The causes of the origin, the progress and the mode of propagation being in great measure known to us, we possess a remedy at hand, which, if carried to its legitimate ends, will result in immense good. I do not mean by this that a law similar to the ancient law of Epirus should be called in requisition to restrict or suppress it; but, by a system of precaution, of segregation, and by regulations influenced and dictated by a spirit of Christian charity—a duty imperative upon England—a certainty may be arrived at, and a means found by which this loathsome disease, if not wholly stamped out, will meet with so effective a check, and be so controlled, as to soften down the ravages it now makes, and curb the facility of its propagation.

SUMMARY OF THREE LECTURES

ON

TRANSFUSION:

ITS

PHYSIOLOGY, PATHOLOGY, AND PRACTICE.

Delivered at the Royal College of Surgeons.

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LECTURE III.

THE respiratory as well as the hæmogenic value of transfused blood is subject to the same conditions, and depends on the same two factors—(1) the quantity of blood transfused, (2) the nature of the blood destruction in progress at the time of the transfusion.

The greater the quantity of blood transfused, the longer are red corpuscles likely to remain within the circulation, and the more likely is their hæmoglobin and the iron it contains to remain within the system. Over this factor, however, we can exercise but little control. The quantity of blood transfusible in man can rarely be more than about 5 per cent. of the quantity of blood already in the body. And the life-duration of the red corpuscles under such circumstances is probably to be reckoned by a period of hours.

Of far more importance as a factor is the nature of the blood destruction at the time of the transfusion and subsequent to it. The more the blood destruction is "active," the shorter is the life-duration of the red corpuscles; and how active this may at times be is evidenced by cases in which the transfusion is followed almost immediately by rigors, fever, and the appearance of free hæmoglobin in the urine. There are certain forms of anæmia in which excessive blood destruction is the essential feature, and these from their very nature are certainly unsuitable for transfusion. We shall presently see that it is possible for us to recognise by certain clinical features the nature of the anæmia we have to deal with, and in this way to avoid the operation of transfusion under circumstances that would probably render it of little, if any, service. In addition to these pathological variations, the activity of blood destruction is, as we have seen, subject to certain physiological variations chiefly having relation to the ingestion of food; and this factor it is in our power to some extent to control by having regard both to the quantity and quality of food subsequent to the transfusion. Our object would be best attained by withholding food altogether, in this way rendering blood destruction, as far as possible, "passive." In any case the food should be as little nitrogenous as possible, since a nitrogenous diet undoubtedly increases blood destruction more than a simple carbohydrate one.

PHYSIOLOGICAL ACTION OF SODIUM PHOSPHATE.

It is by interfering with this—what may be regarded as the primary—indication in transfusion, namely, to reduce blood destruction to a minimum, that the use of sodium phosphate for purposes of transfusion to prevent coagulation of the blood is attended with certain disadvantages that require here to be noted. First recommended now some years since by Dr. Braxton Hicks and Dr. Barnes, the use of this salt has recently been revived, apparently with much success, in the hands of Mr. Cotterill, Dr. John Duncan, and others.

This practice of mixing the blood with saline solutions before injection, and in this way getting rid of certain of the dangers

incidental to the operation, is based on an assumption that is as erroneous as it is widespread, namely, that the behaviour of salts, poisons, etc., on the red corpuscles outside the body affords any clue to their probable behaviour on the blood after their injection. The conditions of an experiment outside the body and those existing within the body are entirely different. Outside, the conditions are physical; we mix the blood with the solution whose action is being studied, and allow the red corpuscles to remain at rest, and in contact more or less prolonged with the substance whose action is being studied under conditions that are entirely without parallel within the body. Within the body the conditions are physiological: the blood is constantly in rapid circulation; all the processes, including the process of blood destruction, are the result of the activity of cells, and may be modified in many ways by the action of the drug introduced.

The facility with which blood can be withdrawn from the body, and the action of drugs on its corpuscles studied, has led to many erroneous conclusions regarding the behaviour of various drugs on the blood. The following observations may serve to emphasise the above conclusions:—I have found a $\frac{3}{4}$ per cent. solution of sodium chloride to cause red corpuscles to break up and disappear in the course of twenty-four hours, while the same solution, after the addition of toluylendiamine in the proportion of $\frac{1}{2}$ per cent. to 1 per cent., preserved them intact for several days. The two observations were made at the same time, and the conditions were precisely the same in both.

Nevertheless, the injection of the simple saline solution into the circulation, even in the largest quantities, is harmless, while the injection of a few cubic centimetres of a 1 per cent. solution of toluylendiamine causes a most marked destruction of the red corpuscles, accompanied, it may be, by jaundice, hæmoglobinuria, or even death.

The bearing which these observations have on the value of the practice of injecting sodium phosphate with the blood transfused will be evident. Its behaviour towards the corpuscles outside the body affords no criterion of its probable behaviour after injection. In all cases bodies so introduced are in the position of foreign bodies. Their action will be harmless only on one condition—namely, that they affect in no way the activity of the cells of the blood on the one hand, or of the blood organs on the other. My observations show that in the case of sodium phosphate this condition is not fulfilled.

In every instance in which the salt was injected along with the blood, the subsequent blood destruction was of a more active character than that observed after transfusion of pure defibrinated blood alone, although the conditions of the experiments were precisely the same in all cases. (Fig. 14.) The evidence of this more active destruction was, in addition to the shorter life duration of the corpuscles as determined by enumeration (Fig. 14), of a twofold nature: 1. The presence of iron in the liver in larger amount than was ever observed in any experiment in which blood alone was transfused, the pigment in which this iron was contained being found in the situation most characteristic of excessive blood destruction—namely, within the liver cells; and (2) an increase in the colouring matters of the fæces pointing to an increased formation of bile pigments.

Clinical evidence of a similar change in the character and amount of the bile excreted after transfusion is, I believe, afforded by an interesting case recorded by Dr. Halliday Croom.¹ On the day following transfusion of a mixture containing $5\frac{1}{2}$ ounces of blood and $2\frac{1}{2}$ ounces of a 5 per cent. solution of sodium phosphate, there was a well-marked attack of jaundice. It is possible that the occurrence of the jaundice subsequent to the transfusion may have been a mere coincidence, but recent observations tend more and more to establish the importance and frequency of that form of jaundice depending on increased destruction of blood, sometimes termed "hæmohepatogenous," but whose essential feature, I believe, may be best described by terming it "hæmolytic." By far the best example of this form of jaundice is that so frequently met with in pernicious anæmia. The sudden onset of the jaundice in the above case after the transfusion, as well as its brief duration (it began to fade at once, and had disappeared at the end of a week), points in all probability to a causal connection of this kind between it and the injection.

The use of salts for purposes of transfusion is, to a great extent, based on the assumption that the composition of the plasma, as regards its richness in inorganic solids, is constantly varying, and that the injection of a little more or less is immaterial. So far

¹ *Edin. Obstetric. Soc.*, June, 1887.

is this from being the case that there is every reason to believe that its composition in inorganic solids remains, consistently with its discharge of great carrying functions, as constant as that of any tissue of the body.

This constancy in composition is most noticeable in the case of chlorides, which form more than one-half of the total percentage of salts in the ashes of the plasma, but it doubtless also applies to the other inorganic constituents. When a rich supply of chlorides is given in the food, the excess is at once excreted by the kidneys.

Fig. 14.—Injection of 100 cubic centimetres of blood and 30 cubic centimetres of a 5 per cent. solution of sodium phosphate into the peritoneal cavity of a rabbit, under the same conditions and with the same precautions as in the preceding series with pure and defibrinated blood. Greater quantity of blood transfused. Life-duration of red corpuscles shorter.

When withheld altogether, the percentage in the blood at first falls very considerably, but ultimately rises again to the normal, while the excretion of chlorides by the kidneys falls to a minimum. The difficulty experienced in removing the chlorides from the serum by osmosis, even with the aid of large quantities of distilled water (Hoppe-Seyler), may be regarded as likewise pointing to the same conclusion—namely, that the inorganic solids of the plasma, as of the red corpuscles, are present, not in free form as such, but in combination with the other constituents. They must be regarded, therefore, as constituting portions of an organised structure built up by the agency of cells, and their amount is, therefore, solely regulated by the activity of these cells. This is specially true of the phosphoric acid of the blood, a considerable part of which is derived from the phosphorus contained in lecithin, one of the most complex, as it is one of the most widely spread, organic compounds in the body. It is also true of the sulphates, some of which are derived from the sulphur of proteids. Hoppe-Seyler has, within the last few weeks, shown that even the hæmoglobin of the corpuscles is not present in the corpuscles as such, but is in intimate combination with other organic and inorganic solids.²

² For independent evidence pointing strongly to the same conclusion, see *Lancet*, ii, 1888, p. 656, where I have described a special variety of hæmoglobinuria characterised by the excretion of hæmoglobin not in free form, but in combination with albuminous constituents of the blood.

The importance of these various facts and observations lies in this, that they point clearly to the conclusion that all salts injected directly into the blood form no part of the blood while present, but are in the position of foreign bodies. They are removed from the blood and excreted from the body with the same rapidity as sugar, peptones, hæmoglobin, and large quantities of neutral saline solutions when similarly injected.³

PATHOLOGY OF TRANSFUSION.

Thrombosis.—Transfusion of blood is an operation at all times attended with certain dangers that fully entitle it to the respect with which it is generally regarded, notwithstanding that the operation is one attended with no great technical difficulties.

Up till 1821, the operation of transfusion consisted in the injection of pure blood. In that year attention was drawn for the first time by two French observers (Dumas and Prévost) to the fact that transfusion of defibrinated blood was equally efficacious in rescuing animals from impending death from hæmorrhage. Their observations were confirmed a few years later by Dieffenbach (1828); but the use of defibrinated blood gained ground so slowly that up till 1860 only 13 cases had been recorded.

The great impetus to its use was given by the researches of Panum (1863). Undeterred by Magendie's experiences as to the dangers accompanying the transfusion of such blood, Panum advocated transfusion of defibrinated blood to the entire exclusion of pure blood, urging as one of its advantages that large tanks of it could be kept ready for use on the field of battle. These were, in truth, the palmy days of transfusion.

The disturbances noted by Magendie following the transfusion of defibrinated blood were chiefly the appearance of blood-stained froth at the nose and mouth, cedema and congestion of the lungs, subpleural hæmorrhage, swelling and congestion of the mucous membrane of stomach and intestine, with occasionally the presence of blood in the feces, and were ascribed by him to an alteration in the viscosity of the blood from the removal of the fibrin. Panum met with similar changes in a number of his experiments; but he attached no importance to them, considering them merely as the result of the rupture of certain of the capillaries from increased action of the heart after the transfusion. Ponfick and Landois, who also met with them, explained their occurrence in different ways; the former regarding them as the result of irregularities in the mode of injection, the latter as the result of blocking up of certain capillary districts with "fibrin-stroma"—the stromata of the injected corpuscles—and the subsequent rupture of adjacent capillaries. None of these explanations serve in any way to account for these various pathological changes.

With regard to the last one more particularly it may be noted that it is possible, as I have found, by means of destructive agents injected into the blood, to reduce the greater number of the red corpuscles to the form of stromata, and to have them circulating in the blood for days without producing any of the disturbances which may sometimes be caused by the injection of a few drops of blood.

The observations that threw most light on the true nature of these disturbances were those of Armin Köhler (1877). The various pathological changes, with their accompanying symptoms, are the results of a widespread capillary thrombosis in various parts of the body, occurring more especially, however, in the capillaries of the lungs and gastro-intestinal mucous membrane, occasionally also in the mesenteric veins and mesenteric glands, sometimes throughout the entire blood vascular system.

The conditions favouring the occurrence of this thrombosis are still in great part unknown. Defibrinated blood obtained by allowing the blood to coagulate spontaneously, and then pressing out the clot, was found by Köhler to be much more active in inducing thrombosis than that obtained in an ordinary way by a process of whipping. The great feature of defibrinated blood in all cases, however obtained, is the uncertainty of its action. It is sometimes quite harmless, at other times highly dangerous, this result being entirely independent of the quantity injected or the care taken in injecting it. The same uncertainty in action applies, although perhaps in less degree, to all blood after its withdrawal from the vessels.

PATHOLOGICAL ACTION OF SODIUM PHOSPHATE.

Nor is this peculiarity in the behaviour and uncertainty in action

³ St. Kikowicz. "Die Regelung der Salzmenge des Blutes." *Archiv f. Physiologie*, 1886. P. 818.

of blood affected in any degree by the use of such salts as sodium phosphate.

The two following experiments may serve to illustrate both the harmlessness of such transfusions and also the dangers they may occasionally be attended with. They will at the same time serve to show how entirely independent the disturbances are of any factors such as overfilling of the system of the blood or too rapid injection, the factors so frequently credited with their production.

EXPERIMENT 13.—*Auto-transfusion.* Rabbit anaesthetised with ether. Twenty cubic centimetres of blood withdrawn from one of the carotid arteries into a vessel containing 15 cubic centimetres of a 5 per cent. solution of sodium phosphate maintained at the temperature of the body; immediately allowed to flow back into the jugular vein. The injection completed without the slightest disturbance of any sort arising.

EXPERIMENT 14.—*Auto-transfusion.* Rabbit anaesthetised with ether. Twenty cubic centimetres withdrawn from carotid artery into 20 cubic centimetres of a 5 per cent. solution of the same salt kept at the body temperature. Blood was immediately reinjected into the jugular vein, with the fullest precautions; my object in doing the experiment being to reinject the whole of the blood back into the circulation. Immediately the blood began to flow the animal became restless and uneasy, its breathing more rapid, and it began to struggle. The injection was stopped, and then resumed after a short pause, the symptoms having apparently passed off. Violent convulsions then immediately set in, the breathing became extraordinarily rapid, a large quantity of frothy blood-stained mucus poured from nose and mouth, and death occurred five minutes after the injection had been commenced and after the injection of 7 cubic centimetres of blood (2 drachms).

An examination made at once revealed the following *post-mortem* changes. Both ventricles of heart distended and motionless, the auricles only moderately distended and still beating. A small quantity of serum within the pericardium. The ventricles on being opened began again to beat, and were both found filled with a firm compact thrombus, red in the left, of darker colour in the right ventricle. In both cases the thrombus extended back into the auricles, and could be traced from the left auricle into the smaller branches of the pulmonary veins. The thrombi were not however continuous, but were in isolated portions of more or less cylindrical shape, tapering off at each end. From the ventricles the thrombi also extended forward into the aorta and into the pulmonary artery, and in the former they could be traced as low down as the descending thoracic aorta, where they gradually tapered off.

The lungs were extremely oedematous, especially at their bases, the bronchi and trachea contained much frothy blood-stained mucus. Over the surface of the lungs were numerous bright red subpleural hæmorrhages.

The ventricles began to beat as soon as they were cut open, and the heart only ceased to beat when cut out of the body some ten minutes after death had occurred.

There could be no doubt in this instance as to the significance of the symptoms which preceded death, and the pathological changes which underlay them. The peculiarity of the thrombosis was that it was complete, extensive, and widespread. The shape of the thrombi in the lung showed that thrombosis had occurred independently at different parts, and had not extended out from one centre. The individual thrombi were remarkable for their extreme toughness. Microscopic examination showed that they were specially numerous in the smaller arterioles and capillaries of the lung. The distribution of the thrombosis in the portal system was, unfortunately, not noted.

In the light of these observations the various disturbances so frequently met with during the performance of transfusion acquire a new significance and importance. The sudden gasping for breath, or the quick and laboured breathing, the feeling of tightness and oppression over the chest, or of precordial anxiety, the forcible cardiac action, or the threatened failure of heart and great weakness of pulse, the restlessness and distress from pains in loins and abdomen, with urgent calls to stool, and the vomiting, these and other symptoms are undoubtedly the manifestation of changes in all respects similar to those found in animals under similar circumstances. Köhler, indeed, found that in animals killed while showing similar symptoms of distress, small thrombi could be discovered in the capillaries of the lungs and gastrointestinal mucous membrane, sometimes in the mesenteric veins.

I have frequently found changes of less degree (numerous sub-

pleural hæmorrhages) after the transfusion of 10 or 20 cubic centimetres of an animal's (rabbit's) blood into its own peritoneal cavity—under circumstances, therefore, that entirely precluded the operation of any factors such as the introduction of air, too hasty injection, or overfilling of the system.

The following cases of Quincke may serve to illustrate the nature of the dangers attending transfusion of blood.

Cases of *Pernicious Anæmia*.—Arterial transfusion of 85 cubic centimetres of defibrinated blood. Towards end of the transfusion face became flushed and covered with perspiration, followed suddenly by pallor and complete collapse. Heart sounds inaudible; pulse not to be felt. Under influence of irritants and stimulants, recovery, but great complaint of cold during the next three hours, with violent abdominal pains and diarrhoea. Urine passed the same day albuminous, and contained a considerable quantity of free hæmoglobin, with casts. The temperature, which before the operation was 98° F., rose in the course of four or five hours to 102°, falling again in the evening to 98.5°.

In another case (Case XII), in which 50 cubic centimetres of defibrinated blood were injected, the transfusion had to be stopped on account of the feeling of great anxiety on the part of the patient with sickness. Half an hour later there was a rigor, which lasted three to four hours, violent pains in the abdomen, and repeated urgent calls to stool lasting several hours. The temperature, which before was 99° F., rose in the course of two hours to 102.4°, and seven hours later still remained at over 100°.

In a third (Case XV), in which 105 cubic centimetres of defibrinated blood were transfused, there was diarrhoea, and icteric tinge of conjunctivæ became more marked.

In another (Case XVI) transfusion of 100 cubic centimetres of defibrinated blood was followed by giddiness and rigors, pulse rose from 84 to 160, temperature to 102°, and in the course of two hours there were no fewer than six loose motions into the bed, urine became albuminous, and contained free hæmoglobin with numerous hyaline and granular casts.

The use of sodium phosphate along with the blood is not untended with dangers of similar nature; "unpleasant though evanescent symptoms," great distress from pain in loins, and forcible cardiac action, were observed by Dr. Duncan in a case of pernicious anæmia after the injection of 4 ounces of a mixture of blood and sodium phosphate, and were ascribed by him to the too rapid injection of so much blood at a time "when the quantity of blood was daily increasing." As has been seen, the same train of symptoms may follow the injection of a few cubic centimetres of the animal's own blood, and may be absent after the injection of fluid to the amount of 100 per cent. or 130 per cent. of the quantity of blood in the body (Lesser).

There can, I think, be little doubt that their cause is to be sought in changes in all respects similar to those found in animals—in the occurrence, namely, of capillary thromboses, the pains felt being probably due to spasm. It will be noted how constantly the abdominal pains are met with, usually attended by diarrhoea more or less severe. In this connection it will be remembered that the radicles of the portal system within the gastro-intestinal wall have been seen to be the favourite seat for the occurrence of such thromboses, and the subsequent swelling and congestion of the mucous membrane, so well described by Magendie in the first instance, are doubtless responsible for the violence of the symptoms observed, pains, diarrhoea, appearance of blood in stools, etc. Sometimes, though rarely, the effect of transfusion in causing intra-vascular clotting may be observed in a still more striking way, as in the case recorded by Hayem,⁴ in which, immediately after a transfusion, phlegmasia alba dolens appeared, first in one leg, then in the other. The condition of the vessels and their blood was probably such that it never required the extra stimulus afforded by the transfused blood to bring about instantaneous clotting.

The cause of thrombosis in all such cases is by no means clear. It is probably connected with the disintegration of the white corpuscles of the injected blood as well as of the plasma, and is favoured doubtless by certain conditions of the blood of the recipient at the time of the transfusion. The frequency with which the characteristic symptoms are met with in cases of pernicious anæmia is doubtless connected with the excessive blood destruction, with consequent instability of the blood, which characterises that disease. With regard to the action of sodium phosphate, one of the favouring conditions we may judge to be the quantity of the solution injected. In the experiment already recorded the

⁴ JOURNAL, vol. i, 1884, p. 387.

blood and salt solution were mixed in equal proportions, instead of in the usual proportion of 3 to 1. It is possible that the influence of this factor is also to be observed in one of Dr. Duncan's cases, in which the patient suddenly became nearly collapsed; the salt solution had, by an oversight, been made of the strength of 10 per cent. instead of 5 per cent.

Fever and hæmoglobinuria not infrequently follow transfusion of blood. They are of constant occurrence when the blood of one animal is transfused into another of different species. In all cases the occurrence of hæmoglobinuria is of the greatest significance as marking—(1) the sudden and rapid liberation of the hæmoglobin from the injected corpuscles, but still more as pointing (2)¹ to the seat of this liberation, namely, the general circulation. In health no such liberation ever occurs in the general circulation. Active destruction, as I have shown, is limited to the portal circulation—chiefly to the spleen: the hæmoglobin set free being disposed of by the liver before it reaches the general circulation.

The largest quantities of blood may under ordinary circumstances be transfused from one animal into another of the same species without the occurrence of any hæmoglobinuria. The explanation of this is, as we have seen, that the seats of destruction are the same as in health.

The appearance of hæmoglobin in the urine is an indication therefore that the conditions of the blood within the general circulation are entirely inimical to the preservation of the red corpuscles, even for a few hours.

The rigors and fever which mark this occurrence are connected with the liberation of the hæmoglobin. The same phenomena attend the liberation of hæmoglobin in paroxysmal hæmoglobinuria.

Any value which blood transfusion possesses over the infusion of saline solutions, we have seen, depends upon the presence of the red corpuscles and their hæmoglobin in the general circulation. We now find that the chief dangers of transfusion are connected with the presence of the white corpuscles of the injected blood and from changes in the white corpuscles and plasma of the recipient's blood.

Any advantages that transfusion of red corpuscles may have over simple saline injections are counterbalanced by the dangers attending the simultaneous injection of the white. In the case of defibrinated blood the latter so preponderate that transfusion of defibrinated blood is an operation not only dangerous in itself, but one whose practical value by no means serves to compensate the additional risks run in carrying it out.

PRACTICE OF TRANSFUSION.

We have up to this point considered transfusion as partly a physiological, partly a pathological, problem. It is not in health, however, in which condition we have been hitherto studying it, but in disease, that transfusion finds its practical application.

We have seen that transfused blood (1) possesses no nutritive value. Transfusion of blood is, therefore, useless in all forms of "atrophic" anæmia, by which term rather than by the unfortunate term "symptomatic," hitherto given, I would distinguish all forms of anæmia in which the changes in the blood simply correspond in degree to the wasting changes occurring in other tissues. The anæmia of all forms of wasting disease is, therefore, of this character. It is important to note that the degree of anæmia cannot be judged of by the amount of pallor. Examination of the blood alone enables us to determine whether the anæmia is "atrophic" in its nature or not.

(2) If the condition to be met is a want of red corpuscles, or an incapacity on the part of those already present to carry on their respiratory functions, then transfusion of blood may possibly be of value. The red corpuscles transfused remain for a certain time within the circulation of their host. Transfusion of blood may conceivably be of value in carbonic oxide poisoning, where the red corpuscles are incapacitated for their work by a close union of the gas with the hæmoglobin of the corpuscles. Successful cases have been recorded without, however, any clear demonstration, that the most dangerous stage of the poisoning had not been passed before the operation was performed. In most of the cases recorded, chiefly by German observers, the transfusion was not made for many hours after the symptoms of poisoning were fully developed. In any case the transfusion must in this instance always be preceded by a venesection. Even when this is done, the operation is of doubtful value.

As regards the other indication for the transfusion of red corpuscles—the existing want of them—it may be stated that there

is scarcely a single condition of the blood in which the want of red corpuscles is a source of urgent danger. After the greatest losses of blood in animals, a sufficient number of red corpuscles always remain in the circulation to carry on respiration, provided that the circulation is maintained. In animals, after loss of half to two-thirds of the total quantity of blood in the body, the number of corpuscles per cubic millimetre may be found as high as 3,000,000 or 4,000,000. The absolute loss is, of course, great, but the relative loss is slight, and is of little importance. The animal's health is in no way affected injuriously by the loss. In some of my experiments the animals have gained in weight from the day of the abstraction of blood, no indication being afforded of any disturbance at all, except on examination of the blood, which showed the reduction in the number of corpuscles. In man the loss of blood can never be so great as in animals. Syncope occurs earlier. Transfusion of blood is, therefore, never required for the purpose of supplying red corpuscles to carry on respiration after sudden loss of blood in a patient previously healthy. The immediate source of danger in such cases is not the want of red corpuscles, but the disturbance of the relation between the vascular system and its contents.

Nor is transfusion of blood indicated on account of its respiratory value in anæmia of idiopathic or traumatic origin. By idiopathic anæmia I mean those conditions in which the changes in the blood are in excess of the changes in the other tissues, and constitute a characteristic feature of the disease. The best examples of this form of anæmia are pernicious anæmia, chlorosis, and leucocythæmia. It is remarkable how slight the disturbance in respiration may be in cases, for example, of pernicious anæmia in which the red corpuscles may be reduced to 10 per cent., or even less, of their original number. I have observed cases in which the number of corpuscles was as low as 500,000 or 600,000 per cubic millimetre, instead of 5,000,000 as in health, the respirations never rising above 20 per minute; the breathing perfectly tranquil throughout. The great breathlessness on exertion always observed depends on other factors, and in any case never constitutes an indication for the performance of transfusion.

(3) If the condition to be met is a failure in blood formation due, perhaps, to the want of iron in the system, transfusion of blood may be of some value, in so far as we in this way supply the organism with iron in the form in which it can most conveniently be stored up in the body. The two conditions in which this disturbance is most marked are chlorosis, and traumatic anæmia resulting from long-continued and repeated hæmorrhages. There is, I conceive, no disease in which transfusion of blood corpuscles is theoretically more indicated than in chlorosis. The anæmia here is in a special degree the result of an insufficiency of iron in the system, so much so that a chlorosis of old age where, as we have seen, the tendency is for pigment to accumulate in great abundance within the spleen, bone marrow, and other organs, is almost a contradiction in terms. The anæmia of chlorosis we can, however, readily combat without having resort to transfusion.

The question as to the advisability of transfusion in traumatic anæmia is not so easily answered. Our object here is not so much to relieve any passing danger arising from insufficient bulk of fluid, or want of red corpuscles, as to stimulate blood formation. That transfusion appears to be of value in some cases there is no reason to doubt, but how far the result is *propter hoc* as well as *post hoc* it is impossible in any case to determine. If it really is of any value it must be solely by assisting blood formation. I am inclined, however, to regard it of doubtful value even from this point of view, and that for the following reason: that in animals the subsequent recovery after loss of blood is certainly not accelerated by transfusion of blood, but in most cases is actually retarded (Hayem, von Ott). If this be the case where the blood-forming organs are active as in health, it is difficult to understand how the result will be different in disease. The recovery is effected with greater rapidity when simple saline solution (3 per cent. solution of common salt) is injected than when blood is transfused. My own experiments show that the recovery after infusion of saline solution is remarkably rapid. The time required for the return of the red corpuscles to their original number after loss of blood, without subsequent infusion or transfusion, varies from two to three weeks. With subsequent infusion of simple saline solution it is the same; whereas with subsequent transfusion of blood complete recovery is delayed a week longer or more. Further, what is perhaps more striking and certainly is of more importance, is the fact that during the subsequent recovery the

⁵ Hunter, *Lancet*, vol. ii, 1888.

animal generally appears to be in better health after infusion of salines than after transfusion of blood.

Even in traumatic anæmia resulting from long-continued losses of blood, transfusion of blood has in all probability no value not possessed by simple saline solution. The former may actually retard blood formation; the latter is at least always harmless, and might be beneficial if it were required.

In the other forms of idiopathic anæmia, pernicious anæmia, and leucocythæmia, transfusion of blood can, in my opinion, never be indicated. In both, the condition of the blood is the result of changes in the blood-forming or blood-destroying processes, or in both.

In leucocythæmia the disturbance is one of blood formation in the first instance, evidenced by the increase in the leucocytes of the blood, while the diminution in the number of the red I find to be due in great part to excessive blood destruction, probably induced by the activity of the leucocytes. In pernicious anæmia, the condition of the blood is mainly the result of excessive destruction. Transfusion of blood under such circumstances is not unattended by dangers as we have seen, but is followed in most cases by rapid destruction of the injected red corpuscles as evidenced by fever, sometimes by hæmoglobinuria, occasionally also by increase in the slight icterus which so frequently marks the progress of the disease.

It is important therefore to be able to distinguish between profound anæmia of traumatic origin and pernicious anæmia; and this I find it is possible most easily to do, by having regard to the character of the urine in the two cases. I find that the urine of pernicious anæmia contains large quantities of pathological urobilin, recognisable both chemically and on spectroscopic examination, and that its colour is correspondingly high. In marked cases, or during periodic exacerbation of the destructive process within the blood, this character of the urine is a very striking one; more especially as it is unaccompanied by any diminution in the quantity, is frequently quite independent of the occurrence of fever, and the specific gravity is usually very low (1010 to 1015).

The urine of traumatic anæmia, on the contrary, is exceedingly pale in colour, and is free from pathological urobilin. If in addition we note the condition of the blood in the two forms of anæmia, with special reference to the relation between the richness in hæmoglobin and the corpuscular richness—in traumatic anæmia the percentage diminution in hæmoglobin being usually considerably in excess of the diminution in the number of corpuscles; whereas in pernicious anæmia the hæmoglobin percentage is always relatively high, I believe we shall be able in future to draw a sharper line of distinction between these two forms of anæmia than has hitherto been possible.

(4) Lastly, if the condition to be met in transfusing blood is a threatened failure of circulation as the result of sudden loss of blood, then it is unnecessary to have recourse to blood transfusion, as infusion of any neutral saline meets equally well, if not better, all the indications. The value possessed by transfused blood in such cases is almost solely in virtue of its physical properties. The chief physical property of blood for purposes of transfusion is undoubtedly its volume. The immediate source of danger from sudden loss of blood is the fall in the blood pressure to a point where the circulation is unable to be maintained. The obvious indication, therefore, is to raise the pressure within the vessels. In health the blood pressure is dependent mainly upon peripheral resistance. The effect of a loss of blood on the blood pressure is, up to a certain point, completely neutralised by an increase in the peripheral resistance due to stimulation of the vasomotor centre. It is only after very severe hæmorrhage that this relation between the vessels and the amount of fluid they contain necessary for the carrying on of the circulation is disturbed. The pressure falls rapidly and suddenly, and death will ensue unless means be taken to meet the threatened failure of the circulation. The readiest way in which this can be done is to replace the lost blood with a certain bulk of fluid. To meet the danger thus arising, the quantity of blood is of more importance than its quality. In an emergency the infusion of ordinary water (Coates) has been followed by results as successful as any ever obtained after transfusion of blood. Bulk for bulk, pure or defibrinated blood, however, must possess certain advantages over neutral saline solutions free from organic constituents. They doubtless possess a certain physiological value as well as a physical value, inasmuch as blood must have a greater and more immediate effect in restoring the tone of the vasomotor centres

than saline solutions. These advantages, however, are more than neutralised by the other and still greater disadvantages—namely, (1) the difficulty of obtaining blood in sufficient quantity or with sufficient rapidity as compared with the ease with which simple saline solution can be prepared; (2) the dangers attending the transfusion of blood, compared with the absolute freedom from danger possessed by solution; and (3) the doubtful value of the transfusion, whether hæmogenic or physical, when compared with saline solution.

Transfusion of blood will long continue to be practised, and its action studied on account of the many interesting problems connected with the physiology and pathology of the blood on which it is well fitted to throw light. For practical purposes, however, all the advantages to be gained by transfusion may, I believe, be equally well and more readily obtained by infusion of a neutral saline, such as $\frac{1}{2}$ per cent. solution of common salt (about one drachm to the pint). The only pressing indication for the performance of transfusion is the collapse from sudden and severe loss of blood.

With regard to its performance, two points may be noted: (1) that the simpler the instruments used—a simple glass cannula, with a piece of india-rubber attached, and a clean syringe—the more easily will this infusion be effected, and the less likelihood will there be of the injection of air—a source of danger to which far too much importance has long been attached, as it is also one which can readily, with a little care, be altogether avoided; (2) that the temperature of the solution should never rise above that of the body.

Under no circumstances is transfusion of milk or of other mixtures possessing what are supposed to be nutritive properties, ever indicated. They possess no value not possessed by an equal bulk of saline solution.

CASE OF PROGRESSIVE PARALYSIS OF MUSCULO-SPIRAL NERVE CONSEQUENT UPON INJURY; OPERATION; SUCCESSFUL RESULT.

By CHAUNCEY PUZEY,

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In the JOURNAL of May 16th, 1885, I recorded very fully a case of paralysis of the ulnar nerve, due to a fracture of the ulna, in which I operated with a completely successful result; and I concluded by saying that, with the knowledge thus gained, I should feel justified in operating earlier in a similar case.

On March 21st of last year, a Custom-house officer, aged 50, was admitted into the Northern Hospital, under my care, suffering from complete loss of power of extension of the right hand and fingers, the wrist being dropped; and the sensation throughout the parts supplied by the cutaneous branches of the radial nerve being defective. The muscles of the dorsum of the forearm were flabby and wasted, and supination of the forearm was effected with difficulty.

The history given was, that three months before he had fallen down and fractured the humerus rather below its middle. Nothing special was observed about the fracture, which was treated in the ordinary way. On removal of the splints, there was found to be great impairment of motor-power in the forearm; wrist-drop and loss of power in the extensors of the fingers. The flexors acted well.

He was treated by galvanism and massage for some weeks, but instead of improving, his condition became worse, the muscles wasting rapidly. Then it was observed that the signs of "reaction of degeneration" were appearing in those parts supplied by the branches of the musculo-spiral nerve.

The site of fracture presented no noteworthy features, except that there was rather an excessive amount of "callus." Pressure over the course of the nerve elicited the ordinary sensations, until that part over the callus was reached, when they ceased. It was therefore thought that probably the nerve was involved in the callus; at all events, that it must be pressed upon in some way.

He was recommended to come into hospital for operation. To this he agreed; and on March 22nd I operated, making an incision 3 or 4 inches long over the course of the musculo-spiral groove, between the outer and inner heads of the triceps. The nerve was