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Blood transfusion

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"Blood Transfusion."

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INDEX.

Part I.

History.

The history of blood transfusion is one of the most interesting bits of medical history on record. One of the most interesting things concerning it is the way its' popularity has waxed and waned throughout the centuries.

The idea that the blood contained the vital part or the essence of life, if you please, is almost as old as life itself--at least as old as medicine. In proof of this fact one need look no farther than the Holy Bible for many references such as Psalms 72:14; "He shall redeem their soul from deceit and violence; and precious shall their blood be in His sight." There is abundant evidence of the ancient belief in the use of blood as a remedy, the idea being that the healthy blood should be used as a potion for the treatment of various ills.

"Pliny (Natural History, volume IX, Pp 498) describes the drinking of the flowing blood of gladiators in the arena, 'as if out of flowing cups;' for epilepsy. He also describes the employment of baths in human blood by the Egyptian kings as a cure for elephantiasis." (24)

In Thomas Bartholins' famous book, 'De Sanguine Vetito' published in Frankfort in 1673, there are to be found numerous references of the use of blood as a remedy. He speaks of the use of blood from cats, doves, turtles and other animals in the treatment of epilepsy and quaintly tells of a girl at Brealau,

an epileptic who, after taking cats blood, became endowed with the characteristics of a cat. Not content with climbing on the roofs of houses and imitating the manners of a cat by jumping, yowling and scratching, she would even sit by hours and look into a hole in the floor." (24).

Many of the ancient writers, including Galen who died in A.D. 201, advised the drinking of blood as a cure for various diseases such as carcinoma of the esophagus and particularly epilepsy.

It has, of course, been claimed that earlier authors made reference to transfusion of blood but it is now generally agreed that these were not reports of actual transfusion but more of the type of hemotherapy to which Galen ascribed. No really authentic records exist of a deliberate attempt at transfusion until a much later period in the evolution of medicine.

The first and earliest attempts towards a transfusion is said to have been in the year about 1492 A.D., when a Jewish physician, Abraham Meyre, attempted to transfuse blood from three small boys into the veins of Pope Innocent VIII. In this attempt the boys were bled too much and all three died and one report is that the Pope also died. Abraham Meyre disappeared from the civilized world after this unfortunate incident and no further record is to be found concerning him. There seemsto be some conflict concerning to interpretation of this incident, how-

ever, and more recent translators think that merely a draught was prepared for the Pope from the blood of the three boys. (33) and (24)

One of the earlieat references to actual transfusionof blood that has been recorded is to be found in the works of Andreas Libavius of Halle, 1546 - 1616, a native of Saxony who was professor of poetry and history at Jena in 1588. This reference is found in a published piece of his work in 1615, one year prior to his death. This seems almost incredible, however, that a transfusion should have been made before the circulation of the blood had been described and it is thought that this reference is merely ironical and there is no evidence that is was otherwise.

Harvey had been appointed physician to Saint Bartholomews' hospital in 1609 and in 1616 as Lumelian lecturer he started his theory on the circulation of blood, but not until its' publication twelve years later was his work generally known. Thus, we can say that actual transfusion on a truly scientific basis must, of necessity, date from about the years 1628 A.D.

It is not until after the middle of the seventeenth century that we find the first really authentic records. The first references to blood transfusion are found in the writings of Francesco Folli, a Florentine physician, who claims to have demonstrated to the Grand Duke, Frederick II, the art of blood transfusion on August 13, 1654. Folli at this time was only thirty-one years old and it seems hardly

plausible that so young a man would be taken for an authority at this time. He was born in 1624 and no other writers refer to his work and demonstrations.

A few years later experimental work in the same line was going on in England and under the direction of the well known genious, Sir. Christopher Wren, who has really not received the recognition due him in this connection. Dr. Wren, as he was called, was one of the most active members of the recently organized Royal Society, and was himself responsible for many new experiments in several sciences. (33) He was the first author of the noble experiment of injecting Liqours into the veins of animals. By this operation divers creatures were immediately purged, vomited, intoxicated, killed or revived accordingly to the kind of liquor injected: Hence arose many new experiments, and chiefly that of transfusing blood. (33)

Sir Christopher Wren did not actually carry out any transfusion experiments himself but suggested it to a friend of his, Richard Lower, who did his experimental work in the laboratory of Thomas Willis at Oxford..

A method of transfusing blood as described by Richard Lower is as follows: Quote-- First take up the carotidal artery of the dog or other animal, whose blood is to be transfused into another of the same, or a different kind, and separate it from the nerve of the eighth pair, and lay it bare above an inch or more. Then make a strong ligature on the

the upper part of the artery, not to be untied again: but an inch below, v.i.z. towards theheart, make another ligature of a running knot which may be loosened and fastened as there shall be occassion. Having made these two knots, draw two threads under the artery, andbetween the two ligatures; and then open the artery, and put in a quill, and tie the artery upon the quill very fast by those two threads, and stop the quill with a stick. After this make bare in the other dog, about an inch and a half long, and at each end make a ligature with a running knot, and in the space betwixt the running knots draw under the vein two threads, as in the other: Then make an incision in the vein and put into it two quills, one into the descendent part of the vein, to receive the blood from the other dog, and carry it to the heart; and the other quill put into the other part of the jugular vein (which comes from the head) out of which the second dogs own blood must run into dishes. These two quills being put in and tied fast, stop them with a stick, till there be occassion to open them.

All things being thus prepared, fasten the dogs on their sides towards one another so conveniently that the quills may go into each other. After that unstop the quill that goes down into the first dogs jugular vein, and also the other quill coming out of the other dogs artery; and by the help of two or three other quills, put into each other, according as there shall be occassion, insert them into one another. Then slip the running knots and immediately

the blood runs through the quills, as through an artery, very impetuously: And immediately, as the blood runs into the dog, unstop the other quill, coming out of the upper part of his jugular and let his own blood run out at the same time into dishes (yet not constantly, but according as you see him able to bear it) till the other dog begin to faint, and cry, and fall into convulsions, and at last die by his side.

Then take out both the quills out of the dogs jugular vein, and tie the running knot fast, and cut the vein asunder. This done, sew up the skin, and dismiss him, and the dog will leap from the table, and shake himself, and run away as if nothing had happened." (24)

Numerous other recordings of transfusions done from sheep to calves and sheep to dog and horse etc are recorded by the experimenters in the Philosophical Transactions of that time. These men by mention of name Sir Thomas Cox, Dr. Edmond King, Jean Denys etc. In some of Dr. Lowers' early experiments he reports using a silver canula to connect the two blood vessels in place of the quills aforementioned. Some of these experiments, the results of which were published in 1666 force us to give credit to Richard Lower for having performed the first transfusion of blood operation ever performed in England.

Meanwhile Sir Christopher Wrens' work became known in other countries and it is said that transfusion was performed in 1664 by Daniel of Leipsic.

Whether or not this may be the case, the first transfusion done upon a human being was certainly carried out by a French physician in France. This man was Jean Denys of Montpellier, physician to Louis XIV, and his act is admitted in the Philosophical Transactions for July 22, 1667. Of the first of his transfusions on humans he wrote as follows:-

"On the 15th of the Moneth, we hapned upon a youth aged between 15 and 16 years, who had for above two Moneths bin tormented with a contumacious and violent fever, which obliged his physitian to bleed him 20 times, in order to asswage his excessive heat.

"Before this disease, he was not observed to be of a lumpish dull spirit, his memory was happy enough, and he seemed cheerful and nimblee enough in body; but since the violence of his fever, his wit seem'd wholly sunk, his memory perfectly lost, and his body so heavy and drowsie that he was not fit for anything. I beheld him fall asleep as he sate at dinner, as he was eating his breakfast, and in all occurrences where men seem most unlikely to sleep. If he went to bed at nine of the clock in the evening, he needed to be awakened several times before he could be got to rise by nine the next morning, and passed the day in an incredible stupidity.

"I attributed all these changes to the great evacuations of blood, the physitians had been obliged to make for saving his life, and I persuaded myself that the little they had left in him was extremely

incrustated by the ardour of the fever.....accordingly my conjecture was confirmed by our opening one of his veins, for we beheld a blood so black and thick issue forth, that it could hardly form itself into a thread to fall into the porringer. We took about 3 ounces at 5 of the clock in the morning, and at the same time we brought a Lamb, whose carotis artery we had prepared out of which we immitted into the young man's veins about three times as much of its arterial blood as he had emmitted into the dish, and then having stopt the orifice of the Vein with a bolster, as is usual in other phlebotomies, we caused him to lie down on his bed, expecting the event; and as I askt him now and then how he found himself, he told me that during the operation he had felt a great heat along his arm, and since perceived himself much eased of a pain in his side, which he had gotten the evening before by falling down a pair of staires of ten steps; about ten of the clock he was minded to rise, and being I observed him cheerful enough, I didn't oppose it; and for the rest of the day he spent it with much more liveliness than ordinary; eat his meals very well and showed a clear and smiling countenance..... He grows fat visibly, and in brief is a subject of amazement to all those that know him, and dwell with him." (33)

This was truly a therapeutic transfusion and evidently proved successful. The second transfusion performed by Denys was done upon an older man and was purely experimental.

In thr succeeding number of the Philosophical Transactions, October 21, 1667, the remarks of another French experimenter, Gasper de Guyre, are quoted. These are of considerable interest in this evolutionary because it is here that one first finds records of the mixing of incompatible bloods. De Guyre affirms that an expert acquaintance of his, transfusing a great of blood into several doggs, observed always, that the Receiving Doggs pissed blood." Denys quoted similar cases and his recordings are of especial interest also because it is in his writings that the first recordings of hemolysis and attendant symptoms in man which follow the mixing of incompatible bloods are found. In this experiment the blood of a calf was used and he states:

"The patient must have received more than one whole pound. As this transfusion was large so were the effects of it quick and considerable. As soon as the blood began to enter to enter into his veins, he felt the like heat along his arm and under his arm-pits which he had felt before. His pulse rose presently, and soon after we observed a plentiful sweat all over his face. His pulse varied extremely at this instant and he complained of a great pain in his kidneys, and that he was not well in his stomack, and that he was ready to choke unless they gave him his liberty.

"Presently the pipe was taken out that conveyed the blood into his veins, and whilst we were closing

the wound, he vomited store of bacon and fat he had eaten half hour before. He found himself urged to urine, and asked to go to stooll. Hemwas soon made to lie down, and after two good hours straining to void divers liquors, which disturbed his stomack, he fell asleep about 10 a clock, and slept all that night without awakening till next morning, was Thursday, about 8 a clock. When he awakened he shewed a surprising calmness, and a great presence of mind, in expressing all the pains and a general lassitude he felt in his limbs. He made a great glass full of Urine, of a colour as black, as if it had been mixed with the soot of chimneys." (33)

Denys continued his work in Paris until he was arrested and brought before a court with the accusation of having killed one of his patients by the transfusion operation. He did, however, prove his innocence and the court acquitted him, but prohibited further experiments with human beings, except with the consent of the faculty of the University of Paris and then the operation must be performed by one of the registered physicians in the city.

Naturally many accidents and deaths resulted from this early experimentation and thus the faculty of the University of Paris and the faculties of various countries of Europe became divided in opinion and it is not surprising to find that in France transfusion of blood was pronibited by an act of the parliament.

Then further progress in transfusion surgery was haltered and brought to a standstill in almost all parts of Europe by a special edict of the Pope at Rome in the year 1678

The whole matter then fell into oblivion and the possibilities of blood transfusion were almost entirely neglected for a period of more than a hundres years before interest was again aroused in the question.

There are some isolated references in the later writings of the 18th century toward transfusion and of these only two need be mentioned. In 1792, at Eye in Suffolk, blood from two lambs was transfused, by a Dr. Russell, into a small boy suffering from hydrophobia, and he claimed that the recovery was due to the transfusion. Soon afterwards in 1796 Erasmus Darwin recommended transfusion for putrid fever, cancer of the esophagus, and in other cases of impaired nutrition. He suggested a means of performing the operation with the use of quills and catgut but never actually carried out the procedure; perhaps because of like fears of other men of that time who believed that if animal blood were put into the human body that the individual would grow horns and wool on the body.

Interest was again stirred up and revived in England by James Blundell, lecturer in physiology and midwifery at Saint Thomas's and Guy's hospitals. In 1818 he published his first paper on experiment-

al transfusion and described an apparatus devised by himself and used in his experiments.

In the opening paragraphs of Blundell's paper read February 3, 1818 he states: "A few monthe ago I was requested to visit a woman who was sinking under uterine hemorrhage. The discharge had stopped before my arrival, but her fate was decised, and notwithstanding every exertion of the medical attendants, she died in the course of two hours.

"Reflecting afterwards on this melancholy scene, for there were circumstances which gave it a peculiar interest, I could not forbear considering, that the patient might very probably have been saved by transfusion; and that,although there was little opportunity for operating in the usual manner, the vessels might have been replenished by means of the syrings with facility and promptitude. As it seemed doubtful, however, whether the blood would remain fit for animal functions after passage through the instrument, the following experiments were instituted with a view to ascertain the point; and they are now submitted to the Society, under the hope that they may contribute a little to excite the attention of the medical philosopher, and recommend a neglected operationto the experimental investigation which it deserves." (4)

Blundell's first apparatus known as Blundells "Impellor", consisted of a funnel as a receptacle for the blood, connected by a two-way tap and valves with a syringe from which the blood was injected

through a tube and cannula into the recipient.

Blundell's first work was done on animals and much was done on treating exsanguinated animals. Soon afterwards he had opportunities for treating patients and transfusing them with human blood. These results were recorded in his paper of 1824. By this time he had improved his "Impeller" and had fastened it to the back of a chair for stability.

All patients transfused by Blundell were either very ill or moribund, so his results were necessarily bad considered from a statistical viewpoint. Never-the-less he was not discouraged and stated, "His own persuasion to be that transfusion by the syringe method is a very feasible and useful operation, and that after undergoing the usual ordeal of ridicule, neglect, and opposition, it will, hereafter be admitted into general practice." (33) Blundell's work has been discussed rather in detail because it is the second signal-post in the history of transfusion. One can truthfully say that after the experimental work of the seventeenth century, the year 1818 may be taken to mark the real beginning of the clinical application of blood transfusion.

The chief difficulty now of course was the obstacle introduced by the coagulation of the blood. Bischoff in 1835 sought to overcome this by the use of defibrinated blood, and that solution of the difficulty was used by many men. It is recorded that

Sir Thomas Smith in 1873 employed defibrinated blood in the treatment of a case of melena neonatorum at St. Bartholomew's hospital. He defibrinated the blood by whipping it with an egg beater and then strained it through a hair seive and then injected the defibrinated portion into the vein of the recipient. This practice of defibrinating the blood was employed throughout the nineteenth century and even as late as 1914 a method of using defibrinated blood was described by Moss. (39) The results of all men who used the defibrination process in transfusion were about the same throughout the country. Their reports didnot indicate a remarkable degree of success. Fatalities were reported by the more honest men and symptoms were described which we now recognize as those associated with the mixing of incompatible blood. At this time however, they still clung to the idea that deaths and serious aftermaths were the result of the accidental injection of air bubbles into the circulation, although it had been definitely proven by Blundell in 1818 (4) that considerable quantities of air could be injected into the blood stream without serious consequences and that certainly that the small which might get in during a transfusion was negligible.

In 1873 an inquiry was carried out by the obstetrical Society of London into the merits of blood transfusion, the subject having been brought to the Societies attention by a report of a case by Aveling. The results do not seem to have been very encour-

aging, and transfusion was still regarded as a procedure that was only to be used in moribund cases as a measure of last resort. These are not surprising facts however when one finds reports of the use of animal blood even as late as 1875.

After the year 1875, however, there seems to be another decline in the amount of attention given to blood transfusion which lasted about 30 years. This was probably due to the increasing number of fatalities that followed the more general use of blood transfusion and partly because of the increasing popularity of the normal saline for intravenous injection in the treatment of hemorrhage.

Soon after the advent of the twentieth century transfusions received a fresh impetus which has steadily gained in force up to the present time. The use of syringes and cannulae was always hampered by the coagulation of the blood and it was definitely a great advantage to be able to perform a direct transfusion without the intervention of a tube of some sort. This was made possible by the advance in blood vessel surgery which was first due to the works of Murphy, published in 1897; they were still carried further by others, such as Carrel and Guthrie and culminated in the labors of Dr. Geo. W. Crile of Cleveland, Ohio; who in 1907 put the technic of blood transfusion on a more secure basis than it had ever been before.

The presence of agglutinins and iso-agglutinins in the blood was demonstrated in 1900 by Landsteiner and independently in the same year by Shattock. This for the first time gave a rational basis for explaining some of the fatalities previously contributed to the harmless little air bubbles. One can also say that this is the most important single discovery in relation to blood transfusion.

Jansky in 1907 showed that all human blood could be classified into 4 groups. Moss working independently confirmed Jansky's observations in 1910.

The final advance was made in 1914 when Hustin of Belgium and Lewisohn in America and others all arrived independently, but almost simultaneously, at the same conclusion. This was that sodium citrate as an anticoagulant was a safe procedure and that indirect transfusion was now a feasible operation. This idea of an anticoagulant was not a new idea for as far back as 1958 Dr. B. W. Richardson used small quantities of ammonia for the same purpose, and in 1869 Braxton Hicks used sodium phosphate as an anticoagulant in his obstetric work. The supposed toxicity of these substances prevented their use however and it is not until 1913 and 1914 that the idea experienced a rebirth and was put on a practicle basis.

"This great stride forward coincided so nearly with the beginning of the great War that it seemed almost as if a foreknowledge of the necessity for it in treating war wounds had stimulated research." (33)

During the first two years, however, blood transfusion was used very little. It was not until 1917, when the British army medical corps was being reinforced with men from the United States of America, that knowledge of blood transfusion spread through the armies. A large part of this is due to Dr. Oswald Robertson who was an important figure in introducing the citrate method.

Through the experience gained in the war a large number of operators became familiar with the various methods, and transfusion has in consequence been widely used in civilian practice since the war, and it is undoubtedly destined to figure still more largely in therapeutics of the future.

Thus, if one so desired, he might briefly summarize this historical sketch into four periods:

First: That of the early abortive, sporadic attempts, the period dating from the year 1492 with the historic transfusion carried out in order to save the life of Pope Innocent VIII, to Carrel's work on blood vessel surgery which marked a turning point.

Second: The period of "direct transfusion" beginning with Carrel's work on blood vessel surgery which later paved the way for Crile's work on transfusion.

Third: The third period is that of indirect transfusion of whole blood and dates from Lindeman's revival in 1913 of Von Ziemssen's old method. This third period is noted for the general recognition

it inagurated of the necessity for carrying out tests for hemolysis and agglutination prior to transfusion, and the development of the requisite tests. In this period along with the above work the names of Jansky and Moss stand out as pioneers.

Fourth: The fourth period is, one might say, just beginning and may well be called "The Period of Anticoagulation" or indirect transfusion with aid of anticoagulants. (3)

Part II.

Indications For Blood Transfusion.

In the earlier days, when blood transfusion was a real ordeal to accomplish, the indications were few and were practically limited to hemorrhages of the fatal type. But, with the work of Murphy, Carrel, Crile and others the technic of direct transfusion was much simplified and then in 1914-15 when indirect transfusion was put on a rational basis by the use of citrated blood the procedure has gradually risen in popularity and its usefulness has broadened enormously. At the present time it is used without an actual indication in many instances and, strictly speaking, the mere possibility of benefitting a condition by the addition of blood is considered sufficient warrant for its use.

With this preliminary, then, it seems justifiable to formulate the following list of probable indications, which is a combination of the classifications given by Keynes (33) and Ottenberg and Libman (43). Following the list each will be discussed individually.

I. Acute hemorrhage and shock.
   1. Gastric and Duodenal ulcer.
   2. Dysentery and typhoid.
   3. Ectopic pregnancy and autotransfusion.
   4. Preliminary to operation.
   5. For postoperative hemorrhage and shock.

II. For the cure of hemorrhagic diseases.
   1. Purpura hemorrhagica.
   2. Hemophilia.
   3. Hemorrhagic disease of newborn.

III. For blood diseases.
   1. Various anemias.
   2. Leukemia.

IV. For Treatment of infections.
    1. Infections with pyogenic organisms.
    2. Infections with non-pyogenic organisms.
 V. For intoxications.
    1. Acuto poisoning.
    2. Diabetic coma.
VI. For debilitated conditions.
    1. Cancer.
    2. Malnutrition.

I. Acute hemorrhage and shock.

Gastric and Duodenal Ulcer Hemorrhage.

The proper management of severe hemorrhage from the gastric or duodenal ulcer has always puzzled physicians and surgeons alike. (33) It is probably true that patients rarely die from the exsanguination of a single rapid hemorrhage, even if severe, but there is no doubt that death may result from continued or repeated hemorrhages of this type. In recent years the treatment of these cases has swung from the attention of the internist to that of the surgeon and present opinion favors early surgical intervention.

In this method of treatment in these cases the role played by blood transfusion is not minor, for by using transfusion before operation the general condition of the patient is greatly improved and thus they stand the shock of operation much better.

There has always been a fear in the minds of many men in connection with this procedure (12) for they argue that by restoring the blood volume the blood pressure is likewise raised and the hemorrhage might again be started. The fact that the introduction of new whole blood into the vascular system

decreases the bleeding time and makes a firmer clot (33) makes this fear groundless because the advantages are sufficiently gross to offset the disadvantages. Thus a transfusion tides the patient over the immediate danger period and makes surgical treatment possible.

These facts are borne out by Ottenberg and Libman (43) who report on 14 cases of duodenal and gastric hemorrhage treated by preliminary transfusion followed by surgery. Ten of these patients recovered and 2 died--not from hemorrhage but from intercurrent complications incident to surgery. Their conclusions are that frequently the fears mentioned above are responsible for physicians (and surgeons) in charge putting off transfusion too long and thus obtaining unsatisfactory results which merely give their fears new impetus, and that the real benefit comes in early transfusion followed by surgical procedures.

Dysentery and Typhoid.

Mc Clure and Dunn (40)report one case of dysentery treated by transfusion with no benefit while Ottenberg and Libman (43) report six cases where the immediate results were gratifying but there were no prolonged benefits noticed. This is probably due to the fact that patients suffering from dysentery are not anemic from hemorrhage but from nutritional disturbances and transfused blood in these cases readily meets the same fate that the original blood met. (43)

Blood transfusion for typhoid on the other hand is to combat an anemia resulting from hemorrhage and here the results are somewhat more gratifying. Ottenberg and Libman (43) report five typhoid patients all moribund at time of operation, two of which recovered and the transfusion was considered as a life saving measure. Mc Clure and Dunn (40) report four cases of typhoid upon which six transfusions were performed. Four of these were considered life saving and two were of no benefit. Quoting Libman (43) "in all typhoid cases the first appearance of blood in the stools should be an indication to make preparations so that a blood transfusion can be done, if needed, at very short notice. If the transfusion is not needed, little is lost; if it is needed invaluable time is gained. Finally, in all typhoid cases and in especially the very protracted cases of typhoid, transfusion may have life saving value and should be tried more often than it has been."

Ectopic Pregnancy and Autotransfusion.

Transfusion of blood in the early days was practically limited to the field of obstetrics and now, even though it has gained in therapeutic popularity, a large proportion of the patients that need transfusion will be encountered in the practice of obstetrics. It is a known fact, and a point of wonder, that a woman can lose large quantities of blood at the time of delivery, and immediately following, without

serious consequences, but it an equally well known fact that many deaths are occasioned each year by postpartum hemorrhage, placenta praevia, ablatio placenta and rupture of ectopic gestations.

There is perhaps no single condition to which transfusion would seem more ideally suited than to the rupture of a tubal pregnancy, and here we encounter an interesting modification of the usual routine, i.e. that of reinfusion of the patients own blood. This method of course, is applicable only to those cases where the hemorrhage has been into either the peritoneal or thoracic cavity and is consequently used in treatment of rupture of the spleen, liver and tubal pregnancy. The latter condition being much more common we find autotransfusion spoken of more often in the literature in connection with ruptured ectopics.

Autotransfusion was first employed by Thies in Germany (63) in 1914. Burch (6) in his survey of the literature on this subject states that, "since then (the year 1914) there have been 164 cases reported in European literature and only 2 in American literature." The most of the cases reported by Burch (6) were in Germany--only four being outside of that country.

The method most generally employed for this procedure is described by Mc Gee and Axford (41) in 1931 accompanied with the report of a case which

recovered without any ill effects. Their method consists merely of laparatomy and aseptically removing the blood from the peritoneal cavity and straining it through sterile gauze to remove the clots, and then adding a small amount of sodium citrate and slowly reinfusing the citrated blood into a vein in the patients arm. Burch (6) states that many men do not add citrate to the removed blood because the blood in the peritoneal cavity seems to clot very slowly. On the contrary Keynes (33) states "judging from my own experience with intraperitoneal hemorrhage, not much blood would actually be recovered in this way, since so much of it has clotted. In any case, the whole procedure is to be looked upon with suspicion owing to the unknown and probably profound changes that have taken place in partially clotted blood." Burch (6), however, published his article one year later than the date of publication of the work of Keynes (33) and states that the operation has been used by 28 European surgeons and only one advises against it. He concludes by stating:

"1. Autotransfusion is a safe procedure but it is limited in scope.

2. Sodium citrate is nonessential.

3. Extra-uterine pregnancy offers the biggest field of usefulness for this procedure.

4. Contaminated blood should not be discarded but should be used as a rectal drip.

5. Autotransfusion may occasionally be used to advantage in certain obstetrical complications such as, placenta praevia, rupture of the uterus and caesarean section."

About ten years later we find a statement made by Jacobs (27) that "autotransfusion, such as the removal of blood from the abdominal and its reinjection into the patients vein, is not practicle in this day, when donors are so readily accessible." In the conclusion of the same paper he stresses the importance of blood transfusion in obstetrics and considers radical views in this regard as consistent with good conservative practice.

Ricci and Di Palma (52) report 282 cases of ruptured ectopic gestation treated byautotransfusion, which they prefer to call autohemofusion. Twelve of the cases were their own series and 270 case reports were gathered from the German literature with a mortality rate of only 2.2% for the whole group. Their conclusions are as follows:

"1. We suggest the term autohemofusion in lieu of the ill chosen autotransfusion.

2. The procedure is of distinct value for the utilization of the free abdominal blood.

3. The red cells of the intraabdominal blood have been found to be microscopically normal as late as seventy-two hours after the time of rupture.

4. Autohemofusion is blood economy. Even for patients who are not in imminent danger, i.e., not in

urgent need of blood, the salvaging and vascularization of 300 to 500 c.c. of blood (the usual amount found) will help toward an uneventful postoperative reaction and a more rapid recovery."

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"6. Autohemofusion is a life saving therapeutic measure in the occasional ruptured ectopic with a sudden and overwhelming hemorrhage particularly when such a catastrophe occurs in a small community where the ordinary transfusion is not available within a safe margin of time."

This last conclusion quoted from Ricci and Di Palma (52) expresses the modern status of autotransfusion as it is generally accepted.

Preliminary to Operation.

This problem has been discussed in previous paragraphs and will be mentioned from time to time in following paragraphs. Suffice it here to quote from Ottenberg and Libman (43), "among some of the most satisfactory transfusions in our whole series were some of those done preliminary to operation upon patients whose desperate condition would otherwise have contra-indicated any operative procedures. There were thirty-three such preoperative transfusions and in thirteen of them the result was decisive and the patient recovered. The actual effects of such transfusions are even better than these figures show, because a majority among those that died did so as

a result of postoperative complications (such as peritonitis and pneumonia) or a continuation of the original disease (such as metastatic carcinoma). Three died of operative shock; and our experience has led us to believe that transfusion has no specific effect in preventing shock further than its effect in restoring to the patient more or less of his original power of resistance."

Postoperative Hemorrhage and Shock.

I have here elected to combine the two conditions "shock" and "hemorrhage" under one title heading and discuss them together as does Keynes (33). Keynes (33) states that shock and hemorrhage cannot be dissociated, and this is true not only because they so frequently occur together in the same patient, but also because the manifestations of the two conditions are essentially the same. In shock as in hemorrhage are found the same pallor of the face and mucus membranes, the same fall in blood pressure, rapid pulse, the same respiration, and restlessness. The symptoms following hemorrhage have often been described as presenting a "shock-like condition." As will be seen, however, it is more accurate to describe the symptoms of shock as closely resembling those of hemorrhage, and to regard both conditions as a manifestation of deficient blood or fluid content in the circulation.

Until recent years it was customary to suppose the vaso-motor centers had failed and consequently

shock was defined as "vaso-motor collapse." Various hypotheses were formulated to account for the vaso-motor failure. Each of these theories had its group of supporters but none of them were sufficiently proved to be accepted as final proof. For as Keynes (33) states"the whole theory of vaso-dilation and the idea that the patients bled to death into their own abdominal cavity or rather abdominal veins was eventually disproved at the operating tables where many patients were operated upon for major abdominal operations who were in states of extreme shock, but the accumulations of blood that was supposedly to be found there was conspicuously absent." And on the contrary Keynes (33) states that it is not at all unusual to find the opposite condition present, i.e. that of venospasm where the vein walls are collapsed and contracted. It has in addition been shown that the vaso-motor system is still active, and that the heart responds to reflex stimulation and to increase in intra-cranial pressure.

Keith (31) showed by his experimental work on blood volume on soldiers suffering from shock and hemorrhage that the symptoms of shock are due to an actual loss of circulating fluid, and the problem now resolved itself into a search for the fluid which had ceased to be a part of the effectual blood volume.

It has already been stated that there is no accumulation of blood in the veins or arteries and therefore there is only one place for it to be and

that must be in the capillaries since all of the original blood must still be present in the body. For a discussion as to whether the capillary bed is capable of becoming such a resevoir the reader is referred to the work of W. B. Cannon (12) and from this paper it becomes clear that the capillary bed is such a potential resevoir. Additional complicating features of this capillary blood in shock is the fact that there is an abnormal concentration of corpuscles in these capillaries. It was definitely proved by experiments on wounded war soldiers(33) that the number of red cells rose to as high as 8,000,000 and the arterial and venous blood remains at 5,000,000 or less.

Thus, a second factor arises; that of the blood plasma passing out into the tissues and setting up a viscious cycle, for as the stagnation increases the capillary permeability also increases. (33)

Briefly we have mentioned the fate of the lost blood in shock, but nothing has been said of the causative agents initiating capillary stasis. There are of course the predisposing factors of mental insults such as worry and anxiety, cold and pain, but these are not sufficient and it is necessary to find some other factor. It is thought that this may have been identified in a material of obscure nature which is derived from damaged muscle tissue themselves and which circulating in the blood stream is

capable of producing this capillary stagnation. Dale, Bayliss and Cannon (26) carried out experiments in investigation of this field and were able to produse shock in animals by the injection of a substance, called histamine, into their circulation; this substance having been derived from damaged muscle tissue.

Since this paper is to deal with the treatment of these various conditions and with importance of blood transfusions as applied to shock treatment we leave this here and proceed to treatment of shock. It is of course paramount in our minds after this brief discussion of cause and pathology that the matter of prime importance is to combat lowered blood pressure and lowered blood volume. Naturally all factors considered as contributary factors or causes of shock must be treated---apply heat, relieve pain and mental anxiety by morphia, remove damaged tissues etc. None of these however will be sufficient to remove the state of profound shock and it becomes necessary to treat this directly. It is essential that shock be not allowed to persist for too long a period because in so doing a permanent damage is done to the capillary walls which cannot be remedied. Our problem then resolves itself into restoring the blood volume and blood pressure by the most permanent and rapid method. Blood transfusion is naturally the most logical and hopeful means of bringing about this desired result. This is especially true where the condition is complicated by hemorrhage regardless

of the source. In fact, the state of shock and hemorhage are so nearly alike that they can hardly be distinguished from each other. It, however, is misleading to imply that blood transfusion is the only method to which shock is amenable. There are many substitutes for blood such as normal saline, gum acacia solution, Ringer's solution, Hartman's solution etc, but these are not lasting in nature and their effects are only temporary. The gum acacia solution is the best of the group and should be used where the transfusion of blood is not feasible for reason of unmatched donors etc. (33)

In regard to the relative merits of blood and gum acacia solutions one must consider which is the more important blood corpuscles or the plasma. If only plasma is needed in these cases, then, why are not gum solutions as good as blood. Keynes (33) discusses this question quite thoroughly and he is of the opinion that since there is a decrease in the volume of blood there is naturally a decreased oxygenation therefore corpuscles are needed and further he says the fact that the corpuscles and the plasma make up about equal portions of the normal blood volume indicate that the corpuscles are of equal importance where questions of restoring blood volume are considered.

In the foregoing discussion we have dealt mainly with shock and now something must be said of the particular application of blood transfusion to hem-

morhage. This question has in part been dealt with in previous topics, and in regard to traumatic hemmorhage and shock there is little to be added, for these conditions present the problem in its least complicated form. No clear cut rule can be laid down as to when a blood transfusion should be performed but the blood pressure reading is the criterion by which most men allow themselves to be governed. Cutting (12) states that even though there are exceptions to all rules it is well to remember and is generally conceded that patients will not ordinarily survive a reduction of the systolic blood pressure to 80 Mm of mercury, or the diastolic to 40 Mm for longer than an hour.

Secondary hemorrhage following operation is essentially similar to primary hemorrhage but may present a few additional points in cases where bleeding vessels are difficult to ligate, but here again blood transfusion should not be delayed for fear of prolonging the hemorrhage due to increase in blood pressure. As stated previously, Keynes (33) has found that by the addition of whole blood the coagulation time of the blood is shortened and recurrence of hemorrhage is on the whole discouraged, and in many cases a series of blood transfusions for recurrent hemorrhage has saved a patients life when the prognosis had seemed to be almost hopeless.

II. ACUTE HEMORRHAGIC DISEASES.

Of these conditions there are many classifications given. Lucas (36) gives a very detailed classification of these hemorrhagic diseases but since the etiology of all of them is unknown and we are dealing only with the importance of blood transfusion in connection with them a simpler classification better suits our needs. Minot and Lee (38) divide the hemorrhagic diseases into idiopathic purpura hemorrhagica, hemophilia and hemorrhagic disease of the newborn. This latter classification is the one to be followed in our discussion for reason of simplicity and convenience.

Idiopathic Purpura Hemorrhagica.

For a detailed discussion of pathology, etiology, diagnosis etc the reader is referred to the works of Lucas (36), and Minot and Lee (38) and Peterson (46).

In reviewing the treatment of this condition there is no specific found. Splenectomy is advocated by Lucas(36) as offering the most promising results for a permanent cure, but even this meets with utter failure in many cases. In general one may say that until the etiology of the purpuras has been demonstrated that our treatment at best can only be symptomatic. Minot and Lee (38) say that the most important treatment is to check hemorrhage and replace the blood platelets. Blood transfusion is by far the

most satisfactory method of doing this. Lucas(36) in advocating splenectomy for these cases recommends blood transfusion as a"most valuable" supporting measure, both after and before operation to diminish the post-operative hemorrhage risk. Lucas (36) recommends large transfusions in those cases too sick to warrant operation (about 10 c.c. per pound of body weight in early infancy, decreasing to about 5 c.c per pound in older children), for, "not only do these patients need blood but they also need large numbers of platlets."

Ottenberg and Libman (43) report nine cases treated by transfusion in which seven recovered and 2 died; those that died both being cases of post-partum purpura. In both of these cases the transfusions had no effect on the hemorrhages and they suggest that the pathogenesis of these cases is entirely different from that of the other cases.

Hemophilia.

Hemophilia is a definite disease entity and the diagnosis should not be made in any condition where there may be an increased tendency to bleeding. The disease is hereditary and occurs only in the male but is transmitted by the female. The condition is characterized by a greatly prolonged coagulation time resulting in an increased tendency to bleed which is so severe that any slight trauma is often sufficient to instigate a serious hemorrhage.

In discussing the treatment of this condition we must begin by stating that no cure is known. Various attempts have been made to find something which would reduce the coagulation time but there has been nothing discovered to date, which does this permanently. Lucas (36) definitely states that the only sure method of checking excessive bleeding is by the use of whole blood transfusions. Minot and Lee (38) urge the use of direct transfusion or citrated blood in indirect transfusion in preference to any defibrinated blood, serum or plasma because the clotting elements are much more abundant in whole blood and the addition of extra erythrocytes is on the average a great benefit to these "bleeders."

Blood transfusion, however, is only temporary and must be repeated again and again before any severe traumatic lesion will heal. However, even though the transfusion is only temporary in effect it is frequently a life saving procedure in this disease.

The main treatment is by way of prophylaxis in preventing trauma to these people. As a sidelight on the subject there seems to be a bright light in the use of ovarian extract for treating this condition.

Hemorrhagic Disease of the Newborn.

This is a peculiar and definite disease entity occuring in newborn infants. The diagnosis should not be made unless there is spontaneous hemorrhage during the first week of life. The hemorrhage com-

monly occurs from the 2nd to the 5th day of life and is self limiting either in death or in permanent and complete cure within a week or sooner if properly treated.

Welch (65) in 1910 was the first to demonstrate the value of human blood serum in controlling this disease. Quoting Welch (65) "drawing a conclusion from experience with thirty-two cases of hemorrhagic conditions, treated by normal human blood serum, I am convinced that this agent is a specific for this pathological condition." Welch (65) advocated using 30 c.c. three times a day until the hemorrhage stopped. Schloss and Comminsky (57) then modified this by the intramuscular injection of whole blood into the baby's buttocks. This simplified the procedure tremendously because all that was needed was a syringe and the treatment could be given anyplace.

The intramuscular injections were very satisfactory for controlling hemorrhage but this did not restore blood cells lost from the body. Therefore in severe cases for immediate results there is no better treatment than blood transfusion which is absolutely specific for this disease.

The technic of transfusion in these small babies is very often a difficult technical problem in many cases. According to Lucas (36) the most favorable site for injection varies in different babies. Many writers advise the invariable use of the longitudinal sinus while others use the jugular vein, scalp veins,

and veins of the antecubital fossa, wrist or ankle. Lucas (36) and his coworkers recommend the use of any vein which is superficial and the use of the longitudinal sinus only in those cases where they are not able to enter a peripheral vein.

According to Lucas(36) the giving of whole blood in the newborn is not wrought with the danger of hemolysis and in acute cases no attempts at grouping need be done because the danger of waiting is more serious than the giving of unmatched blood.

III. BLOOD DISEASES:

Various Anemias.

Much has been said concerning anemia under the discussions of hemorrhage and pre-and postoperative treatment. Suffice it here to say that for the treatment of anemias of acute blood loss the blood transfusion offers the best line of treatment because it not only supplies the deficient blood elements but it stimulates the blood building organs. (44)

For the anemias due to blood destruction as in infections, malaria, nutritional diseases etc. the treatment is along two lines. First remove the cause and secondly replenish the blood with new elements providing the anemia is sufficient to furnish handicap by lowered resistance and weakness. Lucas (36) is of the general opinion that blood transfusion in these cases is nothing better than palliative therapy, but transfusions in these cases may prove to be a very definite benefit in maintaining the patients

strength and improving the general condition.

Concerning primary or pernicious anemia one can do no better than quote or rather state the opinion of Ottenberg and Libman (43) published fifteen years ago. They were of the opinion that as far as blood transfusion was concerned in treating pernicious anemia it was never curative but merely a symptomatic remedy which overcome the chief symptom (the anemia) more surely than any other known remedy and that it often did more than to replenish the blood--it frequently initiated a remission (about 50% of the cases).

However, in the present day therapy of pernicious anemia blood transfusion has a very small and restricted use, i.e., that of combatting the anemia in cases where it is of very marked degree.

Leukemia.

In regard to the treatment of leukemia by blood transfusion the general opinion is that it is of no value other than combatting the anemia and prolonging life for a short while--there certainly is no curative benefits derived from such a procedure. Bernheim (3) says that blood transfusion has been used in leukemia (his cases) not with any idea of effecting a cure but rather in a hope that the condition could be changed from an acute form to the more chronic type, with a resultant prolongation of life; he also adds that he does not think that transfusion has anything to offer in the condition of leukemia.

Dutton (15) states that transfusion is necessary in leukemia merely to improve the general condition and thus gain time for the use of other therapeutic measures. Keynes (33) considers transfusion an operation not followed by good results when used in leukemic conditions.

Ottenberg and Libman (43) report nine cases of leukemias of various types treated by transfusion of whole blood. They find that transfusion is futile in all cases with the exception of the chronic lymphatic type. They consider that blood transfusion is of some definite benefit in this chronic form of lymphatic leukemia and they suggest only one transfusion preceded by a rather large venesection.

IV. FOR CURE OF INFECTIOUS DISEASES.

Infections with Pyogenic Organisms.

The value of vaccines and bactericidal sera in treating pyogenic infections is known to every medical man. Thus it comes as a natural corollary that the transfusion of immunized blood should be of benefit. Keynes (33) points out how often it was noticed during the war that transfusion greatly aided recovery from pyogenic and putrefactive organisms in wounds inflicted on the battle fields, but this apparent boast was probably more from the improvement in the general circulation rather than to any bactericidal properties of the blood. It has been definitely proven that outside of the body the blood has powers of inhibiting the growth of bacteria and

it is claimed that the best criterion for the degree of immunity is the measurement of the bactericidal properties of the blood. There is, then, as Keynes states (33), justification for attempting to combat pyogenic infection by the transfusion of immunized blood.

Hooker (25) is definitely convinced from experience in his own cases that blood transfusion is especially applicable to chronic staphalococcus septicemias and especially marked are the results where the septicemia complicates bone suppuration. He advises the taking of steps to immunize donors preparatory for transfusions in cases where acute infections have the aspects of becoming chronic.

Hayes (21) is very definite in his opinion that in ear infections with a positive blood culture a transfusion should be done immediately from a heterogeneously immunized donor and at the same time begin injections of vaccine, prepared from blood culture of patient, to immunize another donor. In ten days this donor will be immunized and immediate transfusion should again be done but this time from the autogenous immune donor. In these cases Hayes (21) says that blood transfusion maintains the proper amount of hemoglobin and red cells, secondly it acts as a supporting measure to the patient and thirdly, it overcomes the bacteremia.

Mc Lellan (42) reports a case where blood transfusion was used as a last resort to save a patient

who apparently was going the extremis route after suffering from thoracic empyema for a long period of time. There was copious discharge from the operative wound and the patient was getting weaker every day. He was given 280 c.c. of whole blood by direct method followed a week later by another transfusion of 300 c.c. From the first transfusion the patient seemed to rapidly improve and in a short time was well and back to work. In this case no previously immunized donor was used.

Schoffer and Rothman (58) report 101 cases of erysipelas in infants and children in which nineteen of them were treated by indirect transfusion of citrated blood. The mortality rate of the latter group being decidedly lower than the former, and they conclude that blood transfusion is of definite benefit in these cases.

The value of immunotransfusion in the treatment of bacterial endocarditis is a question concerning which there is a great variance of opinion. Egan (16) reports a case on which two transfusions were performed from a donor previously immunized by six injections of vaccine prepared from the patient who received the blood. From the first there was no benefit noticed but from the second there was a decided improvement. The improvement lasted for three months at which time the patient died of pneumonia. Egan (16), judging from this case, thinks that blood transfusion is of value and that

it should be used as early in the disease as possible.

Ottenberg and Libman (43) report four cases of bacterial endocarditis and from their own reports of the results obtained there were no real benefits derived from the treatment; however, they conclude that it should be tried as a means of keeping the patient alive longer and improving the general conditions.

Non-pyogenic Infections.

The application of blood transfusion to these diseases is mainly to combat an anemia and acute toxic conditions which arise. (33) (37).

V. FOR INTOXICATIONS.

Acute Poisoning.

Blood transfusion for conditions of acute poisoning will of course be of value only in those cases where the blood is particularly involved. The poisons which act in this way are carbon monoxide gas, benzol, nitrobenzol, hydrocyanic acid and possibly carbolic acid. In these cases Ottenberg and Libman (43) state that there is need of a fairly large phlebotomy and then replace the blood volume with pure blood.

Sir C. Gordon and Watson (17) report six cases of carbon monoxide poisoning two of which were treated by exsanguination transfusion, as reccommended by Ottenberg and Libman (43), with very satisfactory results and they consider the transfusion as a life saving measure.

Burmeister (7) by experimentation with animals showed that rabbits and dogs treated with coal gas to a point of near asphyxiation and then transfused without a venesection, 75% of them recovered. Of the control series, which were not transfused, nearly all died. Keynes discourages the use of transfusion in humans without a previous venesection because, as he points out there is a real danger of overtaxing the heart. Keynes (33) also urges the immediate use of blood transfusion in these cases for the chances of recovery are much better when the transfusion is done early.

Nitrobenzol poisoning is pathologically the same condition as poisoning from carbon monoxide and naturally yields to the same therapeutic measures.

In the later stages of some of the acute infestious diseases the patient falls into a state of acute toxemia. Harding (20) and Keynes (33) has drawn attention to this condition in diphtheria and the similarity between this toxemia and shock was pointed out. Blood transfusion gave more beneficial results in this than any other type of therapy.

A similar toxemia stage is seen in pneumonia occassionally and Rose and Hund (55) and Keynes (33) obtained better results in these cases when blood transfusion was employed as a therapeutic measure.

The use of blood transfusion in the treatment of the toxemias of pregnancy is a measure that is found to be most beneficial when used for the first

toxic symptoms, i.e., the pernicious vomiting of pregnancy. Quoting Dr. W. H. Taylor, lecture to seniors on "pernicious vomiting of pregnancy", Uni. of Nebraska College of Medicine, November 14, 1933, "In these cases where other mothods apparently are of no value blood transfusion seems to bring about more striking results than any other procedure. I have had occasion to use it several times and in no instance has it failed to cause cessation of the vomiting."

For the treatment of æclampsia blood transfusion was first introduced by Kimpton (33) and later it was independently suggested by Blair Bell (2). It was found that eclamptic symptoms could be produced in mice and rats by injecting placental extract and that if the extract be first mixed with normal human blood serum there was no reaction. (33) Therefore it was natural to suppose that normal human blood serum contained antibodies which rendered the toxic materials innocuous. The case reported by Blair Bell (2) is so striking in results that, although not conclusive, the procedure certainly warrants further trial in this line.

Blood transfusion has been used in the treatment of diabetes mellitus but there never was any real evidence to show that it was of benefit. Ottenberg and Libman (43) report four cases of diabetic coma on which blood transfusion was performed with no beneficial results obtained. In the present day treatment, since the advent of insulin, blood transfusion

has no part at all; at least no recent references to it are found in the literature.

VI. FOR DEBILITATED CONDITIONS.

Cancer.

It will be remembered that in the historical section of this paper that reference was made of Galen who recommended blood transfusion for carcinoma of the esophagus. Obviously blood transfusion here carries no desired features in a curative aspect, it will combat an anemia and give a little added strength to the already numbered days.

Malnutrition.

Under malnutrition one must consider the deficiency diseases because they are truly a nutritional problem.

Lowe and Cooke (35) discuss the value of blood transfusion in sprue by stating that in the later stages of sprue we get an anemia not at all unlike a pernicious anemia, and some men have even argued the same cause for both conditions. Blood transfusion here seems to stimulate the blood forming organs and their results were as good or better in those cases where pyrexia followed the transfusion.

Cole (9) reports twenty cases of pellagra treated by blood transfusion. In his cases he found no ill effects following the transfusions and reports about 60% recoveries whereas the average recovery rate is about 10 to 20% in cases where transfusion is not employed.

Part III.

Dangers of Blood Transfusion.

Blood transfusion is not an operation that is fool proof and wanting for any objections and dangers, but on the contrary it is a formidable operation and warrants the skill of the most experienced men. As Pemberton (45) says, "the procedure is very often considered only a simple intravenous medication or a minor surgical operation while in reality its potential dangers place it with the major operations."

The principal dangers associated with the transfusion of blood, according to J. Pemberton (45) are: (a) the introduction of air bubbles and blood clots as embloi, (b) acute dilatation of the heart, (c) the transmission of infection and (d) agglutination or hemolysis of the donors corpuscles. For this last group of Pembertons classification I prefer to substitute the classification of Stetson (61) and term this group the "posttransfusion reactions."

The question of air bubbles causing damage and even death was discussed in the historical presentation and by rights should be recognized as being only of historical importance. Since air in the circulatory system, to be dangerous, must be present in large quantities the probabilities for it causing any interference is indeed quite remote. As Pemberton (45) says, "today, with our simple method of transfusion (citrate method), this danger of introducing air into the circulation sufficient to produce

any ill effect can easily be avoided." He also states that by using a small calibre needle for insertion into the recipients vein and by allowing the blood to be under low pressure, the introduction of blood clots of sufficient size to produce harm can be absolutely prevented.

Most of the men who did early 20th century experimentation with blood transfusion can site at least one or two cases in which the outcome was wholly bad and death resulted from cardiac dilatation. Pemberton(45) says this is most apt to be encountered in the old and arteriosclerotic patients and in the extremely anemic where there has been myocardial damage to a greater or less degree. He also states that by limiting the quantity and rate of injection you may avoid overloading the right heart and in this way do away with the danger of acute dilatation.

The ganger of transmitting disease by transfusion is real but fortunately small. Bernheim (3) Pemberton (45) and Keynes (33) and others state that syphilis is about the only disease that need be feared with the exception of a few special cases. By the use of only Wassermann negative donors one can rest in peace, of course, remembering that the Wassermann test is a laboratory test which is quite complicated and naturally affords many chances for error, but it is by far the best method of assuring ourselves and should be used routinely on all donors.

Bernheim (3) and Keynes (33) both report transmitting malaria by transfusion. There are many other reports of unfortunate accidents such as this and certainly many accidents have happened which were not reported. These are truly unfortunate happenstances which might happen to any one and all that can be done to prevent them is more careful examination of the donors.

After all the really serious dangers in blood transfusion are those we have elected to call the pasttransfusion reactions, which include the agglutinating and hemolyzing phenomena along with other reactions which will be mentioned.

Hemolysis is much more frequently encountered and is more dangerous than is agglutination according to Bernheim(3). The cause of this phenomenon of hemolysis is totally unknown.

In human blood there are distinctly four different groups of blood and sera grouped according to their hemolyzing and agglutinating qualities (to be discussed more in detail later). Hemolysis is sometimes seen in patients after mixing of blood in the same blood group and this is explained only by the supposition that there are further divisions of the four main groups as they now are known. Hemolysis is manifest clinically by hemoglobinuria. Bernheim (3) states that there is most likely hemoglobin in the urine after every transfusion due to a breaking and damaging of the cells mechanically during the

operation. This mild degree of hemoglobinuria is neither manifest macroscopically or microscopically and is of no significance.

The grosser grades of hemoglobinuria are of definite significance and usually appear shortly after the close of the transfusion. Bernheim (3) has had the hemoglobinuria cease after the injection of 500 c.c. of normal saline in two different cases. He suggests it as a possible method of treating these cases as it is the only means through which there has ever been any improvement noted. It at least can cause no harm and is worth a trial when a case presents itself.

Prevention (be) tests prior to transfusion is, of course, the ideal and only treatment. Pemberton (45) reports twelve severe reactions out of 1032 transfusions at the Mayo clinic and in these twelve cases the bloods of patient and donor were rematched only to find in every case that there had been an error made in either the matching technic or in the recording of the blood group.

In line with the prevention of reactions one cannot forget the work and experimentation of Doan (13) who in 1926 showed that there were incompatabilities of white cells as well as red cells. Doan (13) would, by his work, have us think that all the reactions following transfusion, not accounted for by other means, were due to such white cell incompatability and lysis. His work lacks verification

by other workers but, should be considered at least until until disproved by further study.

Stetson (61) considers a group of reactions which he terms "proteolytic reactions," of which there are three types:

1. Febrile reactions with or without chills and unaccompanied by any other symptoms.
2. True protein reactions with or without chills and evidenced by the dermal reactions of erythema and urticaria.
3. Anaphylactoid.

In the first group Stetson (61) reports about 20% of all transfusions have reactions of this type. The cause of these reactions has been attributed to the protein content of the donors blood and there have been attempts to remedy this by the use of donors who have previously fasted for at least eight hours. There have been some very striking results reported from this procedure. Stetson (61) has never seen a fatality from this type of reaction and since the use of fasting donors is not practical he suggests that this be tried,not routinely, but in those cases of repeat transfusions where there were previous reactions of this type.

The true protein reactions according to Stetson (61) are encountered in about 10% of all transfusion cases and represent only those cases where there is a true dermal reaction of some sort with or without

systemic manifestations. This type of reaction in the severe form can seriously endanger the life of the individual but the administration of 10 to 15 minims of adrenalin chloride solution 1:10000 will as a rule give prompt relief from symptoms.

The third or anaphylactoid reactions are a very severe form and fortunately do not occur as frequently as the milder types. Stetson (61) says he has seen only three cases which he would place in this category. He places in this group all those reactions of a very severe type, lasting longer than the average, lacking any evidence of incompatability between the bloods of donor and recipient respectively, and lacking any skin manifestations of urticaria etc.

Ravdin (51) in 1924 brought out the idea that the chills following citrate transfusions were due to the citrate solution and recommended that operators purchase extra pure grades of sodium citrate and advised against its repeated sterilization. His conclusion was that with proper care and technic that citrate transfusions should not be followed by reactions any more frequently than is direct transfusion.

Lewisohn and Rosenthal (34) in 1933 published an article in which they quite definitely proved that with proper precautions and technic that the citrate method is the safest method for any and all transfusions. In their own hospital the incidence of reactions following transfusions was reduced from

12% to 1% and they concluded that if one or two men in a hospital did all the transfusions that the present 1% incidence of reactions could be erased.

The dangers of blood transfusion are quite numerous but fortunately they may in the most part be prevented by careful technicians and careful operating technic.

Part IV.

Physiology and Pathology of Blood Groups.

The fact that there are groups in human sera is well known but the reason why one individual should have blood which falls into group 1 of the classification and why another, maybe of the same family, should be in group 3 or 4 is unknown. Concerning this subject much has been written and much is still to be written.

Landsteiner in 1901 discovered that a destructive action was exerted upon blood of certain individuals by that of certain other individuals. Jansky in 1907 and Moss three years later very closely investigated this matter and the practical outcome of this was the grouping of all human individuals into four groups whose blood shows distinctive interactions. (33)

It was found that an agglutinative reaction first occurs, and is sometimes followed by hemolysis; and for this reason the clinical examination of blood prior to transfusions is directed solely to the presence or absence of agglutination. The reactions depend upon two factors, oneresiding in the serum and the other in the corpuscles, termed agglutinins and iso-agglutinins respectively. (67)

Jansky's classification as published by him in 1907 is as follows:

Group I. Serum agglutinates the corpuscles of groups II, III, and IV. Corpuscles not agglutinated by any serum.

Group II. Serum agglutinates the corpuscles of groups III and IV, but not those of I and II. The corpuscles are agglutinated by by sera of groups I and III, but not by those of groups II and IV.

Group III. Serum agglutinates the corpuscles of groups II and IV, but not of I and III. Corpuscles agglutinated by sera of groups I and II, but not by those of III and IV.

Group IV. Serum does not agglutinate the corpuscles of any group. Corpuscles are agglutinated by the sera of groups I, II and III.

Moss's classification in 1909 and 1910 was similar to Jansky's but he reversed groups I and IV leaving II and III the same as they were. Moss suggested this change because he found that there were by far more people in group IV (Jansky) than there was in group I (Jansky), thus thinking it better to have the larger group named group I he suggested this change.

Jansky's classification being in an obscure and inaccessible publication, Moss's work became the standard for group classification in America and other English speaking countries. Jansky's classification, however, was being followed by a sufficiently large following to result in dangerous confusion in many instances and in recognition of this fact a committee in America (28) met in 1921 and recommended that the Jansky classification be universally adopted by reason of priority. This recom-

mendation was not followed however, and in order to obviate the confusion still existing from the reversal of groups I and IV in the two classifications, a new system of nomenclature has been suggested.

Snyder (59) gives this classification but does not claim to be the originator. The grouping in the new method is based on the agglutinophyllic capacity of the cells. In this grouping Jansky's group IV is known as AB, having agglutinogens A and B. Group III becomes B having agglutinogen B. Group II is known as A and group I having neither agglutinogen is known as group O. This is the best classification and if universally adopted would eliminate all confusion.

The question as to whether the blood groups are established at birth or not has been discussed considerably on both sides. Happ (26) in 1920 in a very carefully worked out series of studies concludes the following:

1. "The agglutination reaction of 131 infants and children from birth to 10½ years was examined by testing their sera and washed corpuscles microscopically against the sera and corpuscles of each of the four adult groups."

2. "The grouping as present in adults is rarely present in blood from the umbilical cord."

3. "At birth and during the first month of life isoagglutination is rarely present, but the percentage of infants in whom the isoagglutination

group is established increases with age, so that after 1 year the group is usually established, and after two years is always established as in adults".

4. "The grouping is established in the corpuscles before it is established in the serum. Therefore group I is the first to be formed and group IV is the last."

5. "The early grouping in the corpuscles is apt to change by the acquisition of new receptors before the group is established."

6. "When grouping has been established in both serum and corpuscles it does not change."

7. Isoagglutinins are present in mothers milk and the grouping is identical with that in the mothers blood. These agglutinins are probably not transmitted to the nursing infant through the milk."

8. "On account of the differences between the agglutinating reactions in the blood of the mother and the child it is not safe to transfuse an infant with its mothers blood without making the preliminary tests."

Snyder (59) and most other authorities agree with Happ (26) in his opinion that the group is permanent when once established. If this were not true our common practise of having catalogued donors is sadly in error.

Part V.

The Donor.

The choice of a donor is one of the most important preoperative safeguards of blood transfusion. This, after finding persons who are willing to give their blood, involves attention to the physical, physiological, pathological and even psychological qualities of these individuals as well as the careful laboratory routine of blood examination, including grouping and direct matching tests.

In the larger centers where there is a larger demand for donors there have sprung up a group of professional donors. There are already considerable numbers of these professionals and they have even gone so far as to form a trade union so that as high a fee as possible may be obtained from those who are in the need of blood. (33)

The professional donors are always men and they have their blood type on record in all the hospitals in the city in which they reside as well as in many doctors offices so that as soon as the need for a blood transfusion is apparent the only thing the hospital need do is to look up and call those whose blood falls in the particular group needed.

The donors, whether professional or "ameteur", should be viewed with a scrutinizing eye along the lines previously mentioned. According to Keynes (33) the most satisfactory individuals for donors are

young men between the ages of eighteen and twenty-five, because the younger the donor the less likely he is to be suffering from some of the diseases mentioned previously, and the more rapidly will he gain back his red cell count. The donor should naturally be strong physically and free from any pathological process. The element of fear is a big factor in after effects in the donor and for this reason professional donors are superior.

Part VI.

Technic.

Some references to methods and technic of blood transfusion have already been made in the historical sketch and if the reader will recall the early operators, owing to the difficulties introduced by the coagulation of the blood outside of the body, were constrained to make use of some method of direct transfusion. But, since the advent of sodium citrate as an anticoagulant, the direct transfusion method has decidedly waned in popularity.

There are many methods and technics advocated in the literature by various authors, (39), (15), (33), (59), (5) and (14), but for this paper the methods and technic used at University Hospital, Omaha, Nebr. will be described.

For the direct method of transfusion the Scannell apparatus and technic is used. Scannell (56) states that blood transfusion is wrongly termed direct transfusion when apparatus such as he devised is used. He suggests that the term'whole blood' be used to differentiate modified from unmodified blood. Only those transfusions where the cut end of a recipients vein is in contact with the cut end of a donors blood vessel is it proper to call direct transfusions according to Scannell. (56) This method of classifying blood transfusion is not generally followed, however, and for our purpose we will consider the Scannell apparatus and technic as the direct transfusion method.

Scannell's apparatus and technic as described by him in the Long Island medical Journal for May 1926 is a simple and practical method. The advantages are its simplicity of operation and safety.

The apparatus consists of a three-way valve which is not automatic but is easily operated by the thumb. The valwe may be described as a precision three-way unit with all connections being of a locking type. One tube leads to donor, one to the recipient and the other, middle tube, leads to a basin of sterile normal saline. The valve is so constructed that only one line can be open at a time. The salt solution is present to draw into tubes to begin and thus replace all air and is always present to permit washing at any time during the operation.

The syringe is a 20 c.c. specially constructed type of syringe with a patent locking device for attaching three-way valve unit.

The needles and cannulas are varied in sizes for patients of all ages.

The rubber tubing should be pure gum rubber of about the size of a No. 18 F. catheter. "It is very necessary to wash carefully the inside of new rubber tubing before using." (56)

There are three adapters in the outfit so that any syringe or any needle may be used with the apparatus in case of emergency merely by the use of an adapter.

The technic of the operation as given by Scannell is as follows:-

A. Preparation of apparatus.

1. Tubing, needles and syringes mat be wrapped in gauze and boiled, or they may be dry sterilized in an autoclave and kept ready for instant use.

2. To insure easy and free action of the glass syringe, it should be absolutely clean, and the piston and inner side of the barrel should be lubricated with pure, clean, sterile vaseline.

3. The apparatus is then assembled, the tube with the sinker being placed in the middle, and all the air expelled by filling the valve and the tubes with normal saline solution.

B. Preparation of Donor and Recipient:

1.Both are dressed as for a major surgical operation with no underwear or sleeved gowns.

2. The donor and the recipient should accupy operating tables or beds of the same height. A small stand, covered with a sterile towel, is placed under their arms and between the tables or beds.

C. Inserting Cannulas or Needles--Connecting Apparatus

1. Place rubber tourniquet with a patent buckle around the arm of the donor to the tightness of 60 Mm of mercury (this pressure may also be maintained by the arm band of a blood pressure manometer) and after the veins distend, inject a few drops of procain ½% at the site of puncture and insert the needle into the vein that is most prominent, pointing it

towards the hand. (Do not connect apparatus until blood spurts freely from this vein). Next connect one of the side tubes coming from the valve to this needle and loosen the tourniquet around the arm. Draw up 10 c.c. of salt solution and inject it into the vein of the donor, in order to make sure that the point of the needle is resting wholly within the vein.

3. Place another tourniquet around the arm of the patient (recipient), and after the veins distend inject a few drops of procain ½% at the site of puncture of the most prominent vein and insert a needle or cannula pointing it toward the shoulder. Remove tourniquet and inject 10 c.c. of salt solution into the recipient. Next connect the tube opposite to the one going to the donor.

3. Tighten the tourniquet again around the donor's arm and begin the transfusion.

D. Transfusion:

1. Hold the syringe in the left hand in such a way that the valve handle can be turned readily by the thumb of left hand.

2. Turn the valve handle until arrow points to donor-inlet; then with slight traction on the syringe it should fill.

3. After the syringe is filled with blood, turn valve handle in opposite direction until arrow points to recipient outlet, and empty, Then push the valve handle to donor inlet and repeat these movements.

until the desired amount of blood has been transfused. Never spray ether on the syringe during the transfusion.

4. If, after 300 c.c. or 400 c.c. of blood have been transfused, the piston begins to stick, turn valve-handle until arrow points to outlet to basin of salt solution, and wash the syringe out quickly two or three times; then proceed as before.

5. If for any reason a delay is necessary in the middle of the transfusion fill the apparatus with salt solution through the central tube to prevent clotting in the tubes and needles, during the delay.

6. If more than 500 c.c. of blood have been removed from a donor, remove tourniquet from his arm and inject 500 c.c. of Ringer's solution or salt solution. The middle tube is used in this procedure.

7. At the conclusion of the transfusion, wash and clean the apparatus at once.

8. Anyone who expects to do blood transfusions successfully should not only own, but also take personal care of his apparatus. This includes the sharpening of needles after each transfusion."

The indirect method of transfusion has been practically reduced to the various methods and modifications of the citrate method. Again the technic herein described is the one used at the University of Nebraska Hospital, Omaha, Nebraska.

The advantages of the citrate method are many

and in the minds of a large number of operators, by far outweigh the disadvantages. (8), (10), (14), (30), (34), (49) and (67). Citrate methods have simplified the technic to such a point that any physician with a knowledge of intravenous therapy can perform the operation satisfactorily, but, as stated previously, if performed by experienced operators it is much more satisfactory.

The apparatus required for an indirect transfusion consists merely of the intravenous therapy apparatus plus a large guage needle for letting blood from the donor's vein.

The donor's arm is prepared as for a major surgical operation and the tourniquet is applied. A large needle (10 to 14 guage) is inserted into a prominent elbow vein. The blood is then permitted to flow into a glass receptacle containing a 2.5% solution of sodium citrate (50 c.c. of the citrate solution for 450 c.c. of blood). If a large vein is available it makes no difference whether the needle points toward the hand or shoulder. Gentle stirring with a sterile glass rod will mix the blood and citrate so that no clotting will occur. After the desired amount of blood has been obtained the donors part is complete but he should lie on his back for an hour after after the blood letting is finished.

The vessel containing the citrated blood is kept warm by means of a water bath until the recipient is prepared. In entering the recipients vein

the needle is pointed towards the head. To obviate the danger of injecting small blood clots a smaller needle is used for the infusion. For the actual infusion the intravenous therapy setup is the apparatus used.

A choice of the two methods of transfusion is left up to the individual operator and the success of the operation depends upon the skill and technic of the operator and the care taken to properly execute the necessary preparatory measures.

CONCLUSION.

In concluding this thesis on "Blood Transfusion" I wish to briefly survey the more important features and in this manner arrive at a general conclusion concerning the procedure.

In the first part of the paper the history was briefly presented. The interesting feature in the history is the manner in which the popularity of blood transfusion, as a therapeutic measure, has waxed and waned throughout the years. At the present time we are in a period heightened popularity.

In the second part the indications for blood transfusions were considered. It is questionable if there is any pathological condition to which the human body may submit for which blood transfusion has not been tried as a therapeutic measure. In general we can say that the greatest benefits from blood transfusion are found in those conditions where there is blood loss or where there is actual hemorrhage.

Part three considers the dangers of blood transfusion. Suffice it to say that there are certain inherent dangers in the procedure but that by proper care and technic these can largely be aleviated entirely.

Part four discusses the physiology and pathology of the blood groups. It is only necessary

here to state the importance of the blood groups and to stress the importance of using one classification of the blood groups. The grouping as recommended by Snyder (59) is the most logical and fool proof.

Part five presents the problems of choosing a donor. The success of the transfusion is greatly dependent on the donor.

Part six in taking up the technic presents only two methods both of which are in use at the University Hospital at Omaha, Nebraska at the present time. The method used is a matter of choice with the individual operator and one method is quite as successful as the other at this hospital.

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