WHOLE-BODY METABOLISM DURING AND AFTER ABDOMINAL SURGERY*

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Numerous papers have been written on the effect of general anaesthesia and surgical procedures on one or more of the various aspects of metabolism, but none correlates many measurable variables in the same patients. Better understanding of the changes occurring in the body during and after operation should improve the safety of the operation. Improper oxygenation, acid-base imbalance, and abnormal potassium, calcium, and sodium concentrations have potent ill effects on the heart and body.

Metabolism of non-esterified fatty acids (NEFA) is the major source of energy in the fasting state, and the production of ketone bodies reflects the carbohydrate deprivation of fasting. Lactate and pyruvate are also sources of energy as well as being indicators of anaerobic metabolism. Studies of myocardial and whole-body metabolism in patients undergoing open-heart surgery have delineated patterns of changes and indicated improvements in treatment.¹⁻³

The purpose of this study was to investigate changes in metabolites and electrolytes, on a whole-body basis, in a group of patients undergoing abdominal surgery, and to document their responses to anaesthesia and this type of surgery. Another aim of the study was to help to determine, in the previously studied patients having open-heart surgery, the proportion of the changes due to the cardiac lesion and the whole-body perfusion.

MATERIAL AND METHODS

In 11 adult patients (ages 36 to 79 years; mean 55 years), arterial and right atrial blood samples were drawn simultaneously during abdominal surgery and for the next three days. The samples taken before induction of anaesthesia were used as controls. Six patients underwent insertion of aorto-iliac grafts for occlusive vascular disease, and five had other types of abdominal surgery. The mean weight of the 11 patients was 147 pounds (range, 127 to 194 pounds). The physical status of the patients (American Society of Anesthesiology classification) was: class 1, two; class 2, seven; and class 3, two. All patients had satisfactory post-operative courses and left the hospital an average of 13 days later.

For anaesthesia, nitrous oxide (3 L), oxygen (2 L), and halothane (0.25 to 0.75 per cent) were administered with a semiclosed circle absorber system and manually controlled ventilation. Thiopental sodium (125 to 375 mg) and succinyl-

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FIGURE 1. Electrocardiographic features used to guide placement of right atrial catheter.

choline chloride (60 mg) were given for induction and endotracheal intubation. Intermittent doses of succinylcholine chloride were used when necessary for muscle relaxation. Duration of operation was 55 minutes to 2 hours and 30 minutes.

Simultaneous blood samples were taken in heparinized syringes from the right atrium and a peripheral artery. A catheter was inserted from the brachial vein to the right atrium by electrocardiographic guidance⁴ (Fig. 1). The position was further verified on a postoperative roentgenogram. This method of placement was uniformly successful. Right atrial samples were accepted for mixed venous blood because of the danger of arrhythmia associated with attempts to float a catheter into the pulmonary artery.⁵ Samples were drawn before anaesthesia (breathing air), at the middle of the operation, and at the end of anaesthesia, the latter when the patients were spontaneously breathing oxygen via a tightly fitting face mask. Further samples were taken two hours postoperatively and at 1 PM on each

of the following three days while the patient was breathing oxygen via a face tent (Puritan Co.) for at least ten minutes.

Samples for blood gas analysis were transported in ice and analysed for oxygen and carbon dioxide tensions and pH by electrodes maintained at 37° C (Instrumentation Laboratory Inc.). Haematocrit values were determined in an International clinical centrifuge, and buffer base was read from the Singer-Hastings nomogram.⁶

Serum concentrations of NEFA,⁷ total ketone bodies,⁸ and calcium⁹ were determined by reported methods. Serum sodium and potassium were measured by flame photometry. Enzymatic methods were used to measure blood lactate and pyruvate.¹⁰ Plasma osmolality was determined by freezing-point depression (Fiske osmometer). Whole blood glucose was measured in an AutoAnalyzer (Technicon Corporation). Serum immunoreactive insulin concentration was measured by double-antibody radioimmunoassay.¹¹

The fluid administered intravenously, during operation and for two hours post-operatively, was 5 per cent dextrose in water, approximately 50 ml being given as a vehicle for intravenous drugs. Blood was given when necessary, the average amount being 750 ml. Postoperatively, intravenous fluids were given at the average rate of 1,500 ml/day. The usual regimen per 24 hours was 1,000 ml of 5 per cent dextrose in water and 500 ml of 5 per cent dextrose in saline.

Statistical analyses were done by Student's *t*-test with $p = 0.05$ accepted as the level of significance for comparison of paired data for each parameter: (*a*) arterial and right atrial levels at each sampling time, and (*b*) each subsequent arterial concentration compared to the preinduction control level.

RESULTS

The mean values with standard error of the mean for arterial and right atrial blood for all parameters are given in Table I. Table II shows all the significant differences between arterial and right atrial concentrations of variables. Table III is a summary of significant differences between arterial control concentrations and subsequent arterial samples. No significant differences in any variable were found between the group undergoing aorto-iliac grafting and those having other abdominal operations. All differences to be mentioned were statistically significant.

Acid-base balance. Buffer base did not change across the body, nor did arterial levels change with time (Fig. 2). P_{CO_2} increased across the body and pH decreased significantly across the body at most sample times. Respiratory alkalosis was present throughout operation and on days 3 and 4.

Electrolytes. No arteriovenous differences were found in sodium, potassium, calcium, or osmolality (Figs. 3 and 4). Osmolality was near the lower limit of the normal range at almost all times. Arterial levels of potassium midway through the operation were lower than before induction of anaesthesia. Calcium showed no changes in any respect. Arterial sodium levels were below the preinduction value at all sampling times except at the end of the operation and two hours later. This mild hyponatraemia was still present on day 4.

Metabolites. No arteriovenous differences were seen in any of the metabolites.

TABLE I
SUMMARY OF VALUES*

Variable	Before anaesthesia		Middle of operation		End of operation		2 hr		Postoperatively			
									day 2		day 3	
	A	RA	A	RA	A	RA	A	RA	A	RA	A	RA
Po ₂ (mm Hg)	82	40	121	38	195	40	172	40	93	35	112	38
Oxygen content (vol %)	16.6	13.0	15.9	12.8	17.5	13.9	17.8	12.7	15.1	11.3	14.4	11.4
Pco ₂ (mm Hg)	35	38	28	33	34	38	37	43	38	41	34	36
pH	7.48	7.45	7.54	7.48	7.47	7.41	7.42	7.37	7.45	7.42	7.49	7.47
BB+ (mEq/L)	49	48	48	47	48	47	47	46	50	50	50	50
K (mEq/L)	3.9	3.7	3.8	3.9	4.1	3.8	3.5	3.5	4.1	4.0	4.0	4.0
Na (mEq/L)	139	138	136	135	136	138	136	138	134	134	134	133
Ca (mg/100 ml)	9.48	9.45	9.37	9.31	9.36	9.38	9.54	9.56	9.28	9.29	9.17	9.22
Osmolality (mOsm/kg H ₂ O)	280	281	279	281	281	284	280	281	280	277	278	280
Glucose (mg/100 ml)	82	80	126	131	142	144	162	160	126	131	108	108
NEFA (μEq/L)	927	981	1008	1224	1212	1118	1184	1118	802	789	865	769
Ketones (μg/ml)	23.3	22.1	29.0	26.0	37.7	35.7	28.5	26.3	17.2	14.1	11.7	11.6
Lactate (mm/L)	1.09	1.08	1.74	1.78	2.20	2.19	2.03	1.93	1.31	1.33	1.23	1.35
Pyruvate (mm/L)	0.03	0.03	0.06	0.06	0.08	0.07	0.08	0.07	0.06	0.06	0.05	0.05
Lactate/pyruvate ratio	31.1	31.7	28.0	27.3	28.9	31.7	26.3	27.1	21.8	19.8	23.4	24.7
Insulin† (μU/ml)	9.2	±0.99	10.7	±1.9	10.3	±2.1	13.7	±3.4	20.4	±3.6	18.0	±1.9

*Shown as means with combined SE of arterial (A) and right atrial (RA) values.

†Arterial values only.

TABLE II
SUMMARY OF SIGNIFICANT DIFFERENCES* BETWEEN ARTERIAL
AND RIGHT ATRIAL BLOOD

Variable	Right atrial significantly higher than arterial at:	Right atrial significantly lower than arterial at:
pH	no time	all times except end of operation and day 3
PCO ₂	all times except day 3	no time
PO ₂	no time	all times
O ₂ content	no time	all times
O ₂ saturation	no time	all times

* $p < 0.05$.

TABLE III
SUMMARY OF SIGNIFICANT DIFFERENCES* BETWEEN ARTERIAL CONTROL AND
SUBSEQUENT ARTERIAL SAMPLES

Variable	Significantly higher than control at:	Significantly lower than control at:
pH	day 4	no time
PCO ₂	no time	middle of operation
BB+	no time	no time
Haematocrit	end of operation and 2 hr postop.	days 3 and 4
PO ₂	no time	no time
O ₂ content	2 hr postop.	days 3 and 4
O ₂ saturation	no time	no time
Na	no time	all times except end of operation and 2 hr postop.
K	no time	middle of operation
Ca	no time	no time
Osmolality	no time	no time
Lactate	during operation and 2 hr postop.	no time
Pyruvate	all times	no time
NEFA	during operation and 2 hr postop.	no time
Glucose	all times	no time
Total ketone bodies	no time	no time
Insulin	days 2 and 3	no time

* $p < 0.05$.

Total ketone bodies (Fig. 5) were above normal range before induction of anaesthesia and remained so throughout the study. NEFA was slightly increased before induction and was higher than control during operation and two hours post-operatively.

FIGURE 2. Acid-base balance. In all figures, day 1 is the day of operation and postoperative days are designated days 2, 3, and 4. Buffer base did not change throughout the study. Respiratory alkalosis was present during anaesthesia and on days 3 and 4.

FIGURE 3. Serum potassium and calcium concentrations. Potassium remained in low normal range or below throughout. Calcium showed no changes.

FIGURE 4. Serum sodium concentration and osmolality. Gradual decrease in sodium was seen, with no arteriovenous differences. Osmolality, indicative of the water content of the blood, was usually close to the lower limit of the normal range, signifying high-normal proportions of serum water.

FIGURE 5. Total ketone bodies and non-esterified fatty acids. Ketone bodies increased during anaesthesia and were above normal range at all times. Arterial NEFA concentration remained above normal range on the day of operation.

FIGURE 6. Glucose and insulin concentrations. Glucose remained above normal range from induction through the whole study. Arteriovenous differences were not detected. Insulin remained within normal range but increased above control on days 2 and 3.

FIGURE 7. Lactate, pyruvate, and L/P ratio. Lactate increased to a peak at the end of operation but was not different from control postoperatively. Venous lactate was not different from arterial levels. Pyruvate was higher than control throughout the study.

The intravenously administered glucose contributed to the higher-than-preinduction levels of glucose in the arterial blood through the study period (Fig. 6).

The mean concentration of immunoreactive insulin remained within the normal

range (0 to 25 μ U/ml) throughout (Fig. 6). It increased above preinduction level on days 2 and 3.

Lactate (Fig. 7) was slightly increased before induction and remained higher than control through the operation and two hours postoperatively. Pyruvate and L/P ratio were above control throughout the study.

Large arteriovenous oxygenation differences were present at all times (Fig. 8). Mean venous oxygen tension remained at 38 to 40 mm Hg throughout the day of operation but decreased to 33 mm Hg on day 4. Arterial oxygen tension averaged 93, 112, and 69 mm Hg on the three postoperative days while the patients were breathing approximately 40 per cent oxygen. Oxygen content of the arterial blood was higher than control two hours after operation, because of a higher haemoglobin concentration; on days 3 and 4 it was lower than control, with a decreased haemoglobin concentration.

DISCUSSION

It is essential to have continuous satisfactory arterial oxygen tension during anaesthesia, and this can be accomplished by keeping the $F_{I_{O_2}}$ above 0.4 in the presence of a satisfactory cardiac output. For many years it has been suggested that a $P_{a_{O_2}}$ of approximately 100 mm Hg was a minimal requirement for safe anaesthesia.¹² The factors that may contribute to a low $P_{a_{O_2}}$ when the inspired oxygen concentration is kept adequate are hypoventilation, reduction in diffusing capacity, ventilation-perfusion abnormalities, pulmonary shunting, and decrease in

FIGURE 8. Oxygen tension and content. Mean arterial tension was satisfactory when $F_{I_{O_2}}$ was increased, except on day 4. Right atrial tension remained stable. Postoperatively, oxygen content decreased as blood haemoglobin level decreased.

cardiac output.¹³ The haemodynamic state remained stable in our patients, as judged by clinical criteria, and the carbon dioxide levels were subnormal, showing the absence of hypoventilation. Changes of diffusing capacity were not known. Thus, shunting and uneven distribution of ventilation plus perfusion abnormalities stand out as the major factors contributing to the decreased Pa_{O_2} values.

In our patients, oxygenation was satisfactory throughout the operation, although a mean Pa_{O_2} of 121 mm Hg with an FI_{O_2} of 0.4 indicates considerable shunting. Stephen and Talton found a mean Pa_{O_2} of 80 mm Hg (patients breathing air) two hours after anaesthesia.¹⁴ Hamilton and co-authors found arterial oxygen desaturation for two days postoperatively.¹⁵ The postoperative FI_{O_2} in our series is not definitely known because a loose face tent was used, but the values would have been even lower had the patients been breathing air. The fact that shunting of significant magnitude continues in the postoperative period has been shown by Tarhan and co-workers.¹⁶ Clowes and associates¹⁷ observed that oxygen desaturation was greatest 24 hours after operation. Our lowest mean arterial tension occurred on day 4. Nunn and Payne¹⁸ also have shown that hypoxemia commonly occurs after general anaesthesia, attributable to miliary atelectasis. The likelihood of its presence in every patient should be remembered, and efforts to reduce atelectasis should be made in addition to giving oxygen postoperatively.

The respiratory alkalosis occurring during operation was intentionally produced. Buffer base did not change significantly as blood traversed body tissues, nor did arterial levels change with time. Postoperatively, a mild respiratory alkalosis recurred, greatest on day 4 when Pa_{O_2} was lowest. Tachypnoea and shallow breathing from incisional pain may also have contributed to the decreased P_{CO_2} . As one would expect, right atrial pH was lower than arterial pH because the venous blood contained more carbon dioxide.

It has been documented that severe acidosis and deficient oxygenation of tissues lead to anaerobic glycolysis with increased lactate formation, myocardial depression, and catecholamine release.^{19,20} Acidosis was never present in these patients as a potential cause of these events. The significant progressive increase in lactate concentration throughout operation and its continued high level postoperatively was seen in cardiovascular surgery by others.²¹ This cannot be construed as necessarily indicating that anaerobic glycolysis was occurring, since several factors known to cause increased lactate levels were present: respiratory alkalosis was present throughout the study, and glucose was used as a vehicle for drug administration.²² Halothane has been found not to cause excess lactate production in patients.²³

Significant arteriovenous differences of oxygen, carbon dioxide, and pH were seen as changes occurred in both the tissues and the lungs. With no known exchange of electrolytes or metabolites taking place in the lungs, venous and arterial concentrations must be the same in the presence of steady amounts in the blood. If arteriovenous differences were found, then an unsteady state existed—that is, addition or loss of that constituent to or from the blood. Another possible cause of the data showing significant arteriovenous differences is relative inaccuracy of the method of measurement.

Metabolism of NEFA is the major energy source of the body²⁴ and myocardium

after fasting. NEFA is the transport form of fat, with an extremely rapid turnover rate, and blood levels of it are sensitive to hormonal control. Other energy-producing metabolites used by the body are glucose,²⁵ ketone bodies,²⁴ lactate, and pyruvate. Increase in blood sugar can decrease NEFA concentration,²⁵ as does an increase in insulin. These patients had a sufficient glucose load, but the concentration of NEFA did not decrease to normal until after the operation, probably due to the continued stimulus of catecholamines released during operation.

Ketone bodies, mainly acetoacetate and β -hydroxybutyrate, increase during the carbohydrate deprivation of fasting²¹ and rapidly disappear after administration of glucose or insulin.²⁴ Ketosis persisted in this series, indicating continued use of fat for energy in spite of the increased blood glucose level, but with insulin levels not above normal. Insulin did not increase above preinduction levels on the day of operation, but did double in concentration on days 2 and 3. This is consistent with the known effect of insulin release being inhibited by catecholamines.²⁶ The changes seen in carbohydrate and fatty acid metabolism agree with those reported by Griffiths.²⁷ The mechanisms of action of insulin are well described by Rieser.²⁸

Sodium, potassium, and calcium ions are essential to normal cellular function, and their serum levels reflect extracellular concentrations. Osmolality was subnormal at almost all times, indicating slightly reduced solute concentration in the blood. Hyponatraemia, probably due to water retention, was found by Moore²⁹ to be most marked on the second and third postoperative days. Most noteworthy in the findings relative to electrolytes and water was that they remained so close to normal.

The duration as well as type of operation had little influence on the variables studied. The study showed that patients undergoing anaesthesia and general surgery utilize fat predominantly for energy, in addition to utilization of glucose.

SUMMARY

Oxygen, acid-base components, electrolytes, and energy-producing metabolites were measured in arterial and mixed venous blood before, during, and for three days after abdominal operations in 11 patients. A respiratory alkalosis without a metabolic component was present throughout most of the study interval. Predictably, arteriovenous differences were not found for any electrolyte or metabolite. Arterial and venous oxygen tensions were satisfactory throughout anaesthesia, but the postoperative P_{aO_2} indicated considerable persisting atelectasis. Arterial concentrations of non-esterified fatty acids and ketone bodies were increased before anaesthesia and throughout the operation. Blood sugar increased during the operation and remained above normal postoperatively, probably from intravenous solutions. Mean concentrations of immunoreactive insulin remained in the normal range in spite of this increase in blood sugar. Fat metabolism appeared to predominate, and ketosis occurred in the presence of increased blood sugar. Lactate and pyruvate levels increased steadily throughout the operation and decreased postoperatively.

Careful maintenance of arterial oxygen tension and of the circulation during and after anaesthesia for general surgery results in little change in acid-base balance and electrolytes. The changes in blood levels of energy-producing metabo-

lites are moderate and usually reverse themselves. Duration of operation or type of surgery had little influence on the variables studied.

RÉSUMÉ

Avant l'opération, durant l'opération, et durant trois jours après des opérations abdominales chez onze malades, nous avons mesuré, dans le sang artériel et dans un mélange de sang veineux l'oxygène, l'équilibre acide-base, les électrolytes et les métabolites énergétiques. Presqu'à toutes les phases de cette étude, nous avons observé une alcalose respiratoire sans participation métabolique. Tel que prévu, nous n'avons pas trouvé de différences artérioveineuses pour aucun des électrolytes ou des métabolites. Les concentrations artérielles d'acides gras non estérifiés et de corps cétoxygènes étaient augmentées avant l'anesthésie et durant l'opération. Au cours de l'opération, la glycémie a augmenté et, après l'opération, elle est demeurée au-dessus de la normale, probablement à cause des solutés donnés par voie endoveineuse. Les concentrations moyennes d'insuline immunoréactive sont demeurées à un niveau normal en dépit de cette hyperglycémie. Le métabolisme des graisses a semblé prédominer et l'acétone est apparue en présence d'hyperglycémie. Les taux de lactate et de pyruvate ont augmenté de façon régulière au cours de l'opération et ils ont diminué dans les suites opératoires.

Un soigneux maintien de la tension en oxygène du sang artériel et de la circulation au cours et après l'anesthésie pour la chirurgie générale a été suivi de peu de changements sur l'équilibre acide-base et sur les électrolytes. Les changements sur le taux des métabolites énergétiques sanguins sont faibles et, d'habitude, se rétablissent. La durée de l'opération et la sorte de chirurgie n'influencent que très peu les paramètres étudiés.

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