INTRODUCTION.

DEFINITION OF ANÆMIA. CLINICAL METHODS OF INVESTIGATION OF THE BLOOD.

In practical medicine the term "anæmia" has not quite the restricted sense that scientific investigation gives it. The former regards certain striking symptoms as characteristic of the anæmic condition; pallor of the skin, a diminution of the normal redness of the mucous membranes of the eyes, lips, mouth, and pharynx. From the presence of these phenomena anæmia is diagnosed, and according to their greater or less intensity, conclusions are also drawn as to the degree of the poverty of the blood.

It is evident from the first that a definition based on such a frequent and elementary chain of symptoms will bring into line much that is unconnected, and will perhaps omit what it should logically include. Indeed a number of obscurities and contradictions is to be ascribed to this circumstance.

The first task therefore of a scientific treatment of the anæmic condition is carefully to define its extent. For this purpose the symptoms above mentioned are little suited, however great, in their proper place, their practical importance may be.

Etymologically the word "anæmia" signifies a want of the normal quantity of blood. This may be "general" and affect the whole organism; or "local" and limited to a particular region or a single organ. The local anæmias we can at once exclude from our consideration.

A priori, the amount of blood may be subnormal in two senses, quantitative and qualitative. We may have a diminution of the amount of blood—"Oligæmia." Deterioration of the quality of the blood may be quite independent of the amount of blood, and must primarily express itself in a diminution of the physiologically important constituents. Hence we distinguish the following chief types of alteration of the blood; (1) diminution of the amount of Hæmoglobin (Oligochromæmia), and (2) diminution of the number of red blood corpuscles (Oligocythæmia).

We regard as anæmic all conditions of the blood where a diminution of the amount of hæmoglobin can be recognised; in by far the greater number of cases, if not in all, Oligæmia and Oligocythæmia to a greater or less extent occur simultaneously.

The most important methods of clinical hæmatology bear directly or indirectly on the recognition of these conditions.

There is at present no method of ESTIMATION OF THE TOTAL QUANTITY OF THE BLOOD which can be used clinically. We rely to a certain extent on the observation of the already mentioned symptoms of redness or pallor of the skin and mucous membranes. To a large degree these depend upon the composition of the blood, and not upon the fulness of the peripheral vessels. If we take the latter as a measure of the total amount of blood, isolated vessels, visible to the naked eye, *e.g.* those of the sclerotic, may be observed. Most suitable is the ophthalmoscopic examination of the width of the vessels at the back of the eye. Ræhlmann has shewn that in 60 % of the cases of chronic anæmia, in which the skin and mucous membranes are very white, there is hyperæmia of the retina—which is evidence that in such cases the circulating blood is pale in colour, but certainly not less in quantity than normally. The condition of the pulse is an important indication of diminution of the quantity of the blood, though only when it is marked. It presents a peculiar smallness and feebleness in all cases of severe oligæmia.

The bleeding from fresh skin punctures gives a further criterion of the quantity of blood, within certain limits, but is modified by changes in the coagulability of the blood. Anyone who has made frequent blood examinations will have observed that in this respect extraordinary variations occur. In some cases scarcely a drop of blood can be obtained, while in others the blood flows freely. One will not err in assuming in the former case a diminution of the quantity of the blood.

The fulness of the peripheral vessels however is a sign of only relative value, for the amount of blood in the internal organs may be very different. The problem, how to estimate exactly, if possible mathematically, the quantity of blood in the body has always been recognised as important, and its solution would constitute a real advance. The methods which have so far been proposed for clinical purposes originate from Tarchanoff. He suggested that one may estimate the quantity of blood by comparing the numbers of the red blood corpuscles before and after copious sweating. Apart from various theoretical considerations this method is far too clumsy for practical purposes.

Quincke has endeavoured to calculate the amount of blood in cases of blood transfusion for therapeutic purposes. From the number of red blood corpuscles of the patient before and after blood transfusion, the amount of blood transfused and the number of corpuscles it contains, by a simple mathematical formula the quantity of the blood of the patient can be estimated. But this method is only practicable in special cases and is open to several theoretical errors. First, it depends upon the relative number of red blood corpuscles in the blood; inasmuch as the transfusion of normal blood into normal blood, for example, would produce no alteration in the count. This consideration is enough to shew that this proceeding can only be used in special cases. It has indeed been found that an increase of the red corpuscles per cubic millimetre occurs in persons with a very small number of red corpuscles, who have been injected with normal blood. But it is very hazardous to try to estimate therefrom the volume of the preexisting blood, since the act of transfusion undoubtedly is immediately followed by compensatory currents and alterations in the distribution of the blood.

No property of the blood has been so exactly and frequently tested as the NUMBER OF RED CORPUSCLES PER CUBIC MILLIMETRE OF BLOOD. The convenience of the counting apparatus, and the apparently absolute measure of the result have ensured for the methods of enumeration an early clinical application.

At the present time the instruments of Thoma-Zeiss or others similarly constructed are generally used; and we may assume that the principle on which they depend and the methods of their use are known. A number of fluids are used to dilute the blood, which on the whole fulfil the requirements of preserving the form and colour of the red corpuscles, of preventing their fusing together, and of allowing them to settle rapidly. Of the better known solutions we will here mention Pacini's and Hayem's fluids.

Pacini's solution.	Hydrarg. bichlor.	2·0
	Natr. chlor.	4·0
	Glycerin	26·0
	Aquæ destillat.	226·0
Hayem's solution.	Hydrarg. bichlor.	0·5
	Natr. sulph.	5·0
	Natr. chlor.	1·0
	Aquæ destillat.	200·0

For counting the white blood corpuscles the same instrument is generally used, but the blood is diluted 10 times instead of 100 times. It is advantageous to use a diluting fluid which destroys the red blood corpuscles, but which brings out the nuclei of the white corpuscles, so that the latter are more easily recognised. For this purpose the solution recommended by Thoma is the best—namely a half per cent. solution of acetic acid, to which a trace of methyl violet has been added[1].

The results of these methods of enumeration are sufficiently exact, as they have, according to the frequently confirmed observations of R. Thoma and I. F. Lyon, only a small error. In a count of 200 cells it is five per cent., of 1250 two per cent., of 5000 one, and of 20,000 one-half per cent.

There are certain factors in the practical application of these methods, which in other directions influence the result unfavourably.

[1] For the estimation of the numbers of white corpuscles, relatively to the red, and of the different kinds relatively to each other, see the section on the morphology.

It has been found by Cohnstein and Zuntz and others that the blood in the large vessels has a constant composition, but that in the small vessels and capillaries the formed elements may vary considerably in number, though the blood is in other respects normal. Thus, for example, in a one-sided paralytic, the capillary blood is different on the two sides; and congestion, cold, and so forth raise the number of red blood corpuscles. Hence, for purposes of enumeration, the rule is to take blood only from those parts of the body which are free from accidental variation; to avoid all influences such as energetic rubbing or scrubbing, etc., which alter the circulation in the capillaries; to undertake the examination at such times when the number of red blood corpuscles is not influenced by the taking of food or medicine.

It is usual to take the blood from the tip of the finger, and only in exceptional cases, *e.g.* in œdema of the finger, are other places chosen, such as the lobule of the ear, or (in the case of children) the big toe. For the puncture pointed needles or specially constructed instruments, open or shielded lancets, are unnecessary: we recommend a fine steel pen, of which one nib has been broken off. It is easily disinfected by heating to redness, and produces not a puncture but what is more useful, a cut, from which blood freely flows without any great pressure.

The literature dealing with the numbers of the red corpuscles in health, is so large as to be quite unsurveyable. According to the new and complete compilation of Reinert and v. Limbeck, the following figures (calculated roundly for $mm.^3$) may be taken as physiological:

Men.

Maximum	Minimum	Average
7,000,000	4,000,000	5,000,000

Women.

Maximum	Minimum	Average
5,250,000	4,500,000	4,500,000

This difference between the sexes first makes its appearance at the time of puberty of the female. Up to the commencement of menstruation the number of corpuscles in the female is in fact slightly higher than in the male (Stierlin). Apart from this, the time of life seems to cause a difference in the number of red corpuscles only in so far that in the newly-born, polycythæmia (up to $8\frac{1}{2}$ millions during the first days of life) is observed (E. Schiff). After the first occasion on which food is taken a decrease can be observed, and gradually (though by stages) the normal figure is reached in from 10–14 days. On the other hand the oligocythæmia here and there observed in old age, according to Schmaltz, is not constant, and therefore cannot be regarded as a peculiarity of senility, but must be caused by subsidiary processes of various kinds which come into play at this stage of life.

The influence which the taking of food exercises on the number of the red blood corpuscles is to be ascribed to the taking in of water, and is so insignificant, that the variations, in part at least, fall within the errors of the methods of enumeration.

Other physiological factors: menstruation (that is, the single occurrence), pregnancy, lactation, do not alter the number of blood corpuscles to any appreciable extent. The numbers do not differ in arterial and venous blood.

All these physiological variations in the number of the blood corpuscles, are dependent, according to Cohnstein and Zuntz, on vasomotor influences. Stimuli, which narrow the peripheral vessels, locally diminish the number of red blood corpuscles; excitation of the vasodilators brings about the opposite effect. Hence it follows, that the normal variations of the number contained in a unit of space are merely the expressions of an altered distribution of the red elements within the circulation, and are quite independent of the reproduction and decay of the cells.

Climatic conditions apparently exercise a great influence over the number of corpuscles. This fact is important for physiology, pathology, and therapeutics, and has come to the front especially in the last few years, since Viault's researches in the heights of the Corderillas. As his researches, as well as those of Mercier, Egger, Wolff, Kœppe, v. Jaruntowski and Schrœder, Miescher, Kündig and others, shew, the number of red blood corpuscles in a healthy man, with the normal average of 5,000,000 per mm.^{3}, begins to rise immediately after reaching a height considerably above the sea-level. With a rise proceeding by stages, a new average figure is reached in 10 to 14 days, considerably larger than the old one, and indeed the greater the difference in level between the former and the latter places, the greater is the difference in this figure. Healthy persons born and bred at these heights have an average of red corpuscles which is considerably above the mean; and which indeed as a rule is somewhat greater than in those who are acclimatised or only temporarily living at these elevations.

The following small table gives an idea of the degree to which the number of blood corpuscles may vary at higher altitudes from the average of five millions.

Author	Locality	Height above sea-level	Increase of
v. Jaruntowski	Görbersdorf	561 metres	800,000
Wolff and Kœppe	Reiboldsgrün	700 „	1,000,000
Egger	Arosa ...	1800 „	2,000,000
Viault	Corderillas	4392 „	3,000,000

Exactly the opposite process is to be observed when a person accustomed to a high altitude reaches a lower one. Under these conditions the correspondingly lower physiological average is produced. These interesting processes have given rise to various interpretations and hypotheses. On the one hand, the diminished oxygen tension in the upper air was regarded as the immediate cause of the increase of red blood corpuscles. Miescher, particularly, has described the want of oxygen as a specific stimulus to the production of erythrocytes. Apart from the physiological improbability of such a rapid and comprehensive fresh production, one must further dissent from this interpretation, since the histological appearance of the blood gives it no support. Kœppe, who has specially directed part of his researches to the morphological phenomena produced during acclimatisation to high altitudes, has shewn, that in the increase of the number of red corpuscles two mutually independent and distinct processes are to be distinguished. He observed that, although the number of red corpuscles was raised so soon as a few hours after arrival at Reiboldsgrün, numerous poikilocytes and microcytes make their appearance at the same time. The initial increase is therefore to be explained by budding and division of the red corpuscles already present in the circulating blood. Kœppe sees in this process, borrowing Ehrlich's conception of poikilocytosis, a physiological adaptation to the lower atmospheric pressure, and the resulting greater difficulty of oxygen absorption. The impediment to the function of the hæmoglobin is to a certain extent compensated, since the stock of hæmoglobin possesses a larger surface, and so is capable of increased respiration. So also the remarkable fact may be readily understood that the sudden rise of the number of corpuscles is not at first accompanied by a rise of the quantity of hæmoglobin, or of the total volume of the red blood corpuscles. These values are first increased when the second process, an increased fresh production of normal red discs, takes place, which naturally requires for its developement a longer time. The poikilocytes and microcytes then vanish, according to the extent of the reproduction; and finally a blood is formed, which is characterised by an increased number of red corpuscles, and a corresponding rise in the quantity of hæmoglobin, and in the percentage volume of the corpuscles.

Other authors infer a relative and not an absolute increase in the number of red corpuscles. E. Grawitz, for example, has expressed the opinion that the raised count of corpuscles may be explained chiefly by increased concentration of the blood, due to the greater loss of water from the body at these altitudes. The blood of laboratory animals which Grawitz allowed to live in correspondingly rarefied air underwent similar changes. Von Limbeck, as well as Schumburg and Zuntz, object to this explanation on the ground, that if loss of water caused such considerable elevations in the number, we should observe a corresponding diminution in the body weight, which is by no means the case.