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Muscle Surface pH as an Index of Peripheral Perfusion in Man

NATHAN P. COUCH, M.D., JAN R. DMOCHOWSKI, M.D., JOSEPH M. VAN DE WATER, M.D., DWIGHT E. HARKEN, M.D., FRANCIS D. MOORE, M.D.

From the Department of Surgery, Harvard Medical School, and Peter Bent Brigham Hospital, Boston, Massachusetts

IN THE clinical setting, methods for frequent or constant surveillance of vital functions have largely depended upon properties of the cardiovascular tree, rather than properties of the tissues supplied. These factors have included pulse rate, arterial pressure, central venous pressure, blood volume, and electrocardiography. Such data do not provide a measure of the overall state of tissue perfusion and are particularly inadequate for appraising disorders wherein there is maldistribution of blood flow. Although metabolic disturbances are determining factors in survival, methods for continuously measuring aerobic metabolism in peripheral tissue have not been available.

Since 1875, when Lord Kelvin published "Electrolytic Conduction in Solids—First Example, Hot Glass," [24] it has been known that glass is an electrolytic conductor. In 1909 Haber and Klemensiewicz established that "glass electrode potential" depends on hydrogen ion concentration. Only during the last 10 to 15 years have cation-selective electrodes been generally applied in the biological sciences. In the introduction to his classic text, Eiseman remarks, "Such glass electrodes are useful wherever a direct measurement of ionic *activity* is desired—whether this be in a simple solution or in a complex ionic mixture, *in vitro* or *in situ*—and offer advantages over other methods when non-destructive, continuous high-sensitivity measurements are needed. . . . In many situations the measurement of ionic concentration or activities by glass electrodes now exceeds other methods in precision and accuracy." [7]

As problems with uniform fabrication of glass crystal structures have been solved, the use of such electrodes has widened. The quality of electrodes sensitive to the

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hydrogen ion has exceeded that for all other cation-selective electrodes and has led to their ready commercial availability.

In this laboratory, earlier work demonstrated that glass electrodes could be used for measuring surface pH continuously in whole organs and that acidosis in stored kidneys, livers, and hearts varied directly with temperature and duration of storage.[3, 4] Tissue surfaces were used, instead of deep portions accessible only to puncture, to prevent artifacts due to blood extravasation, trauma, positioning of the electrodes, or damage to the cation-selective glass. It became clear that the method was applicable for any solid organ or tissue in the living animal. Further studies in dogs showed that muscle surface pH (pH_M) fell rapidly after hemorrhage, often before the blood pressure, and usually in the absence of change in arterial blood ph (pH_A).[22, 13] It was also found that when blood volume was normal, pH_M closely matched pH_A in conditions of acidosis or alkalosis, whether the cause was metabolic or respiratory.[21]

These studies thus established that reduced perfusion led promptly to tissue acidosis, presumably due to lactic acid generated from anaerobic glycolysis in circumstances where metabolic demand exceeded oxygen supply, or where there was impaired clearance of acid metabolites.

In early 1969 this work was begun in the clinical setting for the surveillance of patients with low flow states or other metabolic derangements causing disturbances of blood and tissue pH.

Answers were sought for the following questions:

1. What is the normal range of pH_M in man?
2. Does the human develop, like the dog, a prompt muscle acidosis in simple hypovolemia?
3. What is the course of pH_M in human subjects undergoing stress from major surgery without major blood deficit?
4. What changes in pH_M occur in areas of regional ischemia, particularly in patients undergoing arterial reconstruction?
5. Does muscle acidosis occur in patients undergoing open-heart surgery, especially during the cardiac bypass phase? If so, at what time in the procedure is acidosis likely to begin? Does pH_M correlate with later complications, lactate elevation, or mortality?

Materials and Methods

The 41 subjects included eight normal young adult male volunteers, three patients undergoing major abdominal surgery without major blood loss or significant pulmonary disease, eight patients undergoing reconstructive surgery for abdominal aortic aneurysm or lower extremity ischemia, and 22 patients undergoing cardiac surgery with pump-oxygenator bypass.

The plan of observation varied for each group.

Normal Volunteers. After the customary screening, informed consent, history, physical examination, hemogram, chest x-ray, and electrocardiogram on the day prior to study, seven of the eight subjects underwent the following procedure:

While the subject was in a fasting state and in the supine position, an intravenous infusion, a percutaneous radial artery cannula, and electrocardiograph electrodes were placed. The tip of an Instrumentation Laboratories electrode [No. 14183] (Fig. 1) was placed on the surface of the midbiceps muscle through a 2 cm. incision under local anesthesia. The radial artery cannula was connected to a Statham strain gauge for pressure recording, and the pH electrode was connected to an Instrumentation Laboratories pH electrometer.

After a control period of 90 minutes, during which the blood pressure, muscle surface pH, and pulse were recorded, 750 ml. of blood were withdrawn through a

14-gauge needle into Fenwal citrate-phosphate-dextrose blood bags. Observations were continued for a 2-hour period of hypovolemia, at the end of which time the entire volume of blood was returned. There followed a final recovery period of 1 or 2 more hours.

Patients Undergoing Major Abdominal Operations. Three patients undergoing colonic resections under general inhalation anesthesia were studied throughout the operative procedures, which were 5 to 7½ hours in length. The biceps muscle was used as the electrode site in all three patients and muscle pH was monitored continuously and recorded every 15 minutes, in addition to the vital signs.

Patients Undergoing Arterial Reconstructive Operations. The patients who underwent operations for arterial reconstruction included four with abdominal aortic aneurysm replacement, two with aorto-iliac reconstruction, one with an axillo-femoral bypass graft, and one with a femoropopliteal vein bypass graft. The latter patient had the electrode placed on the medial portion of the middle third of the gastrocnemius muscle of the involved leg, while the electrode in all other patients was placed on the lower third of the rectus femoris muscle. In three of the four patients with aneurysm resections, a biceps electrode was also placed.

Observations were continued throughout the procedures until 4 to 18 hours postoperatively.

Patients Undergoing Cardiac Surgery with Cardiopulmonary Bypass. For the entire group of 22 patients receiving intraoperative pump-oxygenator support, the biceps muscle was the site of pH monitoring. In addition, cardiac output determinations were made, using cardio-green dye, a Gilford Densitometer, and a Lexington Analog computer programmed for cardiac output. The latter determinations were made at appropriate points before and after bypass. Frequent samplings for arterial blood P_{O_2}, P_{CO_2}, and pH were made. Samplings for lactate determinations (enzymatic method of Hohorst) [1] were also made before, during, and after bypass, and at other points, as indicated by the clinical course.*

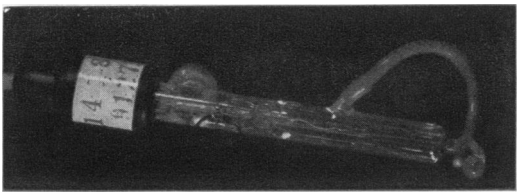

FIG. 1. Right-angle pH electrode for continuous measurement of muscle surface pH. The indicator electrode is the glass portion of the right-angle and is sensitive at the tip; the reference electrode is encased in flexible black plastic.

After return to the Recovery Room, the muscle pH determinations were continued as long as was technically feasible. In most patients this was possible until 24 hours postoperatively.

Results

Normal Volunteers. The mean control pH of resting muscle surface in the eight normal subjects was 7.38 (s.d. 0.05). Of the six subjects who showed a pH_M decline after hemorrhage, only three showed a decline of mean blood pressure of 10 mm. Hg or more, and the mean change of pH_M was −0.24 pH units. The mean pH_M after hemorrhage was 7.16. The single subject whose pH_M did not decrease during hypovolemia showed a drop of blood pressure from 140/75 to 115/65. After return of the shed blood, pH_M in all subjects returned to normal range within 30 minutes.

Except for Subject 4, the arterial blood pH did not change significantly from the control level.

The results for the volunteers undergoing 750 ml. hemorrhage are recorded in Table 1. The course of events in Subject 3 are depicted graphically in Figure 2.

In the eighth normal subject, undergoing a control period in a later study, the control biceps pH_M was 7.48.

* No lactate-containing solution infused during these operations.

TABLE 1. *Muscle pH: Normal Subjects Undergoing Hemorrhage*

Subject	Control		Posthemorrhage		Recovery		Blood Pressure		
	pH_M	pH_A	pH_M	pH_A	pH_M	pH_A	Con.	Hem.	Rec.
1	7.35	7.40	7.35	7.41	7.39	7.42	140/70	115/65	150/70
2	7.42	7.44	7.12	7.39	7.37	7.42	140/60	70/50	160/65
3	7.44	7.40	6.96	7.41	7.44	7.42	130/80	115/70	130/70
4	7.33	7.40	7.27	7.32	7.39	7.41	120/70	90/40	140/80
5	7.40	7.41	7.32	7.39	7.40	7.42	120/70	120/70	150/90
6	7.32	7.42	7.20	7.42	7.42	7.42	150/85	160/80	150/90
7	7.30	7.42	6.92	7.42	7.34	7.44	120/70	120/70	125/60
8	7.48								

pH_M = muscle pH; pH_A = arterial blood pH.

Although pH is not a linear quantity but a logarithmic function of hydrogen ion concentration, the data are expressed in terms of pH for convenience.

The pH electrode measures hydrogen ion *activity* rather than hydrogen ion concentration directly.

Patients Undergoing Major Abdominal Operations. In two of the three patients with major abdominal surgery (one sigmoid colectomy, two Miles resections), the pH_M remained stable throughout the operations, and there was no decline of pH_M below 7.32. In the third patient pH_M was also stable, except for a brief depression to 7.25 shortly after the skin incision; this was accompanied by a drop in blood pressure from 150/80 to 110/70. (The anesthetic was halothane-pentothal-nitrous oxide.) Blood pressure and pulmonary function were stable throughout the three procedures, except for the case cited.

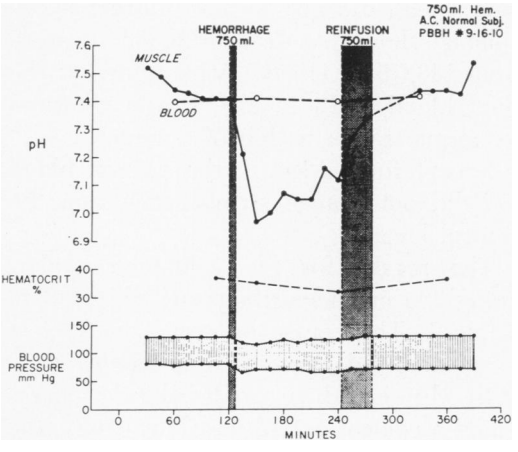

FIG. 2. Normal subject undergoing 750 ml. hemorrhage (No. 3, Table 1). Note the close agreement between pH_M in the control period and after reinfusion, and the marked, abrupt decline of pH_M (to 6.96) during hypovolemia. The blood pressure change was slight.

Patients Undergoing Reconstructive Arterial Surgery. The data pertaining to patients in whom leg ischemia existed preoperatively or in whom intraoperative arterial clamping was performed are outlined in Table 2.

Three of the four patients having abdominal aortic aneurysm resections had abnormally low quadriceps pH_M prior to cross-clamping. All four showed a sharp drop of pH_M duritng cross-clamping, but only three of the four showed a return to normal range after re-flow. The patient who did not show recovery of normal pH_M had a thrombosis. After the thrombosis was relieved, the pH_M returned over a period of 12 hours to a pH_M of 7.30. The biceps pH_M remained nearly or completely normal in the three patients so studied. Figure 3 depicts the course of events in patient H. R.

Of the two patients having aortoiliac reconstructions, only one (J. S.) had an abnormally low pre-clamp pH_M, i.e., 6.94. In the second subject, the control pH_M was normal and did not drop significantly after cross-clamping. In the first subject, however, the pH_M declined to 6.77 after clamping, but returned to 7.59 after reflow. In Figure 4, the date for Patient J. S. are plotted.

The two patients undergoing axillofemoral bypass and femoropopliteal vein bypass also showed abnormally low pH_M

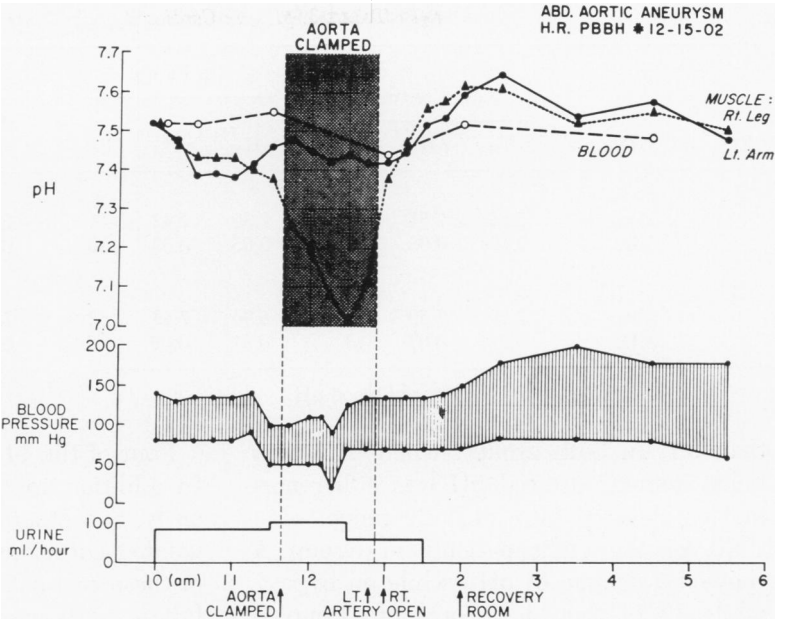

FIG. 3. Patient undergoing resection of an abdominal aortic aneurysm, who had pH electrodes on both the biceps and rectus femoris muscles (Pt. H. R., see Table 2). During the aortic cross-clamp, rectus femoris pH_M dropped to 7.09, while the biceps pH_M remained normal. After reflow, rectus femoris pH_M returned to that of the biceps, and was slightly alkalotic.

prior to repair, with return to approximate normality after re-flow.

Patients Undergoing Pump-Oxygenator Bypass. In the 22 patients of the cardiac bypass group, varying patterns of pH_M were found. The patients were divided into two groups. Group A included those patients whose biceps pH_M at no time during the operation was less than 7.2, and Group B included those whose biceps pH_M fell below 7.2. Table 3 details the pertinent data, and Figures 5 and 6 graphically depict the course of events in representative patients from each group. In only one of the eight patients in Group A did pH_M decline below normal during the pre-bypass period, while ten of the 14 patients in Group 8 showed such a decline. In Group A, when the pH_M was normal it did not deviate from the arterial pH by more

TABLE 2. *pH_M in Peripheral Arterial Reconstruction*

Type	Pt.	Control Immed. Prior to Clamp			During Clamp			Recovery		
					Min.			Max.		
		pH_{TM}	pH_{BM}	pH_A	pH_{TM}	pH_{BM}	pH_A	pH_{TM}	pH_{BM}	pH_A
Abd. aortic aneurysm	N. F.	7.05	—	7.50	6.61	—	7.52	7.40	—	7.61
	H. R.	7.43	7.38	7.58	7.08	7.42	7.44	7.56	7.52	7.51
	E. T.	6.86	7.34	7.64	6.64	7.29	—	6.95*	7.35	—
	A. S.	7.14	7.28	7.47	6.48	7.40	7.44	7.41	7.40	—
Aortoiliac reconstruction	J. S.	6.94	—	7.58	6.77	—	—	7.56	—	7.50
	S. F.	7.39	—	—	7.36	—	—	7.49	—	—
Axillofemoral graft	R. W.	7.05	—	7.53	6.96	—	—	7.21*	—	—
Femoropopliteal graft	T. M.	7.19	—	—	7.14	—	—	7.30	—	—

pH_{TM} = thigh muscle pH; pH_{BM} = biceps muscle pH; pH_A = arterial blood pH.
* Both pts. had thromboses after correction of which pH_M rose to approximately normal.

TABLE 3. *pH_M in Cardiac Bypass*

Pt.	Group	Last Control			On Pump			Recovery			Mortality
		pH_M	pH_A	BP	Min. pH_M	pH_A	BP	Max. pH_M	pH_A	BP	
A	(>7.2)										
	Mean	7.43	7.51	84	7.30	7.42	61	7.38	7.49	76	1/8
	S.D.	0.10	0.08	16	0.05	0.08	20	0.06	0.06	6	
B	(<7.2)										
	Mean	7.19	7.50	69	6.94	7.43	52	7.18	7.47	74	4/14
	S.D.	0.21	0.07	17	0.31	0.09	5	0.28	0.06	11	

pH_M = muscle pH; pH_A = arterial blood pH.

than 0.1. In both groups, when pH_M was below normal, arterial pH was either normal or elevated into alkalotic range.

Six of the eight patients in Group A showed a decline of pH_M while on bypass, while 12 of the 14 patients of Group B showed such a change. Six of the latter group had a decline to less than 7.0. Two of these six patients died. One, who had a minimum pH_M of 6.82 did not regain adequate cardiac output at completion of bypass, and had a pH_M of less than 7.2 for 120 minutes. The duration of cardiopulmonary bypass was 240 minutes. The other patient, who had a minimum pH_M of 6.39, had a bleeding diathesis at the end of the operation, which subsided. However, he developed acute renal failure and severe ischemia of the leg used for arterial perfusion. His pH_M was less than 7.2 for 510 minutes, and the duration of bypass was 180 minutes. Figure 6 depicts the course of his operation.

A third patient of Group B, whose pH_M was depressed to 6.87, maintained his pH_M at a level less than 7.2 for 730 minutes. His immediate postoperative course was stormy and characterized by extreme peripheral vasoconstriction, with cold, pallid extremities, pulmonary insufficiency, and depressed sensorium. After very slow progress he recovered.

Mortality. One of the eight patients in Group A died with a bleeding diathesis on the first postoperative day. All of the other seven had uneventful recoveries.

Four of the 14 patients in Group B died. In addition to the two mentioned previously, two others died in coma without regaining consciousness after operation. One of these two patients had mild, acute renal failure with uremia to the time of death. Both patients had left heart prosthetic valve insertions. Neither showed a decline of pH_M to less than 7.0, and the intervals below 7.2 were 110 and 50 minutes.

No consistent correlation was found between (1) hypotension and low pH_M, or (2) between low cardiac index and low pH_M. However, Figure 7, in which cardiac index is plotted against the simultaneous pH_M, shows a nearly linear relation between the lower pH_M values on the right side of the plot and the cardiac indices. Thus, when pH_M was 7.0, the cardiac index was never greater than 2.5 liters per square meter per minute. And when pH_M was 6.9, the cardiac index did not exceed 2.3 liters per square meter per minute.

On the other hand, there was a wide scatter on the left; for any given cardiac index, pH_M had a wide range into the normal, or alkalotic, levels. This was often attributable to hyperventilation, with lowered blood P_{CO_2} and respiratory alkalosis.

Four patients received sodium bicarbonate, and one received tris-buffer *; these agents were given when the arterial pH was declining, usually *before* it reached

* The standard dose of tris-buffer was 500 mg. and of sodium bicarbonate was 40 mEq.

truly acidotic levels. The patient who received tris-buffer showed no substantial rise of pH_M (from 7.14 to 7.22 ten minutes afterward), as did one of the patients receiving bicarbonate (7.18 to 7.26). The other three patients receiving bicarbonate showed either no change at all, or only a modest rise (7.12 to 7.12, 7.27 to 7.31, and 7.22 to 7.22).

In all patients of both groups there was a rise in serum lactate concentration. In Group A, the mean "peak" lactate concentration after bypass was 3.65 mM./liter (s.d. 1.43), while in Group B, the mean "peak" lactate concentration was 5.32 mM./liter (s.d. 2.05). Hence the patients whose pH_M fell below 7.2 had substantially higher "peak" lactate concentrations than those of Group A, but in this small number of patients the difference was not statistically significant.

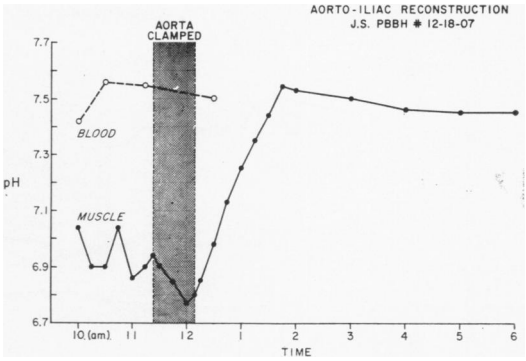

FIG. 4. Patient undergoing an aortoiliac reconstruction (Pt. J. S., Table 2). Note the rectus femoris acidosis prior to cross-clamp, presumably due to chronic ischemia, the further drop during clamping, and the return to normal with reflow.

Discussion

Although skeletal muscle has not been used clinically as an index of peripheral perfusion, it offers several advantages. First, it comprises 40 to 45 per cent of the body cell mass, accounts for 30 per cent of total oxygen consumption when at rest, and contributes a proportionately large quantity of metabolites to the circulating blood.[8] Second, because it has low priority in the body economy, it suffers deprivation of blood flow very early in progressive hypovolemia. A third advantage is that skeletal muscle is easily accessible through a small incision.

Fourth, skeletal muscle vasculature is sensitive to sympathetic nerve activity and circulating vasoactive agents such as the catecholamines and angiotensin. Beyond this, the increase in activity of such humoral agents is known to be virtually instantaneous during hemorrhage. Walker, Moore, *et al.* demonstrated ten- to fifty-fold increases in catecholamine concentration in adrenal venous blood within seconds after onset of blood loss in dogs.[16, 25] Skillman *et al.* showed that increased renin activity (and thus of angiotensin activity) occurred after only 250 ml. of hemorrhage in five of their nine human subjects; they presumed that the prompt release of renin was partly related to sympathetic activity, while recognizing that the effect of decreased blood volume and decreased juxtaglomerular pressure also prevailed.[19] But beyond this abrupt increase of vasoconstrictor activity, with reduction in muscle blood flow and oxygen deprivation, it is important that muscle has a high glycogen and creatine phosphate content, with particularly abundant glycolytic capacity in white muscle.[8] Hence muscle is especially well equipped to shift rapidly from aerobic to anaerobic metabolism, i.e., from oxidative phosphorylation to anaerobic glycolysis, whether the circumstance is decreased blood supply, or increased metabolic demand as in severe exercise.

In addition to promoting anaerobic glycolysis and lactic acid production through vasoconstrictor activity, the catecholamines exert a *direct* influence on energy reactions by effecting formation and accumulation of cyclic-3′,5′-AMP, which in turn increases the activity of phosphorylase a and b kinase, glycogenolysis, and lactate production.[5, 22] This mechanism has been found in skeletal muscle, as well as in liver, heart, fat, intestinal smooth muscle, uterus, lung, spleen, and brain.[22] The response is

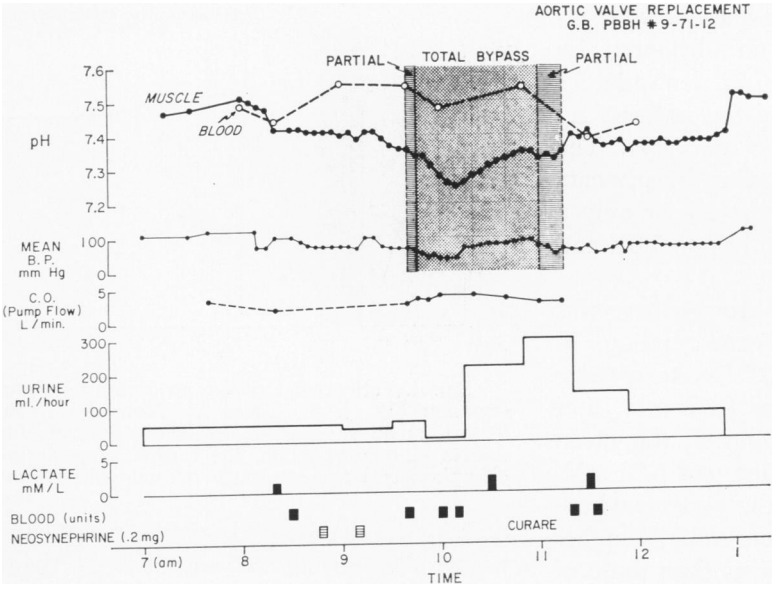

FIG. 5. Patient of the cardiopulmonary bypass series, group A. The biceps pH_M did not reach levels lower than 7.2. The pump flow, blood pressure, and urine flow remained within satisfactory range. There was a modest rise of serum lactate concentration to 2.3 mM. per L. (Table 3).

prompt: using *in vitro* frog sartorius muscle, Helmreich and Cori showed that lactate levels rose within 20 minutes of adding epinephrine.[9]

Finally, for these rapid changes to be measurable by the present technic, diffusion of hydrogen ion and lactate across cell membranes must be swift. In studies of lactate and pyruvate movement across red cell membranes, Huckabee proved that lactate diffusion is indeed rapid, and that it is passive.[10]

It was consistent with such evidence that the response of pH_M to hypovolemia, reduced perfusion, or restored perfusion was consistently rapid, as well as reproducible. The normal range of pH_M in the volunteers was grouped closely around a mean of 7.38, and agreed with the control values seen in the biceps muscle of all other subjects, except for the Group B cardiac patients. When the normal subjects underwent hemorrhage of 750 ml., there was a significant depression of pH_M, often without a major decline of blood pressure, supporting the principle that maintenance of blood pressure for perfusion of vital organs is bought, at the expense of muscle perfusion, by peripheral vasoconstriction. The failure of arterial blood pH (pH_A) to follow pH_M was attributable to the efficient buffering capacity of the blood, the short duration of the hypovolemic period, the low proportion of blood loss, and the dilution of muscle-donated hydrogen ion in the total body water. This failure of pH_A to change in mild hypovolemia underscores the fact that pH_M measures hydrogen ion at its source, whether or not pH_A is altered, and pH_M is thereby a sensitive indicator of the balance of metabolic supply and demand.

The patients undergoing major abdominal surgery demonstrated stable pH_M except for the single instances wherein reduction of pH_M was accompanied by brief hypotension. Normal operative stress and anesthesia, therefore, did not alter pH_M.

Regional ischemia, whether chronic or acute, brought depressions of pH_M in the involved muscle, and the adequacy of flow could be deduced from pH_M. The implications for flow-monitoring in arterial reconstruction are obvious.

The patients undergoing pump-oxygenator support, although affected by more complex factors (including variable blood volume, cardiac muscle function, pulmonary function, and the use of drugs such

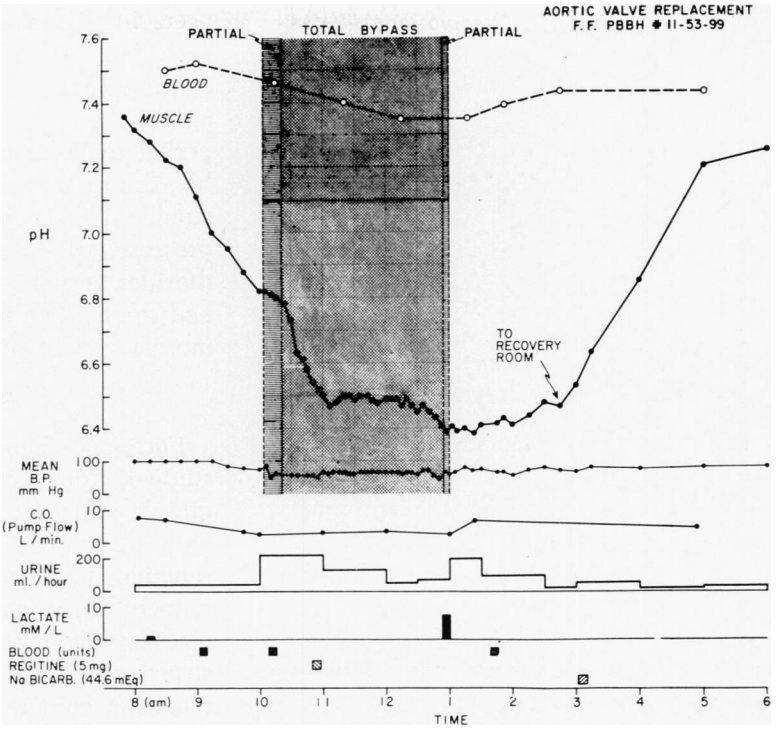

FIG. 6. Patient of the cardiopulmonary bypass series, group B. Note the severe degree of muscle acidosis (to a low of 6.39) while on bypass as well as the decline of pH_M prior to bypass. This patient later developed acute renal failure and ischemic necrosis of his left calf muscles, and did not survive (Table 3).

as vasopressors, vasodilators, and buffer agents) supplied data of particular interest. First, the sharp deterioration of pH_M in the Group B patients quantified, in a novel way, a phenomenon with which anesthesiologists and cardiac surgeons have long been familiar: the poor tolerance for anesthesia of many patients with advanced heart disease, often ascribed to the negative inotropic effects of anesthetic agents, and the stress of large thoracic incisions.

Second, the tendency for pH_M to decline further during cardiopulmonary bypass indicated that muscle hypoxia was occurring, secondary to critical reduction of peripheral flow, a phenomenon which has long been recognized. Thus, when pH_M was depressed in the presence of normal cardiac index or blood pressure, a "centralizing" of flow seemed to prevail, possibly with a disproportionate quantity of blood in the pulmonary circulation.[14] Such maldistribution may be especially pernicious when it is prolonged, and peripheral lactic acid accumulation is accordingly large. The consequences—lactacidosis of the circulating blood—is therefore greatest after flow is restored to the periphery and "washout" occurs. Such acidosis has been shown, by many investigators, to impair the cardiac and peripheral vascular effects of catecholamines [2, 20, 22] and to cause cardiac disturbances, including decreased intraventricular conduction, reduced myocardial contractility [6, 15, 18] and loss of digitalis effect.[15]

The higher arterial blood lactate concentrations found in the Group B cardiac bypass patients came in the wake of greater depression of pH_M than obtained in the Group A patients. Unfortunately, it was not feasible to determine true peak lactate concentrations, because lactate analyses could not be made at short enough intervals to enable such an interpretation. However, the timing of the samples was similar enough to support the validity of this finding.

Huckabee has found that blood lactate elevations in hyperventilation do not exceed 2 mM. per liter, and that in ventila-

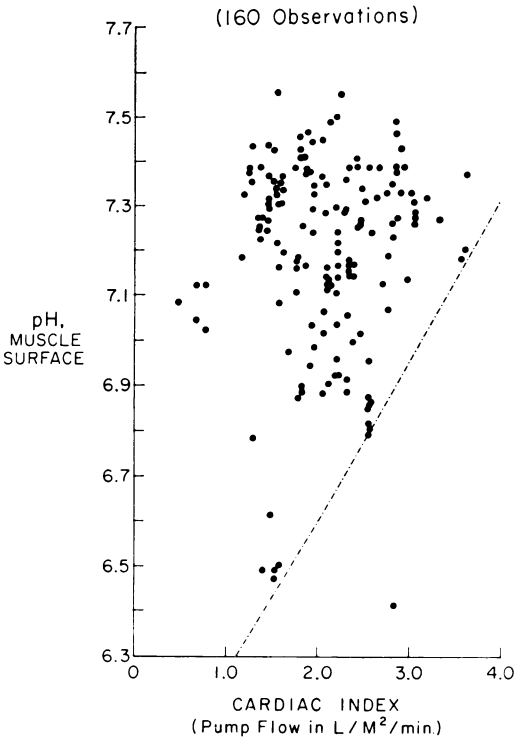

FIG. 7. Muscle surface pH plotted against cardiac index as calculated from pump flow. Note the correlation between declining pH_M and declining cardiac index to the right of the array. On the other hand, a normal or high pH_M did not necessarily indicate a normal cardiac index, because respiratory and metabolic factors could produce compensating akalosis.

tory hypoxia the blood lactate levels do not exceed 3 mM. per liter.[11] On the other hand, lactate concentrations found in clinical low flow states may often exceed 6 mM. per liter, and occasionally 10 mM. per liter.[17]

The prompt return of normal pH_M in the majority of patients after valve repair and completion of bypass circulation resembled the effect found after reinfusion of blood or restoration of flow to an area of regional ischemia, and was attributable to improved hemodynamics brought by the valve repair, improved coronary flow after release of the caval tourniquets with restoration of normal pulmonary flow, and accurate repletion of blood volume.

The appearance of muscle acidosis, often occurring before cardiac bypass and always preceding any elevation of blood lactate concentration, suggested that vasodilator agents should be given early in the bypass period to be maximally effective. Ostensibly, the timing of such vasodilator therapy would depend upon the arterial blood pressure, arterial blood oxygen and carbon dioxide tensions, the arterial blood pH, and the cardiac index, in concert with the muscle surface pH.

Summary

Forty-one human subjects have been studied, using continuous measurement of muscle surface pH (pH_M) in conjunction with other data pertinent to vital organ function. Included were eight normal volunteers, three patients having colonic resections, eight patients undergoing reconstructive arterial surgery, and 22 patients receiving cardiac bypass surgery.

The normal mean biceps muscle surface pH was, in the volunteers, 7.38 (s.d. 0.05). In six of the seven normal volunteers subjected to 750 ml. hypovolemia, a prompt and sharp decline in pH_M was found to a mean level of 7.16; normal pH_M was restored after reinfusion of the shed blood.

In the three patients undergoing major abdominal surgery, moderate surgical stress and anesthesia did not bring significant changes in pH_M. For the eight patients with regional ischemia having operations for correction of chronic impairment of arterial flow, the method showed (1) that seriously reduced flow is accompanied by muscle acidosis, (2) that total interruption of arterial flow by cross-clamping produces profound muscle acidosis, and (3) that restoration of normal flow provides return of pH_M to normal levels. The technic was also valuable for detecting inadequate restoration of flow.

In the patients undergoing cardiac bypass surgery, skeletal muscle acidosis commonly accompanied induction of anesthesia as well as the bypass procedure itself. In

at least two patients with severe muscle acidosis it preceded mortality from ischemic lesions of vital organs. Lactacidosis was more pronounced in the 14 patients who had reduction of their pH_M below 7.2 than in the eight patients who did not suffer such reduction. Therefore, the measurement of muscle surface pH in cardiac patients offers a means for more precise direction of therapy, particularly in the use of vasodilator agents.

Acknowledgments

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References

1. Bergmeyer, H. U.: Methods of Enzymatic Analysis, New York, 1965. Academic Press, Inc., p. 266.
2. Campbell, G. S., Houle, D. B., Crisp, N. W., Weil, M. and Brown, B. B., Jr.: Depressed Response to Intravenous Sympathicomimetic Amines in Humans during Acidosis. Dis. Chest, 33:18, 1958.
3. Couch, N. P., Maginn, R. R., Middleton, M. K., Appleton, D. R. and Dmochowski, J. R.: Effects of Ischemic Interval and Temperature on Renal Surface Hydrogen Ion Concentration. Surg. Gynec. Obstet., 125:521, 1967.
4. Couch, N. P. and Middleton, M. K.: Effect of Storage Temperature on the Electrometric Surface Hydrogen Ion Activity of Ischemic Liver and Heart. Surgery, 64:1099, 1968.
5. Dmochowski, J. R. and Couch, N. P.: Electrometric Surface pH of the Ischemic Kidney and the Effect of Hypothermia. J. Surg., Res., 6:45, 1966.
6. Ebert, P. A., Greenfield, L. J., Austen, W. G. and Morrow, A. G.: The Relationship of Blood pH During Profound Hypothermia to Subsequent Myocardial Function. Surg. Gynec. Obstet., 114:357, 1962.
7. Eisemann, G.: Glass Electrodes for Hydrogen and Other Cations, Marcel Dekker, Inc., New York, 1967, 582 pp.
8. Havel, R.: Utilization of Body Fuels by Muscle, in Energy Metabolism and Body Fuel Utilization. Harvard Univ. Printing Office, Cambridge. P. 20. 1966.
9. Helmreich, E. and Cori, C. F.: The Activation of Glycolysis in Frog Sartorius Muscle by Epinephrine. Pharmacol. Rev., 18:189, 1966.
10. Huckabee, W. E.: Control of Concentration Gradients of Pyruvate and Lactate Across Cell Membranes in Blood. J. Appl. Physiol., 9:163, 1956.
11. Huckabee, W. E.: Relationships of Pyruvate and Lactate During Anaerobic Metabolism. J. Clin. Invest., 37:244, 1958.
12. Lemieux, M. D., Smith, R. N. and Couch, N. P.: Electrometric Surface pH of Skeletal Muscle in Hypovolemia. Amer. J. Surg., 117:627, 1969.
13. Lemieux, M. D., Smith, R. N. and Couch, N. P.: Surface pH and Redox Potential of Skeletal Muscle in Graded Hemorrhage. Surgery, 65:457, 1969.
14. Litwak, R. S., Slonim, R., Wisoff, B. G. and Gadboys, H. L.: Homologous-blood Syndrome During Extracorporeal Oxygenation in Man. New Eng. J. Med., 268:1377, 1963.
15. Moore, F. D.: Metabolic Care of the Surgical Patient, W. B. Saunders Co., Philadelphia and London, 1958. P. 322.
16. Moore, F. D.: The Effects of Hemorrhage on Body Composition. New Eng. J. Med., 273:567, 1965.
17. Moore, F. D., Lyons, J. H., Jr., Pierce, E. C., Jr., Morgan, A. P., Jr., Drinker, P. A., MacArthur, J. D. and Dammin, G. J.: Posttraumatic Pulmonary Insufficiency. W. B. Saunders Co., Philadelphia-London-Toronto, 1969. 234 pp.
18. Peretz, D. I., McGregor, M. and Dossetor, B. M.: Lactic Acidosis: A Clinically Significant Aspect of Shock. Canad. Med. Ass. J., 90: 673, 1964.
19. Skillman, J. J., Lauler, D. P., Hickler, R. B., Lyons, J. H., Olson, J. E., Ball, M. R. and Moore, F. D.: Hemorrhage in Normal Man: Effect on Renin, Cortisol, Aldosterone, and Urine Composition. Ann. Surg., 166:865, 1967.
20. Smith, L. L. and Moore, F. D.: Refractory Hypotension in Man—Is This Irreversible Shock? New Eng. J. Med., 267:733, 1962.
21. Smith, R. N., Lemieux, M. D. and Couch, N. P.: Effects of Acidosis and Alkalosis on Surface Skeletal Muscle Hydrogen Ion Activity. Surg. Gynec. Obstet., 128:533, 1969.
22. Sutherland, E. W. and Robison, G. A.: The Role of Cyclic-3′,5′-AMP in Responses to Catecholamines and Other Hormones. Pharmacol. Rev., 18:145, 1966.
23. Thrower, W. B., Darby, T. D. and Aldinger, E. E.: Acid-base Derangements and Myocardial Contractility. Arch. Surg., 82:56, 1961.
24. Thomson, W.: Electrolytic Conduction in Solids—First Example: Hot Glass. Proc. Roy., A23:463, 1875.
25. Walker, W. F., Zileli, M. S., Reutter, F. W., Shoemaker, W. C., Friend, D. and Moore, F. D.: Adrenal Medullary Secretion in Hemorrhagic Shock. Amer. J. Physiol., 197:773, 1959.