasionally present, but not often marked. The *white corpuscles* show, in the majority of cases, an absolute or relative increase in the number of polymorphonuclear neutrophiles. This increase, as has been said, is not constant and may be of any degree up to very marked leucocytosis. In rare cases, the leucocytes are diminished in gross, or the lymphocytes may be relatively or absolutely increased. Myelocytes in small percentages are not infrequently seen; indeed, in one of Ehrlich's cases six days after hemorrhage there was 13.7 per cent. of myelocytes with poikilocytosis and occasional normoblasts. Three days later the myelocytes disappeared.

* La médecine moderne, January 13, 1897.

The coagulability of the blood is increased and may take place twice or thrice as quickly as usual.

Other Symptoms.—Pallor of the skin, lips, and conjunctivæ, coolness of the extremities, a weak and tremulous voice, spots before the eyes, and noises in the ears, with dyspnœa, thirst, rapid, weak pulse, low temperature, and perhaps fainting, are to be observed even after hemorrhages of moderate severity. In severer cases there may be marked cerebral symptoms, aphasia, delirium, hallucinations, nausea, and vomiting, also cold sweat, increased secretion of urine, and tremor when movement is attempted. In fatal cases, one sees near the end of life the evidence of a great lack of fluid in the system, the skin becomes dry, the eyes lustreless; fibrillary twitchings or cramps may lead on to true convulsions. The temperature falls far below normal, and the pulse becomes almost imperceptible.

Albuminuria has been frequently observed associated with hyaline and granular casts within the first twenty-four hours after the hemorrhage. The urine is pale, and its daily amount increased, owing to the great thirst. A tendency to spontaneous bleeding is occasionally manifest in the gums or as a nose-bleed or uterine hemorrhage. The heart sounds are weak, often irregular, and frequently accompanied or replaced by murmurs, which are almost always systolic and loudest in the pulmonary area, though by no means confined thereto.

Besides the nervous symptoms already mentioned, neuralgia, especially of the cranial nerves, may be very obstinate. Amblyopia and amaurosis are occasionally observed. A certain amount of neuro-retinitis with occasional hemorrhages has been reported.

Post-Mortem Appearances.—(*a*) The most important change is fatty degeneration of the heart muscles, which may appear after hemorrhage even in cases which have proved fatal within a day or two, while if life had been prolonged a few days more, similar fatty change appears in the capillary system (especially in the brain), and in the secreting cells of the liver, stomach, and kidney. This fatty change is not to be explained, as was formerly supposed, by a diminished oxidation of the tissues, for all recent observations have shown that the oxidation processes are, if anything, increased in acute as in chronic anæmia.

(*b*) The bone marrow of the long bones undergoes, within a few days, a transformation in which the fat cells are replaced by enormous numbers of normoblasts, so that its color in gross is changed from yellow to red.

Diagnosis.—The diagnosis is doubtful only in cases of internal concealed bleeding. Under these circumstances it may be both difficult and important in cases of (1) Extra-uterine pregnancy with rupture; (2) internal hemorrhage, ante partum or post partum; (3) post-operative or secondary hemorrhage; (4) violent accidents involving "shock."

1. *Extra-Uterine Pregnancy.*—In cases of extra-uterine pregnancy, the diagnosis may be difficult before rupture occurs, but the symptoms of that event are very characteristic. Severe pelvic pain suddenly ceases, and then the patient begins to feel weak, restless, faint, and thirsty, and presents a pale skin and a weak, rising pulse. Such symptoms can only mean hemorrhage, and demand immediate operation.

2. *Internal Hemorrhage, Ante Partum or Post Partum.*—Any other concealed hemorrhage, such as may occur ante partum or post partum, shows its existence by the same symptoms. In case it is intra-uterine, an increase in the size of the organ can be made out by palpation and percussion.

3. *Post-Operative or Secondary Hemorrhage.*—Secondary hemorrhage after operation gives us the same symptoms and signs which have already been enumerated.

4. *Violent Accidents Involving "Shock."*—In cases of surgical shock, it is often important to determine how far the "shock" means anæmia from hemorrhage. If hemorrhage is going on, the worst thing we can do is to wait in the hope that time and stimulation will improve the condition, for time will, of course, make the matter constantly worse as the hemorrhage goes on. A blood count will often give us information of the utmost importance in such cases. Should it demonstrate the existence of a marked anæmia in a patient whom we have no reason to suppose previously anæmic, the diagnosis of internal hemorrhage is clear. I recently saw a little girl who had been run over in the street and was seen in a condition of what is often called "shock." There was no evidence of hemorrhage from any part of the skin or mucous membrane. A blood count showed a marked anæmia. A rapid laparotomy showed that hemorrhage was going on from a ruptured kidney. The hemorrhage was checked and the child recovered.

Treatment.—In the treatment of acute anæmia due to hemorrhage, when once the bleeding point is found and tied, the next thing is to restore to the depleted vessels an amount of fluid sufficient to keep up the heart action by giving it something to contract on. Transfusion of human blood has now given place to the introduction of normal salt solution, either subcutaneously, into the rectum, or into a vein. If the patient is unconscious, fluid may be infused subcutaneously with great ease and in considerable quantity. If the patient is conscious, this procedure gives considerably more pain than an intravenous injection. The introduction of salt solution into the rectum may be combined with either one or the other of these procedures.

Chronic Anæmia.

Among the commonest causes for chronic deterioration of the blood may be mentioned the following:

1. Repeated hemorrhages, such as occur in cases of gastric ulcer, menorrhagia or metrorrhagia, hemorrhoids, and hæmophilia.

2. Prolonged drain upon the albuminous materials of the blood, such as occurs in chronic dysentery, long-standing suppuration, phthisis, lactation, and cirrhosis of the liver with ascites.

3. Poisoning due to lead or arsenic, or in some less obvious way to toxic materials absorbed from the diseased gastro-enteric tract, or during the course of a case of nephritis. The fact is worth emphasizing that the anæmia which occurs in nephritis is due not to the drain of albumin out of the blood through the kidneys, but to a toxæmia. In chronic diffuse nephritis, for example, the amount of albumin lost through the kidneys is often trifling in comparison to the amount of anæmia. Probably under this same heading (*i.e.*, as a toxæmia) should be reckoned the anæmia occurring in connection with malignant disease. It is not simply starvation which brings about the deterioration of the blood, either in malignant disease or in other conditions in which the amount of food is insufficient, for it has been shown experimentally that starvation as such has no tendency to produce anæmia. After a forty-days' fast the blood of a professional faster has been found to contain more corpuscles per cubic millimetre than at the beginning of the fast.

4. Infectious diseases, especially malaria, syphilis, typhoid fever, acute articular rheumatism, and septicæmia due to pyogenic organisms, are apt to result in anæmia. We have already mentioned under the section on Acute Anæmia how grave a deterioration of the blood may occur in septicæmia. Tuberculosis rarely leads to any considerable degree of anæmia, unless a mixed infection with pyogenic organisms is engrafted upon the original disease, as indeed almost always occurs in pulmonary tuberculosis. Even here it is very surprising how little anæmia we often find, even though the

patient is deathly pale. In no other disease that I am acquainted with is there so little anæmia to be demonstrated in comparison with the degree of pallor. In this connection we may allude to the so-called tropical anæmia occurring in members of white races who have resided a long time in very hot climates, which has been shown to be no true anæmia at all, but only a blanching of the skin, due very possibly to the effect of the heat upon the circulation or upon the pigments of the skin.

5. The anæmias occurring in insanity are so frequent and so pronounced that the association of the two conditions can hardly be considered accidental, nor can the anæmia be explained as a result of taking too little food, for reasons given above.

6. Intestinal parasites may give rise to a very grave form of anæmia, either of the secondary type or in a form indistinguishable from primary pernicious anæmia.

Symptomatology. — *The Blood.* — In some cases of anæmia the impression is often almost irresistible that the total amount of blood is reduced. We have no means of proving this, but hints are given by the difficulty of obtaining blood from a puncture of ordinary depth, and by the relative emptiness of the retinal vessels as seen by the ophthalmoscope. The color of the blood as it emerges from the point of puncture may be nearly normal in relatively mild cases, while in the severer grades of the disease it looks pale and watery or possibly particolored and streaky. This last appearance usually means an anæmia of the very severest type.

A good general idea of the severity of the case may be obtained by the estimation of hæmoglobin. The lowest percentages are seen in connection with malignant disease, acute septicæmia, and any affection involving profuse hemorrhage or suppuration. Readings as low as fourteen per cent. have been made by competent observers. It should be said, however, that in using the Fleischl hæmoglobinometer for percentages of twenty-five or less, the technique, as ordinarily carried out, gives us very faulty results. It is much safer, in any such case, to fill the capillary pipette of the instrument several times in succession, washing the contents each time into the same chamber of the cell in which the blood and water are mixed, and then after making the reading to divide the result by two or three, according as we have used two or three pipettes full of blood. The reduction in the amount of hæmoglobin is almost always out of proportion to the diminution in the number of corpuscles, that is, the individual corpuscles which are left contain less hæmoglobin per corpuscle than is normal. This condition is especially marked in the milder grades of the disease, and at such times the conditions may be exactly the same as those found in chlorosis; for example, one of Laache's cases of consumption showed 5,148,000 red corpuscles with only thirty-five per cent. of hæmoglobin. Similar figures are not infrequently to be recorded in anæmia secondary to malaria, malignant disease, or nephritis.

Red Corpuscles. As suggested in the last paragraph, the number of red corpuscles shows in the earlier stages of a case of secondary anæmia relatively little diminution despite a considerable falling off in the amount of hæmoglobin. If, however, the cause of the anæmia persists, for example, if the patient goes on having malarial chills, or if the nephritis or cancer be incurable, a considerable reduction in the number of red cells gradually makes itself evident, and may finally reach a figure as low as that characteristic of pernicious anæmia. The lowest count that I have come across is that recorded by von Limbeck—306,000. This case fully recovered. Counts of 1,500,000 or less are not at all infrequent in malaria.

The specific gravity of the blood runs practically parallel to the percentage of hæmoglobin, and the same is true of the amount of solid residue. The coagulability of the blood in secondary anæmia takes place considerably more rapidly than is normal. Hayem's pupil, Le Noble, who studied this subject extensively, has shown that in cases in which the number of blood corpuscles is less than 1,000,000 per cubic millimetre clotting takes place in about half the time occupied in normal cases.

Stained Specimens.—1. The pallor of the microscopical preparation in gross may be quite noticeable in severe cases, and in specimens stained with Ehrlich's triple stain it is not uncommon to notice in the mounted cover-glass preparation a bluish tint, instead of the orange-yellow color which we see in similarly mounted specimens of normal blood. I have observed this bluish tint more frequently in secondary than in primary anæmias. The blood is unusually easy to spread between cover glasses; excellent specimens may be prepared even by a beginner, who would have difficulty in handling normal blood. Under the microscope the most striking change is the sparseness with which the corpuscles are spread over the field and the pallor of the individual cells. This pallor does not affect the whole cell equally, but shows itself especially in the central portions, the rim or periphery of the cells being left relatively well stained, even when the centre of the corpuscles is colorless. The amount of "orange G" (of the triple stain) which the cell takes up corresponds very accurately with the amount of hæmoglobin which the cell contains. So far as we know, it is only the hæmoglobin which takes the stain. To the extreme form of this staining anomaly Litten formerly gave the name of "pessary-shaped" corpuscles, which were at one time supposed by him to be characteristic of pernicious anæmia, in which disease, as a matter of fact, they are rarely seen. Not every corpuscle shows equal changes in respect to its staining properties. Side by side with extremely pale cells one may see some relatively well-stained ones. This is especially the case in the relatively mild cases. Where the hæmoglobin is as low as twenty or thirty per cent., one rarely sees a single well-stained corpuscle in the whole preparation, and there may be nothing but the "pessary shaped" cells to be found.

2. Normal red corpuscles have relatively slight affinity for basic stains and relatively strong affinity for acid stains In many anæmic conditions these staining affinities are so modified that some of the corpuscles take up both acid and basic stains, resulting in a diffuse coloration by a tint intermediate between those of the acid and the basic stain; for example, a purple color in case eosin and methyl blue are used. In other cases there appears, in specimens stained with Chenzinsky s solution," a spotted bluish pigmentation on a pink ground. These irregular staining reactions may be seen even in relatively mild cases; indeed, it is not always best seen where the hæmoglobin is lowest. Ehrlich still maintains that abnormal staining reactions, known technically as polychromatophilia, represent simply degenerative changes, but the weight of recent research has tended entirely in the opposite direction, and has proved to my satisfaction that polychromatophilic corpuscles represent immature forms which have been prematurely sent out from their place of manufacture, the marrow.

3. Poikilocytosis. Abnormalities in the size and shape of the corpuscles may be seen even in mild cases. It is important to observe that the abnormalities in size consist in various degrees of diminution in the diameter of the corpuscles, and rarely, if ever, in an increase of their size. In the extreme cases almost all the red corpuscles may be undersized; some may be not more than 2 μ in diameter as compared with 7 μ, the normal size. Deformities of shape, even of the most extreme and bizarre description, may be met with in ordinary cases of secondary anæmia, and are in no way characteristic of any one type. Although a very great variety of shapes may be seen, there is a strong tendency to a repetition of certain irregularities. The commonest of these are: (*a*) Battledore shaped forms; (*b*) sausage shaped forms; (*c*) ovals; (*d*) irregular triangles or quadrate forms.

Quite active pseudo-amœboid movements are not infrequently to be seen in the projecting points of deformed corpuscles or in the corpuscles as a whole. The central biconcavity may or may not remain visible.

4. Nucleated Red Corpuscles. In any form of secondary anæmia, especially in the severer grades, one may find nucleated red corpuscles, usually normoblasts. The number of normoblasts to be seen does not run parallel to the degree of anæmia, nor is any especial variety of anæmia particularly apt to show their presence, unless it is the post-hemorrhagic cases. In the latter condition they appear in a relatively large percentage of cases, and apparently with a certain regularity; in the other forms of secondary anæmia their appearance and disappearance seem very arbitrary and unaccountable. Different cases of equal severity may differ very widely in the number of normoblasts seen, and even in the same case at different times one finds a very great variation; to-day there may be many of them, to-morrow none. Megaloblasts are not very infrequently to be observed in very severe cases, but never, so far as my experience of several thousand cases goes, do they preponderate over the number of normoblasts.

5. White Corpuscles. In certain varieties of secondary anæmia, for example, after hemorrhage, in suppurative diseases, and malignant neoplasms, one usually gets a considerable increase in the total number of white corpuscles, the increase being made up largely or wholly of the polymorphonuclear forms. In one case of cancer of the kidney I counted 92,500 white corpuscles per cubic millimetre, ninety-four per cent. of which were polymorphonuclear neutrophiles. On the other hand, there are many cases of very severe anæmia, such as those associated with nephritis or due to malaria, in which there is no leucocytosis or in which the leucocytes may be diminished. The eosinophiles are usually diminished whenever the polymorphonuclear neutrophiles are increased. In anæmias due to intestinal parasites the eosinophiles may be increased.

6. Blood Plates. After hemorrhage and in some other varieties of secondary anæmia the number of blood plates will be greatly increased. Van Emden,* in an anæmic child with splenic tumor, found 829,000 blood plates as against from 180,000 to 256,000, the normal number.

Other Symptoms.—(*a*) The effects of anæmia upon the central nervous system are shown in manifold ways, almost all of which, however, can be brought together under the title of "*irritable weakness.*" The neuro-muscular system is both irritable and weak, the irritability being shown in increased reflexes and a tendency to cramps and to "nervous," jerky, restless movements, while the weakness is shown in the great proneness to fatigue on slight exertion and the inaptitude in performing delicate movements requiring skill. Brain action likewise shows both irritability and weakness. There is little power for a continued attention or for self-control, and marked irritability and emotional abnormalities. Blurring or dark spots before the eyes and tinnitus aurium are common. Headache, vertigo, and fainting easily occur.

(*b*) The gastro-intestinal tract is easily irritated, as is shown by the frequent occurrence of hypersecretion and occasionally of diarrhœa, but it is also weak and unable oftentimes to perform its functions of digestion and peristalsis. It is hard to decide, however, whether these symptoms are truly the results of the anæmia or of the underlying cause of which the anæmia is symptomatic.

Appetite is almost always lost or very quickly appeased. Painful digestion, due to gastric hyperæsthesia or fermentation, is the rule. The amount of hæmoglobin is normal or increased in the great majority of cases, and the motor functions of the stomach are well performed. Despite the frequency of constipation there is usually no increase of intestinal fermentation, and the intestine seems to absorb normally.

(*c*) On the part of the respiratory tract we find usually superficial breathing, which easily becomes labored and frequent on slight exertion.

(*d*) The heart's action is weak, yet easily irritated to violent palpitation. Œdema of the extremities is common, and effusions into the serous cavities are seen occasionally in marked cases. Hemorrhage, presumably due to fatty changes in the vessel walls, is rare in acute cases, but not at all uncommon in chronic ones; it is usually small in extent, and affects the skin and mucous membranes, especially those of the mouth, stomach, and intestine. Hemorrhages are also common in the meninges and in the retina. Occasionally a considerable amount of blood may be lost by epistaxis or from the gastro-intestinal tract.

The urine shows no characteristic changes; it is oftentimes pale and of low specific gravity, and may contain a trace of albumin and an increase over the normal number of casts. The temperature may or may not be raised. An interesting point in this connection is the relation of temperature to temperament in acute post-hemorrhagic anæmia. After profuse gastric hemorrhage due to peptic ulcer I have twice seen continued fever (from 101° to 103° F.), lasting several days. Both these cases were in patients of markedly neurotic temperament. In the great majority of cases of post-hemorrhagic anæmia, in which there is no specially neurotic element, the temperature remains normal.

Differential Diagnosis.—1. Many cases are dubbed anæmic on the evidence of pallor of the skin, especially if this is associated with symptoms of general debility or neurasthenia. R. T. Edes and others have shown that neurasthenics are rarely anæmic, and it is important to recognize that pallor of the skin is consistent with perfectly normal blood and with good general health. The condition, therefore, most frequently mistaken for anæmia is probably neurasthenia and debility or a simple congenital pallor of the skin unassociated with any disease. Pallor of the mucous membranes, especially those of the lips and conjunctivæ, is a better test of anæmia, but not very infrequently we see considerable pallor of the mucous membranes, as well as of the skin, and yet no anæmia by blood examination. This is especially apt to be the case in pulmonary tuberculosis, in which we may find a normal or even an increased count of red corpuscles with extreme pallor of the skin and mucous membranes.

2. I have known myxœdema mistaken for simple anæmia with obesity and so treated. In both diseases we may have subnormal temperature, muscular and mental weakness, pallor, and œdema; indeed, the two diseases may, and often do, coexist, but simple anæmia does not cause the marked changes in facial expression and cutaneous nutrition, nor the peculiar mental hebetude and hesitating speech characteristic of myxœdema. In case of doubt, the therapeutic test, the use of thyroid extract, would easily decide.

3. Cases of incipient pulmonary tuberculosis, especially in the female sex, are not infrequently mistaken for simple anæmia or chlorosis. Only the most careful examination of the sputum and a most thorough auscultation of the apices of the lungs after cough will suffice to exclude tuberculous disease, which may exist entirely without cough or with so little cough that the patient's attention is not called to it. Any fever occurring in a case supposed to be simple anæmia should make us suspicious of tuberculosis.

4. Pernicious anæmia is at times difficult to distinguish from the symptomatic form of the disease. I have known some of the cases of anæmia secondary to gastric cancer or to chronic bleeding hemorrhoids in which only the blood examination made it possible to exclude pernicious anæmia. In the severest grades of secondary anæmia (which are those most likely to be mistaken for pernicious anæmia), we are very apt to have leucocytosis, a low color index, an absence of macrocytes, and a predominance of normoblasts over megaloblasts. There are, however, periods in the course of some cases of pernicious anæmia—namely, periods of remission—in which the blood may be indistinguishable from that of secondary anæmia. Earlier or later the typical blood picture appears, but for a time diagnosis may be impossible. I have twice mistaken cases first seen during this period

* "Bydragen tot de Kennis von het Bloed," Leyden, 1896.

for secondary anæmia. From chlorosis a case of secondary anæmia occurring in a young girl may be indistinguishable. The characteristics of the blood are identical, and if the etiology of the case is not clear there may be nothing to set us right.

PROGNOSIS AND COURSE.—The duration of the disease and the severity of the symptoms depend largely upon the nature of the underlying cause. In post-hemorrhagic anæmia, in which less than one per cent. of blood mass is lost, it should be made up in from two to five days; where from one to three per cent. of the blood mass is lost, it should be made up in from five to fourteen days; finally, in the severest hemorrhages, in which over three per cent. of the blood mass is lost, it may be a month or more before regeneration is complete. Young and well-nourished persons are naturally much quicker in making up losses than are feeble or elderly persons. Where the hemorrhage is secondary to such diseases as typhoid, phthisis, or cancer, regeneration after hemorrhage may be very slow, or may not take place at all. Bierfreund found that after operations for mammary cancer the hæmoglobin is much slower in beginning to rise toward normal than after operations for non-malignant diseases (a week later on the average), and he asserts that the hæmoglobin never reaches the point at which it was before. This statement is all the more extraordinary because Bierfreund has specially noted a gain in weight in the same patients on whose blood the above observations were made. In Bierfreund's experience, it is usually from twenty-three to twenty-seven days after operation on malignant tumors of the breast before the hæmoglobin begins to rise.

The improvement of cases of anæmia is likely to be interrupted by periods of relapse. This is not so true of secondary anæmia as it is of pernicious cases, but nevertheless holds to a certain extent.

TREATMENT.—Obviously the first and most important indication is to discover and, if possible, remove the cause to which the anæmia is secondary. Many cases will recover with no further treatment. As a rule, however, recovery is considerably hastened by therapeutic measures, and where the cause is unknown, as not unfrequently happens, we have to devote our attention to the following therapeutic agents.

Nutrition.—There is no especial diet appropriate to the treatment of anæmia; what is needed is a full and varied nutrition, which should certainly include red meat, owing to its relatively large proportion of hæmoglobin and so of iron. The digestion may need attention, but it is important to refrain from giving pepsin and hydrochloric acid in any case before we have made sure that there is not already a hypersecretion such as statistics show to be very frequent in anæmia. The bowels often need treatment either for diarrhœa or constipation, more especially the latter, and relief of this symptom will help the general nutrition, and so the anæmia.

Climatic change is undoubtedly of service in some cases, partly through its psychical and partly through its physical effect. Of late years it has been recommended that we send patients to high altitudes. Experience has shown that patients are very favorably affected by altitude, and the rapid increase in blood corpuscles per cubic millimetre which every person, sound or sick, shows in high altitudes appears to be not entirely transitory.

Medicinal treatment consists largely of proper administration of iron and arsenic. Wide experience in all parts of the world has shown that in the great majority of cases iron is best administered in the form of Blaud's pills. As a rule, they cause no irritation of the gastro-intestinal tract, and do not tend to constipation. I think it is a common mistake to use them in too small doses. To an adult I never give less than six five-grain pills a day, two after each meal, and after a week or ten days I often increase this to nine a day, three after each meal. In the rare cases in which Blaud's pills are not well borne or are not effectual in increasing the amount of hæmoglobin in the blood, it is advisable to try one of the newer organic preparations which contain hæmoglobin as such or some substance nearly allied to it; for example, ferratin. The only objection to these latter remedies is that in order to get sufficient quantity of them into the system to give an equivalent to six of Blaud's pills per day, or one-tenth of a gram of metallic iron, one has to spend a good deal of money. The tincture of chloride of iron should rarely, if ever, be given, on account of its strong tendency to produce constipation, its deleterious effects upon the teeth, and its very disagreeable taste. All preparations of iron should be given after meals, never upon an empty stomach. Occasionally arsenic is useful, especially in the severer grades of anæmia. It is best given in the form of Fowler's solution, two drops after meals, well diluted, and increasing one drop daily until the physiological limit is reached, as shown by the occurrence of itching or burning of the eyelids, nausea, or vomiting. *Richard C. Cabot.*

ANÆMIA, SPLENIC. See *Hodgkin's Disease.*

ANÆSTHESIA AND ANALGESIA.—Definition of terms: *Anæsthesia*, accurately speaking, denotes the loss of sense of touch. The term is often used to indicate the loss of all forms of sensibility—as pain, temperature, muscular location, etc. In this article, when the word is used without qualification, it shall mean the loss of tactile sense. Tactile sensibility is subserved by structures that take cognizance of change of contact, and are stimulated by motion of an external object in contact with the surface.

Analgesia is a term employed to denote the loss of sensibility to painful impressions.

Thermo-anæsthesia is a loss of temperature sense.

Ataxia is a symptom of loss of muscular sensibility.

"Muscular sense" is a complex affair, including several different forms of sensibility. There is the painful sensibility to traumatic impressions, to passive stretching and powerful contractions, as in cramps. The most characteristic "muscular sense," however, is that by which is determined the character of movements and postures due to muscular action, also the character of passive movements and postures of muscles at rest. It also includes the recognition of resistance to contraction, by which is estimated the difference in weight of objects; articular sense is included.

Methods of Testing Sensibility.—The determination of the varying degrees of anæsthesia and analgesia is made difficult by the fact that the physician must depend upon the statement of the patient for his information. The intelligence, attention, and sincere co-operation of the patient are necessary to secure reliable responses. Furthermore, individuals vary, within the limits of what is normal, quite appreciably in their sensibility to external irritation. Finally, in patients suffering from lesions which cause either a slight or perhaps a greater degree of loss of consciousness, sensibility is more or less diminished up to entire loss of sensation, even though the lesion may cause no anæsthesia directly.

In testing sensibility the patient should be blindfolded or in some other way prevented from seeing what is being done, in order that simulation or self-deception may be avoided. It is remarkable how vividly one can feel the prick of a pin or touch of a feather through the medium of sight. When the lesion is unilateral, a comparison of the two sides is very desirable. Various instruments of precision have been devised by neurologists for testing sensibility. These are convenient and desirable for scientific purposes, but for clinical use they are not essential. A much more important element is the cultivation of the judgment of the examiner by constantly using the same method of examination. No amount of paraphernalia will make up for a lack of that cultivation. A feather or camel's-hair pencil or the tip of the finger may be used for testing tactile sensibility. The objection to the finger is the possibility that there may be a difference in temperature between the examiner's finger and the patient's skin, and consequently that contact may be recognized by temperature sense

even when anæsthesia exists. A common pin is a valuable instrument in testing for analgesia. By alternately using the point and head and requiring the patient to distinguish between them by saying "head" or "point," the physician can determine whether his answers are based on pain or tactile sense. When testing for anæsthesia the patient should be instructed to say "yes" each time he is touched; or he may be asked to name the point touched. This gives information as to his power of localization. If more definite information is desired, he may be asked to touch the exact spot that had been touched by the examiner.

On some accounts a better test for analgesia is to pick up a fold of skin and pinch the rounded portion. By practice one is enabled to determine quite satisfactorily the degree of sensibility by the degree of pressure required to produce a painful impression.

Thermo-anæsthesia may be present when tactile and pain sense are normal. To ascertain its existence one may employ two test tubes, one filled with hot and the other with cold water. More accurate means of measurement are needed for scientific record.

In the presence of a localized disturbance of sensibility the characteristics should be noted as accurately as possible. If there is an area of anæsthesia its boundaries should be definitely determined. The task is not difficult when the area is sharply defined, but it becomes more so when it passes gradually into the normal. Anæsthetic areas often exist without the patient's knowledge and will escape notice unless especially sought for. This should always be done in cases presenting obscure abnormal conditions of the nervous system.

For convenience of study the anæsthesias and analgesias may be divided into two great classes: I. Those of functional origin; II. those due to some organic lesion.

Functional Derangements of Sensibility.—I use the word functional advisedly and with a full knowledge and appreciation of the position of those who regard every derangement of function as evidence of organic lesion. I shall not argue this question further than to say that in the manifestations of the nervous system the evidence is convincing that temporary and more or less permanent suspension or derangement of function may and does occur without the existence of organic lesion.

Hysterical anæsthesia may involve all varieties of sensation. In such cases there will be no response to any kind of sensory stimulation—such as touch or pain or heat or cold or muscular action or change of posture or location of a part. Or the anæsthesia may be confined to one variety of sensation while the others may remain normal. Or again, any two or more of them may be involved. Analgesia is the form of anæsthesia most frequently observed in hysteria. Then follow, in order of frequency, loss of tactile sense, temperature sense, muscular sense, and articular sense. The last is quite rare as an hysterical manifestation, but has been noted by several observers. The physician should not assume that a case of ataxia is hysterical until he has discovered other stigmata and has excluded all other probable sources of ataxia. For further discussion of the stigmata of hysteria, see under *Hysteria*.

The anatomical distribution of anæsthesia, in hysteria, is extremely variable. No part of the body is free from the liability of a loss of sensibility from this cause. But it may conveniently be considered under three types: I. Hemianæsthesia; II. segmental; III. disseminated.

Hemianæsthesia is the most common type, and when present without motor disturbance it is most suggestive of hysteria. It involves exactly one-half the body vertically, the middle line, anteriorly and posteriorly, forming a distinct and abrupt line of demarcation between the normal and anæsthetic portions of the skin. The mucous membrane of the same side is also involved. Among the cases of hemianæsthesia from lesion of the posterior portion of the posterior limb of the internal capsule, there have been reported some which resembled those of hemianæsthesia of hysterical origin. These cases are so rare, however, as to be a curiosity.

In the segmental type of anæsthesia a hand and more or less of the arm, or a foot with more or less of the leg is anæsthetic—sometimes called the glove or stocking form of anæsthesia; or a part of the face or head may be involved.

In the disseminated type anæsthetic patches, irregular in size, shape, and distribution, occur. Any conceivable part of the surface may be the site of anæsthesia. I wish to call attention to three characteristic features of these anæsthetic areas, that should always be borne in mind when making a differential diagnosis: (1) The areas do not correspond to the distribution of nerves; (2) the borders are sharply outlined, the change to normal sensibility being abrupt, there being no gradual fading of one into the other; (3) the borders are not constant, but are subject to sudden changes. This feature has been especially emphasized by Dr. Patrick, of Chicago. This shiftiness of the borders is so pathognomonic that it should always be looked for in testing a case. A very soft pencil is needed to mark the outline so that no irritation of the skin is produced whereby the patient's subsequent replies may be influenced. I do not care to discuss the treatment of this condition, as it doubtless will receive proper consideration under *Hysteria*. But I may say in passing that the suggestiveness of the treatment is a most potent factor. Therefore the application of electricity to the anæsthetic area in the form of a powerful static spark or a strong galvanic current is among the most efficient of agents.

Any of the special senses may be involved in hysterical anæsthesia. We may thus have impairment or loss of sight, hearing, taste, or smell. Hysterical amblyopia most often consists in a concentric constriction of the visual field. Besides this there may be a disturbance of the color field, either a total loss of color perception or, what is more common, a reversal of the color fields; the most common form being that in which the field for red is larger than that for blue.

Pharyngeal anæsthesia is commonly due to hysterical disturbance of the function of the glosso-pharyngeal and vagus nerves, of which "globus" is another manifestation, and ageusia or loss of taste still another. Laryngeal anæsthesia is not an uncommon stigma of hysteria. The well-known tolerance of examination of the pharynx and larynx on the part of hysterical patients is due to anæsthesia of these parts.

Anæsthesia and Analgesia of Organic Origin.—In studying the organic lesions of the nervous system with their consequent impairment or loss of sensation, we cannot do better than to adopt an anatomical classification. We shall consider: 1. Lesions of peripheral nerves; 2. lesions of the cord; 3. intracranial lesions.

Trigeminal anæsthesia, more or less complete, results from a destructive lesion in any portion of the nerve from its central origin to its peripheral terminations. The location of the lesion may be determined by the extent and distribution of the anæsthesia, and—in the case of a lesion located at the base of the brain—by noting the disordered function of other nerves involved in this lesion. Peripheral lesions are indicated by the small portion of the nerve involved. If a portion of the face with a corresponding mucous surface is involved, one branch of the nerve is affected at or near its exit from the cranium. If the anæsthetic area comprises the distribution of an entire nerve and is complicated by trophic disturbances, the lesion is in the Gasserian ganglion or its immediate vicinity. A lesion in the posterior portion of the posterior limb of the internal capsule will produce anæsthesia of one side of the face and of the same side of the body, resembling hysterical hemianæsthesia (to which the reader is referred). If one side of the face and the opposite side of the body are anæsthetic, the lesion is probably pontile.

The pathological diagnosis is made by considering the history and development of the abnormal condition. Among the more important factors to be considered are