THE GULSTONIAN LECTURES

ON
ANÆMIA.*Delivered before the Royal College of Physicians.*By SIDNEY COUPLAND, M.D., F.R.C.P.,
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LECTURE I.—PART II.

Etiology of Anæmia: Loss of Balance between Blood-Formation and Blood-Destruction; Deficiency in Income or Excess in Expenditure, or both combined. (a) Defects of Blood-Formation:—Quantity and Quality of Food—Oxygen—Derangement of Digestion, Assimilation, Sanguification. (b) Excess of Blood-Destruction:—Prolonged Muscular or Nervous Activity—Excessive Secretion—Catarrh—Inflammatory Effusions—Suppuration—Hæmorrhage—Albuminuria—Malignant Growths—The Cancerous Cachexia—Tubercle—Fever—Special Blood Changes, as in Scurvy, Rheumatism, Syphilis, Malaria. Mineral Poisons: as Lead, Mercury, Phosphorus (?)—Parasites:—Anchylostomum Duodenale. The Influence of Age—Sex—Hereditry—Occupation—Light, Air, and Temperature—Climatic Conditions.

HAVING thus considered the chief points regarding the composition of the blood and its variations in anæmia, I pass now to inquire in what way and under what influences the anæmic condition is induced. This inquiry involves the whole subject of the nutrition and expenditure of the body, together with other factors which, inherent in the individual or operating from without, tend to place the organism in a state unfavourable to the complete performance of the functions of the blood. All the complicated processes of the living animal organism are comprised in a series of changes in composition of the elements of the body, and especially of the blood, for it is through that fluid that the normal balance between decomposition and reconstruction takes place. The cycle of changes must be complete, the amount of nutriment conveyed by the blood must be sufficient to replace the waste occasioned by tissue-change, and this latter must not be out of proportion to the amount of nutriment, if the balance is to be maintained. If there be defects in the supply, the blood and tissues suffer inanition; if excess in expenditure, they suffer undue consumption. In other words, in so far as its vital processes are concerned, the body may be regarded as a complex machine requiring a definite supply of oxidisable material and of oxygen for the performance of its functions—functions which may be expressed in terms of mechanical force and its correlative, heat. We have, therefore, to consider the means whereby such material is supplied, and its supply maintained and regulated; to deal with the manner in which the body takes in this material, and how it disposes of it. If the material itself be deficient in quantity or quality, or if the methods by which it is prepared for disposal be defective, the mechanism of the body will, *pro tanto*, be deranged. The blood will be poorer in the material to be disposed of. On the other hand, if the mechanism for the conversion of the material into force be faulty, so that an excessive amount is used up in the work of the body, the blood again will be impoverished. In seeking, then, for the known causes of anæmia, we may expect to find them in these two directions—deficiency of income and excess of expenditure. I will speak shortly of each of these in turn.

In dealing with the subject of food in relation to the blood and tissue changes, attention may be mainly directed to the nitrogenous ingesta, which serve the purpose of building up the tissues, whilst the waste of tissue is measured by the amount of nitrogen excreted in the form of urea. The other organic constituents of a mixed diet—fats, carbohydrates, and gelatine—do not directly influence tissue metamorphosis; but are none the less important in maintaining the body in a state of health, supplying by their direct oxidation heat and force, which otherwise would have to be furnished by the conversion of proteids. A sufficiency of water and of salts is also necessary to enable the processes of nutrition to go on normally, and indirectly their diminished supply induces blood-changes allied to those of hypalbuminosis. The whole blood is reinforced by taking food; both red and white corpuscles are increased, and the capacity of the blood for oxygen thereby augmented. There are differences of opinion as to the precise

manner in which the proteid constituents of food are disposed of, but this much is clear: that part is directly converted into fats and urea, the former to be further oxidised and eliminated as carbonic acid, or stored up in the form of adipose tissue; part retained by the liver to subserve its glycogenic function; part devoted to tissue metabolism; and perhaps a further portion to remain in storage in the blood, to be utilised in case of need. This last-named destination of the proteids is disputed by Dr. Michael Foster (to whose work I am largely indebted for this portion of the subject) on the ground that metabolism does not take place in the blood itself, but only in the tissues; and that the comparative excess of consumption of proteids in the early days of inanition, as shown by Voit and others, only proves that there is a store of material above the immediate wants of the body, not that the place of this storage is the blood. It is found also that nitrogenous food directly provokes tissue-change up to a certain point, the limit being in great measure determined by the amount of oxygen available, so that the increased metabolism must be in relation to the increase of hæmoglobin in the blood and of its capacity for oxygen. Therefore, also, oxygen is as essential as food; and when, from defective blood-formation, the amount of oxygen in the blood is diminished, tissue-change is arrested, and certain retrograde metamorphoses take place which form the leading effects of the anæmic state. Quinquaud found in certain cases of inanition a reduction in the hæmoglobin to one-sixth of the normal, and proved also the rapidity with which this constituent is reinforced when food is taken by starving persons; and Voit's well-known experiments established the fact that, in starvation, the blood wasted in direct proportion to the loss of body-weight.

This obvious cause of anæmia finds abundant illustrations in disease. There is no anæmia so profound as that which accompanies grave organic disease of the stomach. Indeed, Dr. Fenwick is of opinion that the fatal forms of progressive anæmia, to which hitherto no satisfactory cause has been given, are due to atrophy of the gastric glands. That such an atrophy—if it be primary—would suffice to produce this grave anæmia, is possible; but it should also, one would think, be more often accompanied by general wasting of the body—a wasting which is not by any means a constant feature of "idiopathic" anæmia. When there is wasting, latent gastric disease may be suspected. A few weeks ago, there was admitted under my care at the Middlesex Hospital a man sixty-three years old, who had been attacked with hemiplegia the day before. For six months past, he had suffered from dyspeptic symptoms, and had grown very pale. The pallor had rather rapidly increased of late, and on his admission it was most extreme; but there was no history of any hæmorrhage, and only equivocal evidence of its occurrence in the blackening of the fæces. He was, further, much emaciated, but careful examination failed to detect any abnormal condition of the abdominal organs. One could only suspect some latent gastric disease—cancer or ulceration, with unnoticed hæmorrhages—and attribute the recent increase in the pallor to the supervention of a cerebral hæmorrhage. The number of corpuscles was 25 per cent. of the normal. For upwards of two weeks, he lay in an impassive, corpse-like state; and, on his death, we found a chronic ulcer of the pylorus, with general chronic gastritis. The hemiplegia was due to blocking of the left internal carotid and middle cerebral artery, the former vessel being much narrowed by atheroma at its origin. Such cases as this must be eliminated before diagnosing an idiopathic anæmia.

Any interference to the reception or proper digestion of food, as imperfect mastication, hindrances to deglutition, functional dyspepsia, and also irregularities in taking food, as well as deficiencies in its quantity or quality, rank among causes of anæmia needing no further illustration. And as oxygen is as necessary as the ordinary elements of food for tissue-metamorphosis, any interference with its due supply favours anæmia, as proved in the persons of those who habitually dwell under conditions of bad ventilation, or impurity of the atmosphere—conditions so universal and prevalent that they may fitly be included under predisposing influences. They explain the anæmiating influence of life in a crowded city, with its smoke-laden atmosphere, as contrasted with the conditions obtaining in the purer air of the country.

Derangements in digestion, especially those of simple functional dyspepsia, are maintained by the anæmic state they induce, and it is often difficult to find where the vicious circle commenced; hence the liability to mistake effects for causes, which is one of the chief problems connected with this subject.

Of the glands which aid the peptic in the labour of digestion, the liver and pancreas may severally, when deranged, be the cause of profound inanition and anæmia. The liver has so many other important functions, and is probably so directly concerned in the process of blood-destruction (and possibly of its formation also), that the manner of its action in producing anæmia is more complicated than that of the pan-

creas, which is more purely concerned in the digestive process. Of diseases of the pancreas, however, there is only one with which we associate definite symptoms—including a marked anæmia—and that is cancer; when we have introduced a new element, the abnormal cell-growth, aiding in the impoverishment of the blood. But the marked wasting and bloodlessness accompanying such disease are surely out of proportion to the development of the cancerous mass, and are readily accounted for when the large share taken by the secretion of the gland in the digestion of proteids is borne in mind.

Passing to the processes of assimilation and absorption, it would appear from physiological data that the lacteals are little concerned in the removal of products of proteid digestion, being mainly devoted to the absorption of fatty matters. This, however, is hardly consistent with the extreme degree of inanition associated with chronic mesenteric disease, which points to a lacteal as well as to a portal absorption of nitrogenous matters. We are thus led up to the final stage of blood-formation; for derangements of the whole lymphatic system, and of the allied blood-forming glands, play a very notable part in the etiology of anæmia from inanition. For, in the work of nutrition, the share taken by the lymph is hardly less important than that of the blood itself. Of the two fluids, the lymph, which has its analogues in the whole animal kingdom, would almost seem to be the more necessary. But the lymph contains no hæmoglobin. This special substance—found in all vertebrates—is that which gives the blood its distinctive character, and enables it to perform its respiratory function in the widest sense. The lymphatic system is not a mere appanage to the blood-system; it is an essential complement to the latter, and reinforces it in blood-corpuscles.

As I have previously pointed out, the process of blood-formation, in so far as its distinctive cellular elements are concerned, appears to take place in several organs and regions of the body, where blood and lymph-systems blend, and we look naturally to disorders in their mechanism to explain imperfections in the composition of the blood, not accounted for on more obvious grounds. Such derangement might result in the imperfect formation of corpuscular elements, in an overabundant supply of leucocytes, or a relative increase in these, and of immature corpuscles failing to be transformed into the red corpuscles. Such conditions do occur; and until we are in a position to give a name to the morbid change in the cytogenic organs themselves, we are bound to use provisionally such terms as leukaemia and anæmia to denote the diseases of which the blood-state is only a secondary result. We may be able to distinguish a leukaemia due to splenic, lymphatic, or medullary disorder respectively; and the same may be possible as regards anæmia; and there is nothing incongruous in the idea, for example, that in Hodgkin's disease there may be sometimes a condition of lymphatic anæmia, and sometimes a condition of lymphatic leukaemia, the question as to the distinction between such forms being one of the relative degree to which leucocytes and red corpuscles are respectively increased or diminished in number. It is from the analogy afforded by the existence of such diseases that we are driven to conclude that cases where anæmia is throughout the leading and only symptom, depending on no derangement of normal nutrition, either in the way of income or expenditure, are due to changes in these blood-forming viscera. At present, but little progress has been made in this direction; and, as I hope to show, the derangement at the root of idiopathic anæmia is hardly more known to us than it was to Addison, who, in his search for some definite change in these organs in such cases, discovered the suprarenal disease, and brought to light a new clinical entity, whereby his name has become famous to all posterity.

Having thus slightly, and, I fear, imperfectly pointed out how the blood may be impoverished from defects either in the materials of its formation or in the manner in which these materials are converted into blood, I pass to the remaining and far more extensive causes of impoverishment, where there is undue expenditure of tissue and of blood.

The whole work of the body if effected by oxidation, not in a simple manner by the direct combustion of material contained in the blood, but of that which is stored up in the tissues to which it has been brought by the blood. Setting aside the conversion of carbon compounds, and considering only the subject of nitrogenous metabolism, we find that the nitrogenous matters brought by the blood are utilised to repair tissue waste and to aid in the actual production of energy—i.e., mechanical motion and heat. Every molecular change is accompanied by the production of heat; and mechanical motion appears under different forms in many of the vital acts. Muscular action is the chief source of this expenditure. It is marked by heightening in temperature, the separation of carbonic and lactic acids out of proportion to the amount of oxygen consumed, indicating that some highly complex molecule is destroyed, the nitrogenous portion of which is retained by the muscle.

Such changes go on, but to a lessened extent, in the muscle during rest. The nutrition of muscle, then, consists in a constant formation of contractile material periodically greatly decomposed, and as this decomposition is accompanied by heat, much force is expended. Over-work of muscle does not impoverish the blood so much as might *prima facie* be expected, and this for several reasons. The circulation is accelerated by muscular activity, and tissue-changes go on more rapidly so long as a sufficient amount of oxygen and carbon compounds is supplied to the working muscle; and hypertrophy of a muscle called forth by extra work enables it to utilise more material. This, however, implies an increase in the intake of the blood; and were it not that a limit was placed by the condition of fatigue, the blood would be greatly impoverished. As it is, long-continued exhausting physical labour, and its frequent repetition, undoubtedly cause anæmia. I might remark in passing that, if any good is to be derived from the extravagant feats of physical endurance at present so popular, it should be by utilising them for physiological inquiry in these directions.

The opposite condition—that of lack of normal muscular activity—is a more prolific cause of blood-impoverishment than excessive action; but its mode of operation is, of course, very different. There is then diminished tissue-change, diminished oxidation, and the blood suffers from being imperfectly renewed, and not from being drawn on for extra supply. Conversely—inability to physical exertion, and the readiness with which this is followed by fatigue, are prominent features of the anæmic state, and are readily explained by the lessened power of oxygenation.

As regards expenditure in the production of nervous energy, there is less certain knowledge than is the case with muscle. The actual chemical changes taking place in a nerve during the passage of a nervous impulse are comparatively insignificant, but those which occur in the central mechanism are probably much greater. The complexity of the construction of a cerebral molecule, for example, is very great, and its activity must, no doubt, depend upon a due supply of oxygen, as in the case of other tissues; and it is probable that for every act initiated by the nerve-cells the energy must be supplied by oxidation changes in these complex molecules. More than this, however, is probably concerned in the question of the influence of the nervous system. Its intimate relations with all parts of the body point to an exercise of control over blood formation, as over nutrition and secretion, so that under certain conditions the nervous system may bring about an anæmia other than by the exhaustion of material supplied it by the blood. It is only on such an assumption that the occurrence of a profound, lasting, and even progressive anæmia following great mental shock or emotional disturbance can be explained. I am not prepared to say that this same influence does not operate in the production of anæmia from exhausting mental labour, from anxiety, or from want of sleep. It may be one factor of which the other is the disproportionate expenditure of material.

In the act of secretion, there is more obvious reason for believing that excessive function entails a loss of material from the blood. The secreting cell not only takes up material and converts it into its peculiar product, but such conversion often demands the destruction of the cell itself. Some secretions are composed of more complex substances than others; and the drain on the blood must be proportionately greater when these glands are too freely exercised. One of the best known instances of a symptomatic anæmia is afforded by such excessive and prolonged activity of the mammary gland, which yields a product rich in all the main elements of the blood. A like instance is afforded by the product of the male generative organs—a product of a peculiarly stable character, and endowed with highly specialised properties. It is plain, on mere *à priori* grounds, that an excessive production of this secretion must cause undue drain on the blood; and such is a well-recognised fact, although in both these instances the effect on the nervous system as the controller of blood formation must not be entirely lost sight of. Probably it is the same with every other secreting gland, in extent varying with the quality of the secretion. The transition from conditions of excessive discharge of normal products to those of perverted and abnormal discharges is slight. We may comprehend in one view all the abnormal fluxes—from a simple mucous catarrh to an abundant purulent discharge from a mucous tract, where the formed elements of the blood compose a great part of the discharged material. Such outpourings not only impoverish the blood directly, but where, as in the case of the intestine, they involve organs subservient to digestion and assimilation, they of course interfere with the formation of blood; and the rapidity with which a diarrhoea produces anæmia is well known.

Such causes of impoverishment of blood may lead us to other conditions, where either the blood itself or its albuminoid constituents are passed out from the vessels. Of hæmorrhage nothing need be said.

Even the monthly loss by the catamenia is represented by an actual fall in the richness of the blood. Inflammatory effusions into serous sacs, when abundant, must necessarily entail anæmia; but I do not know if the degree to which this occurs has been much studied. Quinquaud, in three cases of acute pleural effusion, found a marked reduction of hæmoglobin and of the solids of the serum, and also noticed that paracentesis was followed by the further reduction of these constituents. Large inflammatory exudations, such as occur in acute pneumonia, are also accompanied by a fall in these constituents, but, according to this writer (and in that respect the observations of Drs. Baxter and Willcocks coincide), not to a very marked extent, especially when the high degree of pyrexia is taken into account. And, passing from simple inflammatory exudations to suppuration, we meet with conditions of drain on the blood too obvious to require illustration.

The anæmia of chronic albuminuria forms another example in this lengthy category. A notable deficiency in red corpuscles has been shown to occur in chronic Bright's disease, whilst the supervention of dropsy is apparently due to the replacement of albumen by water in the blood.

The relation of malignant growths to the composition of the blood involves a subject complicated with the question of cachexia. Undoubtedly, when malignant disease is of rapid development, it must deprive the blood of much nutriment, perverting it to its own ends, and living on the body in a truly parasitic manner. Or if the disease involve organs essential to digestive or nutritive functions, it must obviously indirectly interfere with the formation of blood. It is said that in cancer the red corpuscles are not only diminished in number, but are smaller in size than the normal, and that the hæmoglobin in cancerous subjects becomes reduced in a very remarkable degree. But that this precedes the development of the disease there is no warrant for saying; or that there is in cancer a cachexia apart from the circumstances of the growth itself, and the additional drain frequently occurring from the ulceration and hæmorrhage of the diseased mass. I have seen cancer arise in the robust and plethoric, and in such subjects it grows with terrible vigour; but it is not, of course, always so, and the problem is to discriminate between an underlying blood-condition and that induced by the malignant growth itself. It seems to be otherwise with regard to tubercle; and amongst the numerous points in which medicine is indebted to Trousseau is that where he declared the fact of the existence even of marked anæmia in subjects of tubercular tendency, before the local manifestations of the diathesis appear. Whether it be that, in these individuals, the lymphatic system is primarily deranged, and the work of sanguification impaired, or whether we may look upon tubercle as a true blood-disease, I do not know. When, however, tubercularisation is declared, other factors come into play to aid in the production of the anæmic state; there are abundant cell-formation and destruction of tissue, whilst prominent among all the influences is *fever*. On the special influence which it has in inducing anæmia, I must now say a few words.

The central fact in the febrile process, next to the heightened body temperature, is the increased metamorphosis of the albumen of the body, as shown in the rapid wasting of the tissues and increased elimination of urea. When to this is added the impairment of the digestive and assimilative functions, we get in fever a combination of both the conditions of impoverishment of blood. The blood suffers as well as the other tissues; its corpuscles appear to be more rapidly disintegrated, their number is notably diminished, the hæmoglobin is reduced, and the pigment excreted in excess. Consequently, to maintain the increased oxidation, the circulation is accelerated, and the respiratory changes are more rapid. Wagner says (*Elements of General Pathology*, Seguin's edition, page 660): "Without any doubt, metamorphosis is increased in fever. This does not occur as a simple and uniform increase of the normal process of metamorphosis, but the process of oxidation of nitrogenous substances is made more active than that of the non-nitrogenous. More especially, there occurs a greater destruction of albumen, chiefly indicated by increased excretion of urea, and that, in spite of the fact that the conditions for its separation are less favourable in fever because of the diminution in the amount of urine. Even under the most favourable circumstances, we find in fever patients an average increase in the excretion of urea, amounting to more than double what is thrown out in non-febrile states under otherwise similar conditions. According to a number of investigations, it is the red blood-corpuscles—that is to say, those elements which we know to take up oxygen from the air and serve to transport it to the tissues—which suffer most in fever. If the organism in fever cannot appropriate as much oxygen as in the same dietetic conditions in the non-febrile state, it likewise cannot furnish as much products of oxidation. But, as larger quantities of oxygen are used in the formation of greater amount of urea, it is probable that an excessive formation of other products of combustion (so often asserted)

does not take place." The present methods of blood analysis have not wholly substantiated these inferences (Baxter and Willcocks); but, as these methods take no cognisance of alterations in the density of the blood, these results can hardly be quoted against the manifest effects which fever produces in its subjects, and the plain evidence of increased tissue metamorphosis afforded by urinary analysis.

I must also enumerate—to complete the list of known causes of anæmia—certain diseases (in many of which fever plays a part) which are specially characterised by alterations in the composition of the blood. Scurvy is an example of such a disease. Arising in defects of diet, it is, as Dr. Ralfe has demonstrated, productive of a diminished alkalinity of the blood, which, in its turn, leads to corpuscular disintegration, and all the effects following upon this. These effects are probably then largely dependent on the anæmia of the disease, for the changes in the viscera and blood-vessels are similar to those met with in profound anæmia. Quinquaud has noted a very marked reduction of hæmoglobin in scurvy. In acute rheumatism, anæmia is a prominent symptom from the first, and it is an example of a disease in which the blood is directly influenced. Diminution in corpuscles has been noted both in acute rheumatism and in acute gout. The anæmia induced by the malarial poison is sufficiently accounted for by the degree to which the more important organs concerned in blood formation are influenced by it. The subject has been especially studied by Kelsch, who found in simple intermittent fever a considerable decrease in the number of red corpuscles after each febrile paroxysm, followed by a partial return to the normal—a renovation which was not accomplished, owing to the recurrence of the paroxysm, so that the anæmia is maintained and intensified as long as the fever lasts. The subsequent malarial cachexia is marked by a lowering in the number of blood-corpuscles. Quinquaud's estimations of hæmoglobin teach the same fact; and, in addition, he remarks upon the considerable diminution in the solid matters of the serum in malarial disease. Lastly, in syphilis we have an animal poison, probably directly affecting the blood, and showing its effect in diminution of the red corpuscles and hæmoglobin.

Amongst mineral poisons, lead and mercury are powerful agents in the impoverishment of the blood. Workers in lead are always anæmic, often to an extreme degree. This may be in part due to the direct action of the metal on the blood; but it is at least an open question whether, in view of its action upon the nerve-tissues, it does not also operate by impairment of sanguification through disordered innervation. Observations are not wanting to show that there is a considerable diminution in corpuscles and colouring matter in chronic lead-poisoning. I have included phosphorus in this category, although its precise mode of action is doubtful; acute poisoning by phosphorus leads to changes which seem related to deprivation of the blood of its oxygen; but whether this is in consequence of a directly noxious effect on the corpuscles, or not, I cannot say.

Lastly, some forms of anæmia in tropical climates, especially that form known as "Egyptian chlorosis", are explained by the discovery of a blood-sucking nematoid parasite, the *anchylostomum duodenale*, which may exist in large numbers in the upper part of the alimentary canal, where it is conveyed by the ingestion of impure water. The obscure disease which proved fatal to some of the workers in the St. Gothard tunnel has been shown to be due to the presence of this parasite, which "bites its way into the mucous membrane, pierces the sub-mucous cellular tissue, and subsists on the blood. After its removal, there remains an ecchymosis, the size of a lentil, the centre of which presents a white spot of the size of a pin's head, with a fine hole. Out of these wounds the blood oozes into the intestinal cavity" (Wagner).

Having thus reviewed the conditions liable to lead to the impoverished state of blood known as anæmia—conditions of defective nutrition and impaired sanguification on the one hand, excessive expenditure and loss of nutritive elements on the other, and certain specific and other poisons, and parasites, there yet remain for consideration certain influences in the individual, or in his conditions of life, which operate powerfully to the same end. These influences—to which, for want of a better term, the word predisposing is usually given—include the factors of age, sex, heredity, and occupation; and the influence of light, air, and climate. With a reference to each of these in turn, I shall conclude this portion of my subject.

In the growing organism, the process of blood-formation is at its height. We have seen how, in foetal life, the elements of the blood are developed from the mesoblastic tissues almost indiscriminately. As parts become more specialised, this function is limited to certain special tissues, which are embraced under the term "cytogenic". In infancy and childhood, the cytogenic tissues attain their acme of development, and share, with all the nutritive processes, in the work of building up the body. The whole organism is thereby modified; it is mobile and plastic; repair and renovation are more rapidly effected; tissue-change,

and therefore oxidation, are increased, the temperature of the body heightened, and circulation and respiration accelerated. I cannot forbear quoting the terse sentences of Dr. Michael Foster, as he sums up the nutritive conditions obtaining in the infant organism. He says (*Text-Book of Physiology*, 3rd ed., p. 633): "Metabolism is directed to constructive ends. The food taken represents, undoubtedly, so much potential energy; but, before that energy can assume a vital mode, the food must be converted into tissue; and in such a conversion, morphological and molecular, a large amount of energy must be expended. The metabolic activities of the infant are more pronounced than those of the adult; for the sake, not so much of energies which are spent on the world without, as of energies which are, for a while, buried in the increasing mass of flesh. Thus the infant requires, over and above the wants of the man, not only an income corresponding to the energy of the flesh actually laid on, but also an income corresponding to the energy used up in making that living sculptured flesh out of the dead amorphous proteids, fats, carbohydrates, and salts, which serve as food." Thus, then, in the growing organism, we have not only a greater instability in the nutritive processes, but also a direct source of expenditure in the very fact of growth itself. In consequence of that instability, we find how comparatively slight causative influences may lead to considerable defects in the blood, reducing it below the physiological standard; and, in the fact of growth, we see how the tissues may demand more nutriment than the blood can supply, and an anæmia special to the period of childhood and adolescence may readily be provoked.

At the other extremity of the cycle of life, when the demands are lessened, when all tissues and organs more slowly perform their functions towards the close of the long years of activity through which they have passed; when all the nutritive processes take place with a sluggishness in contrast to the period of active growth; the blood, too, no longer required for the purposes of growth or the renewal of tissues, loses in corpuscular richness and in hæmoglobin, so that one feature of the natural decline of life is the presence of slowly deepening anæmia, which in its turn, probably aids in the diminution of the vital powers. It is plain that a very slight derangement, either in the direction of intake or that of undue waste, must readily influence and intensify this senile anæmia and marasmus.

Turning now to the contrast afforded by the sexes, which up to the age of puberty advance almost in parallel lines, we find, in the first place, that there is a difference in the precise composition of the blood (see Table I), that of the female being notably less rich in corpuscles and hæmoglobin than that of the male; and although, of course, this difference in health is, doubtless, in precise relation to the amount of work called for in each sex, yet, in consequence of it, the female is rendered more liable to become anæmic. She is also subjected to influences special to her sexual function. Ovulation and menstruation go on in health with regularity, and the blood loss they entail is readily renovated. But they are most easily influenced by derangements in health and nutrition; and, on the other hand, when diminished or excessive, may be important factors in the production of anæmia. Pregnancy, the puerperal period, and lactation—severally subject the female to anæmiating conditions, and the cessation of the menstrual function is often the period at which anæmia is developed. Upon the special relations which this function bears to chlorosis I shall have to speak later.

I have no doubt that heredity plays some part in disposing the organism to anæmia, but it is not easy to give instances. A tendency to anæmia may certainly be transmitted, just as a tendency to hæmorrhage, in hæmophilia.

The other conditions, which I have included under predisposing causes, frequently co-operate. Occupation may involve deprivation of a due amount of light and air, the exposure to heightened temperature, and a want of due amount of sleep. I need hardly particularise them further; they are influences which are almost as much exciting as predisposing causes of anæmia; they stand, at any rate, on the borderland between the two groups in the etiology of the condition.

The influence of climate is well known as favouring the anæmic state, the subjection to prolonged tropical heat having a direct influence over and above that which is due to the inertia called forth by life under such conditions.

In conclusion, it must be borne in mind that any given anæmia may arise from a multiplicity of causes, each of which is sufficient of itself to have induced the state; and in the second place the impoverished blood itself reacts on the organism in such a way as to maintain and intensify the anæmic condition. For all the vital processes are influenced by blood defective in the oxygen-carrying substance—hæmoglobin. Hence the capacity of blood for hæmoglobin must be increased, as well as the removal of the primary cause or causes; if any given anæmia is to be remedied. Metabolism must be quickened, and oxygen supplied for that

purpose. I should have hesitated about taking you over—in this hasty survey of the known causes of anæmia—ground so familiar, if this were all that the subject comprised; were that the case, there would have been no need to discuss the subject at all. But when the category of known causes is exhausted, there remain cases of more or less profound and progressive anæmia, to which hitherto no sufficient explanation has been given, leaving the question still open for inquiry and speculation. It is the existence of such a class of "idiopathic" cases that has made me feel it to be necessary that I should speak to day of the factors known to operate in producing the anæmic state, before proceeding to the consideration of that class of disease to which I shall invite your attention in my next lecture.

CLINICAL LECTURE

ON FOREIGN BODIES WITHIN THE EYE,

AND

THE ELECTRO-MAGNET AS AN AID TO THEIR REMOVAL AND DETECTION: WITH CASES.

Delivered at King's College Hospital.

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TO-DAY, I wish to call your attention to the most serious class of injuries to which the eye is subject. Foreign bodies, buried in or within the organ of sight, are most fruitful sources of blindness, not only to the eye originally hurt, but to its fellow, through sympathetic mischief. You may take it as an established truism, that every eye, whilst lodging a foreign body, is threatened with destruction by its tenant. Neither the position nor the size of the foreign body negatives this, though both are factors of very material importance in estimating the degree of serious gravity attaching to such a case. Moreover, you must recollect that, as I have just hinted, the danger is not confined to the injured eye, the risk of blindness being shared by its fellow. Sympathetic ophthalmia, an affection indefinitely deferred, insidiously developed, obstinately progressive, and deplorably blinding, often attacks the fellow to an eye rendered useless by a penetrating foreign body, which may be located in any part of the globe.

You may judge, therefore, something of the importance attaching to the detection and removal of such foreign bodies, and the responsibility incurred by one who, undertaking to treat an injured eye, does not do his utmost to arrive at a correct diagnosis regarding the presence or absence therein of a foreign body.

The investigation of these cases should be commenced by the aid of focal illumination; the pencil of light being thrown from every direction on to every visible surface of the globe, so that the position of any superficial indication of a wound may be fully lighted up and searched for by the aid of a magnifying-glass. For this purpose, the two object-glasses commonly supplied in the case with many of the hand-ophthalmoscopes will answer admirably; but if, as I believe is the lot with most of you, your ophthalmoscope be one of those excellent *multum in parvo*, practically efficient, simple, and strictly economical instruments* which I recommended you to procure, then, using the single object-glass thereof for concentrating the light, you will need a second as a magnifier. This may be an ordinary pocket-lens, one of twenty dioptries from the trial-case, a common burning glass, or watchmaker's loupe. I mention this, lest the possession of only a single object-lens with your ophthalmoscope should be conjured into an excuse for the inefficient examination of these cases. The scrutiny, with the two lenses, of the superficial parts, must be extended to the anterior chamber and surface of the iris. Here let me remark on the importance of conducting the examination thus far before applying any mydriatic to dilate the pupil, as it happens at times that foreign bodies which penetrate the cornea, or corneo-scleral junction, remain partially bedded in the tract along which they passed, whilst projecting into the anterior chamber, where the interposition of the iris may serve to screen the capsule of the crystalline lens from injury.

In other instances, a foreign body may be so situated, loose in the anterior chamber of the aqueous humour, that it would be liable to

* Wecker's compounded metrical refraction ophthalmoscope by Crété, Paris, price forty francs; or thirty-five shillings, by Pickard and Curry, London.