"Washout" Acidosis following Resection of Aortic Aneurysms:

Clinical Metabolic Study of Reactive Hyperemia and Effect of Dextran on Excess Lactate and pH

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IF ARTERIAL inflow to an extremity is occluded for even short time intervals and then reinstated, blood flow increases two to six fold and the rapid increase in flow continues until the metabolic deficit resulting from temporary ischemia has been repaid.[8] This phenomenon has been called "reactive hyperemia" and is in a large measure responsible for the hypotensive episode associated with aortic declamping. Although the precise mechanisms responsible for "reactive hyperemia" have not been clarified, several have been suggested:

1) that there is a vasodilator material elaborated by ischemic tissue [12]

2) that vessels themselves are affected by a metabolic deficit during periods of relative ischemia and hypoxia [8]

3) that vascular tone (especially the response of vessels to catechol amines) is adversely affected by the accumulation of acid metabolites resulting from anaerobic metabolism.[8, 14]

It is the purpose of this study to define more accurately the degree of anaerobic metabolism which occurs distal to the cross-clamped aorta and to determine the effect of a substance (commercial dextran) which has been shown to enhance capillary perfusion in areas of relative ischemia.

Methods

In 15 patients undergoing elective resection of atherosclerotic aneurysms of the abdominal aorta, the femoral artery and vein of one extremity was exposed through a separate inguinal incision. Immediately prior to aortic and iliac artery cross-clamping aliquots of blood were removed for study. Additional arterial and venous samples were obtained 30 minutes following occlusion, immediately prior to release of the cross clamps, and at 1–5, 10, 20 and 30 minute intervals following restoration of arterial continuity. Microtechnics of the Astrup analyzer [1, 2] were utilized for the determination of pH, pO_2, pCO_2, standard bicarbonate, base excess and buffer base in all patients. O_2 saturation was calculated from the pH and pO_2 values. The method of Barker and Summerson [3] was utilized to measure lactate levels, and pyruvate levels and were determined by a modified Friedman and Haugen technic.[6] Excess lactate was calculated according to Huckabee [10]:

$$\text{Excess lactate } (XL) = (L_n - L_o) - (P_n - P_o)(L_o/P_o)$$

L_o and P_o are control lactate and pyruvate
L_n and P_n are experimental lactate and pyruvate

In eight patients the serum water concentration, serum specific gravity and total proteins were determined from the serum re-

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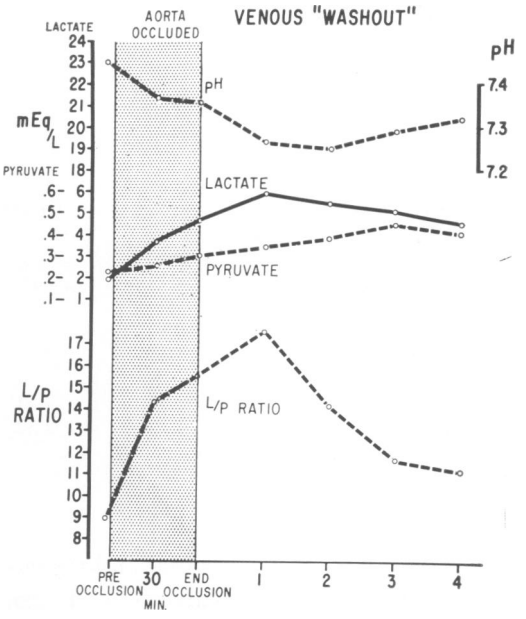

FIG. 1. Mean values (total patient group) in femoral vein blood for lactate, pyruvate, L./P. ratio and pH prior to, during occlusion and at 1–5, 10, 20 and 30 minute intervals following aortic clamp release.

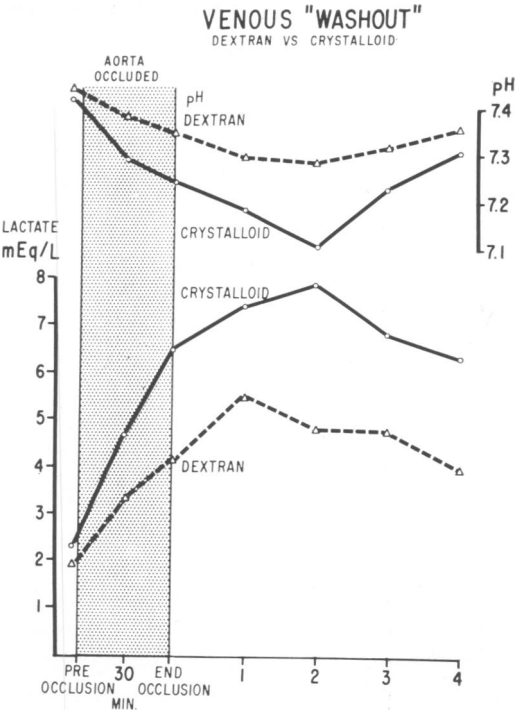

FIG. 2. Illustrates differences in mean values in femoral vein blood for pH and lactate in those patients infused with Dextran and those not infused with Dextran. Post-release samples obtained at 1–5, 10, 20 and 30 minutes.

fractive index utilizing a total solids meter.[4, 13] Serum sodium, potassium, chloride and magnesium levels were analyzed in six patients by standard laboratory methods.

Halothane anesthesia was utilized on all patients following induction by pentothal, nitrous oxide and oxygen. Ten patients had intravenous infusion of commercial Dextran into the upper extremity at a rate of 2.5 cc./Kg. body weight per hour. Five patients were infused with crystalloid solution only (5% Dextrose in water).

The venous "washout" of one additional patient was studied who had successful restoration of arterial continuity following 20 hours of occlusion (inadvertant ligation of the right iliac artery during a left hemipelvectomy). One baseline arterial inflow sample only was obtained on this patient. Aliquots of blood obtained were analyzed as outlined in the preceding studies.

Results

Mean values for lactate ranged in all patients from 1.99 and 1.93 milliquivalents per liter in venous and arterial blood, respectively, in the preclamping specimens to a maximum of 5.98 and 4.80 mEq./L. ($p < 0.01$) after the cross clamps were released (Table 1). Venous lactate levels of those patients not infused with Dextran varied from 2.32 mEq./L. in the preocclusion samples to a maximum of 7.80 mEq./L. in the postocclusion samples (Table 2) (Fig. 2). Similar changes were noted in arterial samples of these patients. Patients infused with Dextran also showed positive changes in lactate and pyruvate levels but of lesser magnitude. Striking changes were noted in excess lactate values of venous blood but arterial excess lactate values were only slightly elevated subsequent to declamping.

Although there were significant reductions in mean venous pH values ($p < 0.02$), the mean arterial pH values were never in an acidotic (Table 1) range (Fig. 1 & 2).

TABLE 1. *pH, Excess Lactate (mM./L.), Lactate and Pyruvate Levels (mEq./L.): 15 Patients (Mean Values)*

		Pre-occlusion	½ hr.	Pre-release	1–5 min.	10 min.	20 min.	30 min.
Lactate	F.A.	1.932	2.582	2.844	4.001	4.804	4.348	3.877
	F.V.	1.991	3.643	4.681	5.981	5.474	5.194	4.501
Pyruvate	F.A.	0.222	0.289	0.306	0.341	0.397	0.414	0.398
	F.V.	0.224	0.254	0.302	0.341	0.386	0.446	0.402
Excess lactate	F.A.	−0.52	−0.56	−0.48	+0.41	+0.54	−0.10	−0.40
	F.V.	+0.13	+1.49	+2.10	+3.06	+2.17	+1.39	+1.03
L/P ratio	F.A.	8.7	8.9	9.3	11.7	12.1	10.5	.7
	F.V.	8.9	14.3	15.5	17.5	14.2	11.6	11.2
pH	F.A.	7.55	7.45	7.50	7.44	7.42	7.43	7.43
	F.V.	7.45	7.37	7.36	7.27	7.25	7.29	7.32

F.A. = Femoral artery; F.V. = Femoral vein.
Excess lactate calculated from mean values.

However, if one analyzes changes in pH of individual patients it is apparent that the arterial pH of certain individuals was significantly affected by the venous washout of increased numbers of hydrogen ions. When the pH values of arterial and venous blood of patients P. P. (Table 3) and J. B. (Table 4) are compared it becomes apparent that the former developed a significant acute arterial metabolic acidosis while the

TABLE 2. *Lactate and Pyruvate Levels (mEq./L.)*

A. No Dextran		Excess Lactate—mM/L						
		Pre-occlusion	½ hr.	Pre-release	1–5 min.	10 min.	20 min.	30 min.
Lactate	(F.A.)	2.401	3.432	3.581	5.297	5.214	5.261	5.382
	(F.V.)	2.320	4.652	6.429	7.375	7.800	6.792	6.264
Pyruvate	(F.A.)	0.251	0.347	0.399	0.421	0.455	0.453	0.450
	(F.V.)	0.267	0.281	0.401	0.485	0.497	0.660	0.583
Excess lactate	(F.A.)	−0.35	−0.32	−0.70	+0.69	+0.34	+0.41	+0.56
	(F.V.)	+0.06	+2.76	+2.97	+3.15	+3.47	+1.90	+1.98
L/P ratio	(F.A.)	9.6	9.9	8.9	12.6	11.5	11.6	11.9
	(F.V.)	8.6	16.5	16.0	15.21	15.69	10.29	10.74
B. Dextran								
Lactate	(F.A.)	1.760	2.377	2.594	3.512	4.651	3.983	3.547
	(F.V.)	1.900	3.337	4.162	5.496	4.769	4.720	3.968
Pyruvate	(F.A.)	0.213	0.261	0.275	0.313	0.375	0.399	0.379
	(F.V.)	0.217	0.247	0.274	0.311	0.351	0.376	0.363
Excess lactate	(F.A.)	−0.59	−0.48	−0.30	+0.16	+0.58	−0.3	−0.53
	(F.V.)	−0.81	+1.26	+1.73	+2.82	+1.75	+1.48	+0.84
L/P ratio	(F.A.)	8.2	9.1	9.4	11.2	12.4	9.9	9.3
	(F.V.)	8.7	13.5	15.2	17.7	13.6	12.6	10.9

Excess lactate and L./P. ratios calculated from mean values.
F.A. = Femoral artery; F.V. = Femoral vein.

TABLE 3. *Patient P. P.*

		pH	pCO_2	Base E.	S. Bicarb.	Lac.	Pyruv.	L./P. Ratio	Excess Lactate
Pre-occlusion	F.A.	7.48	34	−0.5	23.5	1.981	0.275	7.20	−1.01
	F.V.	7.350	39.5	−3.5	21.2	2.761	0.268	10.30	+0.49
½ hour	F.A.	7.37	38.5	−2.8	21.7	1.966	0.276	7.12	−0.84
	F.V.	7.25	52	−6.6	19.2	3.614	0.276	13.09	+1.03
Pre-release	F.A.	7.37	40	−2	22.9	2.072	0.276	7.51	−0.73
	F.V.	7.24	46.2	−8.9	17.7	5.060	0.261	19.39	+2.85
1–5 minutes	F.A.	7.26	47	−6.5	19.0	4.337	0.234	18.53	+1.76
	F.V.	7.17	67	−8.2	17.2	5.455	0.235	23.21	+4.48
10 minutes	F.A.	7.25	45.3	−7.8	18.1	4.578	0.281	16.92	+1.52
	F.V.	7.15	61	−9	17.2	5.253	0.375	14.01	+2.00
20 minutes	F.A.	7.26	46	−7.1	18.5	3.952	0.310	12.75	+0.59
	F.V.	7.20	52	−9.9	17.0	4.867	0.440	11.06	+1.04
30 minutes	F.A.	7.33	39	−5	20.1	3.421	0.365	9.37	−0.51
	F.V.	7.24	47	−7	18.6	4.289	0.401	10.07	+0.921
1 hour	F.A.	7.26	58	−3.8	21	2.458	0.340	7.23	−1.23
	F.V.	7–26	47	−7	18.7	2.819	0.279	10.10	+0.45

F.A. = Femoral artery; F.V. = Femoral vein.

TABLE 4. *Patient J. B.*

		pH	pCO_2	Base E.	S. Bicarb.	Lac.	Pyruv.	L./P. Ratio	Excess Lactate
Pre-occlusion	F.A.	7.630	18.5	+3.2	26.5	1.107	0.120	9.23	−0.01
	F.V.	7.490	22.5	−2.5	22	1.821	0.132	13.80	+0.77
½ hour	F.A.	7.630	18.2	+2.2	25.7	1.214	0.132	9.20	−0.01
	F.V.	7.290	30.0	−11	16.7	6.071	0.247	24.58	+3.97
Pre-release	F.A.	7.620	18.5	+2.5	26	1.964	0.179	10.97	−0.04
	F.V.	7.290	32	−10	17	6.785	0.273	24.85	+4.48
1–5 minutes	F.A.	7.600	12.3	+1	24	3.571	0.190	18.79	+2.30
	F.V.	7.150	44	−13.6	14.2	6.963	0.199	34.99	+5.34
10 minutes	F.A.	7.59	11.3	−6.8	19	6.428	0.241	26.67	+3.75
	F.V.	7.150	27	−19.7	11.8	7.142	0.312	22.89	+4.47
20 minutes	F.A.	7.52	18.5	−2.9	21.8	3.750	0.321	11.68	+0.27
	F.V.	7.14	37	−17.8	12.9	7.142	0.487	14.66	+2.92
30 minutes	F.A.	7.56	19	+1	24.5	3.213	0.304	10.51	−0.08
	F.V.	7.25	28	−14	14.2	7.142	0.450	15.87	+3.23
1 hour	F.A.	7.600	18.5	+2	25.5	2.500	0.281	8.90	−0.56
	F.V.	7.290	40	−12	15.2	6.785	0.360	18.85	+3.68

F.A. = Femoral artery; F.V. = Femoral vein.

TABLE 5. *Patient H. A.*

		pH	pCO_2	Base E.	S. Bicarb.	Lac.	Pyruv.	L./P. Ratio	Excess Lactate
Pre-occlusion	F.A.	7.62	18.5	0	24	2.46	0.229	10.75	−0.06
	F.V.	7.48	25.5	−2	22.3	2.75	0.251	10.96	+0.53
½ hour	F.A.	7.45	24	−2.7	20	3.76	0.217	17.33	+1.36
	F.V.	7.45	26	−4.3	20.6	4.78	0.298	16.06	+2.51
Pre-release	F.A.	7.54	19	−3	21.5	3.08	0.230	13.38	+0.55
	F.V.	7.48	22.5	−4	21	4.45	0.240	18.52	+2.43
1–5 minutes	F.A.	7.29	45	−6.2	20	3.42	0.303	11.28	+0.13
	F.V.	7.22	53	−7.5	18.5	3.76	0.334	11.26	+0.90
10 minutes	F.A.	7.23	49	−6	18	2.94	0.309	9.51	−0.23
	F.V.	7.18	73	−7.8	19.5	3.25	0.281	11.56	−0.13
20 minutes	F.A.	7.18	66	−7	18.8	3.33	0.251	13.28	+0.58
	F.V.	7.16	68	−8.5	17.8	4.27	0.248	17.23	+2.17
30 minutes	F.A.	7.15	72	−7	18.2	2.21	0.215	10.26	−0.16
	F.V.	7.08	98	−8.5	18	2.91	0.238	12.21	+0.91

F.A. = Femoral artery; F.V. = Femoral vein.

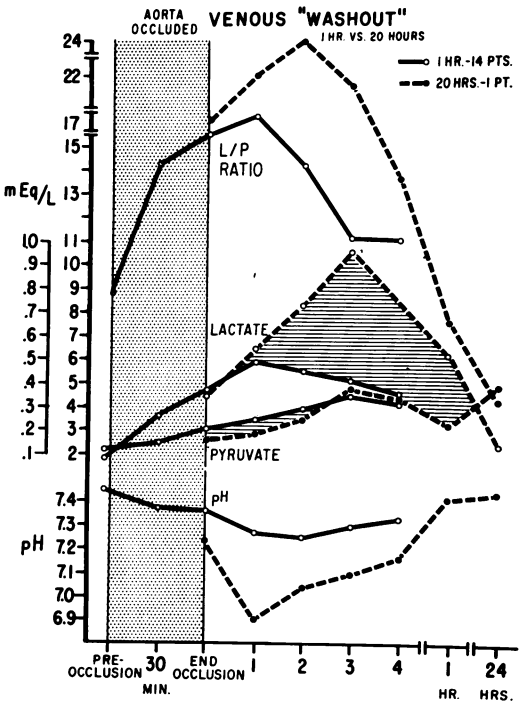

FIG. 3. Illustrates the differences in femoral vein blood values for pH, lactate and L./P. ratio between the mean of the total patient group and a single patient whose inflow was occluded for a total of 20 hours. (Sample times are as described in text.)

latter did not, even though the magnitude of venous pH changes in J. B. were far in excess of those encountered in the venous washout of patient P. P. A further glance

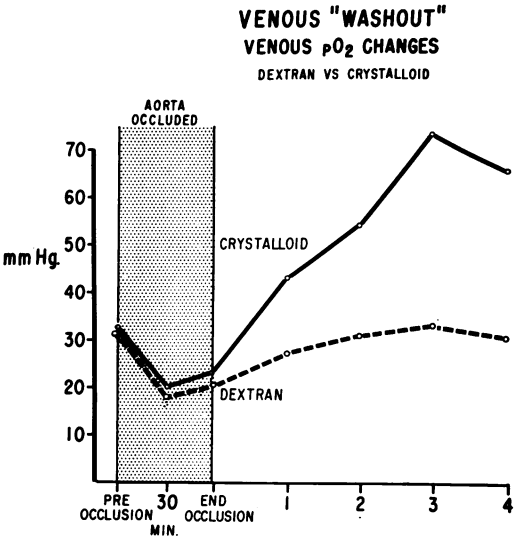

FIG. 4. Comparison of mean venous pO_2 values (from femoral vein) in Dextran infused versus crystalloid infused groups. Note post release increase in the latter group to values approaching those for arterial blood, suggesting the presence of A-V shunt in the human extremity. (Sample times are as described in text).

TABLE 6. *Peripheral O_2 Studies (Mean Values)*

		pO_2 (mm. Hg)						
		Pre-occlusion	½ hr.	Pre-release	1–5 min.	10 min.	20 min.	30 min.
N.D.	(F.V.)	33	16	23	43	54	73	65
D.	(F.V.)	28	18	23	30	32	34	32
N.D.	(F.A.)	165	141	125	175	190	170	135
D.	(F.A.)	142	100	132	154	162	163	194
				O_2 Sat. (%)				
N.D.	(F.V.)	60.2	27	34.4	48.4	73	89.4	89
D.	(F.V.)	57.5	38.6	40.3	48.1	57.8	58.4	57.5
N.D.	(F.A.)	100	95	99	100	100	100	100
D.	(F.A.)	96	97	100	100	98	99	100

N.D. = No Dextran; D. = Dextran; F.A. = Femoral artery; F.V. = Femoral vein.

at the standard bicarbonate levels, base excess and pCO_2 values make it clear that not only did patient J. B. have a more effective buffer mechanism but also that he was maintained in relative respiratory alkalosis throughout the procedure. The tendency in well-conducted anesthesia toward respiratory alkalosis was in a large measure responsible for the maintenance of normal to slightly alkalotic arterial pH values in these patients. Patient H. A. (Table 5) on the other hand developed a significant respiratory acidosis during the procedure and this factor, combined with a relatively mild metabolic acidosis, was reflected by a drop in arterial pH to dangerous levels. A more severe degree of metabolic acidosis and potential catastrophe was fortunately avoided by a short occlusion time (29 minutes) in this patient. The decision not to keep the aorta clamped for one hour (for study purposes) in this patient was made because of the potential hazard of infection. (H. A. had a draining sinus in his left anterior abdominal wall at the time of operation and his aorta was resected through an extraperitoneal approach.)

That a gross correlation exists between the length of time the aorta is cross clamped and the degree of "washout" acidosis is suggested by the increase in lactate levels and drop in venous pH observed in C. B. whose arterial inflow (except for collateral circulation) was occluded for 20 hours (Fig. 3).

Mean venous pO_2 levels ranged from 31 mm. Hg prior to clamping to a low of 16 mm. Hg 20 minutes following clamp release. However, inspection of results comparing the Dextran-infused group with the group receiving Dextrose infusion reveals that the extremely high venous pO_2 and O_2 saturation values following restoration of arterial continuity were limited exclusively to the latter group (Fig. 4). Arterial values for pO_2 and oxygen saturation were within normal or slightly greater than normal ranges throughout the period of observation (Table 6).

Mean values for the specific gravity of the serum of venous blood varied from a preclamping level of 1.0246 to 1.0234 following release of the cross clamps (Fig. 5). Total protein values ranged from a mean of 6.2 grams per cent prior to clamping to 5.8 grams per cent after clamp release and the serum water concentration of venous blood increased from 94.1 Gm./100 ml. to 94.5 Gm./100 ml. at the same intervals. In each patient, the most precipitous fall in venous serum specific gravity occurred during the first half hour of occlusion. Arterial measurements of this parameter were not carried out on all patients. Arteriovenous differ-

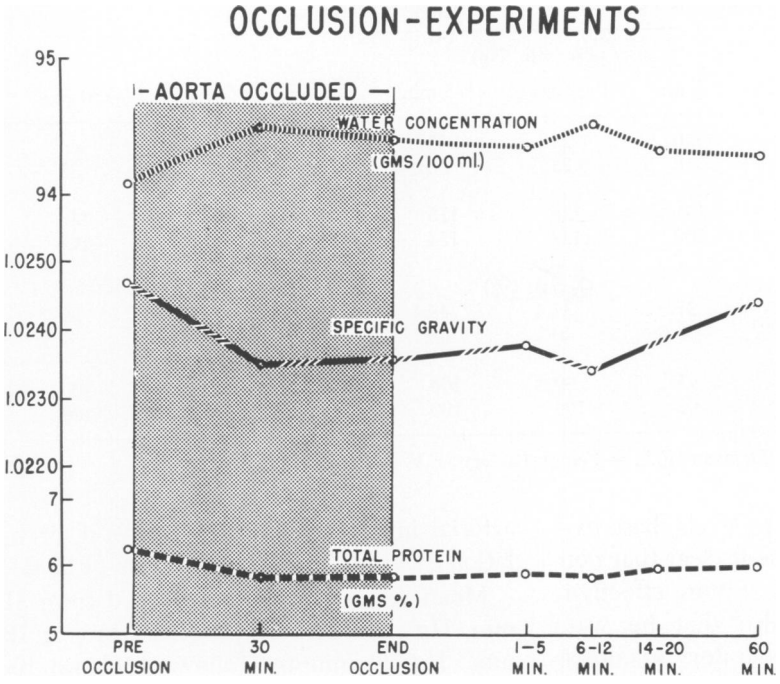

FIG. 5. Mean values from femoral vein of eight patients illustrating fall in specific gravity and total protein and rise in water concentration suggesting net flow of interstitial fluid into capillary bed during occlusion.

ences of a single patient are presented in Table 7.

There were no significant changes observed in the levels of sodium chloride. potassium or magnesium during occlusion or in the period immediately following the restoration of arterial flow.

Discussion

The precipitous fall in specific gravity during the first half hour of cross clamping represents in part the result of decreased hydrostatic pressure in the capillary bed with a net flow of interstitial fluid toward the intravascular space. Since the interstitial fluid of the extremities is low in protein content the net effect on venous blood should be a fall in total protein content and a rise in the relative percentage of water. Such were our observations in this group of patients.

In this study all arterial blood oxygen levels were normal to slightly elevated. Thus any tissue hypoxia which occurred did so despite adequate arterial oxygen saturation and must be related to decreased tissue perfusion. Venous pO_2 and venous O_2 saturation fell to extremely low levels during occlusion. Restoration of arterial continuity resulted in a prompt return to normal values for pO_2 and oxygen saturation in the venous blood of Dextran-infused patients, while those patients not infused with Dextran demonstrated a rise in the venous levels of these parameters to values approaching those of arterial blood (Table 6) (Fig. 4). These findings suggest that Dextran infusion enhanced capillary perfusion during occlusion and in the period following clamp release. On the other hand the high value for venous oxygen saturation and pO_2 in the group not infused with Dextran would seem to indicate that many capillary beds were bypassed via metarteriolar shunts in the extremities. This interpretation is further enhanced by the observed differences in values for absolute lactate levels and those for excess lactate in the two groups (Table 2) (Fig. 2).

That the increases in lactate are not due

TABLE 7. *Specific Gravity, Water Concentration and Total Protein: A/V Difference—Patient P. P.*

		Pre-occlusion	½ hr.	Pre-release	1	2	3	4
Serum Spec. Grav.	F.A.	1.0236	1.0236	1.0225	1.0222	1.0220	1.0220	1.0211
	F.V.	1.0239	1.0222	1.0217	1.0208	1.0214	1.0211	1.0214
Total Prot. Gm./100 cc.	F.A.	5.9	5.9	5.5	5.4	5.3	5.4	5.0
	F.V.	6.0	5.4	5.2	4.9	5.1	5.0	5.1
Serum Water Conc. Gm./100 cc.	F.A.	94.4	94.4	94.7	94.8	94.9	94.8	95.1
	F.V.	94.3	94.8	94.9	95.2	95.0	95.1	95.0

F.A. = Femoral artery; F.V. = Femoral vein.

to anesthesia is evidenced by the lack of excess lactate in samples obtained prior to clamping and subsequent to approximately 1½ hours of Halothane anesthesia. This observation would tend to corroborate the findings of Lowenstein, Clark and Villareal [11] who were unable to demonstrate any excess lactate and only minimal changes in the absolute concentration of lactate and pyruvate during Halothane anesthesia. Bank blood preserved in acid citrate dextrose solution contains from 1.1 to 2.9 mEq. of lactic acid and from 0.04 to 0.11 mEq. of pyruvic acid per 500 cc. unit.[9] Since a mean of 900 cc. of bank blood was administered to these patients during the period of study, the contribution of this amount of lactic acid and pyruvic acid to the total was insignificant. The efficiency of the body buffer mechanisms in the presence of normovolemia and adequate ventilation is not only indicated by the maintenance of an adequate arterial pH but also by the relatively low levels of excess lactate in arterial blood as compared to those in the venous washout. These observations tend to reinforce those of others who have demonstrated that hypotension associated with declamping and reactive hyperemia is not primarily the result of the sudden venous "washout" of acid metabolites and its effect on myocardial function.[5, 7] However these studies show that the venous blood distal to the cross-clamped aorta contains significant amounts of acid metabolites and under certain circumstances might contribute significantly to the refractiveness of a hypotensive state, should one occur. For example, a recent survey of mortality rates following resection of ruptured aortic aneurysms in 131 patients from the personal series of one of us (C. T. F.) showed a distinct correlation between operative mortality and the size of the retroperitoneal hematomata encountered at the time of operation. In this group of patients the hypotensive episode associated with aortic rupture is not only more severe, but requires the rapid infusion of large quantities of bank blood for resuscitation. In addition, technical difficulties secondary to the large hematoma often requires a slightly prolonged period of cross clamping. Howland, Schweizer and Boyan,[8] studying the effect of exogenous buffering on the mortality associated with massive blood replacement, stated that bank blood is a most important source of acid during massive transfusion, since it contains a pCO_2 of 152 to 210 mm. Hg, a standard bicarbonate of only 1.2 to 7.8 mEq./L. and an average buffer base of only 31 mEq./L. These same authors showed that the administration of 44.6 millimoles of sodium bicarbonate, given to

counteract the theoretical acid load of each 5 units of bank blood, decreased the mortality rate from 38 to 8 per cent in patients transfused with 20 or more units of blood.

The three-pronged mechanism cited above (massive transfusion, hypotension and cross clamping) must result in large quantities of acid metabolites in the circulation of patients undergoing resection for ruptured aortic aneurysms. It would seem that in this group of patients the still excessively high mortality rate might be reduced to a respectable level if buffer agents were administered from the onset of therapy.

Summary and Conclusions

1. Metabolic studies distal to the cross clamped aorta demonstrate:
   a) accumulation of significant amounts of acid metabolites as evidenced by a significant fall in venous pH
   b) significant elevations in the absolute values of lactate and pyruvate and of excess lactate during occlusion
   c) a profound fall in venous pO_2 and venous O_2 saturation
   d) a precipitous fall in the specific gravity of the serum
   e) that the effect of venous washout acidosis on arterial blood is minimal under circumstances of normovolemia and adequate ventilation and oxygenation.
2. The infusion of commercial Dextran above the cross clamp at the rate of 2.5 cc./Kg. body weight/hour is effective in reducing anaerobic metabolism during the period of occlusion. This effect is probably secondary to enhanced capillary flow associated with Dextran infusion.
3. The use of buffers (Na bicarbonate) would seem to be helpful in reducing the mortality rate associated with the resection of ruptured aortic aneurysms.

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