tents of the stomach are filtered or dialyzed, and sulphide of ammonium is added to the clear fluid thus obtained. If chloral is present an orange yellow colour is formed, which gradually becomes more and more brown, then turbid, and finally an amorphous precipitate falls, and a peculiar odour is developed. Ten milligrammes in 1 cubic centimetre of water give a marked reaction and a precipitate, 1 milligramme in 1 cubic centimetre a yellow colour, the odour, but no precipitate, and 0.1 milligramme in 1 cubic centimetre a slight pale straw colour and no odour. This reaction may be distinguished from that of antimony by adding an acid, when the latter falls as an orange yellow precipitate; but if chloral alone is present, there is only a light whitish precipitate of sulphur.

One apparent flaw in this case is the fact that the analyst said he only found a "trace" of chloral. But it must be remarked that he did not try to estimate the actual amount present, but merely showed its presence by decomposing and obtaining the reactions for chlorine and hydrochloric acid. Now, as he got each of these tests three times, it is, perhaps, hardly accurate to speak of a "trace." But taking it for granted for a moment that only a trace was found, this does not in the least alter the arguments in favour of chloral having caused the death; for it must be remembered as a fundamental principle in all analyses of the contents of a stomach in poisoning cases that the portion of poison found in the stomach is only the residue of what has been administered, and is not the actual part which has caused death, this, of course, having been absorbed. This principle is well pointed out by Guy and Ferrier, who state: "When poison is found in very small quantity, the objection is sure to be advanced that it was not enough to account for death; but to this the reply is obvious that the quantity found must needs fall short of that actually taken and that the quantity found in the stomach is only the surplus of what may have been sufficient to cause death by absorption. The discovery, therefore, of a quantity of poison insufficient to destroy life is scarcely even a presumption that the substance was not administered in a poisonous dose." Woodman and Tidy also state that: "The discovery of a very small portion in the stomach is no criterion of the quantity taken." With a body so rapidly absorbed as chloral, this principle is all the more important to remember.

Finally, all the symptoms, the *post-mortem* examination, and the analysis coincided with the fact that chloral had been administered. Taking this for granted, no one can for a moment doubt that the administration of this body to a man whose heart was already enfeebled with alcohol and slight fatty degeneration most certainly hastened the death if it did not actually cause it. Now, if in this manner death was accelerated even by a single minute, then it is perfectly correct to say that the administrator of the chloral caused the death.

SUMMARY OF THREE LECTURES

ON

TRANSFUSION:

ITS

PHYSIOLOGY, PATHOLOGY, AND PRACTICE.

Delivered at the Royal College of Surgeons.

By WILLIAM HUNTER, M.D., M.R.C.P., M.R.C.S., F.R.S.E.,

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LECTURE II.

RESPIRATORY PROPERTIES OF TRANSFUSED BLOOD.

Life Duration of the Red Corpuscles.—We have now to consider what value is possessed by transfused blood in virtue of the presence of the red corpuscles. So long as they remain within the circulation of their host, they will act as carriers of oxygen, and will thus have a certain respiratory value. What, then, is their life duration after transfusion? This subject I have discussed at length elsewhere.¹ After transfusion of large quantities of blood, there is a gradual and steady fall in the number of corpuscles till the normal is reached two to three weeks later. This lengthened life duration is only found when large quantities are in-

jected, and only applies to rabbits. With smaller quantities the life duration is correspondingly shorter. In dogs a longer life duration than ten days was not observed. The two factors influencing it in all cases are—(a) the quantity of blood transfused; (b) the condition of the animal at the time of the transfusion and subsequent to it. As regards the latter, the following conclusions could be drawn from a study of the results obtained in the different experiments:

1. Any condition in which metabolism is diminished, as in starvation, tends to prolong the life of the red corpuscles. This applies both to the animal's own corpuscles and to the corpuscles of transfused blood (Fig. 7).

Percentage of red corpuscles.

Fig. 7.—Life-duration of red corpuscles after transfusion of defibrinated blood into the peritoneal cavity (Experiment 10). The animal remained in good health throughout, although the original weight was not regained till close of the experiment. The weight is represented by the interrupted line.

2. Any condition approaching that of health, in which metabolism is active, tends to shorten the life duration of the transfused corpuscles (Fig. 8).

3. In any condition in which metabolism is increased, the life duration of the red corpuscles is shortest of all (Fig. 9).²

The quantities of blood transfusible in man are so small that, under the most favourable conditions, the life duration of the red corpuscles is probably rarely longer than two to three days.

Effect of Defibrination.—Defibrination destroys the character of the blood as a tissue by destroying its matrix. On the red corpuscles, however, it has little or no injurious effect. Their life duration after defibrination is, under favourable circumstances, the same as when pure blood is transfused. (Fig. 7.) This conclusion is opposed to the one arrived at by Hayem, according to whom the corpuscles are by the act of defibrination doomed to a certain death—"are killed, beaten to death." So long as they remain within the circulation, they act as carriers of oxygen. They are ultimately destroyed as the animal's own corpuscles are, but that they are not killed is clear from the circumstance that they remain within the blood for days, sometimes even for weeks, whereas red corpuscles killed by the action of poisons—for ex-

¹ Life Duration of Red Corpuscles after Transfusion, etc., JOURNAL, i, 1887.

² For fuller discussion of these curves see my paper in *Journal of Anatomy and Physiology*, vol. xxi, 1887.

ample, by pyrogallie acid—are seized upon by the leucocytes and removed from the circulation in the course of a few hours.

Percentage of red corpuscles.

Fig. 8.—Life-duration of red corpuscles after transfusion of pure blood into peritoneal cavity. The health of the animal exceptionally good throughout.

Percentage of red corpuscles.

Fig. 9.—Life-duration of red corpuscles after transfusion of pure blood into peritoneal cavity (Experiment 9). The animal remained in poor health from the time of the experiment.

ULTIMATE FATE OF TRANSFUSED BLOOD.

The red corpuscles are thus the only elements of transfused blood that remain within the system for any length of time. After a time even they disappear. What becomes of them? Where and in what manner are they destroyed? Like all other tissues, the blood must be affected by the discharge of its functions as

the carrying tissue of the body. A certain wear and tear is connected with this process, which must affect in varying degree the various elements—plasma, white corpuscles, and red corpuscles.

Fate of the White Corpuscles.—The white corpuscles are most active during digestion. The changes in the blood at this time are, as we have seen, most marked within the portal blood and the organs connected with it. It is in this system that the changes in the leucocytes are also most marked at this period. There is an increase in their number, and their activity is otherwise shown by the number and variety of the karyokinetic changes presented by their nuclei. Since increased metabolism implies increased disintegration, we should expect to find some evidence of this latter change in the blood. Such evidence is, I believe, to be found in the greater tendency of the portal blood to coagulate. After transfusion of blood, as my experiments show, it is not infrequent to find large compact thrombi in certain of the branches of the portal vein within the liver at periods varying from ten days to several weeks after the transfusion. This thrombosis was found most marked when the destruction of blood had been most rapid. It was, in all probability, connected more particularly with the breaking up of the white corpuscles.

A similar thrombosis was found by Wooldridge to follow the injection into the blood of an extract he obtained from the lymph glands, testis, and thymus gland. The intravascular clotting was usually instantaneous and complete throughout the whole vascular system, causing sudden death; but under certain circumstances it was limited to the blood of the portal system. Wooldridge credited the leucocytes with but little share in this process; the "tissue fibrinogen," by whose union with the fibrinogen of the blood fibrin was formed, was derived from the lymph corpuscles, not from the leucocytes. I find no reason to believe that such a difference of structure or function exists between the leucocytes and the lymph corpuscles as Wooldridge supposed. Both of them are extremely active cells, and there is, therefore, some degree of probability in the view now advanced that the greater liability of the portal blood to coagulate both after transfusion and to a less degree in health is connected with the great activity and correspondingly greater disintegration of the cells, whether leucocyte or lymphoid, in and around the portal radicles. This conclusion is of some importance, as serving in part to explain the peculiar distribution of the thrombosis which so often occurs after transfusion of blood. The gastro-intestinal tract and the mesenteric veins are its chief seats.

Fate of the Red Corpuscles.—The evidence of any destruction of white corpuscles in health is thus but slight. The case is very different with the red corpuscles. The source of the bile pigments is the hæmoglobin of the blood, and the daily excretion of these pigments points to the existence of some cause at work in the blood leading to a certain destruction of hæmoglobin, and presumably therefore to a certain daily destruction of red corpuscles. The first question which naturally arises is why there should be any such destruction. The rôle of the hæmoglobin in respiration is a comparatively passive one; the mere carrying to and fro of oxygen does not appear to demand the exercise of much functional activity, or necessitate very great metabolism on the part of the red corpuscles. Nevertheless, change is involved in this process. There is evidence that even if the sole function of the blood were respiratory, the red corpuscles would after a time become unfit for their work, relatively slight though it be. Their hæmoglobin cannot carry oxygen for an indefinite period. Hence it is that the outworn hæmoglobin has to be got rid of. The appearance of the red corpuscles in the animal scheme is contemporary with the appearance of an organ—the liver—one of whose special functions it is to remove pigment matters from the system.

When blood destruction is spoken of, we refer more particularly therefore to the destruction of the red corpuscles. What is the nature of this destruction? What are its seats, the agencies by which it is effected, and the conditions influencing it? The subject is one of no little complexity. In the following account, based on the results of a lengthened series of investigations, I shall confine myself to a consideration of such facts as bear more especially on the ultimate fate of the red corpuscles after transfusion.

THE NATURE OF BLOOD DESTRUCTION.

Two forms of blood destruction are to be recognised, distinguishable alike by their character, the conditions influencing them, and their relative importance to the organism.

1. The first is a slow and gradual decay of the red corpuscle, manifested chiefly by changes in colour and shape, and

its resistance to the action of reagents. The hæmoglobin remains within the corpuscle to the last, and becomes gradually converted into a globule of inert blood pigment, retaining the size and spherical shape of the red corpuscle. To this form of blood destruction I propose to give the name of *Passive destruction*. It is the mode of death of the red corpuscles which would occur were the blood subjected to no other changes than those involved in carrying on its respiratory functions. It is to a great extent independent of the action of cells. The final conversion of the hæmoglobin into effete blood pigment is, however, the result of the activity of cells. The chief evidence of passive destruction is the presence of pigment in certain organs of the body, chiefly in the spleen, capillaries of the liver, and bone marrow. The chief character of this pigment is the large and varying size of the individual pigment particles, and their irregular shape. This feature is best seen in animals in which the red corpuscles are normally very large; for example, in frogs and birds. The larger the animal's red corpuscles, the larger the pigment particles resulting from their passive destruction.³ (Figs. 10 and 11.) When once formed this blood pigment is remarkably resistant to the action of reagents; it can be recognised long after the death of the original red corpuscles. Hence the amount of pigment found in the organs specified affords a most reliable indication as to the amount of passive destruction that has occurred. Its absence from these organs can also be relied upon as showing that but little passive destruction has occurred—that the conditions have not been favourable to the persistence of the red corpuscles within the circulation for a sufficient length of time to allow them to undergo a process of natural decay.

Fig. 10.

Fig. 11.

2. The second form of blood destruction is one in which the hæmoglobin, instead of remaining within the red corpuscles, escapes from them into the plasma, and is in great part excreted by the liver as bile pigments. To this form of blood destruction I propose to give the name of *Active destruction*. It is the change in the blood corpuscles caused by the action of water, various salts, etc. It differs from passive destruction in being closely dependent upon the activity of cells. The chief evidences of this active destruction are—(1) the formation of bile pigments by the liver, to which organ the hæmoglobin is mainly carried; (2) to a less and altogether subsidiary extent in health, the formation of blood pigment. The chief character of this pigment is the small uniform size and spherical shape of its individual particles. (Figs. 12 and 13.) The assumption of this form by the pigment is independent of the action of the cells; but the conversion of the hæmoglobin into blood pigment is as much the result of cellular activity as in passive destruction.

The size of the red corpuscles has no influence on the size of the pigment particles resulting from active destruction. It is the same in mammals as in birds or amphibians. The pigment is formed from free hæmoglobin.

No trace of blood pigment is usually found in the liver cells as the result of the breaking up in and excretion of this free hæmo-

globin from the body. Under certain conditions of excessive active blood destruction in disease—for example, in pernicious anemia—pigment may be found in great abundance in the liver cells; sometimes, also, in the capillaries of the liver. In both cases alike it possesses the features already described as characteristic of pigment resulting from active destruction. The presence of this kind of pigment within the liver cells is in a special degree an evidence of excessive active destruction, and a further characteristic is that it is always most abundant in the liver cells of the portal zone of lobule. (Figs. 12 and 13.) Pigment resulting from passive destruction, however great it may be, is never found within the liver cells, but always lies enclosed in leucocytes within the capillaries, and it possesses the character belonging to pigment resulting from passive destruction. (Figs. 10 and 11.) This distinction is one of great importance. In the spleen and bone-marrow the character of the pigment is our only guide as to the nature of the blood destruction that has occurred. In the liver we have to consider not only the character of the pigment, but also its situation, whether within the liver-cells or within the capillaries.

Fig. 12.

Fig. 13.

CONDITIONS INFLUENCING BLOOD DESTRUCTION.

Age.—What is the relative amount of active and of passive destruction in health? It varies first of all according to the age. The spleen and bone marrow in young healthy animals—for example, in rabbits, dogs, cats—contain but little pigment. The amount of pigment tends to increase with age, and in old animals, especially in dogs, it may be found very abundant, not only in these two organs, but also in the capillaries of the liver. We must conclude, therefore, that in the young animal there is but little passive destruction; it is, indeed, at a minimum in young healthy animals, at a maximum in old animals. The significance of this is that in the former the conditions are not favourable to the slow and gradual decay of the red corpuscles; whereas, as age advances, the conditions become more favourable. With active destruction the very reverse is the case. It is greatest in youth, and diminishes gradually with advancing age. The proof of this is that the formation of bile pigments is most active in young and healthy animals; and this process is entirely subserved by active destruction of blood. There is, in fact, no relation between the amount of passive destruction and the formation of bile pigments, a conclusion differing from that come to by previous observers (Quincke, Kunkel, Naunyn, and Minkowski). On the other hand, there is an extremely close relation between active destruction and the latter process.

Food.—The liberation of hæmoglobin from the red corpuscles in active destruction implies the existence of conditions unfavourable to the continued existence of the corpuscles. What are these? The first fact to be noted regarding them is that they are not in equal operation at all times. We have a guide to the amount of active destruction that occurs at any time in the quantity of bile pigments formed. In starvation the formation of bile pigments never entirely ceases, but it is at a minimum. In health it is much greater, varying, however, from time to time, according to the amount and quality of the food. It is greatest during digestion, and is most marked of all five or six hours after the ingestion of food. Since we cannot conceive of an increased formation of bile pigments without a correspondingly greater supply of hæmoglobin to the liver cells, we must conclude that the ingestion of food is followed by increased active destruction.

³ The pigment formed from extravasated blood or as the result of congestion presents the characters of that resulting from passive destruction. The description about to be given of this process has no reference to the occurrence of extravasation or congestion, the pigment resulting from which can at once be recognised by certain other features which need not here be specified.

SEATS OF BLOOD DESTRUCTION.

Active destruction must therefore depend on certain changes in the blood, most marked during digestion. We have seen in our study of the physiology of the blood that the changes in the blood at this period are by no means great, and that any changes met with are most marked in the blood of the portal system, in the spleen, liver, and radicles of the portal vein.

Active destruction in health is almost entirely limited to the same system. The hæmoglobin set free is carried to the liver, where it is broken up and excreted in the form of bile pigments. The spleen is *par excellence* the seat of active blood destruction. The same structural features that favour the active destruction of red corpuscles—namely, slowness of circulation, closeness of relation of the cells of the pulp to the blood flowing through it, capacity for accommodating large and varying quantities of blood—favour also the seizure of red corpuscles in process of becoming effete by slow and gradual decay. The spleen is thus also the great seat of passive destruction. This circumstance explains the presence of blood pigment in that organ when it is entirely absent from the liver, a condition found in many of my experiments after transfusion. Next to the spleen the red bone marrow is the most important seat of passive destruction. It is the only tissue outside the portal circulation in which a destruction of blood of any consequence takes place. Within the liver the seats of active destruction are the capillaries.

The changes in the blood within the spleen, radicles of portal vein, and liver are compatible with the liberation of hæmoglobin in so small a quantity at a time, that it is impossible to recognise free hæmoglobin within the blood of the portal vein.

Active destruction of blood is not a mere physical process. It is not the result of the action of the constituents of the food on the red corpuscles, but is dependent on the activity of cells in the various situations in which it occurs, and on the changes in the plasma induced by this activity.

Summary.—The foregoing may be regarded as the first systematic attempt to bring the various facts connected with this subject into relation with one another. According to Voit, in Hermann's *Physiologie*, we have hitherto had no knowledge as to whether the corpuscles are destroyed in greater number in health than in starvation: "There is no reason why there should be a greater destruction of red corpuscles during digestion than during the fasting state." We have seen that it is precisely during digestion that the greatest and most active destruction of blood occurs. The greater accumulation of pigment in the spleen and other organs in old age, in the fasting state, in conditions of wasting disease, is not an evidence of greater destruction of blood, but indicates that the conditions have been peculiarly favourable to the slow and gradual decay of the red corpuscles. In all these conditions blood destruction is at a minimum. The changes in the red corpuscles are most marked at the period of greatest activity of the leucocytes of the blood, and of the cells of the spleen and follicular tissue of stomach and intestine. The activity of these cells is regulated by the character and amount of the food given. With a rich supply of food their metabolism is greatest and the destruction of blood is also greatest. Since, however, with a rich supply of food the process of blood formation is most active, it follows that in the blood, as in all other tissues, anabolism and catabolism are closely associated. The conditions that favour its building up lead also to its breaking down. The final argument is thus supplied in support of the conclusion previously arrived at, that the blood is in all respects a tissue—in structure and behaviour, in its formation and its destruction.

ULTIMATE FATE OF THE TRANSFUSED CORPUSCLES.

The appearances presented by the various organs most intimately concerned—great accumulation of pigment within the spleen and bone marrow, its absence altogether from the liver, or presence in only slight amount within the liver-cells—point to the conclusion that their fate is precisely the same as that of the animal's own corpuscles. Transfusion of red corpuscles is a real implantation. Their destruction is effected in the same way and by the same agencies as in health. It is partly active, partly passive. The existence of the latter form of destruction is important, pointing as it does to the conclusion that the conditions may be so entirely favourable, that the corpuscles transfused are allowed to undergo a process of natural decay. The seats of their destruction are the spleen, the radicles of the portal vein, the capillaries of the liver, and the bone-

marrow. The agencies by which this is effected are the same as in health.

Lastly, the conditions influencing its character and amount are the same; it is specially affected by the amount and character of the food. Passive destruction is favoured by abstention from food, active destruction is favoured by increasing the supply of food. The bearing these conclusions have on the utility of transfusion will be seen when we come to consider the *rationale* of this operation. So far as transfusion of blood may be supposed to serve any respiratory purpose, any value it possesses depends on the life-duration of the red corpuscles, hence the importance of determining precisely what the most favourable conditions are for prolonging their existence within the circulation of their host.

HÆMOGENIC PROPERTIES OF TRANSFUSED BLOOD.

Fate of the Hæmoglobin.—Its fate varies according as the destruction of the red corpuscles is active or passive. Passive destruction is conducive to the storing up of a large quantity of blood pigment within the body, chiefly within the spleen and bone-marrow. This pigment contains all the iron of the original hæmoglobin. Anything that tends to render destruction more active than passive favours the removal of the hæmoglobin from the body in the form of bile pigments, and along with the bile pigments a certain proportion of the iron is always excreted in the bile. The chief advantage of having iron in the system is that it may afterwards be used for purposes of blood formation. This object is best served when the iron is deposited in the organs concerned in that process, namely, the bone-marrow, and to a less extent the spleen. The presence of iron in large quantities within the liver cells, as in some forms of anæmia in which the destruction is very active, does not serve any useful purpose. It is in process of excretion, and must interfere to some extent with the proper action of these cells.

Transfusion of blood may thus have a certain hæmogenic value in virtue of the presence of hæmoglobin in the form best suited to enable its iron to be stored up in the body. Free hæmoglobin introduced into the blood is removed at once as a foreign body; mainly by the kidneys, and in part also by the liver. Hæmoglobin introduced in the form of red corpuscles remains within the circulation for a period commensurate with the life duration of the corpuscles. Under favourable conditions, it is afterwards stored up in the spleen and bone-marrow in the form of blood pigment. Little or none of it is then removed from the system.

ABSTRACT OF THREE LECTURES ON TUBERCULOSIS IN SOME OF ITS SURGICAL ASPECTS.

Delivered at the Royal College of Surgeons of England.

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LECTURE III.

In describing the results to be obtained in the treatment of surgical tuberculosis, by means short of excision, I shall keep chiefly to hip disease, because this is the instance in which operative interference has been most strongly advocated. But, in the first place, I may briefly allude to the case of the other joints, and of the spine. Speaking of the general group of tubercular diseases met with in surgery, I believe that when they are detected early and are adequately treated by prolonged rest, in not more than at the most 10 per cent. do they develop to any formidable degree. It is a rule to which I have seen but few exceptions that when, for example, a knee, or an elbow, which is the seat of tubercular disease of less than three months duration, is enclosed in well-fitted splints, and is kept at rest, the case gives no further real trouble. The symptoms begin at once to subside, and the improvement, though it is slow, goes on without material check until the joint is apparently free from disease; while, after a longer period of rest, complete recovery is secured. I am confident that the period