Myocardial Metabolism in Patients Having Aortic-valve Replacement

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Concentrations of metabolites and electrolytes in arterial and coronary sinus blood were studied in ten patients undergoing whole-body perfusion for aortic valve replacement. The study continued through three postoperative days. A comparison was made between five patients whose hearts were beating during perfusion and five whose hearts fibrillated. Oxygen consumption of the myocardium was reduced during hypothermic coronary perfusion; the reduction was greater in the beating hearts. Significant arterial–coronary sinus differences in electrolytes and osmolality were not seen. Arterial concentrations of energy metabolites utilized by the myocardium were elevated throughout operation, and all except glucose were utilized by the heart. Ketosis persisted after operation in the presence of above-normal glucose levels. Other than greater consumption of oxygen during perfusion, no consistent difference was seen between the performances of hearts that fibrillated and those that continued to beat. (Key words: Myocardial metabolism, Aortic valve replacement, Electrolytes, Oxygenation.)

SURVIVAL after open-heart surgery depends ultimately on the continuing ability of the myocardium to maintain cellular function and to do adequate work. Documentation of the response of myocardial metabolism to the stresses of whole-body perfusion and the postoperative period may help to provide better care and survival. Previous studies demonstrated the arterial concentrations of metabolites presented to the myocardium.[1] The present study examines arterial and coronary sinus levels of oxygen, acid–base parameters, electrolytes, and metabolites in ten patients during operation for aortic valve replacement and during the following three days.

Material

PATIENTS

Two groups of five patients each, in whom Starr-Edwards aortic prostheses were inserted for aortic stenosis or insufficiency, underwent identical studies. The heart continued to beat during perfusion in one group and was electrically fibrillated in the other. The "beating" group included three women and two men, whose mean age was 44 years (range 24 to 68), mean weight 136 lb (range 103 to 187), and mean surface area 1.65 sq m (range 1.4 to 2.0). Three patients had been taking digitalis and two patients diuretics. Mean time of whole-body perfusion was 82 minutes (range 70 to 94). The "fibrillating" group included two women and three men whose mean age was 56 years (46 to 65 years), mean weight 162 lb (125 to 190), and mean surface area 1.83 sq m (1.54 to 2.04). Four patients had been given digitalis and diuretics. Mean duration of whole-body perfusion was 91 minutes (range 80 to 101).

Clinically manifest low cardiac output did not develop in any patient, and no patient received assisted ventilation or catecholamine infusion after operation. All patients survived.

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Methods

Anesthesia

As in the previous study,[1] nitrous oxide, oxygen, and halothane were used, with halothane administration continued during perfusion. The tracheas were extubated at the end of operation.

Perfusion

The priming solution consisted of diluted acid-citrate-dextrose (ACD) blood, as noted in a previous paper.[1] The mean rates of whole-body perfusion were 2.26 (beating group) and 2.20 (fibrillating group) l/min/sq m at 30 C. Both coronary arteries were perfused by separate pumps through plastic catheters while the aorta was open. Only the left coronary flow was considered for calculation of left ventricular oxygen consumption, since 80 to 90 per cent of the blood appearing in the coronary sinus drains the left ventricular myocardium.[2] The left coronary pump and the arterial pump supplying the whole-body perfusion were calibrated volumetrically after each perfusion.

Sampling Schedule

Arterial blood was taken from the patient, or pump oxygenator (during perfusion), as shown in table 1. Samples were drawn simultaneously from the coronary sinus via a small catheter placed by the surgeon after thoracotomy. The catheter was brought out through the chest wall and used for postoperative sampling. Arterial samples were obtained after operation from a left atrial catheter emerging through the chest wall, or from a peripheral artery.

Analyses

Methods of analysis of the arterial and coronary sinus blood have been reported in a previous study.[1] Tensions of oxygen and carbon dioxide, as well as pH, were determined, and temperature was corrected when lower than 36 C. Concentrations of calcium, sodium, and potassium were measured, and osmolality was determined by freezing-point depression (Fiske Osmometer, Model G). The energy-producing metabolites measured were nonesterified fatty acids (NEFA), total ketone bodies, glucose, lactate, and pyruvate. Levels of blood glucose were determined in an Auto-Analyzer (Technicon Instruments). Ratios of lactate to pyruvate were calculated, as were coefficients of extraction or production [•] of oxygen, NEFA, and lactate. Oxygen content was obtained by multiplying the values for hemoglobin by 1.34 and by oxygen saturation of the hemoglobin.

Statistical analyses were done by use of Student's t test, with $P < 0.05$ as the level of significance. Paired data for each parameter in each of the two groups were compared: (1) arterial and coronary sinus blood levels at each sampling time, and (2) each subsequent arterial level compared to preinduction level. Analyses of unpaired data, comparing arterial levels of the two groups at each sampling time, also were done.

Table 1. Schedule of Obtaining Samples in Patients with Aortic-valve Replacement during Open-heart Surgery

Event	F_{IO_2}	Temperature of patient, C
Before perfusion*:		
Patient	0.40	35.5
Prime	0.97	28.5
5 min of left coronary perfusion	0.98	31.3
Before rewarming	0.98	30.1
End of left coronary perfusion	0.98	34.4
30 min after perfusion	0.40	36
5 min after extubation	1.0	—
2 hours after operation	0.4†	—
Day 2, 8:00 AM	0.4†	—
3:00 PM	0.4†	—
Day 3, 8:00 AM	0.4†	—
3:00 PM	0.4†	—
Day 4, 8:00 AM	0.4†	—
3:00 PM	0.4†	—

* Arterial sample only was drawn before induction, breathing air. Coronary sinus samples were also drawn at all other times.
† Approximate.

Results

Mean values (with the standard errors) for all parameters in the "beating" group are given in table 2 (during operation) and table

[•] (Arterial-coronary sinus)/Arterial × 100.

TABLE 2. Data for Group with Beating Hearts during Open-heart Surgery for Aortic-valve Replacement

Parameter	Before Anesthesia	Before Perfusion		Perfusion			After Perfusion	
		Patient	Priming Blood	Early	Before Rewarming	End	30 min	End of Operation
P_{O_2} (mm Hg)	75 —	158 ± 24* 25†	505 —	383 ± 62 56	309 ± 38 45	211 ± 40 34	159 ± 31 28	280 ± 70 25
O_2 content (ml/100 ml)	17.7 —	17.1 9.2	11.8 —	14.4 13.6	15.0 13.0	15.5 12.2	16.5 9.2	10.2 7.7
P_{CO_2} (mm Hg)	30 —	30 ± 1 29	11 —	22 ± 1 27	26 ± 1 30	29 ± 2 30	26 ± 3 31	40 ± 3 54
pH	7.42 —	7.51 ± 0.7 7.40	7.60 —	7.55 ± 0.01 7.48	7.51 ± 0.01 7.50	7.47 ± 0.01 7.41	7.50 ± 0.02 7.44	7.37 ± 0.01 7.32
Buffer base (mEq/l)	46 —	44 ± 1 47	35 —	44 ± 1 43	46 ± 1 46	45 ± 1 46	45 ± 1 46	45 ± 1 47
K^+ (mEq/l)	4.1 —	4.0 ± 0.02 4.0	10.2 —	5.1 ± 0.05 5.0	4.7 ± 0.17 5.0	5.2 ± 0.07 5.2	4.0 ± 0.09 4.0	3.5 ± 0.07 3.7
Na^+ (mEq/l)	140 —	137 ± 0.4 138	113 —	130 ± 0.6 130	132 ± 10.0 137	131 ± 0.5 131	133 ± 0.9 134	138 ± 1.1 138
Ca^{++} (mg/100 ml)	9.7 —	9.4 ± 1.4 9.5	26.6 —	14.1 ± 0.4 14.3	13.4 ± 0.1 13.6	13.2 ± 0.1 13.3	12.0 ± 0.1 12.0	13.0 ± 0.1 13.0
Osmolality (mOsm/kg H_2O)	283 —	282 ± 2 284	353 —	293 ± 2 295	293 ± 1 293	292 ± 2 293	292 ± 2 293	293 ± 2 290
Glucose (mg/100 ml)	87 —	141 ± 2 144	1,440 —	452 ± 5 456	403 ± 11 383	383 ± 10 397	305 ± 9 289	188 ± 4 184
NEFA‡ (μEq/l)	912 —	2,812 ± 91 2,538	427 —	1,620 ± 32 1,587	1,473 ± 31 1,378	1,468 ± 56 1,352	685 ± 41 607	620 ± 53 534
Total ketone bodies (μg/ml)	15.8 —	17.7 ± 4.3 35.0	7.4 —	28.8 ± 2.2 26.7	20.6 ± 2.9 22.5	32.5 ± 4.2 21.3	18.8 ± 0.9 14.9	14.7 ± 1.4 11.9
Lactate (mmoles/l)	1.00 —	2.01 ± 0.17 1.70	5.06 —	3.02‖ ± 0.13 3.30	3.38 ± 0.21 3.31	3.08 ± 0.76 4.12	1.80 ± 0.15 4.22	4.16 ± 0.18 3.03
Pyruvate (mmoles/l)	0.12 —	0.17 ± 0.02 0.14	0.11 —	0.22 ± 0.01 0.20	0.26 ± 0.01 0.23	0.31 ± 0.03 0.30	0.41 ± 0.03 0.25	0.38 ± 0.02 0.16
Ratio of lactate to pyruvate	8.8 —	12.2 12.5	54.1 —	20.7 23.5	14.4 15.8	14.1 15.5	12.3 16.9	10.7 14.0

* Mean ± SE for arterial blood (top line in each block).
† Value for coronary sinus blood (bottom line in each block).
‡ Nonesterified fatty acids.

TABLE 3. Postoperative Data for Group with Beating Hearts during Open-heart Surgery for Aortic-valve Replacement

Parameter	Day 1	Day 2		Day 3		Day 4
	2 hours postop.	8:00 AM	3:00 PM	8:00 AM	3:00 PM	8:00 AM
P_{O_2} (mm Hg)	199 ±37* 24†	210 ± 73 25	121 ± 55 27	192 ± 48 30	168 ±58 24	119 ± 18 23
O_2 content (ml/100 ml)	18.0 8.2	18.3 8.8	18.4 10.1	16.7 9.3	16.8 7.6	14.5 7.2
P_{CO_2} (mm Hg)	39 ± 2 51	34 ± 2 45	35 ± 1 42	35 ± 1 43	33 ± 1 43	33 ± 2 41
pH	7.41± 0.01 7.46	7.45± 0.01 7.40	7.46± 0.01 7.42	7.47± 0.01 7.43	7.48± 0.01 7.44	7.47± 0.01 7.44
Buffer base (mEq/l)	47 ± 0.25 50	45 ± 1 50	49 ± 1 50	48 ± 1 49	47 ± 2 51	47 ± 1 51
K^+ (mEq/l)	3.7 ± 0.09 3.7	3.9 ± 0.05 4.0	4.1 ± 0.05 4.1	3.8 ± 0.02 3.8	3.7 ± 0.05 3.8	3.4 ± 0.02 3.4
Na^+ (mEq/l)	137 ± 0.4 138	135 ± 0.2 136	134 ± 0.7 135	131 ± 0.3 133	131 ± 0.2 133	132 ± 0.2 133
Ca^{++} (mg/100 ml)	12.3 ± 0.1 12.3	10.4 ± 0.1 10.5	10.1 ± 0.1 10.2	9.1 ± 0.2 9.1	9.1 ± 0.2 9.3	9.0 ± 0.1 8.9
Osmolality (mOsm/kg H_2O)	286 ± 2 288	280 ± 2 281	277 ± 2 279	273 ± 1.5 271	269 ± 1 268	268 ± 1 269
Glucose (mg/100 ml)	153 ± 4 149	119 ± 8 105	117 ± 5 118	109 115	111 ± 2 113	88 ± 6 97
NEFA‡ (μEq/l)	919 ±93 771	1,431 ±232 1,067	1,198 ±123 856	1,210 ±121 951	1,110 ±70 899	1,171 ±109 988
Total ketone bodies (μg/ml)	13.2 ± 1.1 12.0	45.4 ± 3.6 51.5	48.1 ± 3.4 46.2	40.8 ± 7.5 25.6	34.1 ±10.7 15.9	48.7 ± 4.5 26.0
Lactate (mmoles/l)	3.33± 0.06 2.65	1.46± 0.15 1.31	2.11± 0.15 1.60	1.32± 0.10 1.26	1.00± 0.24 1.14	0.90± 0.7 0.89
Pyruvate (mmoles/l)	0.21± 0.03 0.16	0.23± 0.03 0.16	0.22± 0.03 0.15	0.11± 0.01 0.10	0.11± 0.02 0.10	0.12± 0.19 0.11
Ratio of lactate to pyruvate	16.7 15.8	8.8 10.1	10.7 10.5	12.1 12.0	9.2 11.0	5.7 8.3

* Mean ±SE for arterial blood (top line in each block).
† Value for coronary sinus blood (bottom line in each block).
‡ Nonesterified fatty acids.

3 (after operation). Significant differences of arterial levels and arterio-coronary sinus concentrations between the beating and fibrillating groups were few and did not follow any consistent patterns; therefore detailed data for the fibrillating group are not presented. Table 4 shows the details of left coronary flow and left ventricular oxygen consumption during direct coronary perfusion in the beating and fibrillating groups. Only statistically significant differences will be discussed specifically.

ACID–BASE BALANCE (FIG. 1)

Buffer base did not change across the heart or in arterial levels except in a few instances. Arterial *p*H was higher than before induction at each sample time, except for the period from the end of perfusion through two hours after operation. Coronary sinus *p*H was lower than arterial *p*H, and P_{CO_2} increased across the heart, except during perfusion. Respiratory alkalosis was present throughout operation and for the three postoperative days.

ELECTROLYTES (FIG. 2)

No differences in levels of potassium, calcium, or osmolality were found across the heart. Coronary sinus levels of sodium were higher than arterial levels in the "beating" group on the third postoperative day. Arterial sodium levels were lower than before induction throughout operation, and this hyponatremia recurred after operation in the "beating" group. Arterial potassium levels were elevated during perfusion, and decreased to

TABLE 4. Myocardial Oxygen Consumption during Coronary Perfusion in Patients Undergoing Open-heart Surgery for Aortic-valve Replacement

Mean levels	Beating heart			Fibrillating heart		
	Early	Before Rewarming	End	Early	Before Rewarming	End
Left coronary flow, ml/min	219	207	203	197	192	192
Difference* in O_2 content, ml/100 ml	0.8	1.1	3.3	2.7	4.5	6.8
O_2 consumption, ml/min	1.8	2.3	6.7	5.4	8.5	12.8
Body temperature, C	31.5	30.2	34.3	31.3	30.1	34.4

* Arterial and coronary sinus blood.

below preinduction levels in the "beating" group on the fourth operative day. Calcium levels were elevated above preinduction levels from the beginning of perfusion through two hours after operation.

METABOLITES (FIGS. 3 AND 4)

Total ketone body levels were above normal before induction of anesthesia. Arterial levels were elevated sporadically throughout the study except at midperfusion and shortly after perfusion. Extraction by the myocardium was seen at most sample times when arterial concentration was high.

Glucose levels did not show any arterial-venous differences at any time. The large amount in the priming fluid resulted in higher-than-preinduction concentrations in arterial blood throughout the day of surgery. Similarly elevated levels of blood glucose were seen for all patients at all times except on the last postoperative day.

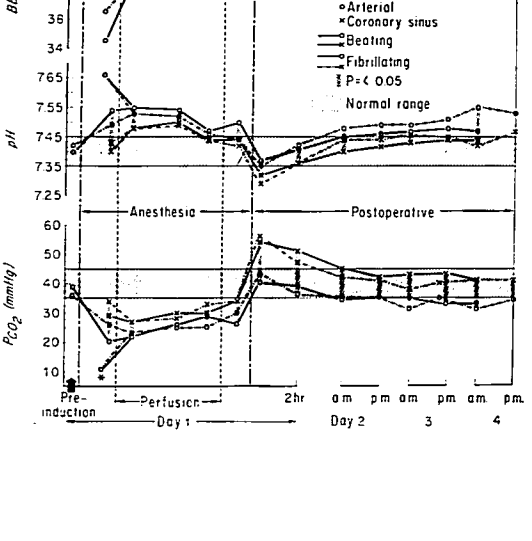

FIG. 1. Arterial and coronary-sinus mean levels of buffer base, *p*H, and P_{CO_2} through surgery and for the three following days in the "beating" and fibrillating" groups. Significant differences across the myocardium are indicated. Above-normal *p*H and below-normal P_{aCO_2} were present through most of the period studied.

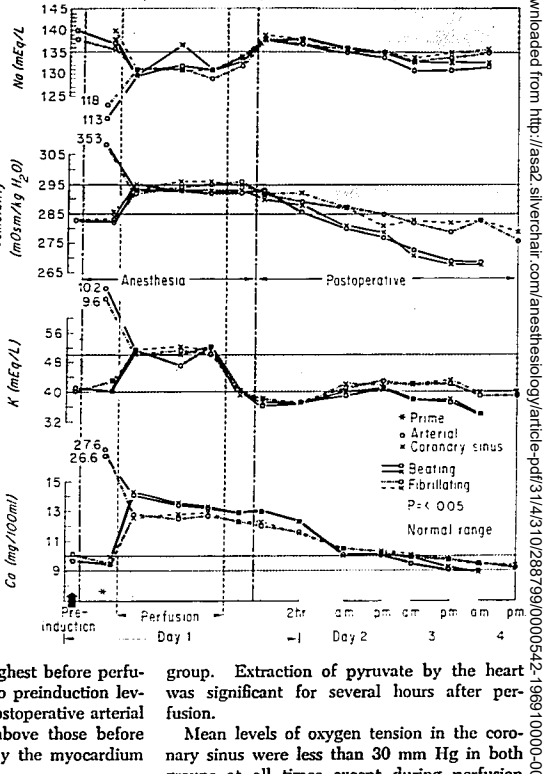

FIG. 2. Arterial and coronary-sinus mean levels of sodium, osmolality, potassium, and calcium. Significant arteriovenous differences were almost never seen at any time. Levels of Ca, K, and osmolality were elevated during operation, and level of Na was below normal. Levels of all parameters but Ca were below normal after surgery.

Levels of NEFA were highest before perfusion but did not decrease to preinduction levels until after perfusion. Postoperative arterial levels were generally not above those before anesthesia, but extraction by the myocardium was more consistent.

Arterial lactate levels increased before perfusion, rose steadily during perfusion, and were highest shortly after perfusion. Levels on the subsequent postoperative days were not different from preinduction levels. Myocardial extraction of lactate was evident when arterial levels were high for several hours after perfusion.

In the "beating" group, pyruvate values increased over preinduction levels, before perfusion and throughout operation. This increase was seen from midperfusion through two hours after operation in the "fibrillating" group. Extraction of pyruvate by the heart was significant for several hours after perfusion.

Mean levels of oxygen tension in the coronary sinus were less than 30 mm Hg in both groups at all times except during perfusion (fig. 4). Arterial mean levels were above 90 mm Hg at all times, although individual readings after operation were as low as 68 mm Hg during breathing of 40 per cent oxygen. Oxygen extraction by the myocardium was significant at all times.

Mean coefficients-of-extraction values, along with individual values for NEFA, oxygen, and lactate are shown in figure 5. NEFA decreased during hypothermic perfusion and increased gradually after operation toward the normal mean.[4] Oxygen extraction was below the normal ranges [5] before perfusion, very low

during hypothermic perfusion, and remained below normal after operation.

Extraction of lactate of less than 10 per cent or frank production is considered abnormal or evidence of anaerobic metabolism.[3] Mean lactate extraction remained in this zone throughout perfusion and sporadically after operation. The greatest extraction occurred while arterial levels were highest after perfusion.

Discussion

We have reported the arterial levels throughout operation [1] and the arteriovenous differences of metabolites and electrolytes across the heart during perfusion.[6] The present study examined cardiac metabolism throughout the operative day and for three postoperative days after aortic-valve replacement. An additional aim was to find out whether the beating or the fibrillating heart had different responses during the direct coronary perfusion and afterward.

Oxygenation

Oxygen tension and content in the coronary sinus increased during hypothermic coronary perfusion, compared with before perfusion, indicating that extraction of oxygen by the heart was reduced. Reduced extraction was more striking in the hearts that continued to beat, the oxygen consumption being a third that of the fibrillating heart. On rewarming, oxygen consumption of the beating heart was half that of the fibrillating heart. However, it is also true that the patients whose hearts were fibrillated were probably more severely ill, had larger hearts, and underwent more

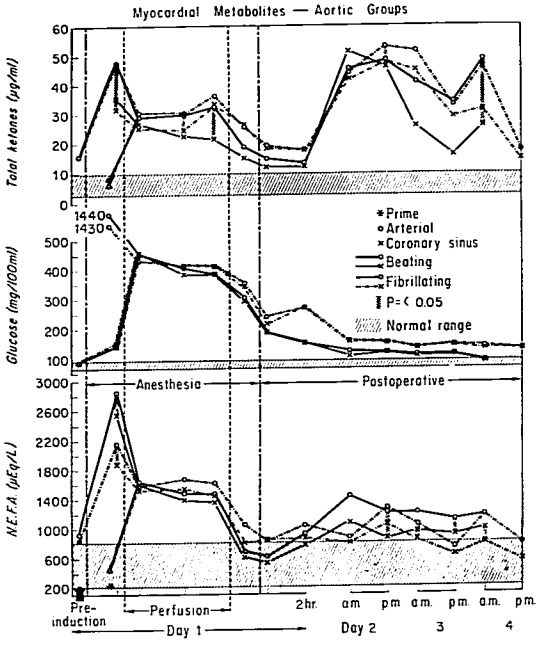

FIG. 3. Mean levels of total ketone bodies, glucose, and NEFA throughout the study. NEFA and total ketone body levels were increased at most of the sample times, with significant extraction frequently found. Sugar level was increased in arterial blood, but utilization by the myocardium was not detected.

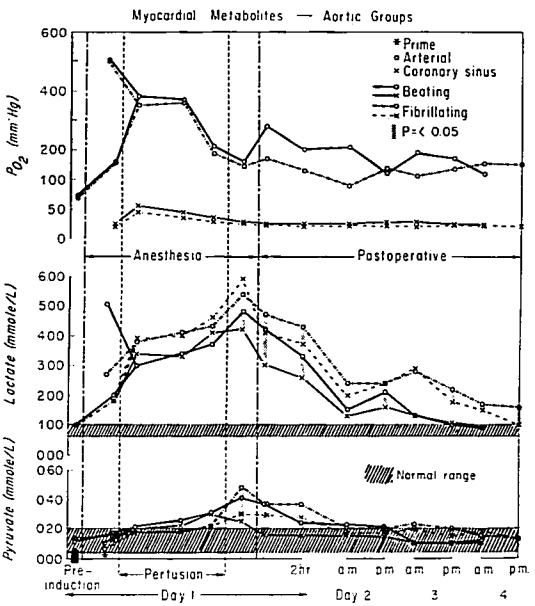

FIG. 4. Arterial and coronary-sinus mean levels of P_{O_2}, lactate, and pyruvate during and after operation. P_{CSO_2} was below 30 mm Hg except during hypothermic coronary perfusion. Lactate and pyruvate levels increased steadily throughout perfusion, with significant extraction when arterial levels were high.

prolonged coronary perfusion. Oxygen consumption by the myocardium increased in both groups as perfusion continued. Oxygen consumption of the dog (left ventricle) perfused at 38 C has been reported as 3.4 ml /100 gm/min in the empty beating heart, and 3.8 ml in fibrillation.[7] In the present study, the arterial oxygen content decreased late in the postoperative period, as hemoglobin values decreased, probably owing to hemodilution and destruction of erythrocytes. Coronary sinus content also decreased after operation, more so in the fibrillating group (larger patient, larger heart).

The "fibrillating" group had a higher percentage of oxygen extraction throughout the entire study, and only the fibrillating hearts reached the normal range of oxygen extraction[8] for several hours after operation. Messer and coauthors[5] found that the coefficient of oxygen extraction was 70 per cent ± 6 (SD) for normal subjects; 66 per cent ± 8 for patients with coronary insufficiency, and 73 per cent ± 5 for patients in congestive heart failure. They found increased oxygen extraction in the group with congestive heart failure in the presence of low cardiac output. The lower-than-normal myocardial oxygen extraction in our patients after operation could result from (1) coronary flow in excess of need, because coronary arteriolar regulation had not adjusted to the lower requirements for work permitted by the competent aortic valve, or arteriolar control was influenced by some other effect of coronary perfusion; (2) coronary arteriovenous shunting, which is either anatomic or physiologic (that is, transport of oxygen from capillary to mitochondrion is impaired); and (3) reduced mitochondrial utilization of available oxygen. Frank production of lactate occurred in some hearts after operation, suggesting anaerobic

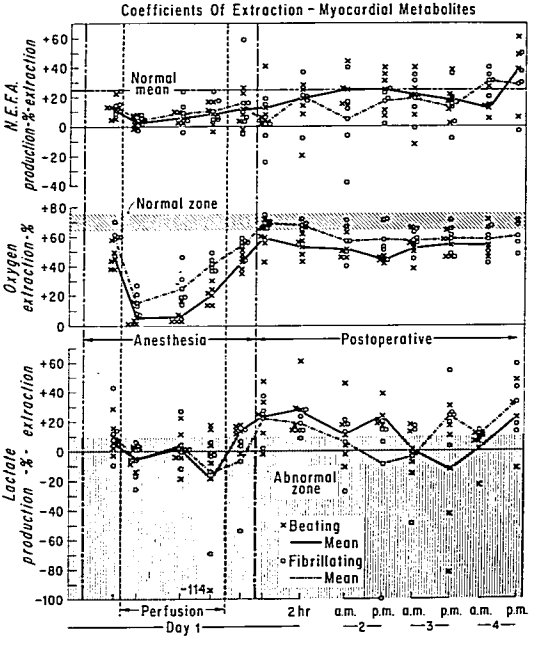

FIG. 5. Coefficients of extraction of NEFA, oxygen, and lactate for the myocardium. All individual values and the means for both groups are shown. Extraction of each of these metabolites was below normal for most of the period studied. References for normal means and ranges are given in the text. Herman and associates [3] consider a lactate extraction of less than 10 per cent indicative of deficient aerobic metabolism.

energy production, which does not support the hypothesis that excessive coronary flow was the cause of the decreased oxygen extraction. Mueller and his co-workers [9] similarly found a decrease in oxygen extraction after operation, along with reduction of cardiac output, mean arterial pressure, and left ventricular work. They suggested reduced oxygen requirements as the major cause.

ACID–BASE BALANCE

The respiratory alkalosis that occurred during operation was produced purposely by hyperventilation. The only other deviation from normal was mild respiratory alkalosis in the days subsequent to operation. As expected, *p*H decreased and carbon dioxide increased across the myocardium.

ELECTROLYTES

All the electrolytes measured in this study, as well as the osmolality, were significantly altered by the nature of the priming solution. The value for sodium was reduced, whereas values for calcium, potassium, and osmolality were increased. Homeostatic mechanisms resulted in the return of concentration to preoperative ranges by the end of operation, except for calcium, which returned to normal by the next day.

Osmolality was measured to study the degree of dilution of the blood.[10] The hypoosmolality that developed after operation undoubtedly was due to increased extracellular water volume, both intravascular and interstitial.[11] The significance of this abnormality and its relationship to disturbances of cardiac rhythm and cerebral aberrations warrant fur-

ther study. It has been demonstrated that the kidneys retain sodium and excrete potassium after open-heart surgery.[12] It is likely that earlier promotion of diuresis by drugs may prevent hypo-osmolality of the serum and its probable adverse effects.

The significantly-higher levels of calcium, owing to recalcification of the ACD blood used in the priming solution, returned to normal by the next morning. Although most of the extra serum calcium seen on the day of surgery is probably bound to citrate or protein, if the level of the ionized calcium component is elevated, positive inotropic effects on the heart are likely. Characteristically, the cardiac output of our patients remained good during hypercalcemia.

We were unable to detect significant gains or losses of electrolytes by the heart. Exchanges at the cell membrane possibly were too small to be detected by the methods used.

Metabolites

Continued utilization by the myocardium of the usual fuels was demonstrated: fatty acids, ketone bodies, pyruvate, and lactate. Extraction of glucose was not detected, perhaps because the normal arteriovenous difference is only about 3 mg/100 ml.[8] It appeared that extraction of NEFA and lactate was slightly impaired to approximately the same degree that oxygen extraction was impaired, possibly for the same reasons.

A common alteration was the elevated concentration of all the metabolites in arterial blood. The high concentration of glucose came primarily from the priming solution and, later, from intravenous therapy. The continued mobilization of fat in the body is a known effect of elevated endogenous catecholamines,[13] as is hyperglycemia and hyperlactatemia.

Another effect of catecholamines is to inhibit the release of insulin,[14] causing decreased utilization of glucose and increased formation of ketone bodies.[13] The normal balance between catecholamines and insulin seemed tipped toward inhibition of insulin activity throughout this entire period of stress.

Levels of arterial lactate increased before perfusion, as seen previously, when cardiac output was low,[15] probably indicating whole-body production of lactate. Other possible causes are respiratotry alkalosis and hyperglycemia. But the progressive steep rise during perfusion and afterward was probably the combined effect of THAM converting glucose to lactate [16] and of glucose itself, as observed after ingestion of glucose.[17] Elevated levels of lactate have a glucose-sparing effect as well.[18] Levels of arterial pyruvate were elevated for several hours after perfusion, as glucose was converted to it and then to lactate. Significant usage of pyruvate by the heart was seen at this time. Whether there exists a decreased ability of pyruvate to enter the Krebs cycle or a greatly increased production is not known. Ratios of lactate to pyruvate increased across the heart at almost all sampling times. Anaerobic metabolism in the myocardium would be indicated by higher levels of lactate in the coronary sinus than in arterial blood. This was seen in both beating and fibrillating hearts having coronary perfusion after reversal of hypothermia.

None of the metabolic aspects were different in the hearts that fibrillated and those that continued to beat other than a greater consumption of oxygen during perfusion in the fibrillating hearts.

The findings in this study that have contributed to better care and survival are several. (1) A priming solution that includes the organic buffer THAM results in metabolic alkalosis during and after open-heart surgery, which is preferable to acidosis. (2) Although some degree of hemodilution is used by most groups and has many advantages, intravascular and extravascular water retention occurs. Early administration of diuretics after operation should eliminate this accumulation. (3) The possible beneficial effects of an increased level of serum calcium on cardiac output for several hours after surgery suggest that calcium may be an effective drug for treating low cardiac output at any time. (4) The predominance of lipid metabolism with resulting ketosis raises the possible desirability of giving extra glucose plus insulin after operation to increase utilization of carbohydrate.

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Muscle

NEUROMUSCULAR BLOCKADE Specific characteristics enable one to determine which type of neuromuscular blockade is present. The normal untreated muscle will contract when an effective stimulus is applied. Repeat stimuli will cause appropriate muscle contraction under normal circumstances. Stimuli applied to the nerve in a rapid, repetitive fashion will cause tetanic contraction in a normal muscle. A depolarizing block is characterized by: 1) absence of fade, 2) absence of posttetanic facilitation, 3) well-sustained tetanus, and 4) potentiation by cholinesterase inhibitors. A nondepolarizing block is characterized by: 1) presence of fade, 2) presence of posttetanic facilitation, 3) poorly sustained tetanus, and 4) antagonism by cholinesterase inhibitors. (*Way, W. L., and Miller, R. D.: Clinical Pharmacology of Neuromuscular Blocking Agents, Gen. Pract. 38: 100 (Nov.) 1968.*)