THE LENGTH OF LIFE OF TRANSFUSED ERYTHROCYTES IN PATIENTS WITH PRIMARY AND SECONDARY ANEMIA*

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Introduction.—During recent years, and especially since the introduction of the sodium citrate method, blood transfusion has become one of the most common forms of treatment of the various types of primary and secondary anemias. Thus far, however, little is known as to the length of life of the transfused erythrocytes in patients with primary and secondary anemia, and until the recent work of Ashby [1] no observations had been made on this subject. This investigator studied the length of life of transfused red corpuscles in pernicious anemia and found the average to be about three months. Previous to this time various observers had claimed the length of life of the red corpuscles to be from fourteen to fifty-two days.[2] Information on this point seemed desirable in that it might demonstrate the practical value of transfusion, serve as an aid in deciding what the proper intervals between transfusions should be, and because of its relation to the debated problem as to whether or not there is an increase of hemolysins in the blood serum of individuals with primary and secondary anemias.

It is generally known that the transfusion of blood is a safe procedure when the donor's cells are compatible with the plasma of the recipient. The fact that the donor's plasma may agglutinate and hemolyze the cells of the recipient is negligible because the donor's plasma is diluted so rapidly as it enters the recipient's blood stream that agglutination and hemolysis are impossible. It follows then that Group IV blood (Moss classification) may be transfused without ill effects into persons whose bloods fall into Groups I, II and III. In a similar manner a recipient in Group I may be transfused with bloods of Groups II, III and IV.

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1. Ashby: J. Exper. M. **29**:267, 1919.

2. Ashby: M. Clin N. America, November, 1919; J. Exper. M. **29**:267, 1919. Ward and Muller; Von Ott; Hunter, W.: Quoted by Ashby, J. Exper. M. **29**:207, 1919.

Technic.—Ashby has devised an ingenious method of following the life of the transfused red blood cells by means of group agglutination.[3] Blood is taken from the recipient's finger and mixed with citrated blood serum which will agglutinate the cells of the recipient but not the cells which have been transfused. The unagglutinated cells (i. e., those that have been transfused) may then be counted. The technic of the method is as follows (assuming a Group II recipient and a Group IV donor): The blood of the recipient is taken in a leukocyte counting pipet up to the 0.5 mark, and is diluted up to the 11 mark with the agglutinating fluid, which is made up of Group IV serum and a 4.4 per cent. solution of sodium citrate in the proportion of 1:20. The pipet is shaken and the mixture expelled into a small test tube in which it is incubated at 37 C. for forty minutes, with thorough shakings every ten minutes. It is then left in the icebox over night. Just before counting, the mixture is shaken and a drop placed in the blood counting chamber and, as directed by Ashby, "160 small squares in each of the two chambers are counted, the average of the counts taken and multiplied by 1100/2 to give the number of unagglutinated or transfused corpuscles per cubic millimeter of blood." Controls on the activity of the agglutinating serum are made by using the technic described above on blood of an untransfused individual in Group II. Theoretically, all the Group II cells should be agglutinated by the Group IV serum; practically, however, there remain unagglutinated on an average of from 20,000 to 50,000 cells per c.mm. Serum which will agglutinate the blood of a normal person in Group II, leaving only 50,000 cells per c.mm. unagglutinated may be considered to be active. When the unagglutinated cell counts in transfused individuals remain higher than these control counts, it may be assumed that the number of unagglutinated corpuscles in excess of the control count represent the number of unagglutinated donor's cells present in the circulation. Cases have been studied by us according to Ashby's method and technic. All counts have been made in duplicate, and the figures in the accompanying tables represent the average. In the cases reported, controls on the serum were made as described above, and, except in two instances, the same agglutinating serum was used throughout for all patients. Control counts of the new and old serums were shown to be practically identical before the changes were made.

Observations on Patients with Pernicious Anemia.—Four patients with pernicious anemia, whose bloods were in Group II, were transfused with citrated blood from donors in Group IV. Counts were then made of the transfused or unagglutinated cells in the bloods of these recipients, and repeated many times until the total transfused cells dropped to the level of the control counts. These patients presented the clear cut and classical signs and symptoms of primary

3. Ashby: J. Exper. M. **34**:147, 1921.

anemia, but among them were representatives of the different stages of the disease. Patient A was in the sixth year of the disease, was bedridden and had been observed in a remission during his stay in the hospital the year before, but in a series of counts taken before his transfusion his erythrocytes were found to be steadily decreasing. Patient C, in the third year of the disease, was also bedridden and his red blood cell counts showed the same general curve as the counts of Patient A. In contrast, Patients B and D were in the earlier stages of the disease, had been able to do some work and were ambulatory at the time of their transfusion.

The observations on Patient D are of especial interest in that the donor for transfusion was another patient with pernicious anemia (Group IV). When the donor was bled, 300 c.c. were withdrawn and he was immediately transfused with 800 c.c. of normal blood. The volume of cells in the 300 c.c. of pernicious anemia blood being very small, the unagglutinated cell count in this recipient never rose above 97,000 per c.mm. Frequent counts were made in this case, and the control counts which were made on untransfused normals in Group II and also on the blood of an untransfused patient with pernicious anemia in Group II, agreed closely.

REPORT OF CASES

CASE 1.—Patient A (Medical No. 13211) was a man, aged 41, belonging to Group II. His symptoms began four years before his entrance to the hospital. They were weakness, pallor, distress after eating and numbness of the fingers and toes. Two years previously, while under observation in the hospital, he had a typical remission with marked improvement of all his symptoms except the numbness of the extremities. Eight months later he again began to grow steadily weaker. In the month previous to his present entrance to the hospital his red cell count dropped from 1,332,000 to 676,000. He was then transfused with 575 c.c. citrated blood of Group IV. Blood findings before transfusion were: white cell count, 2,500 per c.mm.; hemoglobin, 30 per cent.; platelets, 98,000 per c.mm.; reticulated cells, 0.5 per cent. The blood picture was typical of pernicious anemia (Table 1, Fig. 1).

TABLE 1.—BLOOD PICTURE OF PATIENT A

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	Nov. 16, 1920	1,152,000	
18	Dec. 3, 1920	Transfused 575 c.c. citrated blood, Group IV	
18	Dec. 3, 1920	1,024,000	530,000
23	Dec. 8, 1920	1,936,000	535,700
28	Dec. 13, 1920	1,800,000	691,900
49	Jan. 3, 1921	1,552,000	553,850
59	Jan. 13, 1921	1,216,000	464,200
56	Jan. 20, 1921	848,000	349,800
73	Jan. 27, 1921	1,344,000	300,300
77	Jan. 31, 1921	811,436	148,500
78	Feb. 1, 1921	884,268	228,250
79	Feb. 2, 1921	Transfused 600 c.c. citrated blood, Group II	
85	Feb. 8, 1921	1,160,000	229,900
91	Feb. 14, 1921	1,160,000	
95	Feb. 18, 1921	1,088,000	
101	Feb. 24, 1921	904,000	301,400
106	March 1, 1921	1,328,000	351,450
110	March 4, 1921	1,744,000	258,500
116	March 10, 1921	1,312,000	122,650
120	March 14, 1921	1,094,808	100,650
128	March 22, 1921	848,000	73,150

CASE 2.—Patient B (Medical No. 15159), a woman aged 46, also belonged to Group II. Her illness began one year before admission to the hospital. The symptoms were gradually increasing weakness and pallor, several attacks of diarrhea and slight numbness of the fingers. She had been able to do a little work around the house. Her blood report before transfusion was as follows: Red cell count, 3,456,000 per c.mm.; reticulated cells, 0.9 per cent.; white cell count, 4,700 per c.mm.; platelets, 151,000 per c.mm. The blood smears showed the typical findings of pernicious anemia. She was transfused with 400 c.c. of citrated blood from a Group IV donor (Table 2, Fig. 2).

TABLE 2.—BLOOD FINDINGS OF PATIENT B

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	Jan. 9, 1921	3,456,000	
1	Jan. 9, 1921	Transfused 400 c.c. citrated blood, Group IV	
3	Jan. 11, 1921	4,152,000	464,750
13	Jan. 21, 1921	4,648,000	381,150
19	Jan. 27, 1921	4,338,000	282,150
24	Feb. 1, 1921	4,256,000	247,500
31	Feb. 8, 1921	3,592,000	307,450
38	Feb. 15, 1921	5,446,000*	
51	Feb. 28, 1921	5,338,000	259,600
55	March 4, 1921	3,688,000	347,600
75	March 24, 1921	4,368,000	216,150
90	April 8, 1921	4,214,000	110,000
98	April 16, 1921	4,320,000	106,150
111	April 29, 1921	4,556,000	35,200

* The sudden rise in the total red blood cell curve was due to a short remission as shown by a sudden increase in the number of reticulated red cells just previous to the rise in the total red cell count.

CASE 3.—Patient C (Medical No. 14705) was a woman, aged 55, belonging to Group II. Two years before entrance to the hospital, a gradually increasing weakness, pallor and gastric distress marked the onset of her illness. Then she developed numbness of the hands and feet. Her blood findings before transfusion were: hemoglobin, 45 per cent.; red cell count, 2,356,000 per c.mm.; reticulated cells, 1.5 per cent.; white cell count, 4,100 per c.mm. The stained smear was typical of pernicious anemia. She was transfused with 600 c.c. citrated blood from a Group IV donor and later had several transfusions of Group II blood (Table 3, Fig. 3).

TABLE 3.—BLOOD FINDINGS OF PATIENT C

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	Jan. 18, 1921	1,268,000	
1	Jan. 18, 1921	Transfused 250 c.c. citrated blood, Group IV	
3	Jan. 21, 1921	1,028,000	238,150
7	Jan. 25, 1921	Transfused 600 c.c. citrated blood, Group II	
10	Jan. 28, 1921	2,356,000	165,000
14	Feb. 1, 1921	2,016,000	161,700
16	Feb. 3, 1921	Transfused 550 c.c. citrated blood, Group II	
17	Feb. 4, 1921	2,776,000	189,750
43	March 19, 1921	1,360,000	124,850
43	March 19, 1921	Transfused 500 c.c. citrated blood, Group II	
71	April 16, 1921	1,544,000	57,750

CASE 4.—Patient D (Medical No. 15642), a man aged 50, belonging to Group II, noticed symptoms of weakness and pallor three months before admission to the hospital. One month later he had a sore tongue, distress after eating and numbness of the fingers. He had been able to work until shortly before he entered the hospital. His blood findings at entrance were as follows: hemoglobin, 18 per cent.; red cell count, 1,224,000 per c.mm.; reticulated cells, 0.9 per cent.; white cell count, 5,600 per c.mm., and platelets, 128,000 per c.mm. The smear was characteristic of pernicious anemia. He was transfused with 300 c.c. of Group IV blood from another patient who had a typical pernicious anemia (Table 4, Fig. 4).

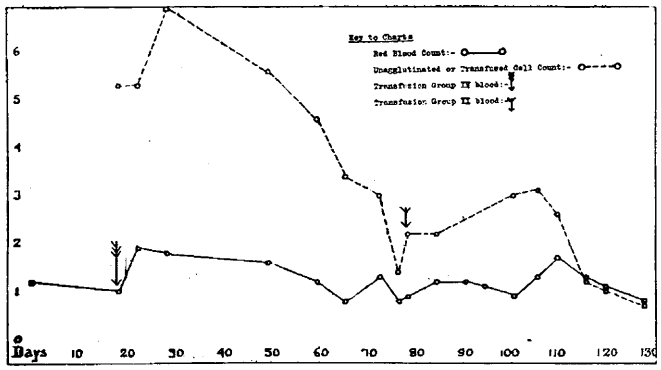

Fig. 1.—Blood findings of Patient A. In this and the accompanying charts the figures on the left border represent millions in the total red blood cell counts, and hundreds of thousands in the unagglutinated or transfused red blood cell counts.

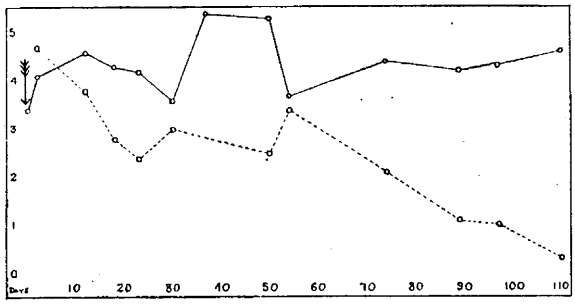

Fig. 2.—Blood findings of Patient B.

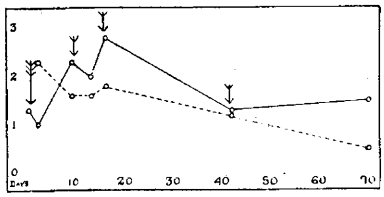

Fig. 3.—Blood findings of Patient C.

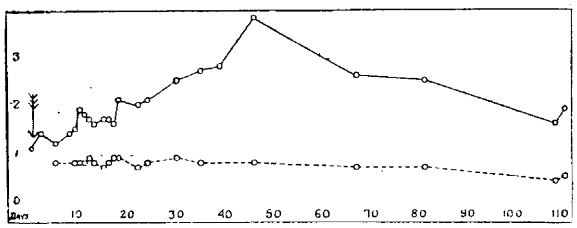

Fig. 4.—Blood findings of Patient D.

TABLE 4.—Blood Findings of Patient D

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	March 19, 1921	1,224,000	
1	March 19, 1921	Transfused 300 c.c. citrated blood, Group IV (P. A.)	
3	March 22, 1921	1,401,000	
6	March 25, 1921	1,200,000	86,350
9	March 28, 1921	1,448,000	
10	March 29, 1921	1,520,000	89,650
11	March 30, 1921	1,928,000	87,100
12	March 31, 1921	1,864,000	86,900
13	April 1, 1921	1,704,000	94,600
14	April 2, 1921	1,648,000	80,850
16	April 4, 1921	1,680,000	78,650
17	April 5, 1921	1,688,000	84,150
18	April 6, 1921	1,568,000	94,050
19	April 7, 1921	2,144,000	90,200
23	April 11, 1921	2,064,000	78,100
25	April 13, 1921	2,120,000	80,850
31	April 19, 1921	2,560,000	96,800
36	April 24, 1921	2,688,000	84,700
40	April 28, 1921	2,804,000	
47	May 5, 1921	3,832,000	82,500
68	May 26, 1921	2,600,000	75,900
82	June 9, 1921	2,528,000	74,250
109	July 6, 1921	1,600,000	47,850
111	July 8, 1921	1,872,000	54,833

Observations on Patients with Secondary Anemia.—Four cases (E, F, G and H) of secondary anemia, accompanying an advanced nephritis, were studied in the same way. Before transfusion, the patients showed progressive anemias as proved by decreasing red cell counts. Patients F and H were bleeding constantly from the kidneys and their urines showed gross blood. Patient E had a very small amount of blood in the urine, averaging from five to six red blood corpuscles per low power field when examined microscopically, while Patient G showed no evidence of hematuria or bleeding elsewhere.

Case 5.—Patient E (Medical No. 15126), a man, aged 32, in Group II, had had chronic nephritis for about six months before admission to the hospital. On entry his systolic blood pressure was 190; diastolic, 110. Phenolsulphonephthalein excretion was 42 per cent., blood urea nitrogen, 20 mg. per hundred c.c. of blood. His urine showed a few red blood cells constantly, averaging about five or six per low power microscopic field. The blood findings were: hemoglobin, 60 per cent.; red cell count, 4,060,000 per c.mm.; reticulated cells, 0.9 per cent.; white cell count, 9,650 per c.mm. The red corpuscles were practically normal in size and shape but showed definite achromia. He was transfused with 600 c.c. citrated blood from a Group IV donor (Table 5, Fig. 5).

TABLE 5.—Blood Findings of Patient E

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	Jan. 15, 1921	4,060,000	
1	Jan. 15, 1921	Transfused 600 c.c. citrated blood, Group IV	
4	Jan. 18, 1921	4,644,000	623,700
42	March 1, 1921	4,992,000	244,750
52	March 11, 1921	4,792,000	332,750
64	March 23, 1921	4,560,000	239,800
70	March 29, 1921	4,656,000	162,250
77	April 5, 1921	4,008,000	143,550
84	April 12, 1921	3,544,000	90,750
92	April 20, 1921	3,368,000	94,600
99	April 27, 1921	3,420,000	82,650
108	May 6, 1921	2,936,000	151,800
119	May 17, 1921	3,248,000	34,650

CASE 6.—Patient F (Medical No. 15371), a man, aged 23, in Group II, had had influenza followed by acute nephritis two years before his entrance to the hospital. He has passed bloody urine constantly since that time and throughout his stay in the hospital the urine showed gross blood. The phenolsulphonephthalein excretion varied from 18 to 35 per cent.; blood urea nitrogen was from 26 to 61 mg. per hundred c.c. on a low protein diet. Blood findings before transfusion were as follows: hemoglobin, 65 per cent.; red cell count, 4,512,000 per c.mm.; reticulated cells, 2 per cent.; white cell count, 11,200 per c.mm. The smear showed slight achromia of the red cells but was otherwise essentially normal in appearance. He was transfused with 550 c.c. citrated blood from a Group IV donor (Table 6; Fig. 6).

TABLE 6.—BLOOD FINDINGS OF PATIENT F

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	March 28, 1921	4,572,000	
9	April 5, 1921	Transfused 550 c.c. citrated blood, Group IV	
10	April 6, 1921	3,664,000	248,050
12	April 8, 1921	3,974,000	275,550
15	April 11, 1921	4,040,000	259,600
17	April 13, 1921	4,160,000	296,450
23	April 19, 1921	4,736,000	294,800
30	April 26, 1921	3,072,000	208,450
36	May 2, 1921	3,216,000	202,950
39	May 5, 1921	3,552,000	242,000
46	May 12, 1921	3,416,000	189,200
53	May 19, 1921	3,208,000	143,000
56	May 22, 1921	4,288,000	176,550
69	June 4, 1921	2,816,000	156,750
92	June 27, 1921	3,828,000	83,600
96	July 1, 1921	3,600,000	68,750
108	July 13, 1921	3,506,448	42,185
114	July 19, 1921	4,016,000	33,000

CASE 7.—Patient G (Medical No. 14976), a man, aged 33, in Group II, had had nephritis for about eight months. Physical examination revealed ascites and considerable edema of the genitals and lower extremities. The blood pressure was: systolic, 128; diastolic, 96. Phenolsulphonephthalein excretion was 13 per cent., and blood urea nitrogen was 25 mg. per hundred c.c. The urinary sediment contained many hyalin, granular and waxy casts but no red blood cells. Before transfusion the red count was 3,736,000 per c.mm.; reticulated cells, 0.9 per cent.; hemoglobin, 45 per cent. The stained smear showed practically normal red cells with slight achromia. He was transfused with 250 c.c. citrated blood (containing 10 000,000 red corpuscles per c.mm.) from a donor in Group IV (Table 7, Fig. 7).

TABLE 7.—BLOOD FINDINGS OF PATIENT G

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	March 28, 1921	3,764,000	
35	May 2, 1921	2,896,000	
45	May 22, 1921	3,736,000	45,650
57	May 24, 1921	Transfused 250 c.c. citrated blood, Group IV	
59	May 26, 1921	5,064,000	253,000
67	June 3, 1921	4,576,000	261,250
74	June 10, 1921	3,984,000	399,850
79	June 15, 1921	4,688,000	280,500
85	June 21, 1921	5,024,000	265,650
94	June 30, 1921	4,416,000	163,350
105	July 11, 1921	4,344,000	179,300
112	July 18, 1921	3,712,000	130,550
142	August 17, 1921	4,456,000	69,300
150	August 25, 1921	4,128,000	56,100
156	August 31, 1921	4,800,000	49,550

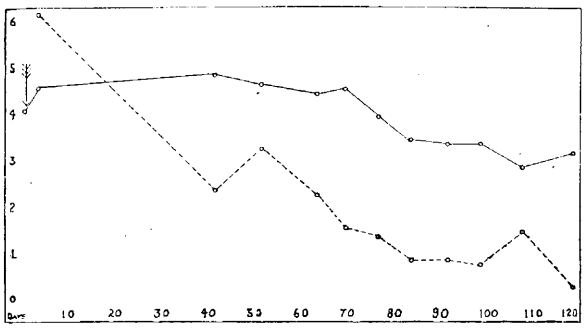

Fig. 5.—Blood findings of Patient E.

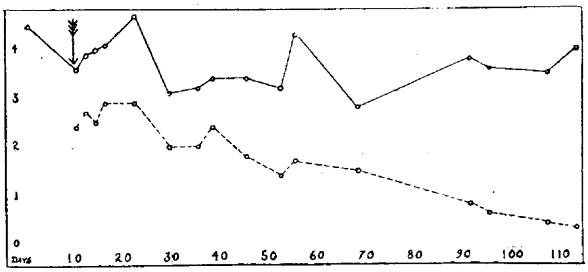

Fig. 6.—Blood findings of Patient F.

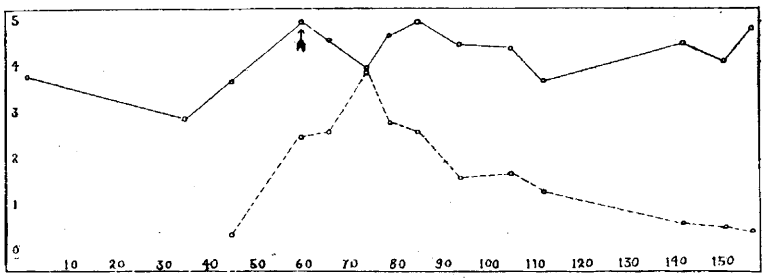

Fig. 7.—Blood findings of Patient G.

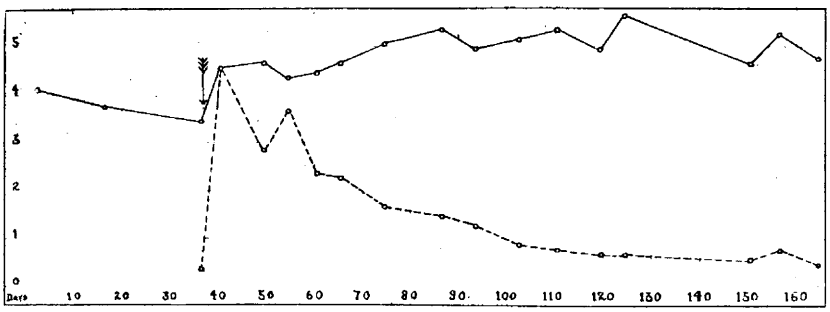

Fig. 8.—Blood findings of Patient H.

CASE 8.—Patient H (Medical No. 15653), a boy, aged 16, in Group II had nephritis, of two months' duration, which followed a respiratory infection. He was not edematous and his blood pressure was: systolic, 148; diastolic, 90. The urinary sediment contained hyalin and finely granular brown casts and many red blood cells so that the blood was visible grossly from time to time. Phenolsulphonephthalein excretion was 50 per cent., and the blood urea nitrogen was 12 mg. per hundred c.c. His red cell count before transfusion was 3,360,000 per c.mm.; reticulated cells, 2.2 per cent.; hemoglobin, 52 per cent.; white cell count, 6,900 per c.mm. The stained smear showed slight achromia of the red corpuscles. He was transfused with 250 c.c. citrated blood (containing 10,000,000 red corpuscles per c.mm.) from a Group IV donor (Table 8, Fig. 8).

TABLE 8.—BLOOD FINDINGS OF PATIENT H

No. of Days	Date	Red Blood Cells	Unagglutinated or Donor's Cells
1	April 16, 1921	4,144,000	
17	May 2, 1921	3,672,000	
37	May 22, 1921	3,360,000	
39	May 24, 1921	Transfused 250 c.c. citrated blood, Group IV	
41	May 26, 1921	4,497,000	451,550
49	June 3, 1921	4,560,000	281,150
56	June 10, 1921	4,344,000	306,350
61	June 15, 1921	4,408,000	238,150
66	June 20, 1921	4,456,000	226,050
75	June 29, 1921	5,000,000	162,250
87	July 11, 1921	5,256,000	141,350
94	July 18, 1921	4,904,000	123,750
103	July 27, 1921	5,144,000	88,000
111	August 4, 1921	5,344,000	79,750
119	August 12, 1921	4,962,000	62,700
124	August 17, 1921	5,616,000	68,200
150	Auguse 25, 1921	4,592,000	58,850
156	August 31, 1921	5,208,000	78,100
164	Sept. 8, 1921	4,688,000	48,950

DISCUSSION

Unfortunately it has not been possible in this investigation to study the length of life of cells transfused into normal individuals, but, in the light of the present findings, further studies on normals should be made. Ashby observed only one normal case until the transfused corpuscles disappeared from the circulation and found that they lived for thirty-nine days, while in her other two cases, which were followed incompletely, the cells lived about thirty-two days. In a later study, this author reports the length of life of transfused red blood cells in eight patients "without blood disease" to be very variable, some living as long as one hundred days, others disappearing in thirty days. The protocols of these patients, however, show that some of them had cancer or other malignant growths, one was in the tertiary stage of syphilis and none can be regarded as normal. Indeed, one finds included in the list patients with some of the most common and frequent causes of secondary anemia, and while in the technical sense of the term they may be "without blood disease" they show a decided disturbance of the blood.

Ashby found the length of life of the transfused erythrocytes in pernicious anemia to be about three months and concluded that there was no hemolytic toxin producing the anemia in this disease. The

results of this investigation show the length of life of the transfused corpuscles in primary anemia, and in the one type of secondary anemia studied, to be from seventy-one to one hundred and ten days, but it is felt that no conclusion regarding the presence of a hemolysin is justifiable, because these observations furnish no direct evidence on this point, and also because of the lack of accurate information as to the duration of life of red corpuscles transfused into normal persons. Furthermore, no evidence could be found to support the claim, made by Ashby, that "on the whole, blood destruction is quiescent in pernicious anemia." The results here show merely that the length of life of transfused erythrocytes is greater in patients with primary anemia and with secondary anemia due to nephritis, than in the one normal case on record; and this is only known to be true when the donor and recipient are of unlike groups. Whether or not the same would hold true when the donor and the recipient are in the same group it is not possible to say. In addition, these observations do not throw any light on what is happening to the patient's own cells during this period, and there is no reason to believe that the rate of destruction of the transfused cells is any indication of the rate of destruction of the patient's own cells, for it is possible that the transfused erythrocytes, belonging to a group foreign to the patient, are not acted on in the same manner as the patient's own cells.

It has not been proved conclusively that the transfused blood cells function during their stay in the circulation, but the fact that many of the patients show some clinical improvement after transfusion suggets that this is the case. Moreover, the observations of several investigators have shown that any foreign material, such as manganese or carbon particles and foreign blood cells, when injected into the blood stream of an animal are removed quickly.[4] This being the case, if the transfused cells were not living and functioning as normal red blood corpuscles one would expect them to be removed from the blood stream.

Several rises in the counts of transfused red cells were noted just before their final disappearance (Figs. 1 and 5). As the control counts on these days did not increase, and there was no variation in technic, differential counts of the number of microcytes were made to see if a breaking up or fragmentation of cells might account for these rises, but no evidence to support this theory was found. In view of the coincident rise of the total red blood cell count, it is not unlikely that changes in the blood volume account for the rise. One other possible explanation of this occurrence is that following transfusion there may be a definite improvement in the circulation with a resulting rise in

4. McJunkin: J. Exper. M. **21**:59, 1918. Lund, Shaw and Drinker: J. Exper. M. **33**:231, 1921. Drinker and Shaw: J. Exper. M. **33**:77, 1921.

the number of circulating cells in the periphery. This seems plausible in Case. 1.

The most striking result of these observations on the life of the transfused cells in the primary and secondary anemias is their surprisingly long stay in the circulation of the recipient. The longest period before the disappearance of the last cells was 113 days and the shortest fifty-nine days, the average for all these observed being about eighty-three days. It must be remembered that in addition to this period of life as transfused erythrocytes in a foreign circulation, that some of these corpuscles were functioning as adult cells in the donor before they were transferred, but of the length of time that they had been in the adult stage nothing is known, nor is there any accurate knowledge of the period of time required for a red blood cell to pass from its immature nucleated stage to its adult nonnucleated stage. These considerations, together with the findings of this investigation, indicate that the life of the human red blood cell is much longer than has been believed to be the case. Whether the duration of life and the stages of development of these cells would have been the same in the circulation of the individual from whom they originally came it is not possible to say.

It is also of interest that the life of the transfused red cells in both secondary and primary anemias was of the same duration. It seems almost probable that the transfused cells are adult red corpuscles of varying ages, and this, if true, would account for their steady gradual disappearance from the circulation of the recipient, also for the fact that some of the cells begin to disappear almost immediately after transfusion. This explanation is also compatible with the idea that new red corpuscles are being constantly supplied to the circulation. There were no sudden drops in the transfused cell count during these observations, but this may be due to the time intervals between counts, and in this connection it will be noted that two of the patients with pernicious anemia were women, both of whom had ceased to menstruate, so that no loss of transfused cells can be accounted for by that route, as noted by Ashby. In Case 6, in which there was constantly a large amount of blood in the urine, an attempt was made to determine the number of transfused corpuscles that were being lost in this way, but this was unsuccessful as the total unagglutinated count of the red corpuscles in the urine after centrifugalization was less than the control counts of the agglutinating serum on normal Group II blood.

Another point that is clearly brought out in this study is that due to the long life of the transfused red cells one may expect to tide patients over the acute stages of primary and secondary anemias by purely mechanical means. The improvement after some transfusions,

except when a real remission begins, might be explained by the increase in oxygen carriers. This improvement, which is generally of about two or three months' duration, is probably governed by the fact that some of the transfused corpuscles seem to function between sixty and ninety days.

CONCLUSIONS

Red blood corpuscles from donors in Group IV transfused into patients in Group II with pernicious anemia and anemia secondary to nephritis, remained in the circulation longer than has been generally believed to be the case. The last of the transfused red blood cells disappeared from the circulation in from fifty-nine to 113 days, with an average of eighty-three days.

No difference was noted in a series of observations in the duration of the stay of the transfused red blood corpuscles in the circulation between patients with primary anemia and secondary anemia (due to nephritis).

In a single observation red blood corpuscles from a patient with pernicious anemia transfused into another patient with pernicious anemia, behaved as did the corpuscles from normal donors.