Then, because in the human case the toxic symptoms had appeared only after a second injection, repeated after five days interval, the first experiment (100 c.c. dose) was repeated on the same dog after five days, but again without hemoglobinuria.

In the next dog a relatively double dose, 224 c.c. (3.2 per cent.), was given during fifteen minutes. Five minutes after the injection was stopped, the urine appearing in the catheter was still yellow and free from hemoglobin; eight minutes later it suddenly changed to a dark claret color, which persisted for more than four and less than sixteen hours. The same results were obtained by repeating the experiment five days later, tending to show that no relative increased or decreased resistance of the blood had thus far been developed. Subsequent experiments seemed to show that the toleration limit in dogs and rabbits was near 2.5 per cent. of body-weight, when the water was injected during a period of from five to fifteen minutes; but in two other experiments, designed to determine whether larger amounts might be given without hemoglobinuria if the injection extended over longer periods of time, bloody urine appeared when less than 2 per cent. of the body-weight had been introduced (once at the end of 13 minutes when 1.9 per cent. had been injected, and once after forty-five minutes when 1.8 per cent. had been injected). It appears, therefore, that considerable individual variation exists, for in contrast to these results we have two earlier experiments in which 2.1 per cent. and 2.6 per cent. failed to give hemoglobinuria.

It was found that much smaller amounts of distilled water would give a transient though distinct hemoglobinemia, without hemoglobinuria. In Dog 2, above mentioned, 0.8 per cent. of body-weight of distilled water sufficed to give a distinct hemoglobinemia by the method described, although before the experiment, as in every case, the serum was absolutely clear. Experiments on Dogs 13 and 15 showed that (disregarding individual idiosyncrasy) the limit at which noticeable hemoglobinemia appear was between 0.4 and 0.6 per cent. of body-weight.

In the few blood examinations made, no anemia was noted, the only change being a decrease in the resistance of the red cells (especially in minimal resistance; that is, some hemolysis occurred in relatively stronger hypotonic salt solution). For instance, with Dog 7, whereas before the injection, complete hemolysis occurred in 0.4 per cent. sodium chlorid; partial in from 0.425 to 0.5 per cent., and no hemolysis at 0.525 per cent., one hour after injection of distilled water, complete hemolysis occurred at 0.425 per cent.; partial at from 0.45 to 0.55, and none at 0.6 per cent. These changes were still present after twenty-four hours.

The same toleration limit for hemoglobinuria, roughly speaking, was found to exist for the rabbit. Another experiment showed that, contrary to Ilkewitsch's statement, as much as 8 per cent. of body-weight might not cause death.

A consideration of the results of these experiments shows that although amounts of distilled water necessary to produce hemoglobinuria in the dog are larger than are apt to be used clinically (2.5 per cent. of 80 kg. being 2 liters), nevertheless the smaller amounts produce an undesirable hemoglobinemia. Also other factors, as lowered resistance or individual idiosyncrasy, might with even smaller amounts produce bad results. Furthermore, although these experiments show

fairly definite levels for the appearance of hemoglobinuria in dogs, it may well be that in man, as in the case above mentioned, these levels are considerably lower.

On account of the constantly growing number of diagnostic and therapeutic measures in which intravenous infusion is used, it is therefore important that clinicians should bear in mind the possibility of causing hemoglobinemia or hemoglobinuria by the use of fluids which are not rendered isotonic by the addition of the particular salt used.

CONCLUSIONS

1. Rapid intravenous injection of distilled water, in amounts equal to from 2 to 3 per cent. of the body-weight or more, will cause in the dog transient hemoglobinuria and albuminuria.
2. Lengthening the duration of injection time from five to forty-five minutes is without noticeable effect, though a much slower injection might give different results.
3. Hemoglobin-stained urine usually appears in the bladder catheter in from twenty-five to thirty minutes after the beginning of the injection. The hemoglobinuria lasts approximately from four to sixteen hours, depending on the severity of hemolysis.
4. Much smaller amounts (as low as from 0.4 to 0.6 per cent.) are sufficient to cause a noticeable hemoglobinemia without hemoglobinuria.
5. Hemoglobinemia appears within from two to four minutes after the beginning of the injection and may last twenty-four hours.
6. In doses that just fail to cause hemoglobinuria, albumin and bile may appear in the urine the next day.
7. No noticeable anemia is caused, but there is a temporary decrease in the minimal resistance of the red blood-cells.

Chestnut Hill.

BLOOD TRANSFUSION

REPORT OF ONE HUNDRED AND THIRTY-FIVE TRANSFUSIONS BY THE SYRINGE-CANNULA SYSTEM*

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The purpose of this paper is to report some of the results of blood transfusion by the syringe-cannula system, in the cases referred to me from time to time. Limitations of space will not permit of a thesis on the scientific aspects of the subject and the many correlated problems, a discussion of the numerous theoretical considerations involved, or full case-reports and blood and hemoglobin records. These are reserved for a later publication.

The cases transfused vary considerably and include the diseases enumerated in Table 1. The ages of the patients are given in Table 2.

In no case was there thrombosis, embolism or sepsis; in no case was a skin incision made; in no case was anesthesia given; in no case was death due to any untoward effects of transfusion.

Post-mortem examinations were made in two cases several weeks after transfusion. Veins punctured were examined by Dr. Charles Norris, director of laboratories of Bellevue and Allied Hospitals, who could find no

* Read before the Clinical Congress of Surgeons of North America, Nov. 11, 1913.

evidence of the puncture. These venous puncture-wounds heal by first intention, and no thrombosis occurs at the site of puncture.

CANNULA INSERTIONS

In the total number of transfusions there were over 243 cannula insertions into veins, a summary of which is given in Table 3.

TABLE 1.—DISEASES IN WHICH BLOOD WAS TRANSFUSED

Diseases	No. of Cases	No. of Transfusions in Each Case	Unimproved
Pernicious anemia (total of 19 cases)	8	1	4
	6	2	3
	2	3	1
	2	4	0
	1	6	0
Aplastic anemia	2	3	2
Splenic anemia with hematemesis	1	5	0
	1	1	0
Anemia (unknown cause)	1	3	0
	2	1	0
Chlorosis	1	1	0
Hemophilia	1	3	0
Hemophilia	1	1	0
Purpura hemorrhagica	1	1	0
	1	2	1
Hemorrhage	4	1	0
Typhoid with hemorrhage (extreme)	2	1	1
Typhoid with hemorrhage (extreme)	1	2	1
Gastric ulcer with hemorrhage	4	1	1
	2	2	0
Gastric ulcer with peritonitis	1	1	1
Hemorrhoids and secondary anemia	2	1	0
Carcinoma	1	2	0
Sarcoma	1	1	1
Diphtheria, septic petechiae	1	1	1
Tonsillitis with petechiae and anemia	1	2	0
Bronchopneumonia	2	1	2
Tuberculosis of lungs	4	1	3
Acute endocarditis	1	2	0
Chronic endocarditis	2	1	0
Sepsis	5	1	1
	1	6	0
Typhoid (septic type)	2	1	2
Postoperative nephrectomy	1	1	0
Postoperative cholecystotomy and hemorrhage	1	3	0
Cirrhosis of liver and secondary anemia	1	1	0
Still's disease with anemia	1	2	0
Acute intestinal intoxication	1	1	1
Malnutrition	9	1	4
Acute lymphatic leukemia	1	1	1
Acute destructive myeloid type of leukemia with pernicious anemia	1	1	1

TABLE 2.—AGES

Ages	No. of Cases	Ages	No. of Cases
Under 6 months	7	From 20 to 30 years	12
From 6 to 12 months	6	From 30 to 40 years	12
From 1 to 2 years	4	From 40 to 50 years	7
From 2 to 5 years	4	From 50 to 60 years	6
From 5 to 10 years	4	From 60 to 70 years	5
From 10 to 20 years	12	From 70 to 80 years	1

The youngest patient transfused was 6 weeks old: weight 6 pounds, 6 ounces. The oldest patient transfused was 73 years old.

TABLE 3.—CANNULA INSERTIONS INTO VEINS

No. of Insertions	Puncture on Which Vein was Entered
	MEDIAN BASILIC VEIN
208	First
7	Second
1	Third
2	Fourth
	EXTERNAL JUGULAR VEIN
15	First
9	Second
1	Fourth

In one case six transfusions were performed at different intervals of time, using the same vein through the same skin-puncture in each operation. Donor McM. was used for eight transfusions at different intervals of time; the cannula was inserted into the same vein through the same skin-puncture on each occasion.

I have described the technic of the work in a previous article.¹

1. Lindeman, Edward: Simple Syringe Transfusion with Special Cannulas, Am. Jour. Dis. Child., July, 1913, p. 28.

QUANTITY OR DOSAGE

Judgment of the amount of blood to be transfused will depend on the size, weight, age, physical condition of the patient; the type of disease to be treated, the object to be gained by transfusion, the presence of other complications, and, lastly, experience. The largest amount I have transfused into one person in one sitting is 2,000 c.c. This quantity was taken from two donors.

DONORS

The quantity of blood that can be drawn from a donor varies. The largest quantity I have taken from one person in one sitting is 1,400 c.c. This man was 5 feet 8 inches in height and weighed 170 pounds. I have frequently taken from 900 to 1,000 c.c. in one sitting, as shown in Table 4.

TABLE 4.—QUANTITIES OF BLOOD TAKEN FROM SOME OF THE DONORS IN A GIVEN LENGTH OF TIME AND NUMBER OF SITTINGS

Donor	Quantity, c.c.	Number of Sitzings	Number of Days
T.	1,200	2	5
J.	2,000	3	5
Sister	1,560	3	6
S.	2,240	2	7
Husband	1,660	2	9
McE.	2,650	3	18
M.	1,500	2	14
Father	1,660	6	41
S.	1,150	1	1
J.	1,550	2	7
McM.	3,000	8	150
McG.	2,150	5	42
C.	2,080	5	28
A. C.	2,340	3	21
W. C.	1,000	2	14
Brother	820	1	1
D.	1,860	2	120
D.	1,260	1	1
J.	2,160	3	6
Mother	2,000	2	3
G.	1,600	2	6
Brother	1,200	1	1
Wife	900	1	1

If the case is not one of infectious disease, two-thirds of the amount of blood drawn from the donor is replaced with normal saline solution through the cannula with which the transfusion is performed. When infection is present the same cannula is not used.

TABLE 5.—REACTION TO TRANSFUSION

Donor	Transfusions	Chills	Temperature
Father	17	1	1 case, 104. 1 case, 104.8. 1 case, 101. 2 cases, Increase of 2.
Mother	15	*	1 case, 100.2. 1 case, 100. 1 case, 104. 1 case, 102. 1 case, 104.
Brother	7	1	1 case, 102. 1 case, 104.
Sister	4	†1	1 case, 102.
Grandfather	1	*	No rise.
Aunt	1	*	No rise.
Son	1	1	102.
Allen	62	22	4 cases, 104-105. 10 cases, 102-104. 12 cases, 100-102. 6 cases, 99-100. 30 cases, No rise.

* None. † Slight.

The recuperative power of a healthy donor is quite remarkable. My records on this phase of the subject are still too meager for publication, but from observations thus far made I am convinced that the recuperative power is greater after the first transfusion and gradually less rapid in the succeeding transfusions. Furthermore, after successive bleedings, while the blood-picture may be normal, there may be a little loss of tissue-weight. The loss of weight in all probability is a compensatory process. I hope at a later date to submit a series of observations now being made on this subject.

If at any time the blood-pressure in the donor should fall so that blood is withdrawn with great difficulty, it is an indication that no more blood can be spared at that time. This it will be found will vary; and when there is considerable psychic disturbance the pressure will fall more readily.

REACTION TO TRANSFUSION

It is quite obvious from Table 5 that the reaction from a blood relative in most instances is less than from an alien; yet the blood of many aliens may be fully as congenial as family blood. Of sixty-two transfusions in which alien blood was used chills occurred in twenty-two instances, and a rise of temperature in twenty-six. Hence, practically in 50 per cent. of the cases in which alien blood was used the mixture proved as good as family blood. In the remaining 50 per cent. of the cases no untoward effects occurred in any but three cases, save the chill and temperature reactions; but in three cases hemolysis occurred from which patients

in only a few cases are liable to disregard them or attach little importance to them, the few cases probably not including a pair of incompatible serums.

My view has always been that unless the serologic report is respected, even when slight reactions are obtained, it is useless to perform the tests. Laboratory work, unless done well, is worthless. It should be remembered, however, that laboratory methods have their limitations even when done well, and only by constant vigilance can untoward effects be avoided.

In one case the laboratory reported hemolytic tests as negative, but a hemolysis was detected clinically when the patient had received 75 c.c. The transfusion was immediately discontinued. The reaction was only slight and the patient recovered. The hemolytic tests were again made by another serologist who reported as follows:

Recipient cells + donor serum = no hemolysis.
Donor cells + recipient serum = slight hemolysis.
Control, no hemolysis.

TABLE 6.—RECORDS OF TEN CASES OF TRANSFUSION

Case No.	Age, Yrs.	Sex	Diagnosis	Date of Transfusion	Quantity Transfused	Blood		Remarks
1	16	♀	Anemia; cause unknown.	4/22 4/27 5/7	500 750 500	R. B. C., 1,400,000 Hb., 15 per cent.	5/12 5,700,000 55 per cent.	12/1. Condition excellent.
2	40	♂	Hemorrhage; traumatic.	5/4	1,200			Complete recovery. Discharged from hospital in two weeks.
3	34	♂	Gastric ulcer with hemorrhage.	7/15	820			Operation after transfusion. Discharged cured on 35th day.
4	34	♀	Postoperative nephrectomy.	8/7	1,000	R. B. C., 2,332,000 Hb., 43 per cent.	7/24 4,096,000 65 per cent.	8/28. Discharged cured.
5	34	♀	Cirrhosis of liver.	8/26	960	R. B. C., 2,960,000 Hb., 50 per cent.	8/8 5,600,000 80 per cent.	
6	34	♀	Pernicious anemia.	9/12 9/21	760 900	R. B. C., 1,448,000 Hb., 16 per cent.	9/26 4,090,000 77 per cent.	Much improved.
7	29	♀	Post-partum hemorrhage and sepsis.	8/31	1,320	R. B. C., 900,000 Hb., 25 per cent.	10/20 4,000,000 75 per cent.	11/1. Discharged much improved.
8	3	♂	Anemia; cause unknown.	9/18	250	R. B. C., 1,000,000 Hb., 20 per cent.	9/11 2,448,000 64 per cent.	10/10. Patient reports to-day. Health excellent.
9	47	♂	Gastric Hemorrh.; pleurisy with effusion; consolidation rt. lower base.	12/23 1/2	800 800	R. B. C., 3,008,000 Hb., 40 per cent.	9/23 4,600,000 71 per cent.	9/26. Discharged from hospital. Condition excellent.
10	28	♀	Gastric ulcer; hemorrhage.	7/26 8/21	600 600	R. B. C., 1,780,000 Hb., 26 per cent.	1/9 3,200,000 70 per cent.	1/15. Patient goes out daily. Cured.
						R. B. C., 950,000	8/29 5,760,000	8/31. Discharged from hospital. Cured.

* In this column ♂ denotes male and ♀ female.

recovered. (It should be borne in mind, however, that hemolysis can occur with family blood.)

Providing the same donor be used, there is frequently no reaction after the second and succeeding transfusions; and if any reaction occurs it is usually very mild.

A given donor of alien blood will cause a chill and a fever in one patient and none in another, though the transfusions be done on the same day and both patients have the same disease and the same quantity of blood be given.

The chill and temperature reactions may be associated with a slight degree of hemolysis incident to serum reaction. I have occasionally observed such hemolysis in a few cases evident only by a slight jaundice-tint disappearing within twenty-four hours. In such cases in the succeeding transfusions, the same donor being used, this tint is less or absent.

BLOOD-TESTS

It is customary before transfusion to make preliminary blood-tests, namely, the Wassermann, hemolytic and agglutinin tests. The question I am constantly asked is whether these tests are reliable and really worth while. I think that some who have had an experience

In a second case, in the first transfusion there was no hemolysis and the tests were negative. In the second transfusion, five days following, the same donor was used; hence no preliminary tests were made. A hemolysis occurred; the patient showed a characteristic reaction clinically and hemoglobin appeared in the urine. Hemolytic tests were then made which showed hemolysis of donor's cells by patient's serum. The patient recovered.

In a third case the hemolytic tests were reported as negative, yet the patient hemolyzed the donor's corpuscles. Opportunity was not afforded to check up the accuracy of the laboratory work; therefore, judgment in this case must be suspended. This patient also recovered.

In the large number of donors tested a certain number of incompatibilities were discovered, and these were eliminated. Only once did the laboratory fail, namely, in the case just cited.

In the actual performance of the work I introduce a small quantity of blood and then pause for a short period of time before continuing transfusion. Opportunity is thus offered for observing the compatibility of the blood introduced. Should an undesirable reaction

ever occur indicative of incompatibility, transfusion is discontinued; no harm is done and another donor is procured. Herein lies a factor of safety in this method which is of not a little importance.

The following case-report may illustrate, in a measure, how the method may be applied, and Table 6, containing the records of a few of the cases transfused, speaks for the value of the method.

There is little necessity for me to discuss the results, as "one who runs, sees."

REPORT OF CASE

D. V., man, aged 21, was admitted to the service of Dr. Frank S. Meara, Second Medical Division, Bellevue Hospital, April 16, 1913, with splenic anemia (large spleen with hemorrhages from bowel and stomach). The Wassermann reaction was positive.

November 18: Splenectomy was performed by Dr. John A. Hartwell. At operation the liver was found nodular. According to the pathologic report of the spleen there were chronic interstitial splenitis and chronic passive congestion.

April 18: Coagulation-time, twelve minutes.

April 19: From Donor T., 500 c.c. of blood were transfused into the median basilic vein. There were no chills and no rise in temperature after transfusion.

	April 17	April 20	April 22
R. B. C.....	1,700,000	2,400,000	1,800,000
Hb.....	20 per cent.		

April 23: Second transfusion; 700 c.c. of blood were transfused from Donor T.

	April 24	April 26
R. B. C.....	2,300,000	1,664,000

There were no chills and no rise of temperature after transfusion.

April 24: Coagulation-time, ten minutes.

April 26: Third transfusion; 750 c.c. of blood were transfused from Donor J. There were no chills and no rise in temperature after transfusion.

April 28: R. B. C., 2,550,000; coagulation-time, 6 minutes.

May 1: R. B. C., 1,992,000; coagulation-time, 6 minutes. Wassermann reaction on all donors negative.

NOTE: May 1, patient's disease seemed to destroy the blood-elements; but transfusion made him stronger, decreased the coagulation-time, and all hemorrhages by bowel ceased.

May 5: Wassermann reaction positive.

May 10: Neosalvarsan, 0.45 gm.

May 12: Mercuric salicylate biweekly.

May 19: Neosalvarsan, 0.9 gm.

May 28: Neosalvarsan, 0.45 gm.

June 22: R. B. C., 4,312,000; Hb., 65 per cent. Patient was discharged from hospital, improved; the size of the spleen was unchanged.

October 1: Patient was again admitted to the hospital on account of hemorrhage.

October 12: R. B. C., 4,496,000; Hb., 75 per cent.

October 21: Patient vomited half a basin of blood and passed blood by bowel.

October 27: Fourth transfusion; 740 c.c. of blood were transfused from Donor W. C.

	Before transfusion	After transfusion
R. B. C.....	1,664,000	2,352,000
Hb.....	18 per cent.	29 per cent.

There was a rise in temperature to 104 after transfusion and a decline to normal next day. There were no chills.

November 10: Fifth transfusion; 930 c.c. of blood were transfused from Donor A. C. (brother of Donor used October 27).

	November 8	November 10
R. B. C.....	2,400,000	3,700,000
Hb.....	34 per cent.	39 per cent.

There were no chills and no rise of temperature after transfusion.

November 12: R. B. C., 4,080,000; Hb., 45 per cent.

November 18: Splenectomy was performed by Dr. John A.

Hartwell. The sixth transfusion was performed during this operation; 220 c.c. of blood were transfused from Donor W. C., who was used October 27. This transfusion was done while spleen was being removed in order to replace the loss of blood incident to operation.

November 24: R. B. C., 5,000,000; Hb., 85 per cent.

December 1: Condition good.

January 21: Discharged from hospital apparently well. An interesting feature of this case is the ability of patient to retain the blood transfused after receiving antisyphilitic treatment and his inability to retain it before this treatment.

Not only is blood transfusion a matter requiring skill, but problems in pathology, physiology, serology, immunity, chemistry and clinical medicine also constantly arise that require special study. Every large hospital in which such work is done should have on the attending staff a hematologist who can give to such work the degree of specialization necessary to meet the many problems and direct the work; thus accidents in the work will be eliminated, a waste of good blood may be prevented and applications seen that might otherwise be overlooked.

This subject has interested medical science and has thrilled the imagination of man ever since Harvey's discovery of the circulation of the blood. In the last quarter of a century some of these dreams have been realized. The difficulties of technic of the old method, the uncertainty of success, the pain, infection, and lifelong scars to patients and donors, the empiricism of its therapeutics relegated its use to the court of last resort. This method makes possible new applications. It opens a new field of therapeutics—a field that will possibly solve some of the present insoluble enigmas in the treatment of disease and in the conservation of human life.

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BLOOD TRANSFUSION IN DIABETES MELLITUS*

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INTRODUCTION

If about one-fifth of the pancreas of a dog with its artery and vein be properly implanted under the skin of the abdomen, the graft will live. Later, the remaining four-fifths of the gland may be extirpated *in toto* without causing more than a transient glycosuria, the graft serving to prevent an outspoken diabetes. If after the animal has recovered from the second operation the encapsulated rest be enucleated, severe diabetes supervenes. On the other hand, the blood of depancreatized animals has not been found to possess positive diabetogenic powers. This experiment embodies the chief supports for the conception that the pancreas elaborates a "something" whose presence in the body is in some way necessary for the normal utilization of sugar. It is generally assumed that this "something" (internal secretion) leaves the pancreas by way of the blood-stream, that is, through the pancreaticoduodenal and pancreatic veins.

Numerous attempts have been made to demonstrate directly its existence in the blood (or in extracts made

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