SYNONYMS.—Idiopathic anaemia; Essential anaemia; Myelogenic anaemia; Progressive pernicious anaemia; Ganglionic anaemia; Anemalosis.

Definition.—By “pernicious anaemia” is now generally understood a variety of primary anaemia, which arises insidiously, and is characterised by progressive diminution in the number and changes in the form of the red corpuscles of the blood, together with a similar but generally less marked diminution in the amount of haemoglobin; which changes apparently depend upon undue haemolysis combined with inadequate compensatory haemogenesis,—a condition which, in the majority of cases, passes more or less rapidly to a fatal termination, the progress being in some cases interrupted by periods of improvement followed by relapse, but rarely resulting in permanent restoration to health, whatever the method of treatment.

It is difficult, even in the light of modern research, to frame a satisfactory definition of this affection—one which shall not be too wide, nor, on the other hand, too narrow to embrace the varied conditions under which this severe form of anaemia is known to arise. There is reason to doubt even the constancy of the “progressive” and “pernicious” characters which were deemed by Biermer to constitute its most characteristic features. On the other hand, the use of such names as “idiopathic” and “essential” anaemia, however appropriate they may have been when Addison directed attention to this class of primary blood affection, can hardly be justified now except as an admission that pathological research has failed to discover the source of a disease which presents such striking clinical features. The difficulty is enhanced by the fact that the clinical phenomena are not in themselves distinctive, not even the characters of the blood; hence, as the advance of knowledge led to the shrinking of the “idiopathic” area, it seemed reasonable at one time to admit the existence of secondary forms of pernicious anaemia side by side with the primary.

However, there is good ground for believing that when all extrinsic causes are eliminated, there remains a residue of cases of progressive anaemia, to which the term “primary” may be assigned; and it is to this class that we may also assign, at least provisionally, the name “pernicious.” For a primary anaemia may be defined as one dependent on the perverted relationship between the two great functions concerned in maintaining the normal composition of the blood. In the active processes of disintegration and renewal of the blood elements, haemolysis is balanced by haemogenesis. The balance may be disturbed by excessive haemolysis on the one hand, or by inadequate haemogenesis on the other.
It will be seen that an explanation of idiopathic anæmia has been sought in each of these directions severally, but, as stated in the above definition, there may be defects in both. Whether the definition should be made more precise by indicating the probable source and character of the hemolytic process is a matter, which I shall discuss under the head of "Pathology."

History.—By common consent the credit of the first general account of pernicious anæmia is due to Dr. Thomas Addison, whose reference to it in his monograph "On the Constitutional and Local Effects of Disease of the Suprarenal Capsules" has often been quoted. Although these passages appeared in 1855 he had been teaching their doctrines for several years. No account of the condition can be considered complete without Addison's description of it:

"For a long period I had from time to time met with a very remarkable form of general anæmia occurring without any discoverable cause whatever, cases in which there had been no previous loss of blood, no exhausting diarrhoea, no chlorosis, no purpura, no renal, splenic, miasmatic, glandular, strumous, malignant disease.

"Accordingly, in speaking of this form in clinical lectures, I, perhaps with little propriety, applied to it the term 'idiopathic' to distinguish it from cases in which there existed more or less evidence of some of the usual causes or concomitants of the anæmic state.

"The disease presented in every instance the same general character, and, with scarcely a single exception, was followed after a variable period by the same result.

"It occurs in both sexes; generally, but not exclusively, beyond the middle period of life; and, so far as I at present know, chiefly in persons of a somewhat large and bulky frame, and with a strongly-marked tendency to the formation of fat.

"It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to his earliest feeling of that languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement. There is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth, and waxy appearance; the lips, gums, and tongue seem bloodless; the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitations being produced by the most trifling exertion or emotion; some slight oedema is probably perceived about the ankles. The debility becomes extreme; the patient can no longer rise from his bed; the mind occasionally wanders; he falls into a prostrate and half-torpid state, and at length expires. Nevertheless to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and
the obesity often present a most striking contrast to the failure and exhaustion observable in every other respect.

"With perhaps a single exception, the disease, in my own experience, resisted all remedial efforts, and sooner or later terminated fatally."

"On examining the bodies of such patients after death I have failed to discover any organic lesion that could properly or reasonably be assigned as an adequate cause of such serious consequences; nevertheless, from the disease having uniformly occurred in fat people, I was naturally led to entertain a suspicion that some form of fatty degeneration might have a share at least in its production; and I may observe that, in the case last examined, the heart had undergone such a change, and that a portion of the semilunar ganglion and solar plexus, on being subjected to microscopic examination, was pronounced by Mr. Quekett to have passed into a corresponding condition.

"Whether any or all of these morbid changes are essentially concerned—as I believe they are—in giving rise to this very remarkable disease, future observation will probably disclose."

Isolated examples of the remarkable condition thus succinctly described by Addison had found their way into medical records prior to the date of his writing. This has been shown by Lépine and Pye-Smith in their historical summaries of the subject. Thus, the latter author refers to the records of seven cases which doubtless fall into the category of "Addison's anaemia"; namely, one recorded by Combe (1823), one by Andral (1823), one by Marshall Hall (1837), one by Pierry (1841), one by Pearce (1845), and two by Barclay (1851). It seems clear, too, that the cases given by Channing of Boston (Mass.), in a paper, written in 1842, dealing with anaemia in relation to the puerperal state and in uterine disorders, probably belong to the same class. However, comparatively little attention was attracted to the subject for several years after Addison wrote, except, it is right to add, amongst those who were most familiar with his teaching. Thus, Sir S. Wilks, in the Guy's Hospital Reports for 1857, discussed idiopathic fatty degeneration, in which he referred to the morbid change which is the most characteristic feature of idiopathic anaemia; and cases were recorded by Habershon and others of the Guy's school. The writings of Guusow and Biermer of Zurich, especially the memoir in which the latter author first uses the phrase "progressive pernicious anaemia" (1871-72), did much to awaken interest in the subject, and, I may add, to ignore the previous work of Addison; thus to Biermer was given the credit, which indeed he himself claimed, of describing for the first time the characters of a condition not hitherto recognised. It is clear, however, that not only had he been anticipated by Addison, but it is also probable that the cases amongst pregnant women to which Guusow drew attention were the same as those indicated by Channing thirty years previously, and by Lebert in a case recorded in 1853 as "puerperal chlorosis." Nevertheless, the service rendered by Biermer was considerable, both
from the clinical and pathological standpoint; and his choice of the name "pernicious" directed attention to the fatal character of the disease. However, we must recognise that, as knowledge has grown, reasons have increased for believing that many cases included by Addison as "idiopathic" or by Biermer as "pernicious" would more strictly find a place amongst the secondary anæmias. For not only have unsuspected causes been revealed of progressively fatal anæmias which exhibit all the characters described by Addison and Biermer (such as anchylostomiasis), but definite, if minute, pathological differences have been shown to exist between pernicious anæmia proper and certain other cases which some years ago I regarded as examples of "symptomatic (secondary) pernicious" anæmia; for in the predominance of the cardinal symptoms masking the underlying condition, these latter cases ran a course and exhibited many characters which resembled those of cases not so associated; and therefore named provisionally "idiopathic." This is not a mere question of nomenclature, it concerns the true interpretation of the pathology of the disease before us, and must be referred to again when we speak of this branch of the subject. We must constantly bear in mind, therefore, that a certain number of the cases on record are not strictly to be ranked in the category of "pernicious anæmia" properly so called.

It is not possible in such an article as this to review all that has been written during the past twenty-five years upon the subject. Many contributions have been made by physicians of Addison's own hospital, namely, by Pye-Smith, F. Taylor, and Hale White. Most of their writings appear in the Guy's Hospital Reports. Dr. Stephen Mackenzie, again, in a clinical lecture published in 1878, did much to invite attention to a subject to which he reverted some years later in the Lettsomian lectures which he delivered in 1891 at the Medical Society of London. Dr. Byrom Bramwell published a full account of pernicious anæmia early in 1876, and drew attention to the value of arsenic in its treatment. To Dr. W. Hunter we owe some of the most profound studies of the pathology of the disease, studies which have materially influenced our conceptions of its nature, and have done more than any other work to give definiteness to them. Other labourers in the same field have been W. Russell, Brakenridge, Gibson, Stockman, and Fraser of Edinburgh; Finny, Purser and Craig of Dublin; Mott, Russell, and James Taylor of London. The disease was studied at an early date in America, the contributions of Osler, Gardiner, and Howard of Montreal being amongst the first; Oser is also the author of many subsequent studies. To Pepper of Philadelphia is due the discovery of changes in the marrow of the bones, observations speedily confirmed by others. Musser, Henry, Kinnicut, and Woods have also contributed to the subject in the United States. Numerous essays and monographs have appeared in the Continental schools by Eichhorst, Quincke, Muller, Neumann, Immerrmann, Lépine, Hayem, Lasche, and others.

Etiology.—To speak of the causation of a disease of which, in the majority of cases, no adequate cause can be discovered seems paradoxical;
yet in pernicious anaemia we detect certain remoter antecedents, which, if not of themselves adequate to give rise to the condition, nor constant in their occurrence, are yet not without importance. These are among the more general causes of anaemia, for anaemia owns an infinity of causes; but they seem to have no bearing on the quality of perniciousness. Whenever the anaemia appears to pass beyond the boundary of the incidental, and becomes so dominating a feature of the illness that, as it increases, all the symptoms are referable to the anaemia, and none to the primary affection, then it is legitimate to infer the intervention of some further agency which has converted the simple into the pernicious type of anaemia. Thus, for example, hæmorrhage is a common cause of secondary anaemia, and repeated small bleedings may produce a condition which progresses from bad to worse, and ultimately destroys life. Is such a state to be regarded as "pernicious anaemia"? Some have thought so, and a recent writer (Stockman) has striven to show that the very hæmorrhagic tendency which belongs to severe anaemia may be the means of its passing by a vicious circle into a pernicious and fatal disease. Such a view, of course, gets rid of the notion that pernicious anaemia is a specific disease; as, thus, any anaemia of sufficiently high degree provides for its own further progress by the effects which it produces on the nutrition of the blood-vessels. On the other hand, that cases of hæmorrhage and of diseases involving large hæmorrhages, or a continued repetition of smaller ones, although leading to a chronic anaemia, do very rarely assume the type under discussion, seems to prove the existence of other determining factors; for it does certainly happen that, although a case of pernicious anaemia may seem to have been initiated by a metrorrhagia or a gastric hæmorrhage, the anaemia advances without any repetition of the loss of blood, whether from the primary source or from secondary sources opened by the anaemic state. Thus, even were there no other distinguishing characters—such, for example, as those of the blood and urine—we should have to assume the presence of some fresh factor to account for the course of the disease. The consideration of some of the more common antecedents of pernicious anaemia may suggest to us where this tertiun quid is to be sought.

Amongst the favouring conditions upon which some stress has been laid are insufficiency or unsuitability of food in persons subjected to hard manual labour, or even not so subjected. The conditions of life of the Swiss peasantry were at one time supposed to determine the many instances of the affection which rendered Zurich a centre for its study. Misery and famine are conditions of anaemia; but unhappily such conditions are as common in the large centres of population as they are in the rural districts, yet pernicious anaemia is a rare disease by no means limited to the poorer classes of the community. Moreover, it is mainly in the writings of the Swiss authors that any reference is made to such etiological factors. Another class of antecedents most prominently cited in the writings of Gussorow and Biermer, to account for the excess of women among their patients, consists of pregnancy, parturition, and
lactation; yet how seldom is this fatal kind of anæmia observed as a direct sequence of these physiological states. Reference has already been made to hemorrhage as an antecedent, and mention must be made of gastro-intestinal disturbance also, which of all factors seems likely to be the most nearly connected with the etiology of the disease. Not only are the earliest symptoms connected with this system in a considerable proportion of cases, such as vomiting, diarrhoea, or irregularities of digestion, but many cases exhibit also definite changes in the gastric or intestinal mucosa; and this to such an extent as to have led some observers to attribute the fatal anæmia to the atrophy or other lesions which attack nutrition at its source (Fenwick, Kinnicutt, Osler). Again, it is well known that patients with chronic gastric disorders, such as ulcer or cancer, are sometimes anæmic out of all proportion to the amount of hæmorrhage which may have occurred during their illness. Indeed, in some cases where there are no direct symptoms of the gastric disorder the resemblance to pernicious anæmia is striking; and cases have been described where anæmia apparently pernicious has seemed to establish itself upon the gastric disease (Eisenlohr). The arguments of Hunter on this point have much force, his contention being that in all these conditions where the clinical features of pernicious anæmia are manifested in association with malignant disease or gastric changes, the lesions essential to the former have been superadded; for, as he points out, pernicious anæmia is a rare complication in malignant disease, whilst the gastric lesions often occur apart from pernicious anæmia. In commenting on the view, advanced by Fenwick, that atrophy of the gastric glands underlies pernicious anæmia, Hunter points out that this observer himself found such atrophy in a large number of cases of cancer also. "Thus, of fifteen cases of cancer of the breast, in only four were no anatomical changes to be found in the gastric mucosa. Some degree of atrophy was found in every case of cancer of the stomach. If atrophy of the gastric glands is to be regarded as the essential anatomical change in pernicious anæmia, it would seem reasonable to expect that pernicious anæmia should be found frequently associated with cancer of the breast, and almost invariably with cancer of the stomach. Curiously enough, however, I have not found a single case recorded in which cancer of the breast has presented the features of pernicious anæmia; and as regards cancer of the stomach, it is the exception and not the rule for it to be marked by the clinical features characteristic of pernicious anæmia" (Hunter). Similar reasoning is employed by Hunter to cast doubt on the alleged etiological importance of the degenerative changes described by Sasaki and by Banti in the nervous tissues of the intestinal wall; for such changes, according to the observations of Scheimpflug, are frequent in wasting and acute infectious diseases. Banti, regarding the sympathetic nerve lesions as a primary defect, went so far as to give the name "ganglionic anæmia" to this affection.

Among the influences which have been known to precede a progressive anæmia must be included those in which the mental and
emotional faculties are concerned. There is authentic evidence that shock, depression, anxiety, or severe mental strain have been followed by the appearance of an anæmia which has run on to a fatal issue. The precise relationship between the disease and such antecedents is, however, quite obscure.

The hypothesis that pernicious anæmia is due to microbic agencies has little to support it; the micro-organisms that have been described in the blood (Fränkenhauser) have not been isolated or cultivated, whilst the condition of the blood itself is such as readily to lead to errors of observation in this respect.

Lastly, pernicious anæmia is mainly a disease of adult life, most cases occurring between the ages of twenty and forty-five. But children are not exempt from it, cases being recorded in patients as young as seven, eleven, and twelve years. The sexes are about equally prone to it, but if all cases of its apparent origin in pregnancy and parturition be excluded, it would probably be found that the disease preponderates amongst men.

Symptoms.—In the vast majority of cases it is extremely difficult to fix the date at which the illness began; its onset being so gradual and insidious that the patient passed imperceptibly from health to disease. It does, however, occasionally happen that a debilitating illness, a great loss of blood, pregnancy, or parturition has been followed immediately by an anæmia of the ingarvescent course characteristic of the disease; and, as has already been pointed out, even some unusual mental shock or emotional disturbance may be directly antecedent to the appearance of the anæmia. Whether or not we are to include in the present category every case which seems to have its origin so directly in an anæmiating cause, it is evident nevertheless that the declared symptoms do not differ in kind from those which are thus produced. There is hardly a single symptom of the protopathic affection which is not to be found now and again in association with profound anæmia clearly due to an ordinary cause. The earliest indications of the malady are so slight and insignificant as to be disregarded, and it is often not until the disease is well advanced that its true nature is recognised. Nor is it possible to assign any period during which these early and indefinite signs may be said to last. It is a stage measured mostly by weeks or even months rather than days, although cases of apparently acute course are on record. These initial symptoms consist in the main in failing strength, and in disinclination for exertion, physical or mental; so that the subject of the malady becomes possessed by an unnatural lassitude which makes all labour irksome, and often renders him despondent, low-spirited, and capricious in temper. Together with this persistent asthenia and loss of energy the appetite fails; there may be complaint of discomfort after food, and the patient will perhaps suffer at times from nausea or even vomiting. If to these gastric disturbances there be added intestinal irregularity, it is natural for him and his friends to ascribe his weakness and depression to some functional derangement of the digestive organs. Yet, as a rule, there is no falling off in nutrition, but even a noticeable
increase in bulk and weight. Gradually, however, the signs of anaemia are more evident, and, as they become pronounced, his weakness increases, he suffers from palpitation, perhaps from syncopal attacks, and shortness of breath on exertion, and at last is compelled to abandon his calling and seek rest and advice. The symptoms which may now be presented, those that is, of the declared disease, may best be described in detail; they occur with variable frequency, and some even which may be thought to be essential and characteristic are occasionally conspicuous by their absence.

The constant symptom is of course the anaemia. The pallor of the skin is striking, often in marked contrast with the previous good colour of the individual. The skin and mucous membranes are almost devoid of colour, save that the former, especially of the face, generally assumes a faint yellowish or lemon tint that is wholly different from the whiteness of the subject of pulmonary tuberculosis, the earthy pallor of the cancerous cachexia, or the muddy tint of the malarial subject; and is quite different from the bronzing of the malady discovered by Addison in his search for an adequate cause of "idiopathic" anaemia. This complexion, however, is sometimes met with in the chlorotic, in those who have suffered from internal hæmorrhage (as, for instance, in cases of large pelvic hematocele in process of absorption), in rare cases of chronic gastric organic disease, and in various toxic anaemias. It cannot be deemed pathognomonic; but occurring, as it does, with so few symptoms, or overt evidence of blood loss, it may lead to the suspicion of the grave nature of the malady. It is all the more suggestive when it occurs in a male subject of mature age whose previous health record has been excellent. There may be some oedema of the lower extremities, often very slight, sufficient to cause slight pitting on pressure over the malleoli: sometimes more extensive, and not seldom entirely absent. Indeed, this symptom is hardly so frequent a feature of pernicious anaemia as it is of chlorosis. In the later stages, however, it may become marked, as also may petechial hæmorrhages chiefly on the lower limbs. There is no constant condition of skin as regards perspiration. Some have noticed undue sweating in the earlier and later periods of illness, but there does not appear to be any regularity in this symptom, and it can hardly be regarded as essential. The skin often assumes the soft and smooth character to be met with in the subject of fatty degeneration.

The temperature of the body is generally normal, and in advanced stages subnormal; but most observers record periods of remarkable pyrexial exacerbation, which some consider to be peculiar to this kind of anaemia. This pyrexia is not as a rule severe, the temperature seldom exceeds 102° or 103°, with morning remissions and marked irregularity. It may last for a few days and then subside, recurring at intervals during the progress of the malady; or it may be of more continued course. This intermittent pyrexia is possibly related to the variations in the hæmolytic process, and may be taken as confirmatory of the toxaemic theory of the disease; another conceivable view is that
it is due to capillary hæmorrhages in the heat-controlling centres of the brain. Whatever the explanation it is seldom entirely absent; but then, it may be remarked, a subfebrile temperature is not uncommon in chlorosis, and may also occur after severe hæmorrhage.

The signs of circulatory disturbance are generally obvious, and may even lead to an erroneous opinion. The patient may complain of palpitation from an early period, and at times may be attacked with faintness or actual syncope. The pulse, generally quicker than normal, is markedly affected by exertion or emotion, the difference between its rates as influenced by posture being considerable. It is mostly soft and fairly full, whilst there may be complaint of throbbing in the neck or a feeling of fulness in the head. The cardio-vascular signs of anæmia are pronounced. The impulse of the heart is undulating, and the apex-beat generally somewhat lower and situated more to the left than normal; percussion confirms this evidence of slight dilatation of the ventricles by revealing an increase of the cardiac area of dulness to the left. An intense blowing systolic murmur is generally audible over the preaortic, most marked at the pulmonary cartilage. In advanced cases this murmur may have a grating character, and be even mistaken for friction. (A diastolic murmur has been noted, but this is not common.) Its haemic origin is confirmed by the presence of a similar murmur in the large arteries, and a loud hum in the jugular vein. The carotids often pulsate violently, and a distinct thrill is to be felt over them and the large veins in the neck.

Examination of the blood reveals a great departure from the normal. The bloodless condition of the skin makes it somewhat difficult to obtain sufficient for its estimation. The drop has a pale watery appearance, and the number of red corpuscles is found to be notably diminished. The degree of this oligocythaemia depends upon the stage and severity of the disease; but it is not unusual to find the number of red corpuscles reduced to 1,000,000 per cub. mm., that is, 20 per cent of the normal; and as the case progresses they may fall considerably below this figure, the lowest estimation on record being 143,000 (Quincke). There is no parallel diminution in the number of leucocytes; in late stages they may exceed the normal amount. With the hæmoglobinometer it will almost invariably be found that although there is a marked reduction in the amount of hæmoglobin this is not proportionate to the reduction in corpuscular richness. Thus in a case, in which the corpuscles have fallen to 10 per cent the hæmoglobin percentage may be as high as 20 or 25 per cent. Hence it follows that the individual corpuscles must have a larger relative content of hæmoglobin than in health. The microscopical examination shows notable changes, which when first observed were thought to be quite characteristic. In the first place, the tendency for the corpuscles to form rouleaux is almost entirely lost, although this is not to be observed in every case. As a rule the scanty corpuscles either form irregular masses, or lie scattered over the field; and it is evident at once that they exhibit very great variations in size and shape. Thus many
are of irregular form, pear-shaped, oval, and deformed, constituting the condition named by Quincke "poikilocytosis," which, however, is not distinctive. Some are much larger than normal, (megalocytes), and any, on the other hand, appear as small spherical bodies (microcytes). Neither of these varieties can be considered distinctive, although some authors think that the prevalence of the megalocytes is greater than in any other condition; others, however, consider that the microcytes are if anything more characteristic. Besides these forms, which may be regarded respectively as immature or overgrown red corpuscles, there are also to be seen nucleated corpuscles, which suggest a reversion to the reptilian type; these, according to their sizes, have been named normoblasts, megaloblasts, and microblasts. Lastly, Ehrlich showed that granular corpuscles which stain with reagents are often present, and are possibly degenerate corpuscles; whilst the readiness with which the hæmoglobin accumulates in a mass within a corpuscle gives the latter a pseudo-nucleated aspect. On the other hand, Dr. Copeman found that hæmoglobin separated from the corpuscles in pernicious anæmia with abnormal readiness. There is no increase in the number of leucocytes; but it has been observed that these are mostly of the smaller (lymphocyte) variety, and granular masses are present. Thus the changes are mainly limited to the red corpuscles, which may be considered to exhibit disintegrating forms and immature corpuscles side by side.

A tendency to hæmorrhage is a noteworthy feature of the disease. This may be seen comparatively early in its course, and may aggravate the anæmia; but in extent and degree it is too variable to be regarded as the direct cause of the progressive character of the affection. The hæmorrhages may take the form of epistaxis, of hæmatemesis, of hæmaturia, or of bleeding into internal organs, such as the brain and the spinal cord. Most commonly, however, they are but small capillary effusions, and occur most distinctly in the retina. It has been shown by Mackenzie that these retinal hæmorrhages are prone to occur in any form of prolonged anæmia if of sufficient intensity (below 50 per cent corpuscular richness); and as this degree of intensity is generally attained in pernicious anæmia their occurrence in this affection is one of its most common symptoms. The retinal hæmorrhage was first pointed out by Biermer, and may be regarded as a sign of some value. As a rule it does not lead to any impairment of vision, but cases have occurred where it has been the cause of amaurosis. Mention has already been made of the cutaneous hæmorrhages which may occur.

Dyspnæa is a prominent symptom, the enfeeblement of the heart adding to the respiratory difficulty caused by the lack of hemoglobin. As the end is approached this symptom may become more marked and distressing, and the physical signs of oedema of lung may supervene. Otherwise there is comparative freedom from pulmonary disease throughout, although bronchitis and pneumonia have been observed as serious complications.

Disturbances of the gastro-intestinal system are among the earliest
and most frequent features of the attack. The pale, flabby tongue denotes the general anæmia and want of tone of the stomach—conditions indicated by nausea, vomiting, epigastric uneasiness, and flatulence. The secretion is deficient in hydrochloric acid, in many cases it may be actually wanting (achlorhydria). Digestion is therefore slow, and the appetite much impaired. Sometimes irregularity of the bowels is marked by diarrhoea alternating with constipation, the former being occasionally profuse. So common and so early is the appearance of such digestive disorders as to give ground for the belief that they have an important influence in inducing the anæmic condition; and the fact that anatomical changes are frequently found in the stomach of subjects of pernicious anæmia has led some observers to ascribe the affection to atrophy of the gastric glands. Jaundice is not common, and when present seldom intense. Palpation reveals enlargement of the liver, with some tenderness over it. The spleen is rarely to be felt. Ascites may be present, but never in large amount.

The urine is generally fairly abundant, of normal or diminished specific gravity, acid, and free from deposit. It is often pale, but even in the course of the illness it may assume a high colour hardly consonant with the anæmic state. The chief cause of this coloration was shown by Hunter to be due to an excess of pathological urobilin, and the significance of this ingredient is considerable.\(^1\) There may be an excess of indican, and free iron has been observed by some (Finny). Uric acid is generally in excess, but there is no constant change in the amount of urea. Occasionally albuminuria is noted, but it is not a prominent feature. Observers have noted the presence of many another abnormal constituent; according to Hunter, the presence of pathological urobilin, renal epithelium, casts containing blood pigment, and increased excretion of iron, is characteristic. There may be hæmaturia.

The symptoms exhibited on the side of the nervous system have received especial attention of late years since the discovery of definite organic change in the spinal cord in cases of profound anæmia. The functional disorders comprise irritability, a growing inability to fix attention upon a subject, loss of memory, and often marked insomnia. Headache is not prominent until the anæmia becomes extreme, when there may be delirium also, or even more violent mental disturbance. In some cases the end is ushered in by convulsions passing into coma; in others a lethargy gradually deepens into coma. But the intellect often remains unimpaired almost to the close, and death takes place from mere exhaustion. The occurrence of convulsions and the appearance of partial or complete hemiplegia, or monoplegia, denotes cerebral hæmorrhage of greater or less extent. Sometimes the paralysis is so slight and transient as to indicate that the hæmorrhage must have been very small; in others a definite apoplectic seizure terminates the illness. The spinal

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\(^1\) Gowlland Hopkins, from examination of five cases, was unable to satisfy himself of the presence of "pathological" urobilin, and was inclined to attribute the spectroscopic indications to an admixture of urobilin and hæmatoporphyrin.
symptoms referred to above consist, in the main, in slight disorders of
domility, mostly ataxic in character, sometimes spastic; and they have
been found associated with pronounced changes in the spinal cord. At
the same time some of these degenerative lesions have been met with in
cases that did not exhibit any disorder of function during life.

Morbid anatomy.—At the time of death the body appears, in the
majority of cases, to be fairly well nourished. The pallor of the surface
is striking, and petechiae may be distributed over the lower extremities,
which may be somewhat edematous. The panniculus adiposus is often
of a deep yellow colour, and the dark red tint of the muscular layers
contrasts with the exsanguine aspect of the skin. Some thin serous
effusion may be found in the peritoneal and other serous sacs. The
blood is thick and watery, and the clots in the cardiac cavities small and
pale. The blood serum has been observed to have a yellowish tint from
admixture with haemoglobin readily liberated from the corpuscles, and
even to stain the hands of the pathologist. The specific gravity of the
blood is lower than normal; in one case it is stated to have been 1028
instead of about 1055. The microscopical characters of the blood have
already been given. The heart is generally well covered by epicardial
fat, and sometimes petechial haemorrhages may be seen on its surface.
The muscular substance is soft, flaccid, and of a tawny, brownish tint,
sometimes compared to that of a faded leaf. The musculi papillares,
especially of the left ventricle, are nearly always variegated by wavy
whitish streaks—the “tabby-cat striation” of Quain. Microscopically
the fibres are found to be in various stages of fatty degeneration, some
wholly converted into fatty granular and oily detritus, others with
accumulated fat granules around the muscle nuclei. The valves are
normal, but small areas of opaque white fatty degeneration may stud the
intima of the aorta. Similar fatty degeneration has been found in the
arterioles and capillaries, leading often to their rupture in various parts
of the body. The lungs present no notable lesion; they are, as are all
the viscera, very bloodless; although mostly the lower lobes present some
engorgement and oedema, and there may be petechiae beneath the pleura.
Occasionally it happens that the disease attacks a subject who presents
some old caseous or cedified tubercle in the lung, and sometimes also an
intercurrent pneumonia terminates life; but of course neither the old nor
the recent changes are essential. The stomach exhibits a striking pallor
of its mucous membrane, which may further show marked evidence of
atrophy of the glands, with or without excessive thickening of the sub-
mucosa. The liver is nearly always slightly enlarged, and fattily degener-
ated. In definite cases the outer zone of the lobules is pigmented by an
accumulation of free iron (haemosiderin) within the cells and around the
capillaries. The presence of this substance is revealed by treating sec-
tions with sulphide of ammonium (not a very trustworthy test) or ferro-
cyanide of potassium, and its discovery by Quincke led to the hypothesis
of the disease that is now mostly adopted. The gall-bladder contains
dark bile. The spleen may be slightly enlarged, but often it is quite
small; in colour and consistence it varies, being often pale, sometimes soft, or again rather indurated. In this organ, too, but never to so marked an extent as in the liver, granules of ferruginous pigment have been met with. The pancreas and suprarenals show no changes. The intestinal plexuses of nerves and the great abdominal ganglia have been found to exhibit evidence of degeneration. The mesenteric and other lymphatic glands are not as a rule affected. The kidneys are smooth and pale, but pigment granules have been found in the cells of the cortical tubules. As regards the nervous system, there may be subarachnoid hæmorrhage on the surface of the brain. The brain itself is strikingly exsanguine. It is instructive to note that although sinus thrombosis has been observed in chlorosis, it has not been recorded in pernicious anæmia. Cerebral hæmorrhage, however, may be present. In the spinal cord, even in cases which have not presented any symptoms of such disease during life, tracts of sclerosis have been met with in the white matter; they are irregularly distributed, sometimes involving the whole of the posterior columns, together with the lateral and anterior, but generally sparing the nerve-roots and the gray matter. Another change is that of miliary sclerosis or minute hæmorrhagic foci scattered irregularly throughout the substance of the cord. Notable changes have been found in the marrow of the long bones, consisting in a reversion to the fœtal type of red marrow; when first met with, this conversion was thought to be distinctive, and no doubt it indicates increase of the hæmogenetic function; but it is also present in anæmia due to hæmorrhage, and may be absent in the disease under consideration.

Pathology.—The interpretation of the clinical and pathological facts of so obscure a disease as pernicious anæmia could not fail to arouse widespread interest, and the attempt to afford a rational explanation of its origin has led to much speculation and to more or less thorough investigation. There is no need to dwell further upon a matter already touched upon in speaking of etiology, but it may be said that for coherence and reasonableness of doctrine there has been no more satisfactory exposition than that given by Dr. William Hunter in his numerous essays upon this disease in particular and upon the subject of blood-destruction in general. For, although in some respects it may be necessary to admit certain modifications in his argument, seeing that some of its premises are not yet verified, yet it cannot be doubted that his contention for the specificty of pernicious anæmia, as a disorder consisting in hæmolsys, affords so far a satisfactory explanation of the phenomena. It has further enabled us to eliminate from the category of pernicious anemia many anæmias which are strictly secondary; closely as they may simulate the primary disease in clinical features, blood changes, and visceral lesions. Nor is it warrantable to include within the class such cases as those of fatally progressive anæmia, associated with the presence of intestinal parasites; unless it can be shown that they depend on the same kind of hæmolsys that underlies the primary malady.

Pernicious anæmia, then, signifies a definite group of clinical and
pathological phenomena dependent upon a special form of blood-destuction, or hæmolysis, induced by toxic agents absorbed from the gastro-intestinal tract. The grounds for this conclusion may be briefly summed up as follows:—(i.) There is abundant proof that hæmolysis does take place in this disease. This is shown by the condition of the blood, its deformed and disintegrating corpuscles, the readiness with which the hæmoglobin escapes from them, and the abundance of microcytes. (ii.) The presence of an excess of pigment in the liver, spleen, and kidneys; this pigment being in the form of iron granules very loosely combined in the cells; whilst the elimination of iron and occasional excess of pathological pigments in the urine further support the hæmolytic view. (iii.) This hæmolysis takes place within the area of the portal circulation and not in that of the systemic; as indicated by the condition of the spleen, the accumulation of the hæmoglobin detritus (hæmosiderin) within the hepatic cells of the outer zone of the lobules, and by the absence of hæmoglobinuria. For Hunter’s researches prove that when hæmolysis takes place in the general circulation hæmoglobinuria occurs; but in pernicious anæmia the pigment, if eliminated by the kidney, appears in the form of granules of iron pigment, or as an excess of other pigmentary matter variously regarded as “pathological urobilin” (Hunter, M’Munn) or as a mixture of “urobilin” and “hæmatoporphyrin” (Gowlland Hopkins). Moreover, iron granules have been found in the tubules of the kidney in renal casts and epithelia. (iv.) Such a disintegration of the blood can take place in the portal system (possibly mainly in the spleen), as is shown by Hunter’s experiments with such hemolytic poisons as toluylendiamin. The source of this hypothetical toxin is reasonably considered to be the gastro-intestinal tract, and that it is of bacterial origin is almost equally probable.

The conception that has thus been framed of the nature of pernicious anæmia is rendered more convincing by the fact that in the forms of anæmia which most nearly approximate to it—such as those due to other toxic agencies, to prolonged and repeated hæmorrhages, to blood parasites as in malaria, to cancer, or to syphilis—so marked an excess of iron in the viscera is never found, especially in the liver, as is found in this disease. Thus Hunter gives 0.7 as the average percentage of iron found by various investigators in the liver in pernicious anæmia, as against 0.078 or 0.12 for other diseases; whilst the late Dr. Beavan Rake found, from an examination of five cases of anchylostomiasis, that in this affection (which so closely simulates pernicious anæmia as to have led to the opinion that, like pernicious anæmia, it may perhaps depend upon hæmolysis in the manner peculiar to this disease) it was only 0.1 per cent. Dr. Rake, it is to be noted, adhered to the opinion that the anæmia of anchylostomiasis solely depends upon the hæmorrhages produced by the parasite from the intestinal wall.

At the same time, in the present state of knowledge it is impossible to avoid the conclusion that a hemolytic process closely akin to that of pernicious anæmia may occasionally intervene in the course of grave
organic disease, and especially of chronic gastro-intestinal disease. If this be so, however, it would be no longer correct to speak of such an exceptional and, so to speak, accidental supernovation of the pernicious process as a "symptomatic" anæmia. The secondary affection should rather be regarded as a complication than as a regular feature of the original disease.

The view of the nature of anemia alternative to that of increased hæmolysis—one, too, which in point of time preceded the promulgation of the latter—is that of disordered hæmogenesis, as suggested by the remarkable reversion of the bone-marrow to its fetal condition originally observed by Pepper and Cohnheim, and since verified by many other observers. The significance of these changes has been materially affected by the recognition of the part played by hæmolysis in the disease, as well as by the fact that they are not invariably met with, nor differ in kind, if they do in degree, from the changes in the marrow which ensue on anæmia experimentally produced by bleeding. It may be that a place should be retained in nosology for a "myelogenic anæmia," but if so it must stand apart from pernicious anæmia as now understood. Whenever these marrow changes are met with side by side with the characteristic hæmolytic features of pernicious anæmia they are more likely to be of a secondary nature, indicating an effort on the part of the hæmogenetic organ to repair the waste that is in progress elsewhere.

And that the marrow should exhibit these changes in some cases and not in others may not be more remarkable than that the spleen should be swollen and apparently in an active state of hæmolysis in some cases, shrunken and inactive in others. The course of the malady suggests an inconstant and variable hæmolytic activity, and it may well be that this is paralleled by varying degrees of hæmogenetic action. In one of the most recent and careful studies of these marrow changes in pernicious anæmia the conditions obtaining in the several stages of the disease are described; the earlier changes are similar to those met with after hæmorrhage, the later are characterised by great abundance of large nucleated corpuscles peculiar to pernicious anæmia, and suggestive of a reversion to the embryonic type.

But both must be considered secondary to the anæmic state (Muir). Dr. Muir is careful to add, however, that "whether or not there are any cases of fatal anæmia, in which marrow lesion is a primary factor, I am not prepared to say. The question ought to be kept an open one, and in all such cases the condition of the marrow should be carefully inquired into, along with any changes in other organs which point to a process of blood-destruction."

There remains another aspect, ably described by Prof. Stockman, in which pernicious anæmia has been regarded which, if correct, would de-throne the disease from the position which it has attained, and relegate it to that of a sequel or result of any form of anæmia of whatever origin. It is based on the fact that the anæmic state, if long continued, provokes fatty degeneration of the walls of the blood-vessels, and thus promotes a liability to multiple hæmorrhages, which in their turn intensify the
anæmia and the proneness to bleed; and further, that the effects of larger hæmorrhage are pathologically indistinguishable from those which in anæmia take place within the tissues and organs. It cannot be denied that such an explanation of the nature of pernicious anæmia, if substantiated, would get rid of many of our present difficulties, for it bridges over the gap between the protopathic and deuteropathic forms of progressive anæmia by referring them all to the same immediate cause. Yet as Addison could find no adequate cause for the production of "idiopathic" anæmia, so too is it difficult to believe that the capillary hæmorrhages which characterise pernicious anæmia are in the majority of cases sufficient to induce the extreme degree of oligocythaæmia, and the indubitable evidences of hemolysis which the disease exhibits. At the same time, Stockman's thesis is one which deserves most careful study, for he does not hesitate to deal with the whole of the pathological and chemical evidence put forward by the advocates of the hæmolytic doctrine.

This doctrine also assumes the operation of a specific toxic agency; and it is interesting to note that those who have studied the degenerative changes in the spinal cord, which are apparently more common in pernicious anæmia than might be supposed from the clinical phenomena, believe also that these changes are best explained by a toxic influence, although some of them are manifestly the result of capillary hæmorrhages. In accordance with the prevalent views upon the subject, the nature of pernicious anæmia is expressed in the classification of anemic disorders put forward by Crozier Griffith and Musser. The anæmias are divided by them into two main groups—the cytogenic and the non-cytogenic. Of the latter there are two classes—the hæmolytic and the oligocythaæmic. The hæmolytic comprise—(i.) Pernicious anæmia; (ii.) other toxic anæmias; (iii.) chlorosis; (iv.) parasitic anæmias (some forms). The oligocythaæmic include—(i.) Parasitic anæmias (some forms); (ii.) post-hæmorrhagic anæmia; (iii.) anæmia from loss of albumin; (iv.) anæmia from malnutrition. Such a division is only provisional, but it recognises at least that pernicious anæmia is entitled to a distinctive place in nosology.

Diagnosis.—The diagnosis of pernicious anæmia does not rest upon any very certain basis, for although, generally speaking, this diagnosis may be justified in the presence of a case of progressive anæmia, arising insidiously, without adequate discoverable cause, and exhibiting the characteristic changes in the blood already described, it must yet be borne in mind, first, that sometimes an adequate cause does exist, but cannot be discovered, and, secondly, that the blood changes are not in themselves pathognomonic. At the same time, when it is considered that the clinical phenomena may be simulated by profound anæmia of secondary origin, no endeavour should be lacking to ascertain whether there is or is not some underlying disease. The task is rendered easier as the number of conditions which are known to give rise to so grave an anæmia are not large. The most likely are malignant
disease, especially of the stomach, and advanced syphilis. In such cases attention to the course of the symptoms and the history of the patient may assist in effecting a separation. The anaemia which is sometimes so marked a feature of chronic parenchymatous nephritis is seldom likely to be mistaken for pernicious anaemia, in view of the predominance of definite signs of the renal affection. Malignant endocarditis is more likely to be mistaken for pernicious anaemia, for here anaemia may be pronounced, whilst the cardiac murmur, and even the pyrexia and the cutaneous or other haemorrhages, may be looked upon as indications of pernicious anaemia. But an examination of the blood will determine the true character of the affection. Purpura and haemophilia are hardly likely to be mistaken for pernicious anaemia.

From chlorosis, which shares with pernicious anaemia the title of a protopathic anaemia, the differences are fairly well marked. Between the two affections the clinical diagnosis, apart from considerations of age and sex, is to be made by examination of the blood. In chlorosis the reduction in haemoglobin is always vastly greater proportionately than the reduction in the number of corpuscles; the chlorotic blood does not show such marked evidence of poikilocytosis, or so many microcytes as that of pernicious anaemia. More difficulty may be experienced in discriminating the anaemias due to intestinal parasites, such as the anchylostomum or the bothrioccephalus, for there are no distinctive features either in the blood or in the symptoms which would serve to distinguish them. It is possible that the urine might afford means for the diagnosis, but it is by no means certain that all cases of pernicious anaemia exhibit that excretion of "pathological urobilin" which is held to characterise the affection. In fact, nothing but a thorough examination of the faeces for the detection of the ova of these parasites can suffice to exclude them, and the fortunate issue of anthelmintic treatment may clinch a diagnosis so made. From splenic anaemia the diagnosis is to be made by the marked and progressive enlargement of the spleen in this disease, as well as by the comparatively small degree of oligocythæmia. In leukæmia the blood condition is manifestly the diagnostic criterion.

Prognosis.—The outlook in a case of established pernicious anaemia is very grave. It would, however, be too much to say that it must necessarily end fatally, for cases are recorded where the patients were restored to health and remained in health for years afterwards. It is nevertheless only too true that what has often been regarded as recovery has proved to be but a temporary rally, however remarkable in degree; the oligocythæmia almost disappearing and the distressing symptoms entirely passing away. Such apparent recoveries often, after an interval of months, give way to relapse, and the end may come in the first or some subsequent recurrence of the illness. This character is so common a feature, after more than one method of treatment, as to raise doubts whether the rally is wholly attributable to the latter, whether, that is, there may not be a "relapsing" form of the disease.
Treatment.—Pernicious anæmia then, as its name implies, tends ordinarily to run a downward course, often un influenced by any treatment that may be adopted; and frequently, too, when marked improvement has followed the use of certain remedies, a relapse has occurred in which the same means are no longer successful. As a recent writer (Dieballa) points out, it may be that much depends on the amount of recuperative power still residing in the blood-forming organs. If the blood-destruction can be arrested, or if the hemogenetic function can be stimulated, then there is hope that the blood will be restored to the normal by the natural power of regeneration. So far as can be judged, most of the therapeutic efforts that have been attended by success, temporary as this may have been, have had for their aim the second of these two conditions; but treatment based upon the theory of intestinal intoxication has not been wanting.

The general principles of the treatment of anæmia naturally apply in this disease with especial force. Rest, bodily and mental, and the avoidance of excitement are not only essential, but are often spontaneously sought by the patient, who is disinclined for exertion of any sort. Removal to pure air and healthy surroundings, when the conditions of the patient's ordinary life are without these benefits, are too obvious to require mention; whilst for the well-to-do much benefit may accrue, if the disease be not advanced, from a winter sojourn in a more equable and brighter climate than this country affords. The matter of diet is one of the greatest importance. The anorexia, nausea and tendency to diarrhoea, which often mark the early stages, make this a matter of difficulty. Experience proves that nitrogenous foods are ill borne, and the dietary therefore must in the main be limited to milk, vegetable and farinaceous foods. It may be necessary to have recourse to peptonised and other easily digestible preparations. When tolerated, pounded raw meat or meat juice and bone-marrow may be taken in small quantities, on bread or toast, with advantage. But the disinclination for food of any kind may be so great as to render it very difficult to supply adequate nourishment. Small quantities of alcohol in the form of claret or burgundy may prove of value as aids to digestion.

In a disease which is primarily dependent on destruction of the elements of the blood, haematinic remedies may reasonably be adopted. It is remarkable, however, that the chief of these—iron—is in the great majority of cases quite inoperative. In this respect the difference between chlorosis and pernicious anæmia is so striking as to suggest at once that the pathogenicity of these two forms of primary anæmia is totally different. Evidence of the inefficacy of iron in the latter is probably to be found in the fact that the system still retains its iron; in greater amount, indeed, than can be properly utilised. At the same time, there are a few cases on record in which iron seemed to do good; the free and frequent administration of the perchloride has been especially advocated. It is possible, however, that the value of this preparation may not depend on the ferruginous element (vide p. 515).
Very different is the experience of the value of arsenic, the introduction of which in the treatment of pernicious anaemia we owe to Dr. Byrom Bramwell. Administered in gradually increasing dose, it is generally well tolerated by these subjects, and although by no means invariably successful in causing improvement, yet this does often follow, and can hardly be ascribed to anything else than the specific action of the drug upon haemato genesis. On the other hand, if there be a natural tendency in the disease towards a temporary rally, it is difficult to estimate the precise share in this which is to be ascribed to the action of the remedy. At the same time, the improvement, when it does take place, follows too closely upon the adoption of the treatment to afford room for scepticism. Although of all remedies arsenic has proved to be most often followed by manifest improvement, yet even in cases where the benefit has been striking, relapses have occurred sooner or later; and it often happens that on the second occasion the drug seems to have lost its efficacy, and other measures have to be devised. The arsenic may be given in the form of Fowler's solution, or of the liquor arsenici hydrochloricus, beginning with doses of 2 to 3 minims, which are gradually increased to 18 minims, according to the tolerance of the subject. The arseniate of iron pill is a convenient form. It is well to continue the drug for some time after the signs of improvement are manifest.

Cases of recovery have also been recorded after the use of antiseptic drugs, such as salol, β-naphthol, salicylate of bismuth, and the like; their efficacy being ascribed to their direct antagonism to the supposed fermentative processes which yield a haemolytic poison in the intestine. A notable instance of rapid recovery, which, moreover, was sustained for a long time, has been recorded by Dr. Gibson; it followed the prescription of β-naphthol, after the failure of arsenic. In another case, where for nearly four months a variety of remedies had been vainly tried in turn—namely, ferratin, bone marrow, oxygen, arsenic, iron, and quinine—the administration of salol (continued with occasional intermissions for three months) produced a restoration in the corpuscular richness which seemed to have been due to the change of remedy (Dieballa).

Other isolated cases of similar good results from this line of practice, including that of lavage of stomach and intestinal irrigation, have been recorded, although not seldom the same methods have led to no good result.

Indeed there are few maladies in which the results of treatment are more capricious. It is impossible to prophesy in any given case whether any given remedy will be useful or not. Dieballa, in commenting on the case of recovery after the administration of salol, points out that the comparatively slight diminution of leucocytes and the persistence of a normal proportion of eosinophilous cells in the blood, as shown in that case, may afford a clue to the integrity of the blood-forming organs, and may justify expectation of adequate recovery if the haemolysis can be arrested.
We have yet to discover the reasons for the frequent failure of a remedy in one case and for its success in another. Thus the success attending the use of red marrow, introduced by Prof. Fraser, has been repeated by some physicians, but never attained by others. A like diversity of experience is to be found in the records of cases treated, often, no doubt, in the last resort, by blood transfusion or saline injections. Excellent and even remarkable results of transfusion have been published—amongst others by Quincke, Brakenridge, and Affleck—results which often seem quite out of proportion to the amount of blood injected; as if the healthy serum had exerted some specific effect, either in stimulating haemogenesis or, as some think, possibly by exerting an antitoxic influence upon the (assumed) haemolytic virus. Yet in very many cases this measure has proved futile.

Thus in pernicious anaemia, where the therapeutical results are so varied and conflicting, it is impossible to frame any uniform plan of procedure; and the inconstancy of therapeutical results may be taken as evidence that there is much yet to learn of the intimate pathology of the disease. All that can be done in the presence of the progressive blood-destruction is to make trial of each of the several remedial measures that have been found at times to be efficacious; of these I would place first the administration of arsenic, and next to it that of intestinal antiseptics.

**SIDNEY COUPLAND.**

**REFERENCES**

SPLenic Anæmia


The above select list is by no means exhaustive of the very copious literature of the subject, which of recent years has been greatly added to. Nor does it take account of the numerous articles and monographs upon the various forms of parasitic anæmia, notably ankylostomiasis and bothriocephalus anæmia.

S. C.

**SPLenic ANÆMIA**

There is a form of profound anæmia, progressive in character, ending fatally, generally of no long duration, associated with great enlargement of the spleen, but without leucocytosis or enlarged glands. Splenic anæmia is the name by which the disease is best known in this country; but it has also been called splenic cachexia, splenic pseudo-leucæmia, lymphadenoma splenicum, and spleno-megalic primitive; under the last name chiefly it is described in French literature.

To Banti, who wrote in 1882, is due the credit of drawing special attention to this malady. In 1891 Bruhl published an exhaustive article on the subject, bringing together all the cases that he was able to find recorded up to that date. The other contributions consist for the most part of accounts of isolated cases.

The total number of cases recorded is still small, and probably does not exceed thirty, including the fourteen cases upon which Bruhl's paper was founded.

Symptoms and signs.—The disease may be divided into three stages: in the initial stage the symptoms are those of extreme anæmia, with great loss of muscular power and some wasting of muscle; though usually without emaciation. As in this stage the disease presents no specific features it can rarely be recognised. The second stage is characterised by progressive enlargement of the spleen, and by attacks of severe pain in the splenic region; the anæmia is more profound, the
loss of strength is extreme, and the patients are liable to repeated attacks of bleeding, especially from the nose; the temperature is now usually raised and of hectic character, reaching 102° or more in the evening. It is in this second stage that the disease is first recognised.

In the last stage the condition is one of progressive asthenia which ends in death; there is in it nothing especially characteristic.

Throughout the disease most of the symptoms present but few peculiarities, for they do not differ from those which occur in any form of profound anemia. Thus there is general pallor and loss of strength, and great weakness and dilatation of the heart with its consequences; namely, shortness of breath, palpitation and pain, all made worse by exertion, together with the usual hemic murmurs. The pulse and respiration are readily accelerated, especially on effort or excitement; and there may be some edema of the feet.

The hemorrhagic condition in the latter stages is only remarkable in that it is more than usually pronounced.

This form of anemia is sometimes said to be of the chlorotic type; as there is little or no emaciation, and the reduction in the hemoglobin is greater than the reduction in the number of red blood cells would account for.

With a disease so rare as splenic anemia the best description of the disease will be an account of a case: —

A man aged thirty-six presented himself with extreme anemia, raised temperature, and a large spleen. The case looked like one of splenic leukocytethmia, but examination of the blood showed no increase of white cells.

The patient had been well till twelve months before he came under observation, when a tooth had been extracted; this operation was followed by profuse bleeding, which lasted several days; from that time onwards he became gradually weaker and thinner, and suffered from repeated epistaxis.

The patient was extremely pale, cachectic, and somewhat sallow; his cheeks were flushed, and the temperature, on the evening of admission, reached 103°. He was constantly spitting up a little blood, which came from the back of the pharynx or from the nose. The respiratory organs were normal. The heart was somewhat dilated, with a blowing, systolic murmur audible over the whole precordium and loud at the pulmonary area, there was increased pulsation in the vessels of the neck; the pulse was 96, of low pressure, but fair volume.

The liver was somewhat enlarged, extending from the upper border of the fifth rib to an inch and a half below the costal arch.

The spleen was greatly enlarged, and extended from a point four inches above the costal arch downwards to an inch above the anterior spine of the ilium on the left side. It was smooth on the surface, moved freely in respiration, but was tender to touch.

The urine was normal.

The left pupil was a little larger than the right. Ophthalmoscopic examination showed the retina to be normal.

There was no tenderness of the bones and no enlargement of lymphatic glands.

On examination of the blood the red corpuscles were found to number
SPLENIC ANÆMIA

2,055,000, and the white corpuscles 50,000, chiefly lymphocytes; the haemoglobin was only 26 per cent of the normal. There was no poikilocytosis or other changes in the cells, red or white.

Three weeks later another examination of the blood was made. The red cells had fallen to 1,900,000, while the white corpuscles numbered 58,000; the anaemia had progressed and the strength failed, there had been occasional attacks of abdominal pain, sometimes in the splenic region, sometimes more diffuse, but not very severe; the temperature had remained of a hectic character, rising to about 103° every evening, as shown upon the chart, and the patient had one or two attacks of epistaxis. The blood was examined for microorganisms, and none found.

A week later the eyes were examined again, and a large haemorrhage was found in the left retina.

A few days later the patient became very hoarse, dyspnoea increased rapidly, oedema of the larynx was diagnosed, and tracheotomy performed with great relief. The temperature remained high, and after the operation reached 105°. There was a good deal of oozing from the incision after the operation, and five days later a sudden haemorrhage took place from the wound; blood was sucked into the trachea, and the patient was suffocated.

The necropsy showed a large spleen weighing 76 oz.; it contained one small infarct. On microscopical examination the Malpighian bodies were seen to be much diminished in size and badly formed, and there was a slight general increase in the trabecular tissue. The liver also was enlarged, weighed 93 oz., and was slightly cirrhotic. The heart was dilated and weighed 12 oz.; all its cavities contained post-mortem clots; there was a small vegetation, as large as a pea, on one of the aortic valves. The muscular substance was not fatty. The larynx was still somewhat oedematous.

A full account of this case is given in the Transactions of the Medical and Chirurgical Society, vol. lxxix.

Williamson’s case is also an interesting one to compare with that just recorded:—

It occurred in a lad aged nine who, for two years, had been growing increasingly pale and anaemic, and had suffered for the last twelve months from fortnightly attacks of epistaxis. He was extremely anaemic and had a very large spleen. The examination of the blood was as follows: red cells, 3,540,000; white, 4000; haemoglobin, 22 per cent.

Four months later the red cells were reduced to 2,510,000, white 2000. A month later the following report of the blood was made. There were a number of poikilocytes, no eosinophile cells, no large mononuclear or granular cells, but a slight increase of lymphocytes. The temperature for the last six months of life was very irregular, with marked daily oscillations reaching to 101° and 102° at times. The patient died with an attack of acute peritonitis.

The necropsy showed a very large spleen weighing 40 oz.; the liver reached two inches below the ribs and weighed 44 oz. There was a small serous effusion in the pericardium, and some recent vegetations on the mitral valve. A small ulcer was found in the small intestines, which had perforated and caused purulent peritonitis.

In the spleen the fibrous trabeculae were increased in thickness, there was
an enormous number of large nucleated cells each containing several red blood-cells. The Malpighian bodies had undergone fibroid change and the lymphoid cells were few. There was a slight iron reaction in the fibrous trabeculae and in the Malpighian bodies, but none in the spleen pulp. Micro-organisms were looked for and none found.

The liver showed a little increase of connective tissue, and gave a very slight iron reaction.

The bone-marrow was dark purple-red in colour, and showed a marked absence of fat. It contained large cells enclosing several red blood-cells, as in the spleen.

With these general remarks we may now pass on to the review of the more special features of the disease.

The affection occurs with much greater frequency in men than in women; thus, out of 24 cases 19 occurred in men and 5 only in women, that is, 4 males to 1 female.

In respect of age the affection seems to be fairly equally distributed through all the age-periods of adult life; thus, of 22 cases 13 occurred between the ages of 20 and 50, and these were fairly equally distributed within this period. Cases, however, occur in children and also in old persons; the youngest on the list was aged 9, and the oldest 72 years.

In infancy and very young childhood I do not know that there is any undoubted case on record; and, although anaemia and large spleens are by no means uncommon in these early years of life—cases which have been described by some writers under the name of splenic anaemia—still a review of these cases and the course they run shows, I think, that we have to deal in them with disease of an entirely different kind.

The Blood. — The blood shows no pathognomonic changes. The condition is simply that of profound anaemia. The red cells are diminished to one-fourth their normal number or less, and their form is preserved, though they are a little reduced in size; usually there is no poikilocytosis. The cells are poor in haemoglobin, which is reduced to one-quarter or one-sixth, and the loss is far in excess of the diminution of red blood cells. Occasionally there is a slight increase in the white cell, but not more than the fever or some intercurrent malady would account for. As the disease advances there is a continuous reduction in the number of red cells, as is shown in the following scheme (taken from Dr. F. Taylor's paper):

<table>
<thead>
<tr>
<th></th>
<th>Red Cells</th>
<th>White</th>
<th>Haemoglobin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sept. 27</td>
<td>3,000,000</td>
<td>no increase</td>
<td>35 per cent</td>
</tr>
<tr>
<td>Oct. 4</td>
<td>2,400,000</td>
<td>1 to 300</td>
<td>35</td>
</tr>
<tr>
<td>&quot; 17</td>
<td>2,400,000</td>
<td>...</td>
<td>30-35</td>
</tr>
<tr>
<td>&quot; 25</td>
<td>2,200,000</td>
<td>increased</td>
<td>...</td>
</tr>
<tr>
<td>&quot; 27</td>
<td>1,550,000</td>
<td>1 to 70</td>
<td>...</td>
</tr>
<tr>
<td>Nov. 11</td>
<td>1,370,000</td>
<td>1 to 28</td>
<td>28</td>
</tr>
</tbody>
</table>
The blood has been carefully examined in several instances for micro-
organisms, microscopically as well as by cultivation, but without success.

In many of the cases, especially those which were recorded some
years ago, the blood examination was not as systematic as it would be in
the present day. In my own case it was made under the supervision of
Professor Kandt, and good accounts of the blood are also given in the
cases described by Williamson and Taylor.

Williamson's case is peculiar in the fact that there was poikilocytosis,
which, as already stated, is usually absent.

With reference to the increased number of leucocytes which is some-
times observed, especially where the temperature is high, it must be
remarked that the increase is chiefly due to lymphocytes; that there is
none of the changes in the eosinophile and other cells which are character-
istic of leucocytæmia, and, finally, that the increase, being due in great
measure to the extraordinary diminution in the number of red blood
cells, is rather relative than absolute.

The Spleen.—The spleen is considerably enlarged and tender, and the
surface usually feels smooth; but sometimes it may be uneven. Signs of
local peritonitis in the splenic region may be present, or of left basic
pleurisy, in both cases due to inflammation spreading from the spleen.
Some general peritoneal effusion has been also met with.

The spleen may extend beyond the umbilicus and as far as the crest
of the ilium, and be of considerable weight, as will be further described
under the morbid anatomy. The spleen is observed, as the case pro-
gresses, to increase in size, especially during the exacerbations; but
occasionally between the attacks it seems to become for the time smaller.
The recurrent attacks of pain in the splenic region, apparently due to
peri-splenitis, are often the cause of very great suffering.

The Liver.—The liver is often somewhat enlarged also, and may
extend, as in the case described, from the fifth rib in the nipple line to
an inch or two below the costal arch. It is sometimes associated with
slight jaundice, and there may be some pain felt in this region from time
to time.

The Digestive system.—The digestion is considerably disturbed and the
appetite lost. There is a good deal of nausea and sometimes obstinate
vomiting; this may occur in such paroxysmal attacks as almost to
constitute crises, and they often coincide with attacks of abdominal
pain. Constipation is usually troublesome; but occasionally diarrhoea is
present, and this may be almost dysenteric in character, with tenesmus
and discharge of bloody mucus: in one or two instances there has been
free haemorrhage from the bowels.

Hæmorrhages.—The tendency to bleeding is pronounced: the hæmor-
rhages are usually of slight degree and of the nature of oozing; but they
frequently recur, are very difficult to control, and add greatly to the
anæmia. Profuse hæmorrhages from any part are uncommon, but they
are recorded as occurring both from the stomach and from the bowel, or,
as in my case, from a wound; in each instance they proved fatal.
Epistaxis is very frequent and usually one of the earliest symptoms. Though rarely profuse, it is of importance on account of its frequent occurrence: it may, however, be so severe as to require plugging of the nares. Oozing from the gums, again, is by no means uncommon, and it is most difficult to check.

Hæmoptysis and hematuria have been met with also, but they are rarer than other forms of hemorrhage.

From the gastro-intestinal organs hemorrhage is rare, and, if in any large amount, it is probably associated with some secondary lesion. A case, however, is recorded by Dr. Douglas Stanley, in which, although profuse and fatal hæmatemesis took place, no lesion in the stomach was found after death; in another case, however, a gastric ulcer was present. Müller records a case of fatal hæmorrhage from the bowels, and there an ulcer was found in the small intestines.

In the skin small petechiae on the lower limbs are common, especially in patients who are not in bed; but they are of no special significance. A purpuric eruption of greater degree than this is not described.

Into or behind the retina hæmorrhages may occur, no doubt, as they do in other forms of anæmia; but I do not know any instance of it except that which I have described.

The Temperature.—Bruhl states that fever is unusual, but in many of the recorded cases the temperature reached a considerable height. It has been of the nature of an irreglar heat, rising even to 103° or 104 every evening (cf. Chart).

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Chart 5.—Maximum (evening) and minimum (morning) temperature daily.

It is probable that something depends upon the stage which the disease has reached; that in the early stages the temperature may not be raised, or be even subnormal, while in the later stages, when the disease is actively progressing, it may be high.

At any rate the rise of temperature, when it occurs, appears to be part of the disease, and not to be connected with any complication.

The nervous system yields no special symptoms.

Urinary changes are indefinite and vary much, but sometimes albumin is present in small amount.

The circulatory system presents only such changes as are common to all forms of anæmia.
In the skin pigmentary changes have been described, but as in the majority of these cases arsenic had been administered in large doses and for some time, they were very probably due to this drug.

Morbid anatomy.—The general pallor of the skin and of all organs, the flabbiness of the muscles, the dilatation and degeneration of the heart are common to all forms of anæmia.

The panniculus adiposus is usually well preserved; and in this respect—namely, in the absence of marked emaciation—the body contrasts with that of malignant disease of the spleen, a still rarer condition, a case of which, however, has been recorded under the name of splenic anæmia.

The Spleen.—The most obvious morbid change is the enlargement of the spleen. This organ may be 12 inches long or somewhat more, and may weigh from 2 lbs. to 7 lbs. It is firm, reddish brown in colour, with well-marked notches and, occasionally, irregularities on the surface. It is surrounded by a thickened capsule, which may be adherent either to the diaphragm or to the parts about. On section it looks as if there were a general hypertrophy of the organ; but occasionally there are one or two haemorrhagic infarcts in it. The surface of the section is dry and yields little juice; it shows grayish streaks or fine granulations; the former, on microscopic examination, prove to be thickened trabeculae, the latter fibrotic Malpighian corpuscles. The Malpighian bodies are stated, in many of the cases, to have been the seat of marked changes, the central artery being thickened, the corpuscle shrunken and shrivelled, and sometimes surrounded by a capsule of fibrous tissue. With the thickening of the trabeculae there has been great disappearance of the spleen cells and dilatation of the veins. In Williamson's case many nucleated cells, each containing six to ten red blood-cells, were found in the splenic pulp; but in the majority of cases no special changes are present in it.

The lesions in the spleen then appear to be: (i.) fibrosis of the organ; (ii.) disappearance of the pulp; and (iii.) the cirrhosis and atrophy of the Malpighian bodies. This last is regarded as the characteristic and most important lesion, and is the exact opposite of the state found in leucocytæmia, in which disease the Malpighian bodies are, as a rule, hypertrophied.

The liver is slightly cirrhosed and is much pigmented. The cells are misshapen, atrophied, and often granular. The iron reaction is usually absent; it is only described as present in Williamson's case, and then it was insignificant in degree.

The pancreas also, in some cases, has been found indurated; but this lesion is not constant, and probably, therefore, stands in no direct relation to the disease.

The lymphatic glands are normal.

The bone-marrow also is usually normal; but in one or two instances it has been described as red and infiltrated with leucocytes.

The heart is dilated, the muscular substance flabby and occasionally fatty. In one or two cases minute vegetations have been found upon the
valves; as in my own case, in Williamson's, and in Strümpel's. In connection with these vegetations may be mentioned, the infarcts which have been found now and then in different organs, notably in the spleen and in the kidneys.

These vegetations and infarcts deserve attention because undue significance has been attached to them. They are indeed absent in all the recorded cases except those which I have mentioned; and in these they were obviously accidental and formed no essential part of the disease.

When haemorrhage has occurred during life the traces of it will be seen after death; but, besides this, haemorrhages of small size, petechiae, for the most part, may be found very widely distributed in many parts of the body—in the lungs, pleura, pericardium, and even in the brain; but these, again, are of no special significance, for they are found in all cases of profound anaemia in which the haemorrhagic tendency has been well marked. For the most part, no doubt, they arise shortly before death.

Pathogeny.—That these cases of anaemia form a definite clinical group must, I think, be regarded as fully established. The cause or pathogeny of the disease is hitherto a matter of hypothesis and opinion.

In the second stage, when the spleen is enlarged, and especially when fever is present, the cases bear a close clinical resemblance to many septic diseases, and especially, perhaps, to some forms of malignant ague. This would suggest that some parasite or septic organism is present in the blood. Careful examinations, however, both of the blood and of the spleen, have been made and have proved negative. In my case the results were negative, as they were also in two cases investigated by Sciola and Carta. In one of them, that of a girl aged 13, injections were made in the spleen of different animals with blood from the spleen of the patient, and after removal of the spleen with splenic substance in all cases without result. In another case, that of a woman aged 29, cultivation experiments were made with the extirpated spleen on different media without result.

So far, then, as our present knowledge goes, bacteriological investigations have yielded no new facts.

The enlargement of the spleen observed during life, standing in close relation as it does to the severity of the disease and the peculiar morbid appearances discovered after death, have suggested that the disease is directly due to the affection of the spleen itself; that is to say, to the peculiar atrophy of the Malpighian corpuscles. So far, however, the number of cases is too small to determine whether the peculiar changes described in the spleen are constant, and we must wait until this is established before we found a hypothesis upon such a pathological basis.

Complications.—The complications may be divided into two groups: first, those which are obviously accidental, and, secondly, those which stand in some possible relation to the disease itself.

In the first group we have instances of death produced by pneumonia and by bronchitis.
In the second group may be placed peritonitis or abscess in the region of the spleen, left-sided pleurisy perhaps, and the severe hemorrhage from the stomach or intestines which has been recorded in a few cases.

The course of the disease is usually continuously progressive: there may be periods of temporary arrest, or possibly even of improvement; but in the end relapse occurs, and the result is the same.

The duration of the disease.—The disease is not of long duration, from six months to two years, rarely longer; yet Müller records a case which lasted four and a half years. It is possible that there may be cases of even shorter duration than six months, for Ebstein records one, under the name of Pseudoleukæmia splenica, but the nature of these rapid cases is somewhat doubtful.

Prognosis.—Prognosis in respect of recovery is hopeless; in respect of duration of life is bad; and in respect of the immediate risks to life must be determined in each case by the condition of the patient.

The mode of death, as a rule, is by progressive asthenia; though the end may come suddenly with cardiac syncope, or it may be determined by hæmorrhage, as in the cases referred to.

Diagnosis.—In the early stage diagnosis is impossible; in the later stages it is comparatively easy on account of the enlargement of the spleen.

1. From pernicious anæmia splenic anæmia is distinguished by the enlargement of the spleen, as well as by the condition of the blood; though in a clinical sense the anæmia is pernicious, being progressive and fatal.

It is especially from other forms of profound anæmia in which the spleen is enlarged that the diagnosis has to be made. Foremost among these stand leucocythæmia and Hodgkin's disease.

2. In leucocythæmia the diagnosis is determined by the characteristic blood changes which are absent in splenic anæmia.

3. In Hodgkin's disease the anæmia is usually not so profound, there is a greater enlargement of the liver, and the lymphatic glands are affected.

4. In malignant disease of the spleen emaciation is a prominent symptom, and the wasting advances as the disease progresses; there may be secondary growths elsewhere, and there is no rise of temperature.

5. In pernicious aæne or malarial fever the temperature is of a more intermittent and irregular character; moreover, the presence of the parasites in the blood and the history of the case will fix the diagnosis.

6. Syphilitic disease of the spleen may possibly cause some difficulty as in Coupland's case; but as a rule the history and other evidences of syphilis will help the diagnosis.

7. With tuberculous disease of the spleen there is generally marked wasting and the evidence of tuberculous mischief in other organs; while as a rule the anæmia is not so profound.

8. In cirrhosis of the liver, with secondary enlargement of the spleen,
there is again not so much anæmia, and the ordinary signs and history of cirrhosis of the liver are obtained.

9. In children anæmia and enlargement of the spleen are not uncommonly associated. The causes are many, but among them it appears that splenic anæmia, in the sense in which it is here used, is not to be reckoned; for a conclusive instance of the disease under the age of nine years has not yet been recorded. The course of these cases in children is also different, for most of them end in recovery, and the hæmophilic tendency is but rarely seen.

On the whole, therefore, it is evident that though splenic anæmia is a rare disease, its diagnosis is not generally one of any great difficulty.

Treatment.—The treatment must be symptomatic, and does not differ from that of other profound anæmias. All the usual remedies have been tried one after another, but so far nothing has been found to check the progress of the disease.

S. W.

REFERENCES


HÆMOPHILIA

Definition.—By hæmophilia we mean a disease congenital and hereditary, marked by a tendency to immoderate bleeding on slight causes, lasting throughout the life of the patient; and further accompanied by a troublesome tendency to a joint affection, which is often as wearisome to the patient, as the tendency to external hæorrhages is dangerous.

The name of hæmophilia is modern, and seems to have been first introduced by Schönlein about 1828. "Hemophil" is, however, the name of one of the dramatis personæ in John Ford's Broken Heart, published in 1633. The disease was not classified or described until the time of Schönlein, though single observations may be found scattered in medical literature, beginning with the Spanish Albucasis or Alsaharavius in the 11th or 12th Christian century. The men who are the subjects of
haemophilia are called "bleeders," a word which appears early in the nineteenth century in the medical literature of the United States of America.

**Etiology.** — Beyond hereditary transmission hardly anything is known of the causation of hemophilia. It affects especially the male sex. Though cases in women have been described, it has never fallen to my lot to see a definite case in a woman, yet the women in the bleeder families pass on the disease to their male offspring.

The mode of the hereditary transmission of haemophilia is noteworthy. In a bleeder family we commonly find all the women free from the disease, while their brothers suffer. Then these women, if they marry and are fertile, bear a family some or all of the boys of which are bleeders, while all the girls escape. But these girls, if they marry, pass the disease on to their sons; and so the disease is continued.

This mode of hereditary transmission is not particular to haemophilia. It is very well marked in colour-blindness; and in 1881 I published a genealogical tree showing the descent of this infirmity in a family since 1684. It is also seen in polydipsia, another congenital disorder, as Dr. Gee has pointed out; and the same mode of transmission may be seen now and then in ichthyosis, in the pseudo-hypertrophic paralysis of Duchenne, and in gout. The disease does not seem to descend from father to son; nor through the sons of a bleeder family, free from the disease, to their offspring. As a general rule, the sons of bleeders, and the sons of the brothers of a bleeder, who are free from haemophilia, show no signs of the disease. But the daughters of a bleeder, like his sisters, pass on the disease to their male offspring; the daughters' offspring often showing the disorder in a highly aggravated form.

There seems at this moment no evidence that the marriage of near kinsfolk causes the disease. Nor is haemophilia peculiar to any race of men. I think, however, that it is found more often amongst Jews, in proportion to the population, than amongst Englishmen. Cases have been described amongst the aborigines of Sumatra; and I notice that Japanese writers have lately begun to describe the disease.

No class in life seems to be exempt from haemophilia; nor can any particular geographical distribution be assigned to it.

**Symptoms.**—As a rule the symptoms of hemophilia appear during childhood; in the large majority of cases before the tenth year. In May 1884, at St. Bartholomew's Hospital, I myself saw a case amongst Dr. Andrew's patients in which no symptoms had been noticed until the lad was 19 years old. Other instances have been recorded in which the first symptoms were seen at the age of 21. But the absence of all early symptoms of haemophilia can seldom be proved.

Haemophilia may even show itself in foetal life. An eight months' foetus, from a bleeder family, has been found with bruising on the brow: and a boy when born had large extravasations over both shoulders. Severe haemorrhage may take place after ritual circumcision, which is usually performed on the eighth day after birth; but as a rule the
haemorrhagic disposition does not show itself until near the end of the first twelve months of life.

There is a rare affection, one of the chief symptoms of which is a haemorrhage on the falling off of the umbilical cord. This haemorrhage rarely occurs in children of bleeder families; and it is separated from haemophilia by the fact that when the child recovers it shows no further disposition to haemorrhage in after-life (vide p. 561).

The joint troubles, which are so prominent in definite cases of haemophilia, may appear early in life. In one of Brigstocke's cases an ankle became distended by effusion a few days after birth; but as a rule the joints do not begin to give trouble until the patient be four or five years of age.

The boys who are the subjects of haemophilia have no external peculiarities. There is nothing constant about their complexion, stature, or muscular strength; nor can it be said that they are always intelligent, or that they distinguish themselves at school. Physical examination detects nothing amiss with chest or belly; neither spleen nor liver is enlarged, and the urine, in the cases in which I have examined it, showed the ordinary percentage of urea, and no decided alteration in its other constituents.

Certain states of the surroundings have been supposed to excite haemorrhages in a bleeder, or to aggravate his haemorrhagic disposition. Such are the difference in the seasons, day and night, cold and heat, changes of the moon, and the like; but these assertions greatly lack confirmation. Some have thought that the use of wine provokes haemorrhages; others that the haemorrhagic disposition is increased after the first traumatic haemorrhage. This sequence, of course, admits of another explanation. Anger and other emotions have also been accused. There can be no doubt, however, that the disposition to haemorrhages in these patients varies very much; and the observer must be very cautious in drawing conclusions as to the action of remedies.

The positive symptoms of haemophilia may be divided into three heads: spontaneous bleedings, traumatic bleedings, and the joint affections.

The spontaneous bleedings are said by some observers to be sometimes preceded by distinct prodromata. I have never been fortunate enough to observe these prodromata, but they are set out at length by Wachsmuth. They occur three or four days before the onset of the bleeding, and are mainly signs of plethora: the face is full, the lips and ears swollen, red, and hot; or the friends remark that the patient is looking remarkably well.

As might be expected, epistaxis is the most common of the spontaneous haemorrhages, especially in childhood. Few bleeders live to any age without suffering from some form of nose-bleeding. Nor does it favour any of the ancient beliefs by flowing more from one nostril than the other. Bleeding from some part of the mouth comes next in frequency, though far behind.

As puberty comes on, haematuria and bleedings from the bowels replace the haemorrhages from the nose and mouth. Very rarely spon-
taneous bleedings are seen from the conjunctiva, the skin, the ears, or
the ends of the fingers.

The amount of blood lost in this way may be very trifling, or it may
be so great as to kill the patient. There may be but a trifling ecchymosis
or petechia under the skin, or the whole of the blood may seem to leave
the body. Of the bleedings from the mucous membranes epistaxis is the
most frequent cause of death; next to that, bleeding from the mouth,
bowel, or lung. Hæmaturia is but rarely mortal.

On the whole, the traumatic hæorrhages are the most to be dreaded.
A mere scratch is sometimes sufficient to put life in danger. Trifling
injuries, like the scarifications necessary for vaccination, the division of
the frenum of the tongue, the application of a leech, or ritual circumcision,
have caused death. The taking out of a tooth is an exceedingly dangerous
act; it is a common cause of death in a bleeder, and should never be
undertaken in a patient of this kind.

These patients vary, however, very much in the amount of injury that
they bear. At one time the same patient will endure injuries the infliction
of which at another time will endanger life; and in some families of
bleeders the traumatic hæorrhages are, as a rule, nothing like so
dangerous as in others. I have myself seen a tooth drawn in such an
one without any remarkable hæmorrhage; but, as a rule, this little
operation is in the highest degree dangerous. Usually the vaccination of
a bleeder is followed by no ill effects; this is also the experience gained
by the practitioners in the canton of Graubünden, where there are many
families of bleeders.

The opening of abscesses, either by the surgeon’s knife or of them-
selves, is usually followed by a profuse hæmorrhage. This is still more
profuse and dangerous when blood tumours or extravasations of blood are
opened.

Death may come on very rapidly, within a few hours; or the bleeding
may last for weeks. Often the uncontrollable hæmorrhage does not
come on with the first infliction of the wound, but some hours or even a
day after the hurt has been given. The quantity of blood lost in a few
hours may be enormous.

Of the composition of the blood thus lost we have no very recent or
exact observations. That first poured out seems to clot naturally, but
after a great deal has been lost, it coagulates feebly or not at all. After
great losses, it looks like water in which meat has been washed, and
hardly stains the linen. With the microscope a certain increase in the
white corpuscles has been noticed after hæmorrhages, as might be
expected.

Symptoms of true anæmia follow the great loss of blood, and the
patient dies bloodless. If, however, the result is to be favourable, the
patient lies long as in a deep sleep, and on awaking he suffers for weeks
and months from pallor and general bloodlessness. The blood lost is
very slowly regained. During convalescence a depraved appetite for
sand, chalk, and the like has been noticed in some few cases.
It has been said already that in haemophilia the affection of the joints
is more troublesome to the patient than the attacks of external haemor-
rhage. The joints become swollen and painful, and are apparently filled
with fluid; this disorder is continually recurring, so that some patients
are rarely free from it, and they become cripples from the state of the
knee. The knee is the joint which suffers the most; after that comes
the ankle, then the elbow, shoulder, and hip joint. The wrist and the
joints of the fingers and toes are seldom affected. When the acute
swelling is over, the joint may recover completely for this turn; or some
impairment of motion may be left; indeed after many attacks the joint
at last may be almost destroyed.

The cause of this swelling is, in my opinion, an effusion of blood into
the joint. Formerly it was thought that its origin was sometimes
rheumatic, but it has been now shown from the necropsies of some
cases that the joints contain blood; and this seems the most likely
cause of the phenomena in all. Allied are, no doubt, the joint troubles
seen in some cases of purpura which are not rheumatic.

Morbid anatomy.—Morbid anatomy has hitherto given a negative
result in haemophilia. As a rule, nothing but great bloodlessness can be
found; and a good number of necropsies have now been made by trust-
worthy observers with this as the only result. Schönllein seems to have
laid great weight upon certain changes in the heart, the deficiency of the
muscular fibres in the walls of the septum; but he may have been
describing only the “unprotected spot” of Peacock. Others have de-
scribed a thinness of the walls of the arteries, but this appearance has
been found in too few cases to justify us in regarding it as a constant
element of haemophilia.

Nor has the microscope anything to tell us in haemophilia. Dr. Klein
examined for me with the microscope several cases dying in St. Bartholo-
mew’s Hospital; but in no case was he able to detect any disease in the
vessels or tissues. Dr. Percy Kidd observed certain changes in one case:
but they have not been found in others, and it may be concluded that
they were accidental and not essential to haemophilia.

Of the pathogeny of a disease like haemophilia it is really useless to
speak. It would be mere speculation, and in a work like the present it
would be undesirable to take up space with a discussion of mere
opinions.

On the morbid anatomy of the joints in haemophilia much light has
been thrown of late years. It would seem that the repeated haemor-
rhages into the joints lead up to a state which cannot be distinguished
from chronic rheumatoid arthritis. The first blood effused into the joint
seems to be reabsorbed, leaving the cartilages free from change. But as
haemorrhage succeeds haemorrhage deep changes make their appearance.
First the cartilages and synovial membrane are slightly coloured from
the presence of blood, but the cartilages remain shining and smooth, and
show no further change. In a further stage the cartilages become deeper
coloured, of the rusty colour so often seen as the result of blood-staining.
and they lose their clear appearance and become clouded and thin. Next fibrous bands pass from the femur to the tibia, the cartilages are rough and greatly thinned so that the bone is almost laid bare, and under the microscope changes very like those observed in the cartilage of chronic rheumatoid arthritis are observed. There are some specimens of this state of the joints in the Museum of St. Bartholomew’s Hospital (740 a. b. c. d.).

Diagnosis.—When a boy, born in a bleeder family, begins to suffer from petechiae, suspicion is at once aroused; and if, later, repeated nose-bleeding, hæaturia, and joint troubles appear, the diagnosis is rendered highly probable; if to these be added a long-continued hæorrhage after slight wounds, there hardly remains room for uncertainty.

Difficulty, however, often arises in practice when a patient presents himself of whose history little or nothing is known, and the trustworthiness of whose statements is somewhat doubtful. In the first place the sex is of the greatest importance. I have said that I have never seen a case of true hæmophilia in a woman, and I am inclined to think that the diagnosis of cases of hæmophilia in women is founded on mistaken observations. Next in importance are uncontrollable hæorrhages after wounds, especially slight wounds, or wounds that ordinarily give rise to little hæorrhage; for example, the taking out of a tooth is often a touchstone in the diagnosis. If no hæorrhage have followed this operation, the opinion against the diagnosis of hæmophilia is materially strengthened. Then the joint affection in persons already suspected of hæmophilia adds something in favour of the diagnosis, though it must be remembered that temporary hæmorrhagic diatheses, like scurvy and purpura, sometimes show a joint affection which appears to be due to hæorrhages into the joint affected.

In some doubtful cases, especially in children of a bleeder family, it may be well to wait a few months or even a year till more decided symptoms show themselves, as nose-bleeding and the like, before giving an opinion.

It should always be kept in mind that hæmophilia is a congenital general disease, which persists throughout the life of the patient. Temporary hæmorrhagic diatheses, like scurvy and purpura, must not be accounted hæmophilia; nor should a long-continued hæorrhage from one single part have this name given to it, as a German writer, who ought to know better, has lately done.

There are certain rare cases with umbilical hæorrhage in infants which may be confused with hæmophilia. They have profuse bleeding from the place of separation at the navel, they are often jaundiced, and they die after having shown signs of a general hæmorrhagic disposition. Such cases of umbilical hæorrhage, however, do not belong to hæmophilia. They occur in children of both sexes, and not especially in bleeder families; and in those which survive, no tendency to hæorrhage is noted [vide following article].

Prognosis.—The remote prognosis of hæmophilia no longer appears so serious as was formerly supposed. In Grandièr’s figures only 10 per
cent attained the age of 21. My own direct experience has been much more favourable. I have watched the boys of many bleeder families from childhood; and they have grown up into manhood, not without pain and suffering it is true, but they have kept their life, and followed easy occupations by which they gained their bread in a fashion. The patients whom I have thus watched have belonged mainly to the lower middle classes. They have known of their tendency to hæmorrhage, and thus in many instances, no doubt, they have been able to ward off wounds. With sufficient care, middle age would seem to be within the reach of many of them.

It is said that with the approach of middle age the tendency to hæmorrhage may disappear. I have never seen such a case; but the fact that it has been noticed by some observers should be remembered.

Treatment.—First of all it may be well to consider the measures to be avoided. All procedures by which blood is drawn—blood-letting, leeches, lancing of gums, scarifications and the like—must be forbidden. The red-hot iron and even blisters are attended by considerable danger in many cases. Surgeons should be warned that when the great operations of surgery have been performed, such as an artery tied in its course, amputation of a member, or lithotomy, the patient has usually bled to death of the wound. It is hard to imagine a case in which the use of the knife would be justifiable.

With traumatic hæmorrhages, it would seem best to follow the ordinary rules of surgery, always remembering the warning given in the paragraph above. Styptics, it may be noted, are generally worthless. The use of the hot iron and of the perchloride of iron is specially to be avoided.

In like manner, spontaneous hæmorrhages should be treated according to the general rules of medicine. Ice may be passed up the nose in epistaxis, or into the bowel in bleeding from the rectum, or placed in the mouth in bleeding from the gums. Whatever may be done will, however, too often prove ineffectual; and if the medical attendant have courage enough for such a line of action, there would almost seem to be a better chance for the patient if the attendant abstained altogether from active local treatment designed to check the bleeding. When all the blood seems to have left the body, and the patient about to die of the loss of blood, it has not infrequently happened that the hæmorrhage has ceased and the patient has slowly and gradually recovered.

Transfusion of blood as a last resort has been practised in some cases with success; and in desperate cases I should feel inclined myself to recommend its employment.

During the intervals between the attacks of hæmorrhage, what shall be done? The hygienic treatment is of great importance; all occasions of hæmorrhage must be warded off; all persons about the boys should be told of the tendency to hæmorrhage, and of the grave consequences which may follow the slightest injury. Nearly all the ordinary games of boys, amongst which are specially to be named cricket, hockey, and football,
HAMOPHILIA

have to be forbidden. Other sports and exercises may be allowed according to their results.

Cold sponge bathing is useful, and well borne. The dwelling-place should be dry, the air bracing; during the winter some have seen good from a removal to a dry and warm climate like that of the Riviera. It is to be regretted that we have so little experience of climatic treatment. Warm clothing seems very desirable, as these patients often feel the cold severely.

As to drugs, a good deal of caution must be exercised in drawing conclusions even from an experience which may seem to be wide. For instance, at the beginning of this century, the American physicians who had treated families of bleeder children tell us that "the sulphate of soda was accidentally found to be completely curative of the haemorrhage" in hemophilia. At the present day no such great confidence is felt in the sulphate of soda. At this moment the chlorides are in greater favour; the chloride of calcium has been recommended in these cases from its supposed power of increasing the coaguability of the blood, and very favourable results have been reported from its use. I cannot, however, say that I have seen anything like a complete disappearance of the haemorrhagic disposition follow even a long-continued use of this drug.

In my own experience I have found very good results follow a course of cod-liver oil and perchloride of iron alternately.

In the treatment of the acute stage of the joint affections, rest is the very first, almost the only element in the cure. The joint must be rendered motionless, as soon as the patient can bear such treatment, by splints of plaster, of Paris or whatever the surgeon may deem suitable. Pain must be neutralised by opiates; and there does not seem much danger in haemophilia from subcutaneous injection of morphia.

J. WICKHAM LEGG.

REFERENCES

LEGG, J. W. Treatise on Hemophilia, Lond. 1872, chap. xi. p. 138; St. Bartholomew's Hosp. Reports, vol. xvii. 1881, p. 317, in which place references to other essays on this subject will be found.

J. W. L.
HAEMORRHAGES IN NEW-BORN CHILDREN

The haemorrhages which occur in new-born children may be divided into two groups: (1) **Traumatic or Accidental Haemorrhages**, which are the direct result of injury at the time of birth; and (2) **Spontaneous Haemorrhages**, which occur without any apparent external cause.

The cases of spontaneous haemorrhage are best again subdivided into (a) **Idiopathic** cases, where the bleeding is the chief or only symptom—the so-called "haemorrhagic disease of new-born children"; and (b) **Symptomatic** cases, where the haemorrhages are secondary to some serious organic disease, such as congenital malformation of the heart, congenital obliteration of the bile-ducts, or some grave affection of the liver. With this group also may be taken the rare cases in which true haemophilia leads to haemorrhages in early infancy.

I. **TRAUMATIC OR ACCIDENTAL HAEMORRHAGES**

The traumatic haemorrhages are mainly due to injuries received during birth, either by the pressure of the maternal parts on the child, or by the artificial means used by the accoucheur to expedite delivery. They are consequently more frequent in the case of first-born and male children, in difficult and prolonged labours, and when the presentation is abnormal. There can be little doubt, also, that increase of the blood-pressure, owing either to asphyxia from pressure on the cord, or to pressure on veins or compression of some other part of the body, may be an important cause of their occurrence.

Traumatic cases are of less importance, from the physician's point of view, than those of spontaneous bleeding. Nevertheless they also are of interest to him, and therefore worthy of brief mention here because, in not a few instances, they form the starting-point of serious nervous disease in later life.

The most important situations in which the effused blood is found may be stated as follows:—(i.) On the surface of the skull, between the pericranium and the bone—cephalhæmatoma; (ii.) Inside the cranium—apoplexia neonatorum; (iii.) Into the substance of the sterno-mastoid muscle; (iv.) Into one or more of the abdominal or thoracic organs.

**Cephalhæmatoma**

Cephalhæmatoma is the name given to a swelling on the surface of the cranium formed by a collection of fluid blood between the pericranium and the bone. The condition is due to rupture of blood-vessels under the pericranium, owing to mechanical pressure during birth; and it is
met with about once in every 200 births. It is much more commonly seen after first labours than after subsequent ones, and is especially frequent after difficult births in which the head has presented. It occurs, however, sometimes after breech cases, and occasionally also with comparatively easy and normal labours.

In the majority of cases the tumour is situated over the right parietal bone—this being usually the presenting part. Less frequently it is found in the left parietal region; and sometimes it occurs on both sides. It is rarely met with over the other cranial bones. The swelling is generally noticed within the first two or three days after birth. It is rounded in contour, fluctuating and not apparently tender; and it shows no heat or redness. Being under the pericranium it is always distinctly limited to the surface of one bone and never crosses a suture. For four or five days it usually goes on increasing in size, and then, after being stationary for a while, it slowly disappears. When the blood begins to be absorbed, the bone can readily be felt through the tumour, and round its margin a raised ring can be made out. This is due to the formation of bone having gone on under the raised peristome. Sometimes also from the same cause there is a crackling sensation experienced on handling the surface of the swelling.

Generally the blood tumour is quite absorbed within four weeks of birth, but it often takes two or three months before all trace of the bony ridge round it has disappeared. The prognosis in uncomplicated cases is invariably good, the cephalhæmatoma always recovering without any treatment. It should, however, be remembered that in a certain proportion of cases the external swelling is accompanied by an intracranial hæmorrhage.

Intracranial Hæmorrhages (Apoplexia Neonatorum)

Intracranial hæmorrhages are unfortunately not very uncommon. They are important, not only because they are a very frequent cause of still-birth and early death, but also because they are responsible for a large amount of bodily and mental defect in after-life.

Etiology.—Although the state of asphyxia into which many children are brought during birth must be regarded as a strongly predisposing element in the causation of these hæmorrhages (Ashby), Spencer's statistics render it almost certain that they are mainly due to external injuries. These may be produced either by the pressure of the maternal parts on the child or by that of the blades of the forceps. Thus he has found that the frequency of cerebral hæmorrhage is greatest with forceps delivery, less when the breech or foot presents, and least of all with natural head delivery.

As to the mechanism by which the lesion is brought about, Spencer suggests that in many cases it is due to displacement inwards of the lower anterior corner of the parietal bone. This corner directly overlies the great anastomatic vein, and being driven inwards during birth, clamps
this vessel so as to cause engorgement in its area of distribution. This explains, he thinks, the fact that the hæmorrhages are often limited to the parietal region and Sylvian fissure. Compression of the internal jugular vein by the forceps may also favour cerebral hæmorrhage in a similar way. S. McNutt has shown that hæmorrhages limited to the convexity are more frequent in breech than in head deliveries.

**Morbid anatomy.**—In a very large majority of the cases the hæmorrhage is primarily meningeal, and the injury to the brain itself is secondary and results from pressure from the surface. In some cases, however, the bleeding takes place into the brain substance. Effusion of blood on the inner aspect of the cranial bones, outside the dura mater (internal cephal-hæmatoma), is sometimes found along with an external cephalhæmatoma. It is said that this does not occur unless a fracture of the bone is present (Holt). Generally the blood is poured out into and beneath the arachnoid and pia.

The lesion is more frequently bilateral than confined to one side, and it is much commoner at the base than on the convexity of the brain. It is also commoner towards the posterior part of the skull than anteriorly. As has been already mentioned, hæmorrhages are frequently found over the parietal region and in the Sylvian fissure. The ventricles are sometimes distended with blood.

When meningeal apoplexy occurs, it sometimes lacerates the underlying cerebral cortex; in any case, it is apt to interfere with its nourishment by tearing through the blood-vessels which pass into it from the membranes. It also injures it by its pressure, so that softening and atrophy soon follow. Thus permanent atrophy and arrest of development of the cortex are set up along with degeneration of the fibres in the motor tract of the brain and spinal cord.

**Clinical features.**—If the damage to the brain be very great, the child will probably be still-born. The hæmorrhage may, however, be tolerably extensive, and yet the infant may survive for several days; or it may even recover and grow to adult age, although with a permanently damaged nervous system.

In many cases where the hæmorrhage has been severe the infant does not at first show any distinctively cerebral symptom, except torpor and feeble or irregular breathing; but other indications may be present. There may be obvious paralysis of one or more limbs, or of the cranial nerves if the hæmorrhage implicates the base. If the child live for some days, convulsions often occur; and they are more frequent in cases where the hæmorrhage is over the cortex than in those where it is at the base of the brain (McNutt).

As the child gets older, although the parents are often slow to see that anything is the matter with him, it will usually soon be found that the limbs are unnaturally stiff and the knee-jerks exaggerated. Later, he is backward in learning to hold his head up, in sitting up, and in walking; or it may be that he displays a lack of interest in his surroundings, which is soon noticed as abnormal. Gradually, as the brain grows,
the extent of the damage to its functions becomes more manifest, and the case passes off into spastic paraplegia, hemiplegia, diplegia, imbecility, or idiocy with or without paralysis.

**Prognosis.**—While extensive haemorrhages at the base are usually fatal, comparatively large ones over the convexity are compatible with life. Small cortical apoplexies may, it is said, be entirely recovered from, but in the great majority of cases more or less permanent injury to the brain results.

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**Hæmatoma of the Sterno-mastoid (Sterno-mastoid Tumour)**

Hæmatoma of the sterno-mastoid is a collection of blood which forms within the sheath of that muscle when some of its fibres have been ruptured during birth. It is met with most frequently in breech cases or cross-births where there has been difficulty in delivering the head; often also in difficult forceps cases, and sometimes after labours which are said to have been quite easy. It is probably caused more often by a sudden twisting of the neck than by simple traction on it. In nearly 300 autopsies on children, who were either still-born or had died soon after birth, Dr. Spencer found this lesion in fifteen.

The swelling may occur at any part of the muscle, but most frequently it is situated about its centre. The muscle of the right side is much oftener affected than that of the left. The tumour is not usually noticed until the second or third week, and often it does not attract attention till much later. This is due to the fact that the swelling caused by the effusion of blood is generally small at first. It is not until the injury to the muscle has occasioned a considerable growth of fibrous tissue ("muscle callus") round it, that it becomes too obvious to be overlooked. It may reach the size of a pigeon's egg, but it is generally smaller. The swelling remains stationary for weeks, and then slowly diminishes. It usually takes six or seven months to disappear; but it may have quite gone by the third month, or it may last more than a year (Pollard).

The connection between hæmatoma of the sterno-mastoid and so-called congenital wryneck is certainly a very close one, but it is difficult at present accurately to define it. Out of 106 cases of hæmatoma which Mr. D'Arcy Power collected from medical records, marked wryneck had resulted in twenty-one at least, while only in fourteen had it been specially looked for and not found. Dieffenbach and other older writers on the subject assumed that the wryneck was the simple result of the injury to the sterno-mastoid muscle at birth; but this explanation has of recent years been much disputed (Golding-Bird, Petersen, Koettntz). The chief difficulty in accepting it lies in the fact that in most if not all of the marked cases of congenital wryneck there is a very decided arrest of growth of all the structures of the face on the affected side, and it is difficult to imagine how any lesion of the neck only could bring this about. What cerebral lesion could cause it, however, is as yet un-
determined. The fact remains that this characteristic facial asymmetry along with wryneck not uncommonly appears as a sequel of hæmatoma of the sterno-mastoid (I have recently watched this sequence in three instances). Usually little can be effected in the way of treatment owing to the age of the child; but it is probable that judiciously applied massage and manipulations may sometimes be of use.

Hæmorrhages into Abdominal and Thoracic Viscera

As Dr. Spencer points out in his valuable paper, hæmorrhages into the abdominal and thoracic viscera are much more frequent after breech cases than after those in which the head has presented. They may occur into any of the organs, being seen frequently in the lungs, liver, kidneys, suprarenals, and intestine, and comparatively rarely in the spleen.

In most cases of internal hæmorrhage the diagnosis is impossible during life for lack of symptoms. Pulmonary infarctions, however, sometimes betray their presence by causing physical signs of consolidation of the lung. They are the cause of death in many cases of children who live for a few days only, and in these the fatal issue is apt to be attributed to congenital heart disease on account of the degree of cyanosis which is present. If the infant live long enough, pneumonia may result. Hæmorrhage into the pyramids of the kidneys may cause death within a few days, with symptoms of suppression of urine; and Spencer records one case in which a large hæmorrhage into the cæcum caused complete intestinal obstruction.

II. SPONTANEOUS HÆMORRHAGES

(a) Idiopathic Cases (the Hæmorrhagic Disease of New-born Children)

Description.—The hæmorrhagic disease of new-born children may be described as a passing morbid condition of the system which shows itself mainly by a tendency to spontaneous bleeding. The hæmorrhages may occur either from the umbilicus, from the stomach or bowel, from the blood-vessels in the subcutaneous tissue, or from other parts; and their occurrence is probably due to poisoning by the toxin produced by any one of a variety of micro-organisms.

The condition is a very rare one. Cases of gastro-intestinal hæmorrhage, which is its commonest form, are said to occur once for every 500-1000 births (Runge, Hermary, Kling); while umbilical hæmorrhage is only met with once for every 5000 confinements (Ribemont).

Clinical features.—In the great majority of cases no family history of bleeding is to be obtained. The sexes seem to be affected in about equal proportions. This point is of interest when we remember the very much greater frequency with which the male sex is affected in
Hæmorrhages in New-Born Children

Hæmophilia—the proportion being stated by Grandier as eleven boys to one girl (*vide* art. "Hæmophilia," p. 549).

Sometimes the patient is in weak health before the bleeding sets in: being premature or feeble, or perhaps the subject of congenital syphilis. Generally, however, he appears quite healthy until the hæmorrhage begins. This takes place usually within the first week of life, and rarely after the end of the second; the exact date varies, partly according to the situation whence it comes.

The site of the hæmorrhage may vary considerably. In the majority of cases it comes either from the alimentary tract (mouth, stomach, or bowel), or from the umbilicus. It may also take place into the subcutaneous tissue, or from the nose, conjunctiva, or ears, or into almost any of the internal organs. The bleeding may come from one situation only, as often happens in the slighter cases, or many parts may be affected, either at one time or successively. Thus, of 50 cases reported by Townsend, the umbilicus was affected in 18 (alone in 3); the intestine in 20; the mouth in 14; the stomach in 14; the nose in 12: subcutaneous ecchymoses occurred in 21; bleeding from an abrasion of the skin in 1; from the meninges in 4; cephalohematoma appeared in 3; hæmorrhages into the abdomen in 2, and into the pleura, lungs, and thymus in 1 each.

The amount of blood lost at a time is usually small; but the loss is generally so frequently repeated that pallor, chilliness, and prostration with failure of the pulse are very soon produced. In some cases the temperature is high, in others it is normal or subnormal throughout. In the cases of recovery the bleeding usually lasts one or two days; in the fatal cases death often occurs within twenty-four hours, and rarely later than three days from the beginning. Sometimes diarrhea appears, and towards the end convulsions not infrequently set in.

In children who recover the convalescence is apt to be prolonged and tedious, although the health is not permanently damaged.

**Gastro-intestinal hæmorrhages (Melena neonatorum).—** The blood in these cases is more frequently passed by the bowel than vomited. When vomited it is sometimes bright red, often dark brown in colour. Its amount varies greatly in different cases. Sometimes the hæmatemesis occurs only on one occasion; more frequently small quantities are brought up repeatedly. When passed by the bowel the blood is generally very black and thoroughly mixed with the motions. Sometimes, when it comes from the lower part of the bowel, it is red, and it may be in clots.

The blood is most frequently seen for the first time on the second day of life, or at least before the fifth; but occasionally the hæmorrhage may begin as late as the second week.

**Spontaneous umbilical hæmorrhage** usually takes the form of a steady oozing from the point where the cord has separated or is about to separate. The bleeding does not generally come from any visible blood-vessel; it is often intermittent; sometimes it is alarmingly free. Some-
times it takes place into the substance of the cord, or from fissures on its surface.

It generally begins about the fifth day of life, but it may occur earlier, and it may be deferred till the seventh or even the ninth day. It does not generally last more than three days, but in rare cases it may go on much longer. It is often fatal within twenty-four hours.

Subcutaneous ecchymoses may occur at any part of the body, and are as common on protected areas as on those which are exposed to pressure and friction. They are often of small size, but occasionally they become very large. If they occur without any hæmorrhages from other situations the prognosis is generally good.

Bleeding from the female genitals occurs occasionally in cases of multiple hæmorrhages. It is, however, much more frequently met with as an isolated symptom; and, when this is so, it is generally the result of some trifling local disturbance and has no serious significance. The hæmorrhage begins usually within the first six days of life, rarely after the twenty-first (Busey). The external genitals appear quite normal, but there is a more or less constant oozing of blood from the vaginal orifice, which lasts from two to five days, or sometimes a little longer. Owing to the trivial nature of the ailment very few opportunities have occurred for investigating its morbid anatomy. Billard asserts that the blood comes from the uterine mucous membrane, and Eröss in one case found acute hæmorrhagic catarrh of the fundus uteri. Only in rare cases does it recur, so that it cannot be regarded as of the nature of menstruation.

Morbid anatomy.—In most cases of children who have died from hæmorrhage there is nothing to be discovered at the autopsy but the traces of the effused blood and a general pallor of all the organs.

In a considerable proportion, however, of the cases of melæna (40 per cent according to Romme), more or less ulceration of the mucous membrane of the stomach or duodenum has been found. The ulcers are usually multiple, and may either consist of superficial abrasions or be of a perforating character. In one case (Landau) a clot was found obliterating the blood-vessels which supplied the area in which the ulcers were situated, but this is not usually the case. In some cases of melæna cerebral hæmorrhages have been found (Pomorski and v. Preuschen), but these also are by no means constant. In syphilitic cases endarteritis of the small and middle-sized vessels in the submucous tissue of the alimentary tract has been described (Mracek).

A considerable variety of micro-organisms has been found in the blood and in the tissues in cases of hæmorrhage, and especially in those of melæna. The first to record an observation of this kind was Klebs, who, in 1875, described a micrococcus which he had found in large quantities in the organs of nine new-born children who had died of hæmorrhage. This he injected into young rabbits, and succeeded in producing hæmorrhages in them. His results were confirmed in the following years by Weigert, Eppinger, and Rehn. Since then various
micro-organisms have been discovered in these cases by competent observers. Thus, streptococci have been found by Baginsky, Babes, and Bar; bacillus pyocyanus and staphylococci of various kinds by Neumann, Bar, and Schäffer, and bacterium lactis aerogenes by Neumann and Schäffer. Further, Babes found in one case an organism with all the characters of the diplococcus pneumoniae, and Dungern one which resembled in every way Friedländer's pneumococcus. In Dungern's case it is also recorded that, while the child was in the ward, three other infants died of severe pneumonia.

In 1894 Gärtnner published an account of two fatal cases of melena in which he found a short bacillus. Cultures of this organism were made and injected into the peritoneal cavity of young puppies, and they set up fatal gastro-intestinal hæmorrhage. In one of Holt's cases a similar organism was found.

Etiology.—A number of very different hypotheses of the causation of this condition have been framed. The following deserve mention:—

1. Von Preuschen and Pomorski have published cases where melena and pulmonary infarction of an apparently spontaneous origin were found after death to be associated with traumatic hæmorrhages into the cerebral peduncles and the fourth ventricle, damaging the vaso-motor centre. They therefore maintain that many if not all of the cases of spontaneous hæmorrhage are secondary to cerebral injury. They were able to strengthen their position by means of experiments on animals; for they succeeded in producing melena in a considerable number of rabbits by puncturing the cerebral peduncles and the walls of the fourth ventricle.

While these observations are certainly interesting and important, they cannot be held as explaining the occurrence of most cases of this disease. Cerebral hæmorrhages have only been found in a few instances.

2. Other writers have laid great stress on the local morbid condition. Thus, for example, in dealing with melena they have given mechanical explanations to account for the presence of ulceration in the stomach and bowel in these cases. The most remarkable of these hypotheses is that put forward by Landau. He noticed that the condition often occurred in premature and weakly infants in whom the function of respiration was established with some delay and difficulty. He accounts for this by supposing that the delayed inspiration favours stagnation and clotting of the blood in the umbilical vein. Then, he further supposes that, from the thrombus so formed or from that in the ductus arteriosus, an embolus is separated and carried through the circulation until it becomes impacted in one of the arterial branches which supply the stomach and duodenum, and ulceration results. In one case of gastric hæmorrhage he was able to satisfy himself that the artery supplying the area from which the blood came contained a clot.

Emboli of this sort have not been found by other observers who have looked for them, and Landau's theory has not, therefore, been generally accepted. It must be remembered in this connection that the formation of ulcers in the stomach and bowel is a frequent result of general infection.
with organisms of various kinds, and even of poisoning by toxins (Demelin).

3. Considerable stress has been laid by some authors on the fact that many of the patients in these cases are syphilitic or otherwise weakly; and it has been supposed that the bleeding might be attributed to some disease causing special fragility of the blood-vessels.

Evidence of vascular disease, however, has not usually been found, and it seems more probable that debilitated states of the system act as remote causes only in so far as they prepare a suitable soil for the growth of micro-organisms.

4. Of recent years there has been an increasing tendency to regard the spontaneous hæmorrhages in these cases as a manifestation of a micro-organismal disease; and, although this view can scarcely as yet be said to be thoroughly established, there are a great many facts in favour of it. It is well known, for example, that many pathogenetic organisms have the property of producing a tendency to hæmorrhage. As already mentioned, a large number of different organisms, known and unknown, have been cultivated from the blood and tissues in these cases; and some of them have even been found to cause hæmorrhages when injected into animals. Further, the symptoms of the cases and their short course point to the disease being an infective one, as do also the facts that they are more frequently met with in hospital than in private practice, and that they have been known to occur as an epidemic.

Diagnosis.—Spurious melæna, that is, the vomiting or passing by the bowel of blood which the child has swallowed during birth, or has sucked from fissures in the mother's nipples, often causes needless anxiety if mistaken for this disease. It is more frequently met with than true hæmorrhage. Or the child may have epistaxis or hæmorrhage from an ulcer in the mouth or throat, and the blood may be passed with the motions and cause a diagnosis of melæna. Such mistakes are not usually difficult to avoid. If, however, the hæmorrhages be confined to the internal organs, they are very apt to be overlooked in the absence of characteristic symptoms.

The occurrence of spontaneous hæmorrhages—especially ecchymoses—has, it should be remembered, some interest from a medico-legal point of view, as they may be regarded erroneously as evidence of violence.

Prognosis.—The condition is always a very dangerous one. In Townsend's cases the mortality was 62 per cent. In cases of umbilical hæmorrhage it is even larger than this, being variously stated by authorities at from 65 to 84 per cent; while in melæna it is usually estimated at from 50 to 60 per cent. Should the infant be syphilitic or otherwise constitutionally feeble, this fact naturally renders the prognosis more unfavourable.

Treatment.—Great encouragement to prompt and persevering treatment of these cases is to be gathered from the fact that the disease is so brief in its duration. The treatment is to be conducted on general principles, and too much reliance is not to be placed on drugs. It is
especially important that everything possible should be done to conserve the child's vitality. He should be kept perfectly quiet, and protected from cold by wrapping in cotton wool; he should also be surrounded, if necessary, with hot-water bottles. French writers recommend the use of a couveuse (Dusser, Oui). He should not be allowed to suck, but at short intervals by a spoon or medicine-dropper should have small quantities of his mother's milk, or diluted peptonised milk, cooled with ice. Small doses of ergotin may be given by the mouth, or, if the bleeding be severe, subcutaneously. If there be much collapse, it may be necessary to give alcohol by the mouth or ether as a hypodermic injection.

In meleina injections into the bowel are to be avoided. They are probably worse than useless, as they stimulate the intestinal movements. In umbilical haemorrhage intelligent and patient digital pressure on the bleeding part is probably the best means of treatment. The actual cautery, nitrate of silver, and the application of plaster of Paris have also been successful in some cases. If other means fail, the base of the bleeding spot should be transfixed by a hare-lip pin and a ligature applied round it.

(b) Symptomatic Cases

Description.—Spontaneous haemorrhages, similar in most respects to those we have been considering, are frequently met with as a symptom of various diseases. Thus we find them occasionally occurring in children with congenital malformation of the heart, rarely in infants who inherit true haemophilia, and frequently in cases of congenital obliteration of the bile-ducts and other serious diseases of the liver accompanied by jaundice.

The tendency to haemorrhage met with in these morbid conditions differs from that seen in the hemorrhagic disease of new-born children in that it is permanent. With few exceptions it lasts as long as the child lives.

Children with congenital malformation of the heart do not often suffer from spontaneous bleeding; and although haemophilia generally manifests itself for the first time in childhood, it is very rare indeed to find it as a cause of haemorrhages as early as the first year of life. Out of 576 cases of haemophilia, of which Granddier collected details, the bleeding occurred in early infancy in 12 only.

In congenital obliteration of the bile-ducts, however, and in all other forms of disease which cause lasting jaundice in young infants, haemorrhages are a common and characteristic symptom. Thus, more than two-fifths of the cases of umbilical haemorrhage collected by Jenkins and Granddier occurred in icteric infants; while in 65 cases of congenital narrowing or obliteration of the bile-ducts tabulated by myself, haemorrhages were noted in more than half of the number of infants which had lived more than a few days. A similar hemorrhagic tendency is of course well known to occur sooner or later in all cases of continued obstruction of the common duct; and is almost equally characteristic of a number of very different morbid conditions, all of which are accompanied by jaundice;
such as acute yellow atrophy, yellow fever, phosphorus poisoning, and so forth.

Clinical features.—The places from which the bleeding occurs in these cases are just the same as those observed in the case of idiopathic haemorrhages. Their onset, however, is generally later. Thus in Grandidier’s cases of umbilical haemorrhage the average date of onset was about the sixth day in the non-icteric and about the tenth in the icteric cases. In the case of gastro-intestinal haemorrhages this difference is very much more marked; for, although jaundiced infants sometimes show a tendency to haemorrhage from the very first, they often do not begin to bleed until several months after birth. When once established the tendency seems rather to increase as they grow older.

Etiology.—The causation of the haemorrhages in cases of jaundice has never been satisfactorily explained, although many hypotheses have been proposed to account for them. By some they have been attributed to impoverishment of the blood (Budd, Murchison); by others it has been supposed that they are due to bile acids circulating in it, and either acting on the corpuscles (Leyden) or setting up a diseased state of the blood-vessels (Wickham Legg).

It seems, however, more probable that the haemorrhagic tendency is caused in some way by the presence in the blood, not of bile acids, but of ptomaines or some similar organic poisons. These are formed in the process of ordinary digestion, and the diseased liver is not able to render them innocuous, as it would do if it were in a state of health. The following facts seem to support this hypothesis. It has been found by Roger that the function of the liver, in virtue of which it neutralizes the organic poisons formed in the alimentary canal, as well as others, is closely connected with the amount of glycogen it contains. Thus, when the liver contained little or no glycogen, he found that a very much smaller dose of these organic poisons was required to produce a given result than was necessary if the organ were healthy in this respect. It has also been demonstrated by Dr. Wickham Legg and others that the obliteration of the bile-ducts by ligature is followed in animals by disappearance of glycogen from the liver. It would appear that the retention of bile interferes with the proper discharge of the function of glycogenesis in the hepatic cells.

In the light of these observations, it seems not improbable that in congenital obliteration of the bile-ducts and other serious forms of jaundice a process of auto-intoxication is set up. If this be so, the poisons which come thus to circulate in the blood will probably induce haemorrhages in the same way as do those toxins which are produced by the action of micro-organisms in the idiopathic cases.

Owing to the serious nature of the diseases present in these cases the prognosis is much worse than in the idiopathic group, and the treatment, which is to be conducted on the same lines as in the others, is even less likely to be successful.

John Thomson.
REFERENCES


PURPURA

Definition.—Spontaneous extravasations of blood into the skin, mucous membranes, and internal organs of the body, sometimes accompanied by free hæmorrhages from mucous surfaces.

Etiology and Pathology.—Morbid anatomy simply reveals the existence and extent of distribution of hæmorrhagic effusions, often accompanied by evidences of anaemia. In a minority of cases in the mucous membranes, and more rarely in the skin, erosions or ulcerations are met with in connection with the hæmorrhages, but these are clearly the effects and not the cause of them; in mucous membranes the moisture of the part, and in some organs the digestive property of the secretions, tend to produce this result. In the hollow viscera blood may be found in considerable quantities, and the serous cavities may contain blood-stained serum. Besides the skin and mucous membrane, hæmorrhage occurs in the solid organs and in the serous membranes. They are found in the lungs, kidney, spleen, liver, brain, and retina; indeed, there is no part in which hæmorrhages may not occur. In the brain, from the delicacy of its structure and feeble resistance, the hæmorrhage may reach considerable magnitude, and may be fatal. The pleura, pericardium, peritoneum, and pia-arachnoid are often dotted over with small extravasations. The hæmorrhages vary in size from a pin's-head to a patch as large as the palm of the hand. On post-mortem examination the most important changes found, other than hæmorrhages, are in the kidneys and lungs. Slight degrees of diffuse or parenchymatous nephritis are relatively common. Congestion and oedema of the lungs are frequently present, and are often the determining cause of death. Ulceration of the intestine and enlargement of the solitary and agminated glands are sometimes present.

With regard to the mode of escape of the blood in this as in other conditions in which spontaneous hæmorrhages take place, it may be by rhëxis—by rupture of blood-vessels, or by diapedesis—by the escape of blood corpuscles through unbroken vessel walls. The former is most probably the process in the great majority of cases. Though many observers have failed to discover rupture of blood-vessels at the seat of the extravasations, Unna and his pupil Sack (20) have shown they are to be detected by certain methods of examination. According to Unna, it is the veins that give way; and he has pointed out that the laceration occurs especially at the junction of the superficial part of the subcutaneous tissue with the lower part of the cutis. At this point, which he regards as one of less resistance, the vessels lose their well-marked adventitia, and lack the support of the highly elastic cutis. The extravasated blood from its seat of origin percolates the epidermis, and occasionally the
sebaceous and sweat glands; in some cases sero-haemorrhagic extravasations take place also in the subcutaneous and intermuscular tissues. The causes that lead up to and actually determine the escape of blood are probably many and complex. Search has naturally been made in the walls of the blood-vessels for changes apt to cause them to give way. In some cases inflammatory changes have been found, and may in such instances have been the cause of the ruptures. In the majority of cases, however, the inflammation is the result of the violence to which the coats of the vessels have been subjected, an inflammation which may extend to vessels at some distance from the rupture. A hyaline degeneration, either of the intima or of the adventitia, or both, has been found by some observers. In the well-known case recorded by Wilson Fox a lardaceous change was found in the vessels of a syphilitic subject. Unna properly remarks, and experience of these changes in other circumstances confirms his opinion, that these hyaline and lardaceous changes would rather have a tendency to restrain than to encourage haemorrhage. Venous thrombosis, as in so-called "purpura thrombotica," has been met with occasionally; but probably it stands in the relation of effect rather than of cause. Capillary emboli have been found in sarcoma (Hilton Fagge), in leucocytæmia, and in pyæmia, and may have a direct causal influence; but numerically such cases are very infrequent, and afford no explanation of the majority of cases of purpura in which they are absent. In recent years great attention has been devoted to the search for micro-organisms in the blood, in the blood-vessels, and in the tissues. Various bacteria have been found by different observers, in some cases, but in other cases the same observers have failed to discover them. The presence of micro-organisms in the blood-vessels, even in large numbers as in diphtheria or anthrax, does not necessarily give rise to hemorrhage; moreover, apart from the negative results of the search for bacteria, the circumstances in some cases in which purpura occurs make it unlikely that its causes are of this kind. Though thus not necessarily leading to rupture of vessels or diapedesis, they may nevertheless affect the vessel walls indirectly, by inducing some chemical change in them, as suggested by Watson Cheyne and Unna. Further, as Watson Cheyne has pointed out, the presence of bacteria does not necessarily imply that their entrance into the blood is the starting-point of the disease; the alternative view, however, may be entertained that, although the primary cause may be of quite a different nature, the result may be such an alteration of the fluids of the body that, of the innumerable organisms present in the mouth and intestinal tract, certain species may be enabled to penetrate into the blood and to live in it. It is quite possible, also, that some poisonous toxin or albumose formed in other parts of the body may be absorbed, and act chemically upon the blood-vessels, or on the vaso-motor nerves, producing variations of blood-pressure which at the weakest points they are unable to resist. In the whole class of specific diseases, whether in those in which micro-organisms have been demonstrated, or in those in which so
far they are only assumed, the bacteria or their products must play an
important part in the production of the cutaneous hæmorrhages which are
an occasional feature of nearly all members of this group of diseases.
The fact that purpuric phenomena are not uncommon in certain of them,
such as scarlet fever and measles in which no specific micro-organisms
have as yet been demonstrated, should make us chary of denying the
possible existence of bacterial influence in the purpura of other diseases
in which up to the present no micro-organisms have been found.

It is certain that cutaneous hæmorrhages are sometimes determined,
and in all probability primarily caused by nervous influences; as in the
case of purpura occurring in the situation of the lightning pains of tabes
(Strauss, 19), and in connection with certain neuralgias (Weir Mitchell).
The mechanism of the hæmorrhage in such cases is hitherto purely con-
jectural; but it seems most probable that, by acting on vaso-motor centres,
it produces variations of vascular pressure under which the blood-vessels
give way in the situation already indicated at the points of least resis-
tance. Though purpura is one of the manifestations of hæmophilia,
the histopathology of the latter need not be fully discussed here (see
"Hæmophilia," p. 552), nor would it materially elucidate the pathology
of the majority of cases of purpura. Hæmophilia is believed, however,
by some authors to be due to a congenital defect in the vascular walls.
It is quite possible that in some cases of purpura a hæmophilic taint
may be an element in the hæmorrhagic tendency.

Venous stagnation plays a part in the production of purpura. Though
not of itself a sufficient explanation of hæmorrhage, it is evidently a
factor of importance, as in nearly all cases of purpura the hæmorrhages
begin and are most marked in the lower extremities, the veins of which
have to support a longer and heavier column of blood than those of other
parts. As a rule, however, something more than stagnation is necessary
to bring about rupture or diapedesis. When hyperæmia co-operates with
stagnation the conditions are favourable to hæmorrhage (Unna).

Next, in relation to the escape of blood from the vessels, we have to
consider the influence of the quality of the blood. The changes in the
composition of the blood in purpura may be of the most varied kind: (i.)
deficiency of the red corpuscles as in pernicious and other severe forms of
anæmia, (ii.) excess of white corpuscles as in leucocyæmia, (iii.) deficiency
or excess of some of the saline constituents of the blood as in scurvy, (iv.)
alterations in the reaction, (v.) alterations in the specific gravity, (vi.)
deficiency in the fibrin-forming elements may all play their parts in
the initiation of changes in the vessel walls and in their permeability.
Lastly, the presence in excess of some organic matters such as bile, urea,
and other products of metabolic changes as in jaundice or ureæmia, or
the addition to the blood of extraneous matters, have all a tendency to
promote some chemical or vital changes which render the vessels liable
to rupture or increase the permeability of their coats. In the latter
category we have important evidence of the effects of certain chemical
substances. The observations of Prussak, confirmed by Wickham Legg,
have demonstrated that chloride of sodium injected into the vessels or subcutaneous tissues of the frog gives rise to diapedesis of coloured corpuscles which, under the microscope, may be seen to pass through the intact walls of the blood-vessels (9). Similarly, in certain persons, iodide of potassium, as well as other drugs, give rise to purpura. Though the exact mode of operation of such agents has not been worked out, we must ascribe some influence, direct or indirect, to chemical action on the walls of the blood-vessels.

Finally, it must be pointed out that a diminution of support to the blood-vessels by the tissue immediately surrounding them may lead to their rupture. Thus purpura occurs in those who have wasted much from severe or protracted diseases (convalescence purpura); in the wasting, loss of elasticity, and vascular degeneration of the aged (senile purpura), and in the newly-born (purpura neonatorum).

Reviewing briefly the pathological conditions under which purpura occurs, we may arrange them as follows:—

I. (a) The infective diseases, in nearly all of which, but especially in small-pox, measles, scarlet fever, cerebro-spinal fever, syphilis, and malaria, purpura is an occasional incident.

(b) Rheumatism, which may be placed temporarily in this class, but requires separate description.

(c) The various conditions under which certain organic matters present in excess in the blood—such as bile, urinary constituents, or certain adventitious organic poisons, such as snake venom—may gain access to the blood.

(d) The presence in the blood of extraneous chemical substances, such as phosphorus, mercury, mineral acids, salicylic acid, iodide of potassium. For clinical purposes group (d) should be considered apart as “toxic” or “drug” purpura, but pathologically it fits in here.

(e) Conditions in which some constituent of the blood is wanting, as in scurvy.

(f) Alteration in the formed elements of the blood, as in anaemia and leucocytæmia.

To Series I. the term “Vascular purpura” may be given.

II. (a) Conditions that offer an impediment to the circulation, general or local; as in diseases of the heart and large vessels, and tumours compressing them, thrombosis, temporary vascular spasm or paralysis; as in convulsive seizures, whooping-cough, or angina pectoris.

(b) Want of mechanical support of blood-vessels, as in wasting, in the newly-born, and the aged.

Series II. may be designated “Mechanical purpura.”

III. Conditions in which the direct influence of the nervous system can be traced, as in tabes, neuralgia, and the like. To this series the name “nervous purpura,” or purpura of nervous origin, may be applied.

IV. Congenital imperfection of the blood-vessels, as in haemophilia—“haemophilic purpura.”

In the absence of a common cause, of a definite clinical course, of
constant pathological changes, it is obvious that purpura is not a consistent or uniform symptom group, but is itself a symptom entering not into one only but into many groups.

The best notion of the circumstances in which purpura occurs will be conveyed by an analysis of 200 cases from the records of the London Hospital. They were not selected, but taken consecutively, so far as the records permitted. They are given in the following table:—

**Table of 200 Cases of Purpura in the London Hospital, arranged as regards probable Causes or associated Conditions.**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatism</td>
<td>33</td>
<td>28</td>
<td>61</td>
</tr>
<tr>
<td>Doubtful rheumatism</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Bright's disease</td>
<td>7</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Heart disease</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Anaemia</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Leucocytæmia</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Scurvy</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Privation and dictotic</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Pyæmia</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Ulcerative endocarditis</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Malaria</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rickets</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Whooping-cough</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Toxæ (drugs)</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Cirrhosis of liver</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Convalescence</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Injuries</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Haæmophilia</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Varicose veins</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral neuritis</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Unexplained</td>
<td>31</td>
<td>37</td>
<td>68</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>112</td>
<td>88</td>
<td>200</td>
</tr>
</tbody>
</table>

This table does not present any instances of purpura in connection with the specific fevers, for these, with the exception of enteric fever, are not admitted. Nor are there any cases of P. neonatorum or P. senilis.

*Age* incidence will be best shown by the subjoined table:—
TABLE of 200 Cases of Purpura arranged in Decades.

<table>
<thead>
<tr>
<th></th>
<th>Up to 10 years</th>
<th>11 to 20</th>
<th>21 to 30</th>
<th>31 to 40</th>
<th>41 to 50</th>
<th>51 to 60</th>
<th>61 to 70</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>24</td>
<td>29</td>
<td>31</td>
<td>13</td>
<td>9</td>
<td>2</td>
<td>4</td>
<td>112</td>
</tr>
<tr>
<td>Females</td>
<td>25</td>
<td>28</td>
<td>17</td>
<td>10</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>88</td>
</tr>
<tr>
<td>Totals</td>
<td>49</td>
<td>57</td>
<td>48</td>
<td>23</td>
<td>16</td>
<td>3</td>
<td>4</td>
<td>200</td>
</tr>
</tbody>
</table>

From these figures, which fairly represent the condition in which purpura occurs, apart from the eruptive fevers and in the newly-born, it will be observed that purpura is more common in the male than in the female sex, in the proportion of 14 males to 10 females—not quite 1 ½ males to 1 female. This holds good for all ages with the exception of the first decennium, in which the females exceed the males by one. It will also be observed that the greatest number of cases occur in the first three decades, 77 per cent in persons under 30 years of age. In the fourth decade the numbers rapidly fall to less than half of those in the third decade; still fewer cases occur in the fifth decade, and only 7 cases occur in persons of either sex over 50 years of age.

The number of cases here dealt with is probably larger than in any published series; but it will be seen how comparatively rare purpura is when I say that 200 cases represent the number occurring amongst 63,834 medical cases in 16½ years. They only amount to 0·3 per cent of the medical cases, and this is probably a fair calculation of its occurrence in purely medical practice.¹

The great variety of supposed causes or associated conditions is sufficiently striking. Still more so is the fact that in one-third of the cases tabulated no explanation was afforded for the purpura, though in several of the cases a necropsy was made. It will thus be seen how extremely complex is the pathology of purpura. All we can do in the present state of our knowledge is to accumulate further information, and to exhaust every means—histological, bacteriological, and chemical—in the investigation of cases. It will be observed that in by far the majority of cases in which anything definite can be ascertained as to the causation of purpura this is of a vascular character—some known or probable alteration of the blood, or some condition which brings about a change in the blood-vessels; and, arguing from the known to the unknown, it seems probable that, in those in which no definite causation can be ascertained, purpura is due to one of these two kinds of change.

**Symptoms.**—Certain phenomena are common to most cases of purpura.

¹ A very few cases, too few to affect the calculation, were omitted as the notes were incomplete.
Changes in the extravasated blood.—Recent extravasations appear of a more or less bright red or crimson colour. They are usually oval or round, but may occur in lines or streaks—vibices. In a short time they become of a dull purple, and later of a brownish red tint; lastly, a brownish stain persists for a considerable time. In some cases a bluish green colour is present. In quite superficial haemorrhages, spots, as they fade, present a yellowish hue, passing into a faint brown. As regards the changes in the blood effused, when the haemorrhage takes place into the cutis, there begins, according to Unna, very soon after the occurrence of the bleeding solution of the haemoglobin, which is partly reabsorbed with the blood-plasma, and partly crystallised in the tissue (precipitated). Where large masses of blood corpuscles are closely packed, they break up, without previously giving up their haemoglobin, into yellow or brownish flakes, which are gradually converted into pigment granules, and as such are partly taken up by the connective tissue cells.

Pyrexia.—A certain degree of fever is present in more than half the cases. In the majority it is slight and transient; in others the disease runs a moderately febrile or highly febrile course (P. febris), and hyperpyrexia has been known to occur. The decidedly febrile cases are nearly always characterised by a greater severity, and are therefore attended with greater danger than those which are non-febrile; otherwise no important differences are noticeable.

Albuminuria, apart, of course, from cases in which it is plainly secondary to Bright's disease, is of rather frequent occurrence in purpura; it occurs in both febrile and non-febrile cases, and corresponds with the statement (p. 568) that in fatal cases the kidneys are frequently found diseased.

Digestive system.—Derangement of the stomach and intestine is common. Apart from anorexia, which is frequent, colic in severe paroxysms, vomiting and diarrhoea are so pronounced in some cases as to have been constituted into a special form of the disease (Henoch's purpura).

Haemorrhages.—Haemorrhage may occur from any of the mucous surfaces. Epistaxis is the most common; next, haemorrhage from the gums and throat, and, following these in frequency, from the intestines, urinary passages, stomach, lung, and sexual organs. Intra-visceral and interstitial haemorrhages also occur; and haemorrhages in the retina may be detected during life by the ophthalmoscope. Retinal haemorrhages are, however, rare in purpura.

On account of the variety of circumstances in which purpura is met with, some classification in the investigation of cases is absolutely necessary. Dr. Radcliffe Crocker's classification has a pathological basis; he makes the following varieties: (i.) Certain blood alterations; (ii.) visceral disease; (iii.) want of support to the vessels; (iv.) sudden changes in the circulation; (v.) diseases of the nervous system.

Dr. Pringle makes the following classes: A. Symptomatic purpura: (i.) Mechanical, due to increased blood-pressure; (ii.) dependent on changes in the blood or walls of blood-vessels; (iii.) toxic; (iv.) due to disordered innervation; (v.) the result of a specific infective virus; (vi.) cases which
cannot be considered as belonging to any of the foregoing classes, and which must provisionally be classified as idiopathic. B. Purpura simplex. C. Purpura haemorrhagica.

Professor Osler gives a very good provisional grouping of the varieties of the condition. A. Symptomatic purpura: (i.) infective, (ii.) toxic, (iii.) cachectic, (iv.) neurotic, (v.) mechanical. B. Arthritic purpura: (i.) a mild form known as P. simplex, (ii.) peliosis rheumatica, (iii.) Henoch's purpura. C. Purpura haemorrhagica.

The following kinds will be described here:—(i.) Purpura simplex, (ii.) purpura haemorrhagica, (iii.) purpura rheumatica, (iv.) iodic purpura, (v.) Henoch's purpura.¹ There is no fundamental distinction between P. simplex and P. haemorrhagica; the former is a mild form of purpura, the latter a severe purpura with haemorrhages from mucous surfaces. Both are symptomatic of a great variety of causes.

**Purpura Simplex.**—With or without preceding constitutional disturbance, haemorrhagic extravasations make their appearance in the skin. They frequently begin in the lower extremities, but become generally disseminated over the whole surface. They may present a rough symmetry, or have a random distribution. The spots are generally circular or rounded, but may occur in streaks; they vary in size from mere petechiae to extravasations as large as half a crown or larger. The attack may be ushered in by a slight rise of temperature, or febrile disturbance may arise in the course of the attack. Many cases are non-febrile throughout their course. The disease is most common in young persons. The patient may be anaemic, or may present a healthy appearance, and be well nourished. There may be some malaise, digestive troubles, and other constitutional disturbance; or these may be wanting. The first spots fade, passing through the changes of colour described, and new ones appear; so that all varieties of colour are present. After lasting a variable and indefinite period, usually a week or two, no fresh spots make their appearance, the old ones fade, and the attack comes to an end, leaving pigmentation of the skin where the haemorrhages have been present, for some weeks or longer.

**Purpura Haemorrhagica (Morbus muculosus Wertheii).**—The etymologically meaningless name P. haemorrhagica—for all purpura is haemorrhagic—is applied to cases in which not only cutaneous extravasations are present, but in which haemorrhages take place from mucous surfaces also. It represents the more severe and dangerous kind of purpura. No more than P. simplex is it to be regarded as a uniform symptom group, for it occurs under a variety of conditions.

¹ Neurotic purpura, or purpura of nervous origin, cannot be made into a well-defined variety; but the name neurotic purpura may be applied to cases in which the haemorrhages can be confidently attributed to nervous influence. Dr. Weir Mitchell has described cases of neuralgia in which haemorrhages occurred in the skin about the penis; Strauss (10) and others, purpura in connection with tabes. Purpura is also met with in angina pectoris, meningitis, whooping-cough and epilepsy. In the latter categories the immediate mechanism is probably vascular, and consists in a local increase of blood-pressure.
It may begin with more or less constitutional disturbance—headache, debility, gastric pain, and vomiting, and be followed by extravasations into the skin and mucous membrane, and free haemorrhages from the latter. Or it may begin as P. simplex and later become P. haemorrhagicus, as bleedings take place into and from the mucous surfaces. The haemorrhages vary in size as in P. simplex, but tend to be larger, and are often accompanied by haemorrhagic oedema in large patches—as large as the hand or larger—appearing in certain parts, raised, reddish, or purple-blue in colour, and pitting on pressure. The orbits, the penis, and scrotum occasionally become extremely swollen, and the skin tense and of a livid colour. The appearance may suggest a fear of sloughing, and indeed the fear may be justified. The cutaneous haemorrhages pass through the same stages as in P. simplex, but appear in rapid succession, and are often of large extent. Haemorrhages in severe cases are usually met with in the mucous membrane of the mouth and throat; and in this situation they may give rise to alarming symptoms, and even occasion a fatal issue. In several recorded cases haemorrhages have taken place into the palate and tongue. When occurring in the latter organ acute swelling of the tongue, resembling acute glossitis, has been produced, necessitating incisions for the relief of the consequent dyspnæa. In one or two cases sloughing of the tongue, with shedding of its apex, has occurred.

Of the haemorrhages that take place from the mucous membranes epistaxis is the most common; haemorrhages from the mouth and throat are also very common: in some cases haemorrhages occur from the stomach, intestines, lungs, and genito-urinary organs. The bleedings from the mucous membranes may be very severe and frequently repeated, and in some cases are uncontrollable. Though in some cases anæmia may not be present at the outset, it rapidly makes its appearance, which is not surprising when we consider the large amount of blood lost from the mucous surfaces and into the skin. Von Leahe has recorded a case in which, eighteen days after the beginning of the disease, the red corpuscles numbered only 2,680,000 per c.mm., and the haemoglobin was 0·067 per c.mg. In another, a woman twenty-one years of age, the corpuscular richness was 2,091,900. When the disease has lasted some time, and, as would be anticipated, when copious internal haemorrhages have taken place, the blood richness, in numbers and colour, shows still greater reduction. Hayem has recorded a case in which the red corpuscles fell below 1,000,000; Quinquand a case with only 740,000 per c.mm.; and Hérard a case in which the corpuscular richness was 1,885,000, when first counted, but fell to 620,000 per c.mm. I have recorded a case (10) in a child eleven months old, in which the red corpuscles just before death numbered only 290,000 per c.mm., or 5·8 per cent, with one white to fifteen coloured corpuscles. In this case the great debasement of the blood was due to uncontrollable epistaxis, and the patient died quite exsanguine. The blood that exudes in such cases of extreme anæmia is only tinged with red, appearing as a thin serous exudation.
Fever is present in the majority of cases of P. haemorrhagica. It may reach a high grade—104° F. or higher, and may be hyperpyrexial—105.5° or higher. Such cases with high fever, extensive extravasations, and copious and repeated haemorrhages from the mucous membranes, may run a very rapid course, and end fatally in the course of a few days. Such cases have been described as P. fulminans. In severe cases haemorrhages may take place into the brain, and may occasionally be seen during life in the retina. In P. haemorrhagica pains are often present in the joints and limbs, even in cases in which there is no reason to believe the condition to be of rheumatic nature. Scheybey Buch has drawn attention to effusion into the joints in non-rheumatic cases. Albuminuria, with or without blood, is often present in cases of P. hemmor-

rhagica. In fatal cases pulmonary oedema, often associated with hemorr-

hage into the lung due to exhaustion, is commonly the determining cause of death.

In cases which pursue a favourable course, or which do not end fatally, the haemorrhages into the skin and from the mucous membranes recur from time to time over a period of days, or, more usually, of weeks, in a fitful manner, and eventually cease; the patient being left extremely weak, anæmic, and often much wasted.

Purpura Rheumatica (Schönlein’s Peliosis rheumatica).—This kind has gradually gained increased recognition, though twenty or fifteen years ago it was scarcely ever diagnosed. Schönlein’s description is worth reproducing, as differences of opinion have arisen as to the meaning of the name he used.

“The patients have either already suffered from rheumatism, or rheu-
matic symptoms accompany the attack: slight periodic throbbing pains in the joints (in the ankles and knees, rarely in the hand and shoulder-
joints), which are oedematosely swollen and tender on pressure. The characteristic spots of the disease in the majority of cases first appear on the extremities, especially on the lower extremities, and here only as high as the knee (rarely on the upper). The spots are small, of the size of a lentil to that of a millet seed, bright red, not raised above the skin, disappearing under the pressure of the finger [italics not in original]; they gradually become dirty brown or yellowish, the skin over them slightly desquamates with a branny scale. The eruption comes out in crops, often during several weeks. Ever so slight a change of temperature, as for example passing into a colder room, may occasion a fresh outbreak. The eruption usually appears with some fever, of a remittent type. Towards evening the symptoms are at their height, with a recession in the morning. There is frequently a deposit in the urine.” It is clear from Schönlein’s own words that he described an erythema papulatum, for he expressly notes the colour “disappearing under pressure.” Further, in discussing the diagnosis, he gives the diagnostic criteria from Werlhof’s disease (P. haemorrhagica). The majority of writers, following Schön-

lein, regard purpura rheumatica as a purpuric erythema, though this is
scarcely justified from his description that the colour disappeared on pressure. Some go farther and appear to regard all purpura as erythematous in nature. Though an allied process, I believe it better to keep the two conditions distinct, and in the following description of purpura rheumatica I shall restrict the name to a condition which is purpuric from the beginning, and in which the spots do not disappear on pressure at any stage. In other respects Schönlein’s description of the eruption coming out in crops, and of the aggravation of disease in the evening, is singularly apt.

The disease occurs with about equal frequency in the two sexes, and is most common in the second, third, and fourth decennia (from eleven to forty); it is rare before ten years of age and after forty. In some cases the purpuric eruption makes its appearance whilst the patient is suffering from acute or subacute rheumatism. More commonly the arthritic symptoms arise coincidently with the purpuric eruption; in a few cases, in which arthritic symptoms are doubtfully present in the attack, or are entirely absent, an attack of arthritic rheumatism may appear at some subsequent period, thus revealing the rheumatic nature of the purpura; or, perhaps, to be more exact, thus demonstrating that the patient is a rheumatic subject. Apart from cases in which acute or subacute rheumatism ushers in the purpura, the very characteristic onset and course of the disease is as follows:—The patient has pain in the lower extremities, which may be of a dull aching character, but frequently and characteristically is a sense of tension—a “sensation of bursting” in the parts affected, as patients frequently describe it; often there is itching. When these symptoms are present (and patients who have had a previous attack know well their meaning), bright red spots, which do not disappear on pressure, are seen on the legs. In the majority of cases when they first make their appearance they are raised (P. papulosa). The eruption and its accompanying discomforts usually make their appearance in the later part of the day, afternoon or evening. The knee and ankle joints are usually painful and often swollen and tender, sometimes the skin over them is slightly reddened. A slight degree of oedema of the lower part of the leg, of the ankle, and of the dorsum of the foot is present in nearly all cases. By the following morning the pain remits, and inspection shows that the spots are now of a purple or dull red colour, and no longer raised. On the second evening, or after an interval of two or three days, the same phenomena are repeated—the aching of the legs, the pains in the joints and oedema, and the appearance of another crop of bright red spots similar to those first observed. The spots pass through the usual stages of discoloration characteristic of haemorrhages into the skin, and if the patient is seen after the occurrence of two or three outbursts, and at a time when a fresh crop has recently appeared, we observe:—1. Bright red raised spots, varying in size from a millet seed to a threepenny piece or larger, not disappearing on pressure. 2. Spots of a similar size of dull red or purple colour, but not raised above the surface, and unaffected by pressure. 3. Yellowish brown
stains. The affected limbs are tender to pressure and slightly oedematous. In most cases, as already stated, there are pain and swelling of the joints of the lower extremities, and in some of the elbows and wrists; even in cases in which the skin of these parts is not affected by haemorrhages. The joint affection often persists between the outbursts of haemorrhages, though exacerbations of pain and swelling occur in the attacks. The first outburst of haemorrhages is usually confined to the lower part of the legs and feet. In subsequent outbursts there is a tendency to an extension of range, so as to involve the upper part of the legs, and, later still, the thighs and buttocks. In slight cases the eruption is limited to the lower extremities, but in more severe cases the forearms and arms are affected also. Usually when the thighs are affected the skin above and below the elbow is the seat of haemorrhages. The eruption is so far symmetrical that if one leg is affected the other leg is affected also; and if it attacks the upper extremity both will be attacked. The eruption shows no marked predilection either for the flexor or extensor surfaces of the limbs. In the great majority of cases it is confined to the extremities; but in the more severe cases, especially those in which the arthritis and pyrexia are great, the trunk and face also are affected. Haemorrhages into and from the mucous membranes are rare, but in a few cases small haemorrhages may be seen in the buccal mucous membrane; and in rare and very severe cases extensive haemorrhages may take place into the tongue (intra-muscular) and throat. In about one-third of the cases some degree of pyrexia is present, and probably, if careful thermometric observations were made in the evening at the time of the eruption, some elevation of temperature would be found in nearly all of them. Sweating is not a marked symptom unless the arthritis be pronounced. The amount of constitutional disturbance is variable, this being slight in the majority of cases; but in some malaise and debility are present. The majority of patients are able to walk about stiffly in the early part of the day, but locomotion is very difficult and painful in the later day, especially at the time of the outbursts of haemorrhages. Any exertion tends to bring on an attack. The department for diseases of the skin, of which I have charge, is open in the morning, and patients tell me they had a bad attack in the afternoon or evening of the days when they had been to see me. Exertion seems to me to determine attacks much more than changes of temperature, to which Schönlein referred them. The eruption usually lasts an indefinite time, unless treatment of a certain kind is adopted for several weeks, or months; I have known it to persist for two years. The disease is occasionally, though extremely, rarely, fatal. Usually it is a benign affection. It is very apt to recur.

The assemblage of symptoms is very definite and characteristic. The occurrence of haemorrhages—usually confined to the extremities, appearing in crops, usually in the latter part of the day—the arthritic pain and swellings, and its protracted course, distinguish it from other forms of purpura, and from erythema exudativum multiforme. It has undoubtedly
close clinical alliances with the latter, which also, in a large proportion of cases, is of a rheumatic nature, and the two may occur in the same subject; but in the cases to which I would restrict the name purpura rheumatica the eruption from first to last is purpuric, and not erythematous. The evidence of its connection with rheumatism is, in the majority of cases, extremely distinct. The arthritis, which is present in many cases, is characteristic, and may precede the purpura; so that the diagnosis of acute or subacute rheumatism is already made. In other cases the patient has previously suffered from rheumatic fever. In a considerable proportion of cases valvular disease, usually mitral incompetence, is present; and in a few it may arise during an attack. Many patients have had other affections belonging to the rheumatic series, such as tonsillitis, endo- and pericarditis, pleurisy, chorea; and a family history of rheumatism is very common. I have seen two brothers with purpura rheumatica at some years’ interval. The second one died of heart disease a few years later. In a certain number of cases the arthritic symptoms in the attack are equivocal or absent; but the complex of symptoms described have been definite and identical with those in which the rheumatic nature was beyond dispute; so that when the symptoms above described are present, I am of opinion that we are justified, even in the absence of arthritis, in diagnosing purpura rheumatica. I have seen a case in which no arthritis accompanied the purpura, yet (at an interval of a year or more) an attack of rheumatic fever subsequently appeared. In the list I have given of the ascertained causes of purpura, rheumatism, it will be observed, stands very high, giving in the 200 cases 30.5 per cent, exclusive of doubtful but still probably rheumatic cases.

IODIC PURPURA.—Fournier was the first to give a good description of this form of purpura. The eruption is generally confined to the lower extremities, and in the majority of cases to the parts below the knee. The eruption consists of discrete miliary hemorrhagic spots, bright red when recent, not elevated, not obliterated by pressure, unattended with heat, pain, or swelling. The eruption comes out at an early period of the iodide treatment, and continues to appear for two or three days. It remains for a certain time as a staining of the skin, the blood undergoing the changes of colour usual in cutaneous hemorrhages, and finally disappears by the end of two or three weeks. During its progress a renewed attack may sometimes be induced by augmenting the doses, and then the bright red recent hemorrhages contrast very markedly with those that are fading. Though usually confined to the legs, it may affect the trunk and the face, as in a case I have recorded. The purpuric spots are usually more pronounced in the anterior than in the posterior parts of the legs. Successive outbreaks are usually less profuse than the original one. It may be accompanied by some edema of the legs, but this is not usually the case. The various salts of iodine seem all to produce purpura, but exceptions to this rule are met with;
some persons can take sodium or ammonium iodide without inducing it, whilst potassium iodide is operative; or potassium iodide may fail to produce it, whilst ammonium iodide may be operative. As potassium iodide is the salt most frequently prescribed, purpura is most frequently met with in patients taking this preparation. It is held by Besnier that pure iodine will not cause the haemorrhages, and he has illustrated this fact in the person of a man who had purpura in the lower limbs every time he took iodide of potassium; yet, although tincture of iodine caused symptoms of iodism in him, no purpura appeared (12). Purpura is a very rare consequence of the administration of potassium iodide. Usually it is quite a benign and unimportant affection, but one to be borne in mind, lest it be misinterpreted. Occasionally, moreover, the salt may give rise to very grave symptoms and even prove fatal; as in a case I have recorded. In this case fatal purpura followed a single dose of $2\frac{1}{2}$ grains of potassium iodide in an infant five months of age. In prescribing iodides to young children a small dose should be first given, and if tolerated, the dose may be augmented.

The reaction is clearly due to idiosyncrasy, as it occurs in a very small minority of persons. It does not depend on the debilitated state of the patient, whose nutrition may be quite good. It is possible that syphilis favours its occurrence; but the frequency with which which iodides are administered for syphilis and the rarity of iodic purpura show that personal peculiarity or idiosyncrasy is the determining factor. It is probable that the cause of the iodide purpura is some chemical action of the drug on vaso-motor centres producing variations in pressure in the area in which purpura appears; but it is possible that the drug may have a selective action on particular vascular areas, rendered more vulnerable than usual by incidental influences.

**Henoch's Purpura.**—Though Willan (21) many years previously had described a case of this kind very graphically, it was not until Henoch published a series of cases that attention was prominently directed to this form, often called "Henoch's purpura" (6). Couty recorded a number of cases which he recognised as similar in nature to those described by Henoch; and Osler, who takes a more general view of purpura than I have done in the present article (including it under erythema exudativum), has particularly directed attention to the visceral complications.

The marked feature of this disease is the association of abdominal symptoms (vomiting, colic, intestinal haemorrhage) with purpura and arthritic swellings. The attack may begin with rheumatic pains and swellings of the joints, and be followed by purpura and colic with vomiting and blood in the stools. Or it may begin with gastro-intestinal derangement, and the purpura and articular swellings and pains follow. What is especially characteristic of it is the occurrence of repeated outbreaks of colic, vomiting, and haemorrhage from the bowels, with purpura and pains and swellings in the joints. The illness generally consists of a series of such events over a period of some weeks or months; but intervals
of months may occur, and fresh outbreaks then take place. Recurrence is one of its most characteristic features.

The colic is generally of a very intense character. The abdomen is usually tender, especially over the colon. The vomiting is often severe and protracted, frequently bilious; occasionally but not frequently bloody. The stools contain more or less coagulated blood, but in some of the attacks no blood may be passed. In some cases albuminuria is present, and well-marked symptoms of nephritis set in which may prove fatal; or this complication may slowly subside. Epistaxis, hæmaturia, hæmoptysis may occur, but are not frequent. In the majority of cases the eruption is purely hæmorrhagic, but in others, in addition to the purpura, purpuric oedema, exudative erythema and urticaia may be present. Most commonly the eruption is confined to the extremities, but it may involve the face and trunk; and hemorrhages may occur in the mouth and throat. In the attacks the joints are usually affected. There may be only pain and stiffness, or there may be effusion and redness of skin over the articulations. The dorsa of the feet are often swollen, as in purpura rheumatica. There is as a rule little pyrexia, and it may be entirely absent. In one of Osler's cases great coldness of the feet was a prodromal symptom of the attacks, and in one case the spleen was enlarged. Silbermann has published a fatal case (7): a child, aged ten years, was attacked on December 15, 1887, with fever and pains in the knees. On the 16th there was an outbreak of purpura, with colic, hæmatemesis, and melena, and after persisting for three days the symptoms disappeared. The attack recurred in January with great severity, and on the 20th, 21st, and 22nd there were signs of peritonitis. The autopsy showed an acute peritonitis, which had resulted from a perforation at the fundus of the stomach. There was no ulceration in the bowels, but the mucosa was swollen and congested. There were necrotic foci in the stomach and intestines, and thrombi were found in some of the blood-vessels.

Henoch's purpura is relatively most common in childhood, but it occurs in adults also. As to the nature of such cases the evidence is inconclusive, and whether the colic and vomiting stand in relation to the hæmorrhage from the bowels and stomach as cause or effect is uncertain. Silbermann's case, however, suggests that hæmorrhage is the primary event and may lead to ulceration and perforation; as hæmorrhage is an exceedingly rare or almost unknown event in colic of the most severe degree, as in lead poisoning. Some of the cases appear to be of rheumatic nature—the patients, as in some recorded by Henoch, having previously had a rheumatic attack without purpura or colic. Conty regards the disease, by the exclusion of other causes, as of nervous origin, affecting the vaso-motor nerves.

Diagnosis of Purpura.—It must be reiterated that purpura is rather a symptom than a disease. It is not sufficient, therefore, to recognise purpura, but the nature of the process in the individual case must be ascertained. To recognise the symptom purpura is an extremely easy matter. The occurrence of hæmorrhages in the skin and mucous membrane is demonstrated by
an eruption of blood-colouring matter not of traumatic origin, the colour not disappearing under pressure. In many forms of exudative erythema there is blood extravasation, but this is accompanied by overfilling of the blood-vessels, which may be emptied by pressure, the colour returning when the pressure is removed. To this condition the name purpuric erythema may be applied; but the name purpura should strictly be applied to cases in which the hemorrhages are primary, unattended with erythema, and not due to injuries.

Having decided that purpura is present the observer has next to search for its cause. It is for this reason that some clinical classification is not merely desirable, but absolutely essential. The first step is to ascertain whether the purpura is an expression of one of the specific diseases prone to be attended with hemorrhage. Small-pox, scarlet fever, measles, pyemia, syphilis, and rheumatism have especially to be borne in mind. The diagnosis of purpura rheumatica has been sufficiently given. Next, the various primary blood diseases have to be considered—pernicious anemia and leukocythæmia in particular. The appearance of the patient may afford a clue, but the most important matter is the examination of the blood. In the next place the possibility of scurvy must be remembered. In this disease, in addition to the cutaneous hemorrhages, subcutaneous and intra-muscular extravasations occur, producing brawny, blood-stained patches in the hamstring muscles and calves of the legs, and in the skin over the patches; and the gums are swollen and bleeding. Evidence of insufficiency of fresh vegetable or animal food is generally obtainable. In doubtful cases the effect of treatment will assist in the diagnosis, as scorbatic cases rapidly improve when treated with fresh vegetables and meat juice. It must be remarked, however, in this connection that in certain cases of pernicious anæmia the gums may be swollen and bleeding as in scurvy. To these cases the name "sorbatic anæmia" has been applied. Scurvy being excluded, the possibility of some poison having been accidentally or intentionally taken must be considered—phosphorus, mercury, mineral acids, etc., being borne in mind; or some medicinal substance, especially iodide of potassium. Nor must the possibility of a nervous origin be forgotten; the history of the case, and an examination of the nervous system, will determine whether this cause be in operation.

Finally, in a considerable number of cases no definite cause can be ascertained for the purpura, and such cases are indicated by the name P. idiopathica. They must temporarily be relegated to the class purpura simplex or purpura hemorrhagica, according to the symptoms presented. It must be remembered, however, that this indefinite name serves but to remind us of our ignorance; and the observer must ever be on the alert to discover the cause which will immediately remove the case to its own category.

**Prognosis.**—Most cases of purpura end in recovery. The mortality is probably about 14 or 15 per cent. Thus of the 200 cases above analysed the mortality was 28, or 14 per cent. Sex does not appear to
exercise any decided influence—the mortality in males, in the 200 cases, being 14·2, whilst in females it was 13·6. Age exercises some influence, the gravity appearing to increase, on the whole, with the age of the patient. But in the 200 cases analysed the mortality in the first decade was 16 per cent; in the second decade, 10 per cent; in the third decade, 14 per cent; in the fourth decade, 13 per cent; in the fifth decade, 25 per cent; in the seventh decade, 25 per cent. It is thus seen that the greatest mortality occurs in patients under 10 and over 40 years of age. Cases of P. simplex almost invariably end in recovery; but, on the other hand, purpura simplex may be the beginning of a severe and fatal case of purpura hæmorrhagica. The gravity of the case is generally stamped early upon it. The severity and frequency of the cutaneous hemorrhages, the occurrence of hæmorrhages from mucous surfaces, the degree of pyrexia, the constitutional depression, the degradation of the blood, as proved by the hemoglobinometer and hæmocytometer, and the occurrence of marked albuminuria, will draw attention to the danger attaching to the case. At the same time it must be borne in mind that the most severe and apparently dangerous cases sometimes end in recovery.

Treatment.—The patient in all kinds of purpura should be confined to bed. Whenever a definite cause for the purpura is discoverable, a clue to the treatment will be supplied. In the infective diseases it invariably indicates a very grave condition, and calls for support by nourishing fluid food and stimulants; whilst at the same time some of the hæmostatics to be subsequently mentioned, especially turpentine, should be administered. In syphilitic purpura iodide of potassium should not be given, for it appears in some cases to increase or to initiate the hæmorrhages. In many cases of P. rheumatica oil of turpentine appears to act as a specific; it should be given in ten or twenty minims doses in capsules, or suspended by means of tr. quillaisa saponariae or mucilage. The following mixture I have used in numbers of cases with the happiest results:—Ol. terebinth M x., quillaisa sapon. M x., aquam cassiae ad ʒ j. To be given three times a day. Prof. Boeck of Christiania recommends antifebrin in five or ten grain doses in these cases. Salicylates, in my experience, as well as in that of Prof. Boeck, have little or no influence for good.

In cases in which no discoverable cause can be ascertained, as well as in many in which there is a recognised cause, turpentine is, on the whole, the best remedy. Ergot and hamamelis may be tried, but they have not proved very efficacious in my hands. Calcium chloride, suggested by Dr. Wright of Netley, is indicated when deficient coagulability of the blood is proved or suspected, and certainly should be tried when other remedies fail. It should be given at first in twenty-grain doses, every three or four hours, the dose being reduced later to fifteen or ten grains; when given in excess it diminishes the coagulability of the blood. Iron as preparations of the perchloride or persulphate, appears useful in some cases in the attack, and should be given in convalescence to remove the anæmia which so commonly results in severe cases. In Henoch's purpura Henoch himself has seen benefit from an ice-bag applied to the abdomen
in chronic cases he recommends perchloride of iron. Osler in two
cases saw benefit from arsenic, which appeared to control the tendency
to recurrences. In other cases, however, it failed.

Petechiae.—Minute haemorrhages in the skin, the size of a flea-
bite. Such haemorrhages vary in colour from bright red, dark red, to
purple; and have this characteristic, that the colour does not disappear
on pressure. Petechiae may be one of the expressions of purpura, in
which case they will be almost invariably associated with larger haem-
orrhages in the skin, and in these circumstances own the most varied causes
(see Purpura). Or they may be caused by the bite of the common flea.
In the latter case, when recent there is a small circular spot of
erythema with a pin-point haemorrhage in its centre. The erythema dis-
appears on pressure, to return when the pressure is removed, whilst the
central punctum remains, as it does also when the erythema spontaneously
subsides. When due to flea-bites, recent lesions, with the above
characters, will almost invariably be found affording a clue to their
nature. Their position, on covered parts of the skin, as well as the
evidence of want of personal cleanliness of the patient and clothes, will
be of assistance in determining their nature. There is some evidence
that cachectic conditions and want of food favour the persistence of the
minute haemorrhages due to flea-bites, and their abundance undoubtedly
implies neglect. When associated with pyrexia they may cause mistakes
in diagnosis, especially as regards typhus and measles; so that the subject
is not unimportant. Care with regard to the above points will enable
the observer to avoid errors in diagnosis. The term petechial is applied
to diseases, especially fevers, accompanied by haemorrhages.

Stephen Mackenzie.

REFERENCES

Berlin. klin. Wochenschr. 1874, and Lectures on Children's Diseases. — 7. Henoch's Fest-
schrift for 1890, quoted by Osler, "Of the Visceral Complications of Erythema Exuda-
crises de douloure fulgurantes," Archives de neurologie, 1881. — 20. The Histopathology
of the Diseases of the Skin, translated by Norman Walker, p. 50. — 21. Willan,

S. M.
SCURVY

SYNONYMS.—Lat. Scorbutus; Fr. and Germ. Scorbut; It. Scorbuto; Russ. Zinga.

SCURVY is a general apyretic and non-contagious disorder consisting of mental depression, extreme debility, a tendency to syncope, and special lesions of the mouth, skin, and muscular system, indicative of a morbid change in the composition and properties of the blood. Of these lesions the most frequent and most marked are swollen deeply congested and softened gums, petechiae and diffused livid patches on the surface of the skin, and swelling and rigidity in the hams. In severe and advanced cases there may be bleeding from the mouth and nose and from internal organs, and rapid breaking down of ulcerated, injured, or scarred skin.

Scurvy is still endemic in certain small districts in the north-east of Europe and in Asiatic Russia. It has occurred from time to time on land in epidemics, differing in extent and severity in different instances, but invariably produced under analogous conditions. The disease seems to have preserved the same type, and the records of recent outbreaks show that it is capable now of presenting characters equal in virulence and intensity to those recorded in past ages. The history of land epidemics proves clearly that it is very seldom met with save in times of war and famine, or under circumstances of neglect; and that it should always be dreaded in besieged towns, in armies in the field, after a widespread failure of crops, and in badly-provisioned and overcrowded public institutions. These conditions being present, scurvy will not spare the members of the most advanced and civilised communities. Paris suffered severely during the last siege, and both the French and English armies were much stricken in the Crimean War. Of about 110 records of epidemics of scurvy in the course of the present century, collected by Hirsch, 11 occurred in Great Britain.

It is chiefly from its former prevalence at sea that scurvy has excited the most interest. To the recorded experience of naval medical officers the profession is indebted for most of its knowledge of the nature of the disease, and, from their successful efforts to banish this grievous scourge from the service, it has learnt not only how to treat, but also how to prevent it. The oft-quoted passages from the history of Lord Anson's expedition in 1740 gave but a partial idea of the ravages caused by scurvy in the Royal Navy in the course of the past century. According to Lind, it killed more men than did the hostile French and Spanish armies; and in 1795 the safety of Lord Howe's fleet was seriously endangered by an outbreak of this disease. From this date, when, at the recommendation of Sir Gilbert Blane, lime-juice was introduced into the Navy, scurvy has gradually decreased; and during the past fifty years, except in some few
outbreaks arising under exceptional circumstances, it has become so rare as to be practically abolished as an important disease (Bryson).

Notwithstanding this example and the striking results from the adoption of so simple a preventive measure, scurvy, until quite recently, prevailed to a very unsatisfactory extent in merchant ships. In 1864 it was pointed out by Dr. Barnes that, during the twelve years following 1851, 1058 cases of scurvy had been admitted into the hospital ship *Dreadnought*. The following table, giving the numbers of cases subsequently admitted into this institution, shows a gradual but interrupted decline, which, during the past six years, has reached such a point as almost to justify the hope that this disease will soon be practically extinguished in the British merchant service as well as in the Royal Navy:

**Table of Cases of Scurvy treated in the Seamen's Hospital, Greenwich, from 1864 to 1896.**

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Of the 302 cases admitted in the course of the past twenty-two years, 240 were brought from British and 62 from Colonial and foreign vessels.

Scurvy may occur in any climate; and neither extreme, heat, nor extreme cold, nor excess or absence of humidity, is to be regarded as an essential factor in the causation of the disease. Though more frequently observed in northern and cold regions it has at times prevailed severely in India and China, and amongst exploring parties in Australia. It attacks in the same way both white and coloured subjects, and no race is exempt. Its greater prevalence amongst adult males is doubtless due to incidental circumstances, as in extensive epidemics on land neither sex nor age affords immunity or even resistance against attack.

Etiology.—There can be no doubt that this disease, though almost
invariably associated with circumstances of privation, is the result of a
defective quality of food, and not merely of a reduced supply. The
large majority of those who have had actual experience of scurvy, and
have carefully studied the records of its epidemics, are convinced that the
defect consists mainly in the want of vegetable matter, which forms part
of every ordinary and adequate dietary. Whether, as it is held by some,
scorbutic symptoms may under certain circumstances be due to the absence
of fresh animal food is still an unsettled question, and so must necessarily
remain until more is known of the essential nature of the disease.
Notwithstanding the doubts of Immermann and Mahé, and the expression
of opinion by the medical members of the Arctic Survey Committee, in
1877, that scorb utic disease may be due to an absence of fresh meat,
it seems difficult, on a review of the evidence that has accumulated since
the middle of the last century, to resist the conclusion, first formulated
by Bachstrom, that the primary and only cause of this disease is an
absence of vegetable food. The question is one of purely scientific
interest, and need not at present be brought to bear on measures of
prevention and treatment. Whatever may be the differences of opinion
as to the causes of this or that epidemic, there is an absolutely unanimous
agreement, amongst both medical men and ship's officers, that the only
sure and effectual means of preventing this disease, and of curing it
when it has shown itself, is the supply of fresh succulent vegetables or
fruits, or of a pure vegetable juice. As the introduction of lime-juice
into the Royal Navy in 1795 was speedily followed by a practical
extinction of scurvy, so in recent years a like result has been attained
in the merchant service by securing for seamen a good supply of this
antiscorbatic, and by a general adoption of a dietary of increased vegetable
and reduced animal food.
If further evidence, beyond that collected and reviewed by Dr.
Buzzard in 1870, were needed in support of the conclusion that scurvy
is exclusively caused by the absence of vegetable nutriment, it would be
found in the accurate and carefully prepared records of subsequent
outbreaks. The appearance of scurvy in Paris in the winter of 1870-71
was due, as Delpech and Bucquoiy showed, to a failure of vegetable and
not of animal food; and in the thorough inquiry into the causes of
scurvy in the Arctic Expedition of 1875-76, the outbreak was unanimously
attributed by the members of the Admiralty Committee to the absence
of lime-juice from the sledge dietaries. The latest official returns of
scurvy on board British merchant ships also support the same conclusion.
It is necessary to bear in mind that the manifestation of scurvy, as
of other constitutional disorders, especially those of a cachectic character,
may be much favoured, though not directly caused, by such conditions as
are likely to impair physical vigour, and to disturb the maintenance of
good health. Amongst the host of such indirect and remoter causes
mention may be made of exhaustion by hard work, poor diet, previous
disease, faulty hygienic conditions such as bad air and water and
overcrowding, deprivation of sunlight, monotonous diet, and an almost
exclusive use of salt meat. In instances of scurvy on board ship, debility from previous disease, especially dysentery and malarial fever the most frequent penalties of tropical service, often plays an important part; and very frequently the first manifestations of a scorbucic taint are excited by extreme cold, or by a sudden transition from warm to cold and rough weather. The latter conditions probably exert in most cases a mixed or indirect influence, as cold and bad weather at sea usually necessitate increased work and exhausting or prolonged muscular exertion.

On the other hand, such conditions as a more or less varied diet, freedom from severe physical labour, a good standard of health and vigour, and fair hygienic surroundings will enable those who have been long deprived of vegetable food to resist and even to escape an attack of scurvy. Although it is not strictly true that this disease is exclusively one of the forecastle, there can be no doubt that even in the most severe outbreaks of scurvy at sea the number of officers affected is relatively very much less than the number of men. The existence of absolute immunity from scurvy under a very long-continued or habitual deprivation of vegetables has yet to be proved. It is not impossible, however, that in individual instances immunity may exist from scurvy as from acute infectious disease and many forms of organic poisoning. This quality of immunity, on which so much stress has been laid by some, does not affect the validity of the generally recognised rule as to the causation of scurvy; for, as was pointed out by the Arctic Commission, "although a deficiency or entire absence of fresh vegetable food is an invariable antecedent of a scorbucic attack, it does not follow that the disease invariably occurs during this deficiency or absence."

General pathology.—Inquiries into the general pathology of scurvy have hitherto consisted in attempts to determine on the one hand the changes in the blood and urine of scorbucic patients, and, on the other hand, the special chemical element of food the absence of which results in the appearance of scorbucic symptoms. Experimental researches on animals, as might have been anticipated, have failed to throw any light on this subject. The experiments of Stricker and Prussak on frogs seem to have been made in ignorance of the physiological peculiarities of these animals; and those of Hoffman, quoted by Ralfe, have but an indirect bearing on the question.

No satisfactory information has yet been attained by the examination of blood and urine. The statements, as a rule, are very contradictory, the results of one observer being diametrically opposed by that of another. This is doubtless due to the difficulty of obtaining a sufficient quantity of either of these fluids for the purpose of strict scientific investigation. At the present day it would be considered unjustifiable to treat a scorbucic subject by bleeding; and the composition of the urine is always rapidly changed by the dietetic and remedial measures which, in a case of well-marked scurvy, it is necessary to prescribe without delay.

The next questions to be asked are what elements of nutrition are withheld in the absence of vegetable food, and to which of these, whether
singly or in combination, the normal immunity from scurvy is to be attributed. We have been taught by wide experience that the most efficient of so-called antiscorbutics are fresh green vegetables, succulent and acaceous fruits, and the juices of the latter, especially of the lemon and lime. Of vegetables in common use the most trustworthy are those represented by the lettuce, cabbage, potato, yam, onion, cress and other cruciferous plants. The most prized and useful fruits are such as are juicy, particularly those belonging to the order of Aurantiaceae. Apples also are good antiscorbutics, and their use has done much to protect American seamen against scurvy. Vegetables retain their antiscorbutic properties when preserved, though to a diminished extent. Probably of all forms of preserved vegetable sauerkraut is the best. As substitutes for succulent fruits lime and lemon juice appear to be by far the most efficient. Malt liquors, spruce beer, and claret possess antiscorbutic properties, and probably cider also, which has certainly had a good reputation in this respect.

It seems to be quite clear that vegetables do not owe their antiscorbutic properties to their free organic acids. Citric and tartaric acids have been found practically worthless as antiscorbutics; indeed the use of the former as a substitute for lime-juice on board British ships has been legally proscribed. Though these acids are present in large proportions in the most succulent fruits, they exist but in small quantities in many antiscorbutic vegetables; and the potato, so it is said, contains no vegetable acids at all.

The simplest hypothesis of the causation of scurvy—which hypothesis, however, necessarily admits the antiscorbutic action of animal as well as vegetable food—is that based by Sir Alfred Garrod on the following conclusions which were published in 1848:

1. That in all scrobutic diets (salt meat, leguminous vegetables, rice, bread, etc.) potash exists in much smaller quantities than in those which are capable of maintaining health.

2. That all substances proved to act as antiscorbutics contain a large amount of potash.

It seems strange that the well-known table on which these conclusions were founded has not been extended by further analyses of other articles of diet, especially of fresh vegetables and fruits. As it stands at present, the support it was to give to the hypothesis that scurvy is caused by a deficiency of potash in the food is much shaken by the fact that its data are opposed to those of common and repeated experience. Potatoes and lime and lemon juices are certainly excellent antiscorbutics, and contain large quantities of potash; but it is no less true that for the prevention and treatment of scurvy a vegetable diet, even though it may not contain these articles, is, to say the least, far superior to animal food; and that onions, for instance, possess far more active and useful antiscorbutic properties than salted or even fresh meat. Another and probably more serious objection is that, except in the case of potatoes, the arrangement of the few vegetables given in the table bears no relation at all to their
comparative value as antiscorbutics. The administration of nitrate of potash, regarded by Dr. Buzzard as a crucial test, has failed both to prevent and to cure scurvy.

Immermann, who, following the late Professor Hirsch and other continental writers on scurvy, favours the potash hypothesis, tries to overcome these difficulties by suggesting that the scurbutic disorder may be due, not to an insufficient supply of potash to the organism, but to an absence or deficiency of this base in the tissues. An insufficient supply in the food, according to this author, is certainly one way, but not the only possible way, in which this absence of potash in the tissues can be brought about. In the first place, the potash combination may be supplied to the blood by the food in sufficient quantity, but in a form ill adapted for assimilation. Green vegetables and potatoes contain potash in easily assimilable form; whilst meat, leguminous vegetables, and bread contain the same alkali in a form less capable of decomposition and assimilation within the body. In the second place, a deficiency of potash in the tissues may arise in spite of an abundant supply in the food, when the food is prevented by intestinal disturbances, such as dysentery and diarrhea, from entering the circulating fluid in sufficient quantities. In the third place, the absorption of the circulating potash by the tissue elements must also be influenced by those weakening agencies, such as deprivation of fresh air and light, want of exercise, excessive heat, and the like, which lessen the trophic energy of the cells, and diminish their capacity for appropriating the potash from the blood. The first of these explanations seems to be a very suggestive one, and likely, if it can be made good by further chemical investigation, to remove some of the most serious objections to Garrod's hypothesis. The second and third are opposed by the well-known clinical fact that in ordinary cases of scurvy a supply of fresh vegetables will speedily remove the purely scurbutic symptoms notwithstanding the persistence of associated diseases and other unfavourable conditions.

The view now in most favour with English authors, and one which seems capable of accounting for these numerous discrepancies, was expressed in a suggestion, made many years ago by Dr. Buzzard, that the antiscorbutic element in vegetable food is not potash alone nor the organic acids alone, but a combination of the two. Thus scurvy is to be attributed to the absence of organic salts of citric, tartaric, malic, and, as seems probable from an interesting Arctic record by Dr. W. H. Taylor, of oxalic acid also; especially of the potash salts, which are present in the growing leaves of plants and in fruits and their juices, and which in the organism are converted into carbonates. This view, as further explained and elaborated by Chalvet, whilst recognising the important part played by potash in the production of scurvy, solves many of the difficulties of Garrod's hypothesis. Potash in combination with citric, tartaric, malic, and (very probably) oxalic acids is readily absorbed, because the organic salts thus formed, being unstable, are converted into carbonates which are taken up into the organism, the potash being absorbed by the tissues, and the gas eliminated. In fresh meat and dry leguminous
vegetables, on the other hand, the potash, though abundant, is much less useful for purposes of nutrition, as it is present in more stable forms such as those of chloride and phosphate. Thus, he says, "mutton containing a given weight of potash fails to protect against scurvy, whilst lemon juice, containing not more of this base, acts as a most efficient antiscorbutic."

That this, however, is not the final and only possible view of the matter was shown by the late Dr. Ralfe, who, in an able paper on the general pathology of scurvy, endeavoured to extend the suggestions of Dr. Buzzard yet further. Ralfe, from observations on the results attending abstinence from fresh succulent vegetables and fruits, and from the analyses of urine from scorbptic patients, came to the following conclusions:—"The primary alterations in scurvy seem to depend on a general alteration between the various acids, inorganic as well as organic, and the bases found in the blood, by which (a) the neutral salts, such as the chlorides, are either increased relatively at the expense of the alkaline salts, or (b) that these alkaline salts are absolutely decreased. This condition produces diminution of the normal alkalinity of the blood; and it is suggested that this diminution produces the same results in scurvy patients as happens in animals when attempts are made to reduce the alkalinity of the body (either by injecting acids into the blood or feeding with acid salts); namely, dissolution of the blood corpuscles, ecchymoses, and blood-stains on mucous surfaces, and fatty degeneration of the muscles of the heart, the muscles generally, and the secreting cells of the liver and kidney."

From the results of his investigations Ralfe was led to surmises rather than to positive conclusions concerning the changes in the blood and urine of scorbptic patients. These surmises, however, are very suggestive, and likely to prove of much value as indicating the lines on which further researches of this kind should be carried out.

Symptoms.—Scurvy, as a rule, comes on slowly and insidiously; and the appearance of its external lesions is usually preceded by a preliminary stage of extreme physical weakness and mental apathy. In this stage the nature of the illness is indicated by shortness of breath, fleeting pains in the back and lower limbs, and a peculiar pallor of the skin. As the morbid condition is displayed and the characteristic signs of scurvy manifest themselves, the following symptoms appear:—The patient is listless and weary; the skin is dry and rough, and marked by small purple spots (petechiae), which are most abundant on the thighs and legs and, in many instances, are met with on the lower limbs exclusively. In addition to these spots there are livid patches of varying size and shape, which resemble bruises. Here and there, most frequently in the soft parts of the ham and calf, and behind the ankle, firm subcutaneous swellings may be felt which are widely diffused, are not well defined at their margins, and are very tender. The eyelids are slightly swollen, and the conjunctive often marked by bright red patches of ecchymosis. In some cases the eye is covered by the swollen and purple lids, and the conjunctiva presents the appearance described by
Dr. Buzzard as "tumid and of a brilliant red colour throughout." The lips are pale and anæmic, and the gums of a deep red colour, very soft and vascular, and much swollen. The tongue is moist and clean. There is a peculiar and characteristic fetor in the breath. The patient suffers from breathlessness, which is increased, by the slightest muscular exertion; he sleeps well and retains a fair appetite. The urine is scanty, and the bowels are usually constipated.

Of these characteristic symptoms of a mild and ordinary scurbutic attack, the earliest and most frequent are those presented on the surface of the skin. In the primary stage, and when all other signs of scurvy are absent, there will be found almost constantly a dirty and pale yellow stained skin, and a decided dryness of the epidermis with a tendency to desquamation. Duchek has directed attention to the frequent presence of a roughness over the extensor surfaces of the limbs caused by elevation of the follicles. The petechial spots, each of which is formed by a small and circumscribed effusion of blood around a hair follicle, are smooth, level with the surface of the skin, and persistent under digital pressure. The centre of each is usually traversed by a hair. These spots are in most cases confined to the lower limbs; but in a severe and prolonged attack they may arise on other parts of the body, with the exception of the face. The patches of ecchymosis which usually appear later than the petechial spots, and are not constant, are likewise met with most frequently in the lower limbs; although within these limits they have no special seats of election, they often occur just over or near a large subcutaneous swelling. Like the patches of ecchymosis observed in the subjects of hæmophilia, they are probably due to slight injuries. The tender subcutaneous swellings which occur so frequently in the popliteal space and the muscles of the calf, and which are sometimes met with in the sheath of the rectus abdominis muscle and the armpit, usually succeed the more superficial lesions.

The affection of the gums and the subcutaneous indurated swelling are the two especial lesions of scurvy. The former, though generally regarded as a test symptom, is by no means constant. In most cases it is an early and well-marked symptom; but sometimes, even though all the other lesions may be present in a severe and advanced form, this may be altogether absent, and the gums may remain smooth and regular, though very anæmic, and of a pale blue colour. The swelling and discoloration may come on suddenly and increase rapidly at an early stage of a scurbutic attack, or may advance very slowly whilst all other symptoms are well marked. The intensity of the gum affection, though, as a rule, most marked in very severe and advanced cases of scurvy, often fails to bear any proportion either to that of the general condition or of the other local symptoms. The first indications of the gum affection are usually redness and swelling of the tongue-shaped extensions of gingival tissue between the teeth. Afterwards the gums along the dental arches, both in front and behind, form soft and pulpy swellings of a deep red colour, which are tender and bleed readily when rubbed. Where any teeth are
absent, there is little or no swelling; and "in very old or young subjects who are edentulous the morbid alteration of the gums is reduced to a minimum, or may be quite absent. The swelling is most marked about the necks of carious and broken-down teeth; but certainly it is by no means always absent from the gums of those scorbutic patients who retain a perfect set of teeth.

If the disease be allowed to progress and to acquire an intensity which fortunately is now very rarely seen, the patient rapidly becomes weaker and more lethargic. He suffers much from shortness of breath and palpitation, and the heart's action is so weak that any muscular exertion, such as an attempt to sit up in bed, may cause fatal syncope. The muscular pains in the back and legs still persist and render him more or less helpless. There is decided emaciation and wasting of the muscles, whilst the feet and ankles become edematous, and the face and eyelids bloated. The petechial spots and patches of ecchymoses become more livid, and make their appearance on the trunk and upper extremities. The indurated swellings increase in size and become more painful, the affected limb, usually the leg, being kept in the flexed position. The swollen gums form large, vascular growths which surround and often hide the teeth, and occasionally project from the mouth and distend the cheeks. These growths break down into large and deep ulcers, which may cause wide destruction of the gingival structure, free exposure of bone, and loosening of the teeth." No other portion of the oral mucous membrane participates in these morbid changes.

At this stage there is a general tendency to effusion of blood or sanguineous fluid. Thus a tender subperiosteal swelling—the so-called scorbutic nodule—may be formed in front of a long bone, most frequently the tibia; the breathing and heart's action may be suddenly disturbed by the pouring out of fluid into the pleural or the pericardial cavity; or, again, all the symptoms of pulmonary gangrene may be caused by the occurrence of hemorrhagic foci in the lung. Scorbutic effusion into a large serous sac or into a large joint is usually of an inflammatory nature, as indicated by pain and rise of temperature. A marked peculiarity of severe scurvy is the readiness of the skin to ulcerate; not only will any existing sore suddenly thus alter its character, but an old scar, a recent wound or scratch, or even a portion of apparently sound and intact integument may become the focus of a rapidly spreading scorbutic ulcer, the characteristic feature of which is a dry black slough which, when detached, reveals sharply cut edges and a base of large livid granulations from which there is a profuse and continuous discharge of ichorous fluid. The formation of large vesicles distended by blood-stained fluid, which, according to Immermann, may result in ulceration of the skin, probably occurs only in malignant and very advanced forms of scurvy; it is very rarely, if ever, met with in the milder and ordinary forms of the disease. The tongue still remains moist, except in cases of visceral complication or extensive ulceration of the skin, but it is usually more or less swollen. There is now a tendency to diarrhoea. The stools in simple cases consist
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mainly of partly digested food and blood-stained fluid, but in a dysenteric patient, or in one who has been treated by strong purgatives, it may be mixed with large and abundant clots.

Notwithstanding the evident gravity of the lesions presented by scurvy patients, and the profound morbid changes produced in almost every part of the body, this disease, in the form known to modern observers, is not only attended with remarkably small mortality, but yields at once to medical treatment and even to a suitable change in diet. Of the 690 cases admitted into the Seamen's Hospital since 1864, 15 only were fatal—a death-rate of 1.89 per cent; and of 182 received during the past seventeen years (1896-7), only one was fatal. A frequent cause of death in the forms of scurvy to which reference has hitherto been made is syncope. In many cases of death, whether during the attack or after the disappearance of most of the special scurvy symptoms, the fatal result is due either to extreme weakness from pre-existing disease, or to a complication with dysentery, malarial fever, or some other such exhausting malady. In an uncomplicated case of scurvy, even though very severe, a supply of lime-juice and suitable vegetable food, together with rest, good nourishment, and healthy conditions, is speedily followed by the disappearance of most of the symptoms and by rapid restoration to perfect health. The external lesions usually, though not always, disappear in the following order:—first the firm subcutaneous swellings, next the swellings of the gums, and finally the petechiae and the cutaneous ecchymoses.

A knowledge of the clinical phenomena presented in the final stage of an attack of scurvy in its worst form can only be obtained by reference to the writings of the older authors of this subject. According to Lind, it was not easy to conceive a scene of more diversified wretchedness than that beheld in the third and last period of this disease. Then the swollen legs were covered with livid and fungous ulcers; there was a profuse discharge of altered blood in the stools and urine, and also from the lungs, nose, and stomach; there was a tendency to effusions into the chest and abdomen, and towards the close of the attack there was much oppression of breathing and extreme dyspnoea; there was a troublesome cough with expectoration of fetid and blood-stained sputa; the gums were black and gangrenous; the teeth became loose and fell out; the skin was covered by cold and clammy perspiration; there was a constant involuntary discharge of stools; the urine was retained, and the patient, unless carried off by a sudden attack of dyspnoea, gradually sank from ashenia.

Although in many of the scurvy outbreaks recorded in the last century scurvy was often confounded with typhus and other infectious diseases, there can be no doubt that the disease itself was then attended by a very high rate of mortality. The ships of the East India Company in their voyages round the Cape often lost nearly one-half of their crew; and in Lord Anson's voyage round the globe 380 out of 510 seamen perished from the disease.

In scurvy it is difficult to draw the line between the ordinary symptoms on the one hand and the complications on the other. Formerly many
lesions were regarded as specially scarbutic which were certainly due to casual and extrinsic causes; of late the tendency has been to reject even the least variable and most characteristic signs, and to reduce scurvy to a simple cachexia associated with much mental depression and muscular weakness. Thus the petechiae are attributed to the rubbing of clothes, the swollen gums to the irritation of carious or dirty teeth, the livid patches and subcutaneous swellings to pressure and injury, and the pleural and pericardial effusions to catarrhal inflammation. There can be no doubt that, from the peculiar circumstances under which it is produced, scurvy must almost always be associated with other morbid conditions due to insufficient as well as to unsuitable food, to overcrowding, to mental depression, and to exposure to cold; as occurred in the siege of Paris, in 1871, from the failure of fuel during an exceptionally severe winter. As the late Dr. Ralfe truly asserted, simple dietetic scurvy is seldom seen, even afloat. In many instances on board ship it is really a secondary and complicated affection in men laid up from injury or some other disease, subjected to the most unfavourable hygienic conditions, and probably unable to obtain lime-juice. In such cases one would expect to find the patient suffering from diarrhoea the result of dysentery; from stomatitis the result of syphilis, or rather of its treatment; from affections of the bones and joints the result of tertiary syphilis; and from one or more fungous ulcers of the legs the result of the chronic ulceration of the lower limbs frequent in seamen. It is very doubtful whether scurvy can exert any particular influence on fractured bones. In the form now observed it never causes the absorption of old callus; and in recent fractures, though like other weakening diseases it may retard union, it is rarely, if ever, followed by a permanent pseudarthrosis. Indeed, notwithstanding the frequent occurrence of fracture on board ship non-union is very rarely met with amongst seamen.

Much attention has been directed to the frequent association of night-blindness with scurvy. This association may occur in epidemics on land, but has been most frequently met with amongst the large crews of warships cruising in tropical waters. Many instances have been recorded by English and French naval surgeons in which a large proportion of men suffering from an outbreak of scurvy also suffered from night-blindness. Some of these writers go so far as to regard this disturbance of sight as a symptom of scurvy, whilst others reject the notion of any connection between the two affections. Mr. Donald Gunn, ophthalmic surgeon to the Seamen's Hospital, to whom I am indebted for much information on the subject, expresses the latest and most rational view, in stating that night-blindness has no more to do with scurvy than with any other exhausting disease, except that instances of the eye affection were first observed in scurvy patients. Night-blindness is a functional disorder depending primarily on exhaustion of the retina from prolonged exposure to bright light. Any cause that lowers the general vitality will tend to accelerate the incapacity of the retina to respond to 'less than the strongest stimuli. Scurvy would be the more likely to act in this indirect way,
as the special conditions which give rise to it are often associated with exposure of the patient to bright light. That the retinal and not the general state is the cause is shown by—

(i.) Perfectly vigorous well-fed men, if exposed to sufficient glare, become night-blind; as in the snow-blindness of Alpine travellers, which is quite independent of the associated conjunctivitis.

(ii.) A man, however depressed by scurvy, or any other disease of malnutrition, will not show night-blindness unless he be also exposed to very bright light. It has been asserted, as the proof of the retinal, or, at any rate, functional origin of the trouble, that if one eye of a nyctalopic patient be bandaged, this eye will recover sufficiently to enable the patient to get about at night, while the other eye remains quite blind.

Blood and Urine in scurvy.—In scurvy, according to Duchek, the blood in the heart and large vessels is fluid, of a dark red colour, and contains soft ruddy clots; thus resembling the blood in enteric fever. In anemic bodies, after long protraction of the disease and extensive hemorrhages, it is lighter in colour, but still coagulable. When taken from a living scurbutic patient it differs but slightly from healthy blood. Microscopical examination has failed to reveal any definite change in it. Hayem found in blood taken during life that the number of white globules was normal, and that there was no alteration in the appearance of the red globules. On the other hand, Laboulbène found the number of white globules or leucocytes considerably increased,—a condition, however, which he considered of no special importance with regard to scurvy, as it is observed in many other pathological conditions. The statement of Mr. Busk, in 1841, that the amount of fibrin in scurbutic blood is increased, though opposed by Andral on the strength of a very doubtful observation of scurvy, and afterwards by Becquerel and Rodier, has been fully confirmed by more recent observers. Chalvet, who has made very careful analyses of blood taken from scurbutic patients, agrees with Busk that the blood globules are diminished and the amount of albumin increased. As a result, no doubt, of the impossibility of obtaining sufficient quantities of blood for such purpose, no endeavour has been made to determine the relative quantities of the different inorganic constituents. The assertion of Becquerel and Rodier, that there is an increase of chloride of sodium and other salts in the serum of the blood, has been disproved by the later investigations of German chemists.

Hæmaturia seldom occurs in scurvy, even in the severe cases. The urine during the course of the scurbutic attack is scanty, dark-coloured, clouded, and in severe cases from time to time slightly albuminous. As the symptoms pass off, and the patient becomes convalescent, it increases in quantity and becomes paler. The specific gravity increases during the attack, and decreases after it. In correspondence with these changes Duchek found a decrease of the solid constituents, except phosphoric acid and potash, in the first stage; and subsequently a restored relation between all the solid elements. In a more recent investigation, to which allusion has already been made, Dr. Ralfe found in the urine of scurvy patients
(i.) an increase of uric acid; (ii.) a diminution of the acidity of the urine; and (iii.) a reduction of the alkaline phosphates. *

The following are the complications most frequently observed in scurvy:

(a) Inflammatory effusion in the pleural cavities; (b) Pneumonia and gangrene of the lungs. These affections were very prevalent amongst scorbutic patients in the Crimea. It would have been interesting to trace their association with ulceration of the gums, as the excellent descriptions of the pulmonary symptoms given by Haspel and Buzzard seem to indicate an infective rather than a catarrhal origin of these lesions. (c) Pericarditis with abundance of sanguinolent effusion. (d) Diarrhoea usually of the simple irritative form, but in severe land epidemics and amongst seamen, often of hemorrhagic character, in consequence of the presence of dysentery. (e) Dropy: dropsical oedema of the foot and ankle is a very frequent complication; rapid effusion into the whole of the lower limb on one side was occasionally observed during the epidemic at the siege of Paris. Ascites rarely occurs, and when present is probably the result of renal or hepatic disease. Hydrothorax and hydrarthrosis are not infrequently met with.

In scurvy there is not, as is generally supposed, any marked tendency to bleeding from internal organs. Epistaxis occurs more frequently than any other form of hemorrhage; melena is met with occasionally as a result of dysenteric ulceration or of the action of strong medicine; hematuria and hemoptysis occur very rarely.

**Pathological anatomy.**—Our knowledge of the pathological changes produced by scurvy still remains very imperfect, notwithstanding the researches of Duchek and the careful observations made by French pathologists in 1871. One important point, that has been well established by the latter, is the exemption of the blood-vessels from morbid change. Another point which, if confirmed by further investigations, will also prove no less important, is the observation made by Leven of a general fatty degeneration of the organs. According to this writer, the striated fibres of the voluntary muscles, and of the muscles of the heart, are destroyed, and are replaced by fatty granulations. This fatty degeneration also invades other organs, such as the kidney, the liver, and the lungs; the blood-vessels alone remaining free. It is very probable, however, that these changes, which have escaped the notice of many competent pathologists, are due to cachectic or other general morbid conditions associated with scurvy but not dependent on it.

The condition of the body after death from scurvy is such as might be expected in a case of cachectic disease marked by a tendency to hemorrhagic effusion. An interesting fact, to which attention has often been directed, is that, except in protracted and very severe cases, there is very little wasting of the subcutaneous fat and the muscles. Decomposition sets in rapidly, and the petechiae and ecchymotic patches observed in the skin during life are soon obscured by post-mortem lividity. The subcutaneous tissue, especially in the lower limbs, is suffused by blood-stained fluid, and here and there are collections, varying
in extent, of effused blood, some quite black and others of a paler colour, from cherry-red to yellow. In the indurated swellings, such as those so often met with at the back of the thigh and knee, the muscles and tendons will be found embedded in a thick and firm clot, and the muscles within their sheaths studded with hemorrhagic foci, which, like the extramuscular effusions, are soft and ruddy when recent, and pale, tough, and scar-like when of long standing. Similar deposits, though of much less extent, may be found in connection with bones, in most instances the tibia, just beneath the periosteum; and also, as Immermann asserts, within the bone, especially in the midst of spongy tissue. Effusions are sometimes found between an epiphysis and the shaft of a long bone in a young subject; and also between the ribs and their cartilages. Many of these effusions do not consist merely of altered blood or sanguineous fluid, but of a fibrous and plastic material which, after a time, is traversed by minute vessels which may be readily injected. In most cases of mild and uncomplicated scurvy the viscera present but few morbid appearances. The lungs, except at their lower lobes, are usually collapsed, pale and anemic. The cavities of the heart are sometimes empty; at other times they are distended by dark-coloured blood containing soft and gelatinous clots. The organ itself, as a rule, is small and flabby. In many cases the only marked indications of a scurbitic taint are hemorrhagic spots scattered over the pleura and over the roots of the large vessels of the heart. The changes observed in cases of grave inflammatory lesions which may involve the pulmonary organs in scurvy have been fully described by Buzzard. Of these the most considerable are complete engorgement of the lungs; a diffusion of ecchymotic deposits which compress and obliterate little by little the pulmonary tissue, and often form large fluctuating tumours composed of fluid blood and gangrene. Many medical men versed in severe scurbitic attacks have made mention of effusions of more or less blood-stained serum into the pleural and pericardial sacs. Such effusions, it seems, take place rapidly, are generally abundant, and always associated with fever and other indications of inflammation. Mention has been made also of similar effusions, which, however, are not so frequent, into the abdominal cavity, together with ecchymotic spots and patches on both the parietal and the visceral peritoneum. The abdominal lesions observed in seamen are usually such as are due to tropical diseases; to dysenteric ulceration or pigmentation of the large intestine; a swollen spleen; and a swollen and an engorged liver. Although transient albuminuria is not of infrequent occurrence in scurvy, no constant morbid change nor any special scurbitic lesions have been observed in the kidney. All pathologists agree as to the rarity of any intracranial lesions in scurvy. It has been pointed out by Dr. Buzzard that, considering the delicate structure of the brain, it is remarkable that scurbitic lesions occur by no means so commonly in this organ as in other and less vital parts of the economy. Here clinical and pathological data are in correspondence; as in even the most severe cases of scurvy the intellect remains clear to the last. In considering the few
records in which paresis and analgesia are recorded as scurbutic lesions, it would be well to take into account the possibility of confounding scurvy with beriberi, especially in coloured men.

Diagnosis.—Under ordinary circumstances no difficulty will be met with in the diagnosis of scurvy. Most of the symptoms are very characteristic: the pulpy and swollen gums and the subcutaneous indurations are not features of any other disease. In a large majority of instances the scurbutic symptoms are observed in several persons living together who have been subjected alike to the influence of a diet of insufficient quantity and deficient in vegetable food. In some few cases, however, the nature of the disease may be readily overlooked, or cannot be determined. Sporadic scurvy may occur on land in consequence of abstinence from vegetables through extreme poverty, of aversion to such food, or of too much zeal in enjoining or in carrying out medical instructions. In such instances an absence of one or more of the special lesions of scurvy might give rise to uncertainty. The gums may remain quite healthy, the lower limbs be free from swelling, and only those symptoms be present which scurvy possesses in common with other diseases. The chief points to be taken into consideration in a doubtful case are the nature of the patient's diet, the presence, both before and during the illness, of cachexia and extreme debility, the absence of continued fever, and the effect on the symptoms of the addition of fresh vegetables, lime-juice, and other antiscorbutics to the patient's diet. The following clinical phenomena may be regarded as indicative of scurvy: the multiplicity of lesions, —not of the skin only, but of the gums, muscles, bones, and some of the viscera also; occasional sudden and brief attacks of fever followed by equally sudden and very abundant effusions of an inflammatory character into large serous sacs (pleural and pericardial).

There is very probably but one disease attacking several persons at a time, which is likely to be confounded with scurvy. On board ship, particularly with coloured men in the crew, it might be found difficult in case of an outbreak of cachectic disease to distinguish between scurvy and beriberi. The latter interesting malady presents many symptoms resembling those of scurvy, and indeed Morehead was thus led to attribute to beriberi a scurbutic origin. It is a cachectic disease causing much muscular weakness; it is associated with severe muscular pains; it gives rise to breathlessness, and often causes sudden death from failure of the heart's action. The patient is often dropsical, especially in the legs (\textit{cit.} vol. ii. p. 443). It certainly presents in general neither petechial spots nor livid patches; but these are signs of scurvy which, even if sought for, would be difficult to make out in a black subject. In beriberi, however, it should be borne in mind that the edema usually begins in front of the tibie, and not in the foot and ankle; the gums are not swollen, and, generally, decided symptoms of peripheral neuritis—such as numbness and paresis of the limbs, and tenderness of the muscles—are present.

Although there is at first sight a strong resemblance between scurvy and purpura, particularly that variety known abroad as Werlhoff's
disease, there are well-marked distinctions between the two affections. Purpura is not due to any special defect in diet, nor is it relieved by an increased supply of antiscorbutics. It is characterised by plethora rather than anaemia, and shows a marked tendency to epistaxis and bleeding from internal organs; it affects chiefly the mucous membrane and the skin, whilst the muscles, bones, and subcutaneous soft parts remain free. There is no swelling of the gums. The ecchymotic spots and patches are more vivid in colour and more generally diffused than those of scurvy.

It would hardly be possible to mistake sporadic scurvy for hemophilia; the latter being a chronic affection of a congenital and hereditary character, met with usually in young subjects, and presenting signs of hemorrhage from time to time, usually after injury. Three other hemorrhagic affections have in the diagnosis of scurvy to be taken into consideration. These are leucocythaemia, splenic anaemia, and pernicious anaemia, which affections, like scurvy, are preceded by cachectic conditions. Leucocythaemia, indeed, in some rare instances, presents hemorrhagic swelling of the gums. Scurvy would, however, be set aside at once by the presence of glandular swellings, of splenic enlargement, and of definite excess of leucocytes in the blood. With regard to pernicious anaemia, which resembles scurvy in many respects, the distinction should rest upon the chronic course of the former disease, the absence of any special dietetic fault, a marked difference between the waxy pallor of those affected and the sallow hue of the scurvy subject, and the examination of the blood (art. p. 408). [For “Splenic Anæmia,” vide p. 539; “Infantile Scurvy,” p. 604.]

Prognosis.—The prognosis of a case of scurvy is favourable if the attack have not lasted long, if there be no visceral complications, and if the patient can be supplied at once with efficient antiscorbutics and placed under other good hygienic conditions. In cases of prolonged scurvy death may occur from prostration and general loss of power. Abundant inflammatory effusion into the pericardial or pleural sacs must be regarded as serious; although, as a rule, such effusions disappear with remarkable rapidity under the influence of an improved and antiscorbutic diet. Dysentery is a serious complication; if it do not lead to a fatal result it will certainly retard convalescence. Notwithstanding the low mortality that has attended scurvy during the present century, care should be taken in every case not to give too favourable an opinion; as, even under the most promising conditions, and at any moment in consequence of a moderate muscular effort,—such, for instance, as that of sitting up in bed,—fatal syncope may occur. Persistence of a normal temperature, a tendency in the hemorrhagic spots and patches to fade, an increased flow of urine, and a clean tongue are all to be regarded as favourable signs. On the other hand, scanty and high-coloured urine, an increased tendency to local hemorrhages, an occasional elevation of temperature, diarrhoea, difficulty in breathing, signs of cardiac failure, are all to be regarded as indications of the steady persistence of the scorbutic attack.
Prevention.—If, as has been concluded, scurvy is invariably caused by a much diminished supply or a total absence of vegetable food, then the means for the prevention of the disease must consist mainly in correcting this fault, and in ensuring a full and mixed diet. On land this question, which, except in children, very rarely presents itself in times of peace and plenty, becomes one of pressing urgency in war; and then forms one of the greatest difficulties in military hygiene. In long sea-voyages it is always necessary to take the matter into consideration, and to endeavour to make good the enforced deficiency of fresh vegetable food by the supply of preserved vegetables and fruits, and of some antiscorbutic preparation. Of these substitutes for natural nutriment the former, though not the more efficient, are certainly the more convenient and trustworthy. Lime-juice, when taken day after day, becomes distasteful, and often disagrees with those who take it; as it is not an article of food there is no certainty of its being regularly consumed except under such conditions of discipline as exist in the Royal Navy and in large mail steamers: moreover, in spite of all precautions it may deteriorate after long storage on board ship. Notwithstanding the improved means of preserving vegetables, and the undoubted value, as antiscorbutics, of preserved potatoes, cabbages, carrots, and so forth, they are still much inferior in this respect to vegetables and fruits that are quite fresh. For this reason short voyages are an important factor in the prevention of scurvy. Dr. Curnow, alluding to the decrease of scurvy in merchant ships in correspondence with the increase of steam shipping and the decline in the number of sailing vessels, justly points out that more rapid voyages mean more frequent supplies of fresh food, and thus eventually lead to the practical extinction of this disease.

Whenever the ship touches at a port no opportunity should be neglected of supplying the crew with fruits and fresh vegetables, and in taking an abundance of these on board. A good supply of preserved vegetables and of lime-juice on board ship would not justify any neglect of this precaution.

To the above-mentioned antiscorbutics, which are strictly of vegetable origin, may be added milk, which contains all the elements required for the nourishment of the body; and also certain beverages such as malt liquors and light wines, especially claret, tea, and very probably cider which was regarded by Lind as the best of all. These beverages are remarkable for the large quantity of potash which they contain in combination with organic acids. Alcohol not only fails to act as an antiscorbutic, but, when taken freely, is undoubtedly an active contingent cause of the disease.

It is necessary, also, to take into consideration the means by which, in the absence of efficient antiscorbutics, an outbreak of scurvy may be averted. These should consist in removing, as far as possible, all other conditions that interfere with the maintenance of good health; in an endeavour to supply good and nutritious food, particularly fresh or well-preserved meat; to avoid exposures to extreme heat and cold; to promote
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moderate but not excessive exercise; to afford suitable clothing, and to maintain good ventilation and other favourable hygienic conditions.

Treatment.—The treatment of scurvy, provided the attack be free from complication, is very simple. The chief indications to observe are the supply of those elements of food which have hitherto been wanting, to restore strength and vigour, and to relieve the more severe local lesions. In most cases all these indications may be fulfilled by strictly dietetic means; the scorbutic taint being removed by the free use of fresh vegetables, and the general weakness overcome by nourishing and readily assimilable food. Under such treatment the more serious symptoms, such as those of pleural and pericardial effusions, will, in most cases, disappear together with those that are less grave and more superficial. In dealing with a scorbutic patient care must be taken to avoid such articles of diet as might intensify any complicating affection, particularly dysentery; and, in the second place, by keeping the patient in the recumbent position, to prevent syncope or sudden death. The local lesions, even the most severe, usually disappear with singular rapidity, and by the end of the second week the patient may be restored to his former state of health. The diet should consist of a free supply of fresh vegetable (potatoes, green vegetables) with oranges and other succulent fruits, and eggs, fresh milk, strong soups, and beef tea; to these, as the health improves and the digestive organs become stronger, may be added chicken and lean meat. There is no need, as a rule, to give medicine; nor, if a good supply of vegetables be at hand, even lime or lemon juice. In complicated cases only will it be found necessary to resort to medicinal treatment. Dysenteric diarrhoea must be met by appropriate remedies; and in a case of extensive pleural or pericardial effusion it may be advisable to remove the fluid by aspiration. The gums, if much swollen and ulcerated, should be touched with solid nitrate of silver or sulphate of copper; or be brushed over with a solution of one part of chromic acid in five parts of water. If there be any scorbutic ulceration, the swollen and sloughing sore should be douched three or four times a day with cold sterilised water, or salt and water, and be dressed in the intervals with some iron lotion, or boric acid ointment. The petechiae will disappear rapidly and need no local treatment. The indurations, if they remain tender and show but little tendency to diminish, should be treated by gentle massage and the compression of a flannel bandage.

W. JOHNSON SMITH.

REFERENCES

INFANTILE SCURVY

SYN.—Scurvy Rickets.

Definition.—The scurvy of childhood, like that met with in adults, is a morbid condition of blood and tissues due to defect of diet. It is characterised by great and progressive anaemia, tendency to syncope, cachectic earthy complexion, marked muscular debility, mental apathy and depression, sponginess of gums, and hemorrhages into various structures, notably under the skin and periosteum and into the muscles, especially of the lower limbs.

The disease has a definite dependence upon the privation of fresh food: in the case of adults usually of fresh meat and fresh vegetables; in the case of infants of fresh milk or other fresh food which supplies the same antiscorbutic property; in both it is immediately relieved and rapidly cured by the administration of the fresh elements which have been wanting.

History.—The existence of scurvy in young children, in sporadic form, apart from its occurrence in common with adults under the special conditions of epidemics, has only been recognised within a comparatively recent period. It appears from the researches of Dr. Barlow that isolated cases of similar character had been observed and recorded in Germany from the year 1859 to 1873, by Mohler, Bohn, Hirschspring, and Senator, as examples of acute rickets. The first suggestion of their real nature seems to have been made by Dr. Ingelev, a Swedish physician, in recording
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a case which came under his care in 1873. The first case observed in this country was recorded in the _Pathological Transactions_ by Mr. T. Smith, in 1876, under the provisional title of Hæmorrhagic Periostitis, but the condition was not recognised as scorbatic. In 1878, in a clinical lecture on three cases in young children, published in the _Lancet_, I identified the affection as true scurvy, and traced it to the want of anti-scorbutic element in the food; and similar cases were reported by me again in 1879 and 1882. In 1880 Dr. Dickinson noted cases of hæmaturia in children which he recognised as scorbatic, and described in his work on _Renal and Urinary Disease_. Other cases, distinguished by swelling of the lower limbs, attracted the attention of Dr. Gee, in 1881, who described them in the _St. Bartholomew's Hospital Reports_ under the designation of Osteal and Periosteal Cachexia. In 1883 Mr. Herbert Page recorded a case of subperiosteal hæmorrhage which he judged to be scorbatic. The credit of completing the investigation of the disease and adding the final proof of its nature belongs to Dr. Barlow, who in the same year published, in the _Medico-Chirurgical Transactions_, an account of 31 cases, with an exhaustive description of the morbid changes found on post-mortem examination, and showed that the lesions found were identical with those met with in the so-called sea or true scurvy of adults. Since that time these conclusions have been fully confirmed by later observers. Many cases have been recorded by Dr. Barlow, Dr. Gee, Dr. Goodhart, and others in this country; by Dr. Rehn and Professor Heubner in Germany; and by Dr. Northrop, Dr. Louis Steer, Dr. Fruitnight, and others in America. In the latter country no less than 106 cases were reported to the New York Academy of Medicine in the year 1894.

These later observations fully confirm the general conclusions previously arrived at as to the nature of the affection and the dietetic causes which give rise to it.

**Symptoms.**—The occurrence of infantile scurvy is almost limited to the period between 6 and 18 months. In rare instances, under special conditions, it may arise earlier or later; but as a rule it appears within the period stated, and most often towards the middle or end of the first year. The onset of infantile scurvy has been regarded as sudden, because the most characteristic symptoms may be manifested somewhat rapidly. There is, however, an antecedent period of pallor, anæmia, and debility; and, although the child may be sufficiently fat, it is soft, and its muscles flabby and feeble; this muscular feebleness is a significant and marked feature. In the majority of instances there is some evidence of rickets, often limited to slight enlargement of the epiphyses and beading of ribs; in others there is in addition projecting forehead, thickening or rarefaction of skull bones (crano-tubes), large fontanelle, delayed dentition, head-sweats, and attacks of laryngismus. But the degree of rickets is rarely extreme, and in some cases the distinctive signs are entirely absent. The first symptom usually noticed is that the child is curiously fretful and uneasy, and that it cries incessantly and violently when being washed or dressed or handled, although toler-
ably quiet and contented when left at rest and undisturbed by movement or pressure. The legs especially are tender; the child no longer kicks them about, but keeps them drawn up and still. As the condition advances, the tenderness becomes extreme; the child screams out, not only on the least movement, but on the approach of a hand to touch it; and the lower limbs lie splayed out, and absolutely motionless, as if paralysed. This extreme dread of touch and movement, this quasi-paralytic stillness of the limbs are together almost diagnostic. On examining the legs, swelling of the periosteum will probably be found along the shaft of one or both tibias above the ankle; the thigh bones may be affected in the same way, and there may be edema of the dorsum of the foot. In some instances this periosteal swelling is slight and not apparent at first sight; in others it is palpable and at once attracts observation. With the subperiosteal changes are associated, in severe cases, deep-seated hemorrhages into the muscles themselves, causing puffy swellings, and brawny indurations. In certain cases these are so great as to excite the suspicion of abscess, and they have led more than once to surgical exploration, which has, however, revealed nothing but blood-clot. There is no heat or redness of the surface, no sense of fluctuation, and no rise of body temperature: the temperature is normal or subnormal, except in a few instances where the hemorrhages are large and recent, when it may run up to 100° to 102° for a period of a few days.

The upper limbs may be unaffected, but there is often some swelling and tenderness of the forearm above the wrist; and more rarely on the humerus. Occasionally other bones are invaded; similar swellings have been observed on the ribs, on the scapula, and on the skull. In one instance under my own care the chief periosteal swelling was on the malar bone. The joints proper escape, although periosteal changes near the epiphyses cause a fulness just above them, which at first sight appears to be connected with them, and is not infrequently mistaken for that of rheumatic arthritis. At these joints also, occasionally, crepitus due to separation of the epiphysis from the shaft may be detected; or more rarely fracture of the shaft itself. In some instances the same fractures are found close to the juncture of the ribs with the cartilages, giving rise to a curious depression of the sternum and costal cartilages connected with it, as if it had been driven forcibly inwards towards the vertebral column. A similar deformity is sometimes observed in rickets without known scurvy; in such cases there is no fracture of the rib bones, but acute bending only.

As these signs of affections of bones and periosteum are manifested, the anaemia progresses also, and the complexion assumes the sallow earthy hue so characteristic of true scurvy, due probably to diffusion or deposit of altered hemoglobin. With this the debility increases, the patient becomes more limp of body and weak of back, and cardiac power grows more impaired. Other characteristic signs also begin to appear, notably the one which is really pathognomonic; namely, sponginess of the gums.
Spongy gums are swollen, soft, boggy, purple, hæmorrhagic. In severe cases, when the teeth have come through, they become so swollen as to protrude between the lips in livid bleeding lobulated masses, sometimes so large as to hide the teeth altogether. These spongy excrescences bleed freely, soon begin to ulcerate, and exhale the horribly putrid odour met with in sea scurvy. The teeth become loose and frequently fall out. In some instances the gums are so tender that a child can only be made to take food with difficulty. The change in the gums is not, however, invariably present. If the incisors have appeared there is almost always some purple discoloration to be seen at their base. If the teeth have not appeared, but are approaching the surface, the same purple colour is found over the gums which cover them, or minute ecchymoses appear there. As Dr. Barlow has aptly pointed out, the manifestations of this condition of the gums depends not upon the severity of the disease only; it has also a definite relation to the number of the teeth; and that this is strictly analogous to the sea scurvy of adults, in which disease where the teeth have fallen out the portion of gum in relation to them does not become spongy, although in that portion in relation to existing teeth the condition is fully established. To undergo this change the gum must be in functional relation to the teeth. Another marked and characteristic feature in severe cases of infantile scurvy, as in that of adults, is the super-
vension of hæmorrhages of various kinds into different tissues and organs; in some cases as petechial spots on the skin, occasionally as larger sub-
cutaneous hæmorrhages, especially on the trunk and lower extremities; sometimes there is extravasation into the loose areolar tissue below the lower eyelid. In one case under my own care the supervention of a well-
marked black eye, which suddenly followed a fit of crying, decided a pre-
viously doubtful diagnosis. The fragility of the capillaries in these cases is further illustrated by the readiness with which discoloration and bruise marks are produced upon the skin by slight injury; such as the pressure of handling or the blow of a slight fall.

Occasionally a curious phenomenon appears in the shape of sudden proptosis of one eye, with slight discoloration of the upper eyelid and redness of the conjunctiva, due to hæmorrhage under the periosteum of the orbit. The hæmorrhagic tendency of the disease is further marked in some cases by hæmaturia, which is occasionally the first or the principal sign of the supervention of the scurbutic state. In addition there may be epistaxis, or hæmorrhage from the bowel; but these occurrences are not common, and the loss of blood is seldom or never very copious. In some of the slighter cases the symptoms of the disease may be limited to one or two signs, the significance of which, when occurring alone, may be overlooked or misinterpreted. In some instances hæmaturia may be almost the only manifestation in addition to anaemia and muscular debility; in others orbital hæmorrhage and proptosis may be the only prominent features. More frequently, perhaps, there is merely slight purple staining over the gums of the erupted or pushing teeth, with some tenderness of limbs and general anaemia and cachexia.
FIG. I.

INFANTILE SOURY

Showing spongy gums, proptosis of right eye, external strabismus due to post-orbital hemorrhage, with ecchymosis and oedema of right upper eyelid.

H. D., æt. 9 months. Sole diet for previous six months, condensed milk and malted farinaceous food. Drawn from life, July 26, 1895.