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## Respiratory Changes Induced by Parenteral Nutrition in Postoperative Patients Undergoing Inspiratory Pressure Support Ventilation

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In the postoperative period following major surgery, patients sometimes require both respiratory and nutritional support. The respiratory support is justified by impaired ventilatory function secondary to the surgical procedure and/or to underlying abnormal pulmonary function. Such support can be provided by controlled ventilation, inspiratory pressure support (IPS) in spontaneously breathing patients, or by a mixed mode as intermittent mandatory ventilation. Nutritional support decreases the multiple adverse effects of malnutrition, particularly the incidence of infections.<sup>1</sup> However, there is no general agreement concerning the quantitative and the qualitative aspects of the nutrition regimen (*e.g.*, caloric load, diet composition).

Nutritional support results in an enhanced production of carbon dioxide ( $\dot{V}_{CO_2}$ ), which requires an increase in minute ventilation ( $\dot{V}_E$ ) to keep  $Pa_{CO_2}$  within normal limits. This effect depends on the diet composition and the patient's respiratory and nutritional status.<sup>2,3</sup>

The present study was conducted during the postoperative period in patients with normal or abnormal pulmonary function. The aim of the study was 1) to observe the ventilatory response to a caloric intake given as glucose alone or as glucose + fat, and 2) to assess the ability of IPS to match the changes in minute ventilation in response to the  $CO_2$  load induced by these two nutritional regimens.

### MATERIALS AND METHODS

The study was performed in eight male patients who required a 4-day respiratory and nutritional support after a major surgical procedure. Clinical data are given in table 1. Patients in group 1 had normal preoperative pulmonary

function tests, whereas patients in group 2 had evidence of chronic obstructive (3 cases) or restrictive (1 case) pulmonary disease. None of them had evidence of diabetes, sepsis, and hepatic or renal dysfunction. They were normovolemic and had normal cardiovascular functions. This protocol was approved by the ethical committee of our institution, and informed consent was obtained from the patients' nearest relatives.

The tracheas of all patients were intubated, and ventilation was spontaneous. Ventilation was provided by a Siemens Servo C ventilator set on a pressure support mode. A 2 cm  $H_2O$  inspiratory effort leads the gas to be supplied at a preset constant pressure (+15 cm  $H_2O$ ) during the entire inspiratory time. Thus, each patient could modify his respiratory rate (RR) and tidal volume.

The general outline of the study is shown in figure 1. Each patient was studied during 60 consecutive hours, which included two 12-h nutritional periods (from 7 A.M. to 7 P.M.), each of them being preceded and followed by a 12-h basal period (from 7 P.M. to 7 A.M.). During the nutritional periods, the total caloric intake was set at 1.5 times the predicted resting energy expenditure (PREE) calculated according to the Harris Benedict formula,<sup>4</sup> with a 1 g nitrogen: 150 nonprotein kilocalories ratio. The nonprotein calories were given as 100% glucose (nutritional period G) or 50% glucose-50% fat (nutritional period GL), according to a randomized order. During the three basal periods (B1, B2, B3), the patients received a very low caloric intake (200 kcal per 12 h provided as a 5% glucose solution).

Throughout the study, glucose, lipids (Intralipid® 20%-Kabi Vitrum), and proteins (Totamine®-Egic) were continuously infused with an electric pump (Ivac Corporation) through a central venous catheter.

During the second half of each basal or nutritional period, oxygen consumption ( $\dot{V}_{O_2}$ ),  $\dot{V}_{CO_2}$ , respiratory quotient (RQ),  $\dot{V}_E$ , and RR were continuously measured and recorded with our mass spectrometer-computer system (mass spectrometer Perkin Elmer MGA 1100-microcomputer Kontron Psi 80). A thorough description and validation of the system has been given in a previous report.<sup>5</sup> The system can be briefly described as follows. Gas samples were drawn from the Y piece of the patient's breathing circuit to the mass spectrometer, and analyzed for

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TABLE 1. Characteristics of Patients

Patient N°	Age (Yr)	Height (cm)	Weight (kg)	PREE (kcal/day)	FEV1 (% predicted)	FVC (% predicted)	Diagnosis and Surgical Procedure
<b>Group 1</b>							
1	62	170	55	1288	115.4	109.1	Esophagus carcinoma: cervicotomy + median laparotomy
2	67	174	72	1507	119.4	115.1	Esophagus carcinoma: cervicotomy + median laparotomy
3	61	167	90	1750	123.4	118.5	Esophagus carcinoma: cervicotomy + median laparotomy
4	65	161	57	1256	120.3	104.7	Esophagus carcinoma: right thoracotomy + median laparotomy
<b>Group 2</b>							
5	62	169	55	1284	72.6	119.7	Cardia carcinoma: thoracophreno laparotomy
6	71	159	58	1225	51.6	55.9	Perforation of peptic ulcer: median laparotomy
7	74	167	66	1363	38.8	65.6	Aneurysm of abdominal aorta: median laparotomy
8	66	167	64	1370	52.9	73.4	Stomach carcinoma: median laparotomy

PREE = Predicted resting energy expenditure; FEV1 = Forced expired volume for 1 s; FVC = Forced vital capacity.

inspired  $O_2$  concentration ( $FI_{O_2}$ ) and  $CO_2$  wave form recognition. The latter analysis allowed rejection of artifacted cycles, *e.g.*, coughing. Then, expired gas was sampled from the outlet of a mixing chamber for the measurements of the mixed expired  $O_2$  and  $CO_2$  concentrations. The duration of the entire analysis sequence was about 3 min. Expired flow was measured by a pneumotachometer. All the signals were collected by the microcomputer, which was programmed to reject artifacted respiratory cycles and to compute the physiologic parameters. Every 30 min, the mean values of these parameters were calculated and stored. Energy expenditure (EE) was calculated according to the Weir formula,<sup>6</sup> neglecting nitrogen losses.  $Pa_{CO_2}$  was measured at the end of each period.

Results are presented as the mean  $\pm$  SE and further statistics calculated using analysis of variance with Duncan's multiple range follow-up tests.<sup>7</sup> Correlations were calculated using regression analysis.

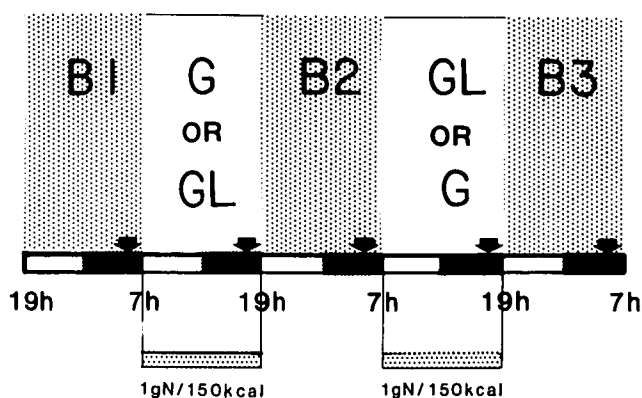


FIG. 1. General outline of the study. The arrows show the time course of  $Pa_{CO_2}$  determinations. During the second half of each basal (B) or nutritional period (G or GL),  $\dot{V}_{CO_2}$ ,  $\dot{V}_{O_2}$ , and RQ are continuously recorded by a mass-spectrometer system.

## RESULTS

The values of the physiologic parameters measured during the three basal periods (B1, B2, B3) were not statistically different, and were pooled for the comparison with the two nutritional periods. As shown in table 2, results were similar in the two groups of patients. EE was found to be 16–17% above the PREE.

In comparison with the basal period,  $\dot{V}_{CO_2}$  and RQ were increased during the nutritional period GL. The other measured parameters were not significantly altered. There was no difference between the values from the two study groups (table 2).

Compared to the basal values,  $\dot{V}_{CO_2}$ , RQ, respiratory rate, and  $\dot{V}_E$  were significantly increased in both groups of patients during nutritional period G. There was also an increase in  $\dot{V}_{O_2}$  and EE, but the level of statistical significance was reached only for EE in patients of group 2. Compared to the nutritional period GL,  $\dot{V}_{CO_2}$ , RQ, and RR were significantly more elevated, whereas  $\dot{V}_{O_2}$  and EE remained at the same level.  $Pa_{CO_2}$  was unchanged (table 2).

Figure 2 illustrates that the changes in  $\dot{V}_E$  paralleled the nutritional-induced changes in  $\dot{V}_{CO_2}$ . Figure 3 shows a typical individual observation during the administration of the different nutritional regimens.

## DISCUSSION

Routine daily therapeutic and nursing interventions can significantly alter metabolic rate in intensive care patients.<sup>8</sup> Thus, measuring energy expenditure in such patients by indirect calorimetry requires multiple and frequent determination of  $\dot{V}_{O_2}$  and  $\dot{V}_{CO_2}$ . We, therefore, used a mass spectrometer system designed to provide an accurate continuous measurement of pulmonary gas exchange during mechanical ventilation.<sup>5</sup> In addition, for each 12-h nutritional or basal period, measurements were per-

TABLE 2. Metabolic and Respiratory Parameters Measured During the Three Study Periods in the Two Groups of Patients

	$\dot{V}_{CO_2}$ (ml·min <sup>-1</sup> ·m <sup>-2</sup> )	$\dot{V}_{O_2}$ (ml·min <sup>-1</sup> ·m <sup>-2</sup> )	RQ	$\dot{V}_E$ (l·min <sup>-1</sup> )	RR	P <sub>aCO<sub>2</sub></sub> (mmHg)	EE/PREE
Basal period							
Group 1	120 ± 4	132 ± 5	0.90 ± 0.02	9.8 ± 0.4	18 ± 0.9	36.2 ± 1.1	1.17 ± 0.06
Group 2	115 ± 4	130 ± 5	0.88 ± 0.02	9.7 ± 0.5	16 ± 1.1	35.7 ± 2.9	1.16 ± 0.06
G + L period							
Group 1	136 ± 6*	140 ± 6	0.97 ± 0.03*	10.7 ± 0.7	18 ± 0.9	33.3 ± 1.3	1.26 ± 0.10
Group 2	129 ± 6*	140 ± 6	0.92 ± 0.02	10.9 ± 1.1	18.5 ± 2.0	35.6 ± 3.7	1.24 ± 0.03
G period							
Group 1	151 ± 7*†	145 ± 8	1.05 ± 0.04*†	12 ± 0.6*	21 ± 1.2*†	36.2 ± 1.2	1.29 ± 0.10
Group 2	145 ± 6*†	139 ± 7	1.04 ± 0.04*†	12.7 ± 0.9*	21.5 ± 1.1*	37.0 ± 2.2	1.29 ± 0.02*

\* Significant ( $P < 0.05$ ) by comparison with basal period.

† Significant ( $P < 0.05$ ) by comparison with G + L Period.

G period = Non-protein calories given as 100% glucose; G + L pe-

riod = Non-protein calories given as 50% glucose-50% fat; EE = Measured energy expenditure; PREE = Predicted resting energy expenditure.

formed only during the last 6 h, to ensure that the patients' energy expenditure reached a steady state.<sup>9</sup> And, finally, both nutritional periods were realized at the same period in the day time.

From the study of metabolic variables, three major points arose. Firstly, the EE measured during the basal period was about 1.17 times the PREE. This finding, which is in agreement with the scale of metabolism developed by Kinney *et al.*,<sup>10</sup> indicates that a major surgical procedure, like esophagogastrectomy, does not necessarily lead to a hypermetabolic state. Secondly, we found that nutrition by glucose alone or by glucose and lipids resulted in minimal increases in  $\dot{V}_{O_2}$  and EE, which are likely related to the thermogenic effect of nutrients. Rodriguez *et al.*<sup>11</sup> failed to observe this effect in acutely ill patients intravenously infused with glucose alone. In fact, the thermogenic effect of nutrient is a very complicated issue. For a given patient, its magnitude depends on several

factors, including the patient's metabolic state, the proportion of glucose and lipids in the diet, the concurrent administration of amino acids, and also the route of administration of the caloric intake, *i.e.*, oral or parenteral, single bolus or continuous infusion.<sup>9,11-13</sup> Thirdly, we found that the shift from basal to nutritional periods resulted, in all patients, in a marked increase in  $\dot{V}_{CO_2}$  and RQ. As expected, this effect, which illustrates the shifting of energy source from endogenous fat to administered glucose,<sup>3</sup> was more pronounced with glucose as the entire

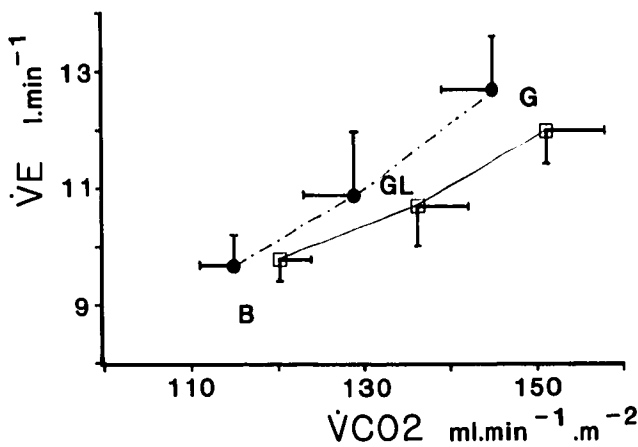


FIG. 2. Relationship between minute ventilation ( $\dot{V}_E$ ) and carbon dioxide production ( $\dot{V}_{CO_2}$ ) for the three study periods: basal period (B), glucose lipid period (GL), and glucose period (G). Open squares = patients with normal preoperative pulmonary function tests; closed circles = patients with chronic pulmonary disease.

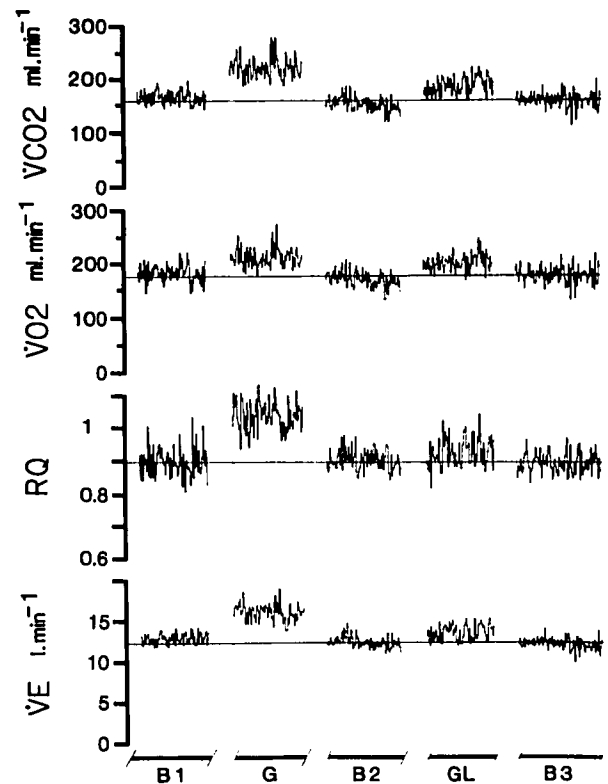


FIG. 3. A typical recording of metabolic and respiratory parameters during the second half of each study period.

source of nonprotein calories, with an RQ greater than 1. Moreover the duration of the nutritional periods was only 12 h, and probably not long enough for glycogen stores to fill.<sup>14</sup> A longer nutritional period might result in a greater effect on  $\dot{V}_{CO_2}$ , since, in these conditions, more glucose might be available for oxidation. Our observations also favor the view that our patients were normometabolic; in hypermetabolic patients, a glucose load is associated with a parallel increase in  $\dot{V}_{O_2}$  and  $\dot{V}_{CO_2}$ , thus leading to an almost unchanged RQ which remains below 1.<sup>3</sup>

The stability of  $P_{aCO_2}$ , which we observed in all our patients, indicates that the nutrition-induced changes in  $\dot{V}_{CO_2}$  were associated with a properly enhanced  $\dot{V}_E$ . The increase in  $\dot{V}_E$  was primarily due to an increase in respiratory rate, as previously observed in spontaneously breathing patients by Rodriguez.<sup>11</sup> The pressure support mode of ventilation allows such adjustments, which the control mode of ventilation does not permit. In fact, an increased  $P_{aCO_2}$  has been observed during a nutrition-induced  $CO_2$  load in patients undergoing artificial ventilation on the control mode.<sup>15</sup>

To augment minute ventilation, our patients with impaired respiratory function exhibited a slight but statistically insignificant rise in  $\dot{V}_{O_2}$ , as did the patients with normal lung function. This finding is in contrast with the results of Campbell *et al.*,<sup>16</sup> who observed that  $\dot{V}_{O_2}$  rose dramatically in patients with obstructive pulmonary disease in response to an exercise-induced increase in  $\dot{V}_E$ . In our patients, the IPS mode of ventilation took over the major part of the work of breathing, thus preventing the abrupt rise in  $\dot{V}_{O_2}$  which would be expected to occur in response to an increase in  $\dot{V}_E$ .

In conclusion, the data of the present study have shown that a major surgical procedure does not necessarily lead to hypermetabolic state. Secondly, as expected, postoperative patients respond to a parenteral caloric load by an increase in  $\dot{V}_{CO_2}$ , which depends on the amount of glucose in the diet. Thirdly, under IPS, an increase in  $\dot{V}_{CO_2}$  is associated with a properly enhanced  $\dot{V}_E$ , even in cases of chronically impaired pulmonary function.

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