Homologous Blood Syndrome: *

I. Preliminary Observations on its Relationship to Clinical Cardiopulmonary Bypass

HOWARD L. GADBOYS, M.D., RALPH SLONIM, M.D.,†
ROBERT S. LITWAK, M.D.

From The Mount Sinai Hospital, New York, N. Y., and The University of Miami School of Medicine, Miami, Fla.

THE OBSERVATION that major physiological alterations occur after homologous blood infusion in dogs has been well established.[3-5] Exchange of as little as 200 ml. of homologous canine blood may precipitate a state characterized by mild or severe arterial hypotension, portal hypertension with splanchnic sequestration of blood, transfer of water and electrolytes out of the intravascular compartment, venous oxygen unsaturation, and fall of the buffer base. The syndrome may be overlooked since the transitory arterial hypotension occurs soon after the onset of perfusion when the animal's status is expected to be the most unstable. The sequestered blood returns in part to the systemic circulation with passage of time.

The purpose of this communication is to describe a group of phenomena occurring during and after clinical extracorporeal circulation that bear close resemblance to the syndrome of anaphylactoid shock from homologous blood exchange in dogs. The principal characteristic of this syndrome is sequestration of significant quantities of blood in areas not measurably in communication with the circulating blood volume. Despite rigid maintenance of blood balance during the course of clinical cardiopulmonary bypass, significant systemic hypovolemia frequently occurs as measured by radioisotopic methods. Failure to compensate for this by blood infusion may result in postperfusion hypotension. Restoration of adequate circulating blood volume often reflects itself in increased total body weight. Furthermore, there is preliminary evidence to suggest that in this group of patients return of part of the sequestered blood to the systemic circulation 24 to 48 hours after operation appears significantly to enhance the pulmonary complications noted after perfusion. Finally, the phenomena in both humans and dogs appear to be influenced by the comparative ratio of the reservoir and recipient blood volumes and by the rapidity and duration of blood transfer.

Methods and Results

Clinical data were obtained from 42 patients undergoing extracorporeal circulation for the correction of cardiovascular defects. The experimental procedures were performed on mongrel dogs weighing 10 to 20 kg. Identification between the canine

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† Post doctoral Research Fellow of the National Heart Institute.

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and human syndromes was demonstrated in the following manner:

Blood Volume Changes

Human studies: Pre- and postoperative blood volumes were obtained on 42 patients undergoing cardiopulmonary bypass for correction of cardiac defects. Radioisotopic methods were employed (RISA and Chromium[51]).[10] Blood balance was meticulously controlled during surgery by careful measurement and replacement of blood loss. The data were analyzed for changes in total blood volume, plasma volume, and red cell volume. These changes are shown in Table 1. The red cell and plasma volume alterations indicate that the deficits involve whole blood and do not simply represent water loss during operation. Blood balance in all patients was maintained at or above control level (Table 1).

TABLE 1. *Total Blood Volume, Plasma Volume, and Red Cell Volume Changes Following Cardiopulmonary Bypass (ml./kg.)*

	Δ TBV	Δ PV	Δ RCV
1.	−15.60	−5.75	−10.70
2.	− 0.96	−13.70	+12.74
3.	−27.96	−14.12	−13.84
4.	− 8.92	−10.39	+ 1.46
5.	− 8.66	− 4.68	− 4.00
6.	− 0.61	+ 0.73	− 1.34
7.	− 0.77	− 0.58	− 0.18
8.	−12.93	−13.76	+ 0.82
9.	− 1.51	+ 2.65	− 4.16
10.	− 5.71	− 6.65	+ 2.99
11.	− 7.60	− 5.20	− 1.83
12.	−36.10	−21.24	− 6.18
13.	−20.40	− 8.09	−12.30
14.	−21.36	−10.00	−16.36
15.	+ 4.27	+ 3.37	+ 0.90
16.	−28.70	−18.95	− 9.88
17.	−12.78	−19.35	+ 6.57
18.	−21.38	−15.17	− 6.20
19.	−14.15	− 1.35	−12.80
20.	−17.90	− 9.60	− 8.20
21.	−20.40	−12.10	− 8.30
22.	−30.40	−22.00	− 8.30
23.	−25.70	−12.60	−13.10
24.	−13.60	− 6.98	− 6.62
25.	+ 4.10	−10.20	+14.30
26.	−48.30	−15.40	−32.80
27.	+ 4.90	− 3.50	+ 8.50
28.	− 1.60	− 8.90	+14.00
29.	−13.90	−10.20	− 3.70
30.	+51.20	+29.80	+21.40
31.	−22.19	− 5.71	−16.48
32.	−27.70	−13.99	−13.71
33.	−42.38	−11.83	−29.63
34.	−66.40	−36.80	−29.60
35.	−19.90	−15.70	− 4.10
36.	−22.46	+ 2.37	−24.83
37.	−11.11	− 3.50	− 7.61
38.	− 5.00	+ 0.9	− 5.90
39.	−35.55	−15.17	−20.38
40.	− 2.42	+ 1.91	− 4.33
41.	+ 3.85	− 2.17	+ 6.02
42.	−15.87	− 8.52	− 7.35
Average	−14.78	− 8.40	− 5.58

Canine studies: Homologous blood exchange was accomplished in ten experiments with a reservoir arteriovenous fistula (Fig. 1) having a priming volume of 2,000 to 3,000 ml. Blood balance was maintained or blood was added by pressure infusion through the arterial limb of the fistula.

Significant sequestration of blood occurred in nine of the ten dogs undergoing

RESERVOIR ARTERIOVENOUS FISTULA

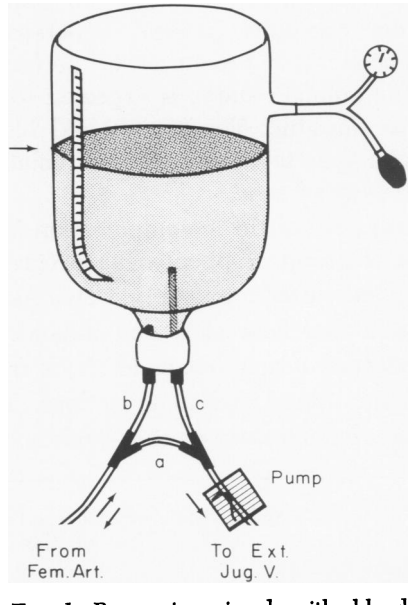

FIG. 1. Reservoir primed with blood. Shunt (a) utilized alone to obtain control hemodynamic data. Limbs (b) and (c) employed to exchange reservoir blood without altering blood volume. Pressure bulb and gauge permit arterial infusion of measured quantities of blood from reservoir.

exchange of reservoir volumes exceeding 2,000 ml. of homologous blood (Table 2). No additional blood was infused in two dogs (No. 1, 2) and subsequent circulating blood volumes were significantly decreased. In Experiment 9, hypotension did not occur and the blood volume data are inconclusive.

Arterial blood infusions were given to the remaining animals either early or late during the hypotensive phase and there was *loss* of blood from the circulating blood volume. The sequence of events is illustrated in Figure 2.

Postmortem examination of the "shocked"

TABLE 2. *Correlative Changes in Arterial Pressure, Blood Balance and Blood Volume During Shock from Homologous Blood Exchange in Dogs*

	Control	Depth of Shock	"Recovery"	Δ Corrected Blood Volume*
1.	a) 116 mm. Hg	15 mm. Hg	Died	
	b) 0	0		
	c) 1,545 ml.	411 ml.		−1,134 ml.
2.	a) 140 mm. Hg	100 mm. Hg	Not performed	−1,161 ml.
	b) 0	−135 ml.		
	c) 2,315 ml.	1,019 ml.		
3.	a) 105 mm. Hg	23 mm. Hg	90 mm. Hg	−494 ml.
	b) 0	0	+450 ml.	
	c) 1,348 ml.	534 ml.	1,304 ml.	
4.	a) 120 mm. Hg	30 mm. Hg	100 mm. Hg	
	b) 0	0	+600 ml.	−1,375 ml.
	c) 1,356 ml.	1,076 ml.	581 ml.	
5.	a) 115 mm. Hg	95 mm. Hg	95 mm. Hg	
	b) 0	0	+1,000 ml.	−225 ml.
	c) 656 ml.	585 ml.	1,431 ml.	
6.	a) 125 mm. Hg	35 mm. Hg		
	b) 0	+500 ml.	Died	−613 ml.
	c) 1,082 ml.	969 ml.		
7.	a) 140 mm. Hg	95 mm. Hg		
	b) 0	+1,650 ml.	Not performed	−543 ml.
	c) 860 ml.	1,967 ml.		
8.	a) 140	130	Not performed	−538 ml.
	b) 0	+1,075		
	c) 1,258 ml.	1,795 ml.		
9.	a) 100 mm. Hg	95 mm. Hg	95 mm. Hg	
	b) 0	0	0	−124 ml.
	c) 974 ml.	—	850 ml.	
10.	a) 120 mm. Hg	115 mm. Hg		
	b) 0	+800 ml.	Not performed	−698 ml.
	c) 1,888 ml.	1,990 ml.		

a)—Arterial mean pressure.
b)—Blood balance.
c)—Blood volume.
* *Corrected Blood Volume* = Isotopic Blood Volume − Simultaneous Calculated Blood Balance. This is probably representative of the amount of blood sequestered.

animals consistently revealed marked hepatic congestion, splanchnic venous distention, and intestinal mucosal hemorrhages.

TABLE 3. *Comparison of Weight and Blood Volume Changes Following Extracorporeal Circulation in Humans*

	Blood Volume (*ml./kg.*)	Δ Corrected Blood Volume (*ml./kg.*)
A. Postoperative Weight Increased		
1.	−27.96	28.0
2.	− 7.60	—
3.	+ 4.27	+ 2.50
4.	−14.15	−19.0
5.	−17.90	−29.3
6.	−20.40	−22.4
7.	−25.70	−32.2
8.	−13.60	−15.8
9.	+ 4.10	− 2.2
10.	−48.30	−54.0
11.	+ 4.90	− 2.4
12.	− 1.60	−20.2
13.	−19.90	−23.4
14.	− 2.42	−11.2
15.	− 5.00	−12.4
16.	− 8.16	−18.9
17.	− 7.10	−19.1
18.	+ 3.85	− 2.7
Average	−11.47	−18.2
B. Postoperative Weight Unchanged		
1.	−15.60	−17.6
2.	− 0.96	− 1.4
3.	− 8.66	−10.6
4.	− 0.61	—
5.	−12.93	− 7.9
6.	−28.70	−28.6
7.	−12.78	−29.3
8.	−30.40	−30.0
Average	−15.72	−17.9
C. Postoperative Weight Decreased		
1.	− 8.92	−19.0
2.	− 1.51	—
3.	−42.38	−42.3
4.	−21.36	—
5.	−21.38	−30.9
6.	−66.40	−79.5
7.	+51.20	+36.6
8.	5.79	− 9.0
9.	−15.87	−19.5
Average	−15.65	−23.4

Weight Changes

Human Studies: Deviations of pre- and postoperative weights were estimated with a metabolic balance (accuracy ± 25 Gm.) before and after cardiopulmonary bypass. Fluids used during the procedure as well as tape, arm boards, etc. were weighed with the patient both before and after operation to exclude these as variables. The weights were correlated with the isotopically determined blood volumes.

No significant correlation could be established between postoperative weight and blood volume changes. A multiplicity of factors—sequestration, length of procedure, evaporation through the thoracotomy incision, and other insensible water loss—appear to conspire against the usefulness of weight changes as a reliable guide to volumetric control. The effect of variables other than sequestration is illustrated by one patient undergoing left heart bypass (priming volume—300 ml.) whose red cell volume rose slightly while weight, plasma volume, and total blood volume fell, suggesting water loss:

	Preop.	Postop.	Change
TBV	3,892	3,398	−497
PV	2,677	2,050	−627
RCV	1,215	1,348	+133
Wght.	—	−200 Gm.	−200 Gm.

As will be shown, the degree of sequestration varies with the length of bypass and the relative size of the patient. Consequently inclusion of these variables would be necessary to validate weight changes as helpful determinants. It should be noted that over 50 per cent of the patients had weight *gain* despite corrected blood volume *deficits* averaging 18.2 ml./kg. The data are summarized in Table 3.

Canine studies: Pre- and postoperative weights were obtained on three dogs having homologous blood exchange with a reservoir arteriovenous fistula. The homologus blood syndrome occurred in all three experiments. The weight changes were

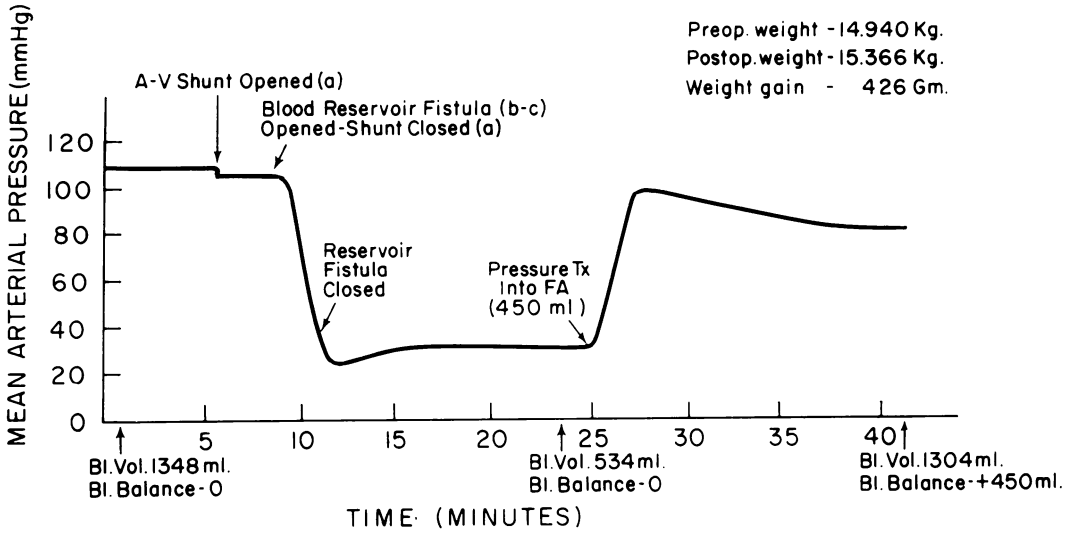

FIG. 2. Sequence of hemodynamic and volumetric data in shock from homologous blood exchange in dog No. 3.

correlated with 1) amount of blood infused and 2) radioisotopically determined blood volumes.

These experiments were performed in closed-chest animals to minimize evaporation. The sizes of the animals and the time intervals for the experiments were essentially similar. Weight changes correlated well with the amount of blood infused and, as would be expected with sequestration of blood away from the circulating blood volume, the changes showed little relationship to isotopic blood volume alterations (Table 4).

Effect of Length of Perfusion on Sequestration in Clinical Bypass

Blood volume data were divided into two groups. Twelve patients underwent surgical procedures employing less than 45 minutes of total perfusion time (partial and total bypass). Perfusion times exceeded 45 minutes in 30 patients. The data for each category were grouped together despite the size of the patients. The average weights for both groups were similar, however. The data were subjected to statistical analysis.

A statistically significant difference ($P < 0.05$) was discernible between the two groups indicating increased sequestration with longer periods of perfusion (Table 5).

Volumetric Influences

Human studies: Since the priming volume of the pump oxygenator remained essentially constant (3,000 ml. ± 200) for all perfusions, data required to assess the effects of relative pump/patient blood volumes were derived by comparing patient weights and postoperative corrected blood volume changes. These data were statistically evaluated for patients weighing greater or less than 30 kg.

A striking tendency for increased seques-

TABLE 4. *Postoperative Weight Changes in Dogs Correlated with Blood Balance and Blood Volume Alterations*

	Δ Weight (Gm.)	Blood Balance (ml.)	Δ Blood Volume (ml.)	Δ Corrected Blood Volume (ml.)
3.	+570	+600	−775	1375
4.	+426	+450	− 44	−406
8.	+915	+1075	+537	−538

TABLE 5. *Length of Perfusion vs. Corrected Blood Volume Changes*

Time (min.)	Wt. (kg.)	Δ Corrected Blood Vol. (ml.)
	0–45 minutes	
27	72.3	−57
29	47.3	−1002
23	23.3	+55
31	57.0	−605
39	69.0	−1308
37	43.6	−347
36	72.0	+112
45	14.0	−412
31	18.6	−26
31	18.6	−847
29	52.7	−85
41	21.1	−412
Average		
33	42.4	−9.7 ml./kg.
	>45 minutes	
49	55.6	−135
46	23.3	−1253
59	44.6	−1317
54	24.1	−673
48	56.3	−681
79	70.5	−2020
80	63.6	−1210
65	38.2	−671
85	47.7	−1136
81	54.5	−1241
82	47.2	−1431
86	10.9	−460
100	74.0	−1172
115	28.6	−886
149	45.2	−99
92	12.5	−994
96	17.0	+623
91	18.0	−362
156	68.0	−844
127	18.0	−1340
80	51.3	−529
59	52.8	−1152
118	63.6	−1661
63	45.4	−972
104	40.3	−1148
111	66.3	−597
108	26.0	−530
70	74.0	−1390
83	50.0	−957
88	50.0	−1212
Average		
87	44.6	−20.5 ml./kg.

tration of blood was seen in the smaller patients. Analysis of those patients who sequestered more than 5 ml./kg. (Fig. 3) revealed a highly significant difference between patients weighing more or less than 30 kg. ($P < 0.001$). Even when those patients who did not show postoperative evidence of diminished blood volumes isotopically were also included, the differences were still statistically significant ($P < 0.05$).

Canine studies: Dogs of approximately the same size (10 to 20 kg.) were utilized. The priming volume of homologous blood was altered and the presence of the *shock syndrome* was ascertained in one or a combination of three methods: 1) significant systemic hypotension; 2) portal venous hypertension; 3) radioisotopic evidence of decreased circulating blood volume. Eighty-four animals had exchange of less than 500 ml. of homologous blood utilizing a reservoir arteriovenous fistula. Twenty-nine dogs had exchanges of 700 to 1,200 ml. of homologous blood by reservoir A-V fistula or partial cardiac bypass. Partial cardiac bypass was employed to exchange volumes of greater than 2,000 ml. of homologous blood in 32 animals. Ten animals had exchange of more than 2,000 ml. of homologous blood by reservoir A-V fistula.

Complete blood exchange was achieved in less than two minutes in each experiment. Blood balance was maintained at or above control levels.

Increasing the volume of homologous blood exchanged resulted in a parallel increase in the incidence of gross hemodynamic manifestations of the sequestration phenomenon (Table 6). The syndrome was observed in 41 of 42 animals (10 to 20 kg.) having exchange of more than 2,000 ml.

Effect of Homologous Blood Exchange

Human studies: Partial cardiopulmonary bypass was instituted in three patients prior to employing total bypass for the correction of intracardiac defects. The ex-

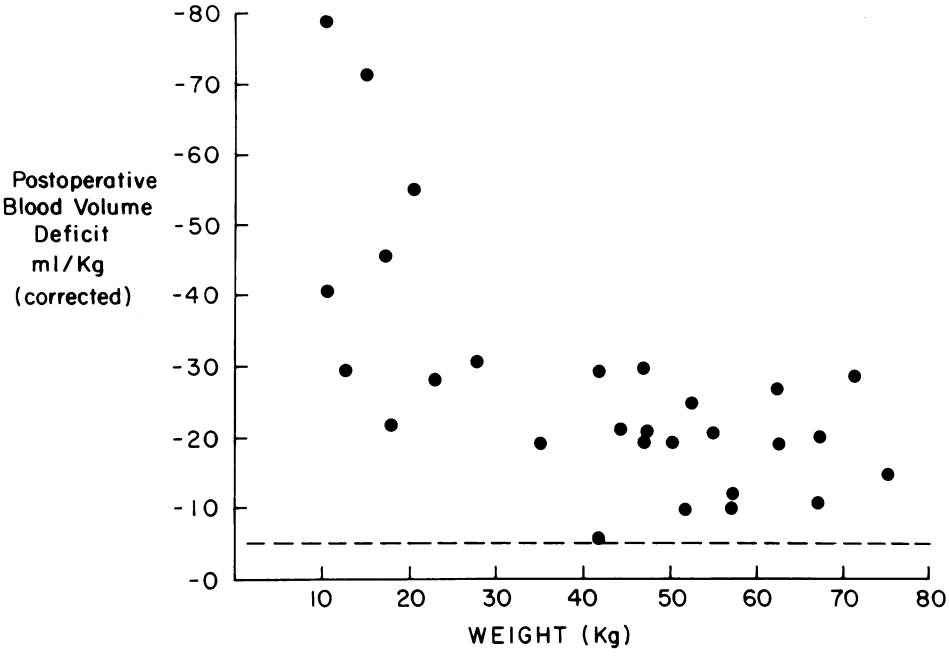

FIG. 3. Corrected blood volume changes vs. body weight in patients sequestering more than 5 ml./kg.

change infusions were performed by returning blood from the oxygenator to the patient at a rate equal to venous return for two minutes. The priming volume was 3,000 ml. ± 200. Control hemodynamic observations were made with cannulas in place for 10 to 15 minutes before commencing blood exchange to rule out mechanical deviations, and both venous and arterial pressures were constantly monitored. At the end of two minutes of blood exchange the arterial and venous lines were clamped. Although it had been planned to observe the hemodynamic changes for ten-minute intervals, the steady progression of the hypotension forced resumption of arterial perfusion in each case. The development of severe postoperative pulmonary congestion in two of the three patients forced abandonment of this study.

An identical procedure was carried out in three patients having left heart bypass (priming volume—300 ml.) for surgery of the descending thoracic aorta.

TABLE 6. *Relation of Volume to Incidence of Shock from Homologous Blood Exchange in Dogs*

Priming Volume	Technic of Exchange	No. Expts.	No. Shock	%
<500 ml.	Reservoir AV fistula	84	30	36
700–1,200 ml.	Reservoir AV fistula	3	2	
	Partial bypass { left heart or cardio-pulmonary }	26	15	59
>2,000 ml.	Reservoir AV fistula	10	9	
	Partial bypass { left heart or cardio-pulmonary }	32	32	97

BLOOD PRESSURE CHANGES FOLLOWING HOMOLOGOUS BLOOD EXCHANGE IN HUMANS

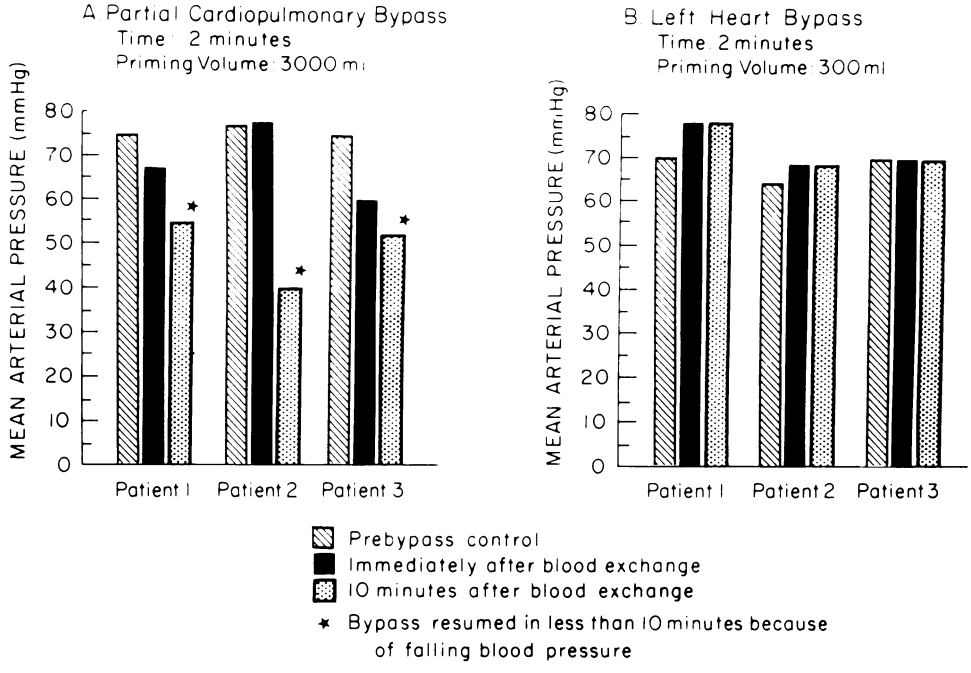

FIG. 4. (See text.)

The effect of rapid exchange of large volumes of homologous blood in humans is illustrated in Figure 4. Despite the fact that the blood balance was meticulously maintained at control level, each patient experienced a precipitous decline of arterial pressure once arterial perfusion was discontinued. Contrasted to this are the findings following rapid exchange of minimal quantities of homologous blood employing left heart bypass for two minutes followed by a period of observation. The hemodynamic status of these patients remained essentially unchanged despite comparable flow rates and time intervals (Fig. 4).

TABLE 7

No. Dogs	No. Shock
A. Effect of Autogenous Blood Exchange	
18	0
B. Preliminary Blood Exchange in Dogs Prior to Cardiopulmonary Bypass	
10	10

Canine studies: Eighteen animals had from 200 to 500 ml. of blood withdrawn into unsterile heparinized containers. The dogs were allowed to adjust to this state over several hours. The autogenous blood was then used as priming volume for the reservoir arteriovenous fistula preparation. Systemic arterial and portal venous pressures were monitored to detect any evidence of the shock syndrome.

Ten additional animals had preliminary homologous blood exchange for two minutes followed by a ten-minute observation period prior to the onset of total cardiopulmonary bypass (priming volume > 2,000 ml.).

The shock syndrome was not detected in any of the 18 animals having exchange of autogenous blood. Preliminary homol-

ogous blood exchange in ten dogs prior to instituting total cardiopulmonary bypass was accompanied by manifestations of the homologous blood syndrome in each case (Table 7).

Discussion

A disturbing problem often noted with *experimental* cardiopulmonary bypass or hemodialysis has been failure to achieve satisfactory venous flow rates without deliberately overloading the circulation. Systemic arterial hypotension may occur if the blood balance is not altered. These features are attended by high mortality rates especially when the perfusion times exceed one hour. It has been shown that these difficulties are the result of anaphylactoid reactions from homologous blood exchange in dogs. The syndrome, further characterized by portal venous hypertension, hepatic engorgement, splanchnic sequestration of blood, and fall of the buffer base, may be precipitated by as little as 200 ml. of homologous blood aseptically drawn from a single donor. In the dog, the primary target organ for anaphylaxis is the liver. A number of stimuli may incite this response including peptone,[19] rattlesnake venom,[6] ascaris extracts,[17] protamine, bacterial endotoxin,[12] and homologous plasma.[1] Since naturally occurring isoantibodies to erythrocytes occur in only about 15 per cent of random dogs,[20] it is not surprising to find no decrease in the incidence of this syndrome in cross matched animals.

Although clinical extracorporeal circulation initially appeared to be free from these distressing complexities, as data have been accumulated difficulties have manifested themselves with relation to 1) satisfactory maintenance of *systemic normovolemia;* 2) unreliability of body weight as a guide to adequate blood replacement; 3) postoperative pulmonary congestion; and 4) poor response to perfusion by tiny infants and by patients requiring prolonged cardiopulmonary bypass. Despite assiduous attempts to meticulously replace all blood losses during total body perfusion, sizeable deficits in the circulating blood volume are frequently detected by postoperative radioisotopic blood volume determinations. Restoration of a *normovolemic* state, as determined by these methods, is often reflected by increased body weight. Unfortunately, the use of arterial and venous pressure measurements has also proven to be invalid as sensitive determinants of satisfactory blood volume replacement.[10]

A similar pattern for both dog and man has been demonstrable by radioisotopic blood volume and hemodynamic studies. Shortly after the commencement of massive homologous blood exchange, the circulating red cell and plasma volumes begin to fall. Normotension can be maintained by venous "overinfusion" or by arterial perfusion. Failure to restore a satisfactory circulating blood volume by infusion of additional increments of blood is often attended by hypotension once arterial perfusion is discontinued. Sequestration increases, however, for varying time intervals. Preliminary data suggest that gradually some of the trapped blood returns to the systemic circulation as exemplified by repetitive blood volume determinations in a patient who underwent cardiopulmonary bypass.*

*

	Preop.	3 hrs. postop.	12 hrs. postop.	3 days postop.
TBV	1,909 ml.	1,501 ml.	1,641 ml.	1,875 ml.
PV	1,221	1,101	1,141	1,292
RCV	688	400	500	583
Bal.	0	+138	+456	+413
Δ Corrected TBV	0	−530	−724	−447

Thus, a disturbing dilemma appears. Should one elect to maintain constant *blood balance* in the face of the sequestration phenomenon, postoperative hypotension frequently becomes a serious problem with which to contend. The alternative, immediate restoration of normal circulating *blood volume* by infusion of blood, permits smoother termination of the perfusion possibly only to result in hypervolemia, pulmonary congestion, and other related abnormalities two or three days later. It is noteworthy that comparison of lung biopsies taken at the completion of perfusion with subsequent autopsy specimens in three patients managed by the latter method has shown the development of severe pulmonary congestion after re-establishment of the circulation. The underlying cardiac lesion and repair could not be incriminated as the cause of pulmonary congestion in any of the three. Complete resolution of this dilemma must unfortunately rest on elimination of the homologous blood syndrome.

The genesis of the homologous blood syndrome is not immediately apparent. It is worthy of consideration, however, that although elaborate precautions are taken to type and crossmatch erythrocytes before blood infusions, the same measures are not readily available for plasma, leukocytes, or platelets. It has been well established that anaphylactoid shock can be produced in dogs by infusion of homologous plasma.[1] Serial electrophoretic studies during and after clinical bypass have demonstrated minimal changes except for occasional slurring between the Alpha 2 and Beta globulin peaks, but Lee[9] has observed striking effects from the infusion of abnormal protein complexes obtained from the air-fluid interface of oxygenator systems. Since the changes occcurring from both experimental and clinical blood exchange appear to be dose related, this militates against the usual all-or-none antigen-antibody reaction. More subtle leukocyte allergies certainly cannot be excluded at this time. An attractive hypothesis can be proposed to incriminate platelets. It has been shown both clinically and experimentally that platelets rapidly diminish following the onset of extracorporeal circulation.[2, 16] A slower decline may then ensue for the next few days. Nelson[18] has demonstrated the formation of platelet thrombi at specific platelet concentrations in homologous preparations. Moreover, Hardaway and McKay[7] have elicited changes in dogs similar to those produced by homologous blood exchange by injection of incompatible (human) blood which produces apparent intravascular thrombosis. Curiously, however, these latter changes were prevented by heparin.

Solution of the dilemma presented by the homologous blood syndrome may lie in one of several areas:

1. *Elimination of Homologous Blood Prime:*
   a) Development of non-prime pump-oxygenator systems which will still have adequate flow characteristics.[15]
   b) Utilization of non-"toxic" priming substances such as dextran, gelatin, etc.[11] The priming requirements of present high flow systems would necessitate dilution of coagulating elements, plasma proteins and antibodies.
2. *Utilization of the Patient's Own Blood to Prime the Extracorporeal Unit:*
   a) Long range blood donation and storage. The use of stored glycerolized autogenous blood is being investigated.[14]
   b) Preoperative exchange transfusion.[8] Experimentally this eliminates many of the measurable phenomena at the time of extracorporeal circulation. A significant hazard may lie in the development of *immunological suicide* in which the entire antibody mechanism of the recipient can be neutralized destroying all immunological responses.[13]
3. *Removal or Antagonism of the Inciting Blood Factors*
   a) Establishment of the responsible blood element.
   b) Identification of the target organ or tissue in humans.

It obviously is incorrect to attribute all of the unsolved ills of extracorporeal circulation to the homologous blood syndrome. Nevertheless, many of the still-clouded issues of perfusion apparently related to this phenomenon require further elucidation, including 1) pump fever; 2) postoperative pulmonary congestion; 3) postperfusion anemia; 4) hemorrhagic complications of prolonged perfusions; and 5) acidosis associated with prolonged perfusions. Experimental evidence suggests that each of these difficulties can be produced by homologous blood exchange under conditions simulating cardiopulmonary bypass.

Summary

A group of phenomena has been identified in clinical cardiopulmonary bypass that bears close resemblance to the homologous blood syndrome in dogs.

The syndrome is characterized by sequestration of both red cells and plasma in areas not measurably in communication with the circulating blood volume as determined by isotopic means.

Maintenance of a calculated normal (zero) blood balance during perfusion frequently results in significant systemic hypovolemia. Failure to compensate for this deficiency by infusion of additional blood may be accompanied by severe postperfusion hypotension.

The evidence suggests that the volume of sequestered blood is represented by the difference between the isotopically determined blood volume change during perfusion and the simultaneously calculated blood balance.

A statistically significant correlation ($P < 0.05$) is demonstrable between the length of perfusion and the degree of sequestration. Moreover, a similar correlation ($P < 0.05$) exists between the priming volume of homologous blood and the size of the patient. That is, there is a striking tendency for increased sequestration of blood in smaller patients.

The sudden exchange of large quantities of homologous blood by a brief period of partial cardiopulmonary bypass produced severe hypotension in three patients in whom this procedure was employed. This is in contrast to the lack of hemodynamic alterations in three patients undergoing rapid exchange of minimal quantities of homologous blood for a similar length of time.

Existence of the sequestration phenomenon appears to militate against the use of postperfusion weight changes as reliable guides to volumetric control.

It is speculated that some of the common clinical complications attending cardiopulmonary bypass (febrile episodes, pulmonary congestion and biochemical aberrations) may relate to the described phenomena.

Addendum

It has been possible clinically to ameliorate many of the difficulties attending the homologous blood syndrome in two ways:

1. Diluents are substituted for a portion of the homologous blood. The over-all volume is unchanged making it unnecessary to restrict flow rates. One diluent utilized is 5.0 per cent dextrose and water to which is added 1.0 Gm. of human serum albumin per 100 ml. The diluent-blood ratio is approximately 1:2. Four-hour postperfusion blood volume studies have revealed a greater deficit with hemodilution, possibly the result of subtle intracorporeal fluid shifts. However, a striking return of the blood volume toward normal is generally observed in the ensuing 24 hours. This is in contrast to the pattern usually observed with whole blood in which sequestration becomes progressively more severe during the first 24 hours following perfusion.

2. Postoperative blood loss is incompletely replaced in anticipation of return of part of the sequestered blood to the circulating blood volume.

These data will be presented in detail elsewhere.*

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