Effect of Epidural Blockade on Protein, Glucose, and Lipid Metabolism in the Fasted State and during Dextrose Infusion in Volunteers

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Background: To interpret correctly the results from studies performed during surgery and anesthesia it is necessary to dissect the separate effect of the anesthetic technique itself. The purpose of this study was to investigate the metabolic effects of epidural blockade (T7-S1) with bupivacaine 0.25% after 12 h fasting and during administration of 4 mg ⋅ kg⁻¹ ⋅ min⁻¹ dextrose in six healthy volunteers.

Methods: Each volunteer was assigned to randomly undergo a 6-h multiple stable isotope infusion study (3 h fasted, 3 h dextrose infusion) with or without epidural blockade. L-[1-¹³C]leucine, [6,6-²H₂]glucose, and [1,1,2,3,3-²H₅]glycerol were infused to measure protein synthesis, breakdown, and amino acid oxidation; glucose production and clearance; and lipolysis. Plasma concentrations of glucose, lactate, glycerol, free fatty acids, insulin, and glucagon were determined.

Results: Epidural blockade with bupivacaine had no influence on protein oxidation, breakdown and synthesis, glucose production, glucose clearance and lipolysis in the fasted state. Plasma concentrations of metabolic substrates and hormones also were not affected. Dextrose infusion significantly increased glucose clearance and plasma concentrations of glucose and insulin, while endogenous glucose production and lipolysis decreased to a similar degree in both groups. Protein synthesis, breakdown, and oxidation did not change during dextrose infusion.

Conclusions: Epidural blockade with bupivacaine in the absence of surgery has no effect on fasting protein, glucose, and lipid metabolism. Epidural blockade does not modify the inhibitory influence of dextrose administration on endogenous glucose production and lipolysis. (Key words: Bupivacaine; glyceral; leucine; stable isotopes.)

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protein-preserving effect of dextrose infusion. In healthy humans significant inhibition of urea synthesis and almost complete suppression of endogenous glucose production has been achieved if glucose was infused at 4 mg · kg⁻¹ · min⁻¹. Glucose administration at a higher rate resulted in a more pronounced decrease of urea production and an increase of glucose oxidation but did not further inhibit endogenous glucose production.

The aim of this project was to establish, whether epidural blockade (T7–S1) in the absence of surgery influences fasting protein breakdown, amino acid oxidation and protein synthesis, glucose production, and lipolysis assessed by stable isotope kinetics. This segmental area of neural blockade was selected as it represents the area of dermatome innervation of subumbilical abdominal surgical incisions. A second objective of this study was to investigate if dextrose, infused at 4 mg · kg⁻¹ · min⁻¹ and in the presence of epidural blockade, further improves glucose utilization and attenuates glucose production, thereby enhancing its protein-sparing effect.

**Subjects and Methods**

This randomized crossover study was approved by the ethics committee of the hospital, and informed consent was obtained from six healthy volunteers (age [mean ± SD], 26 ± 6 yr) with a mean body weight of 62 ± 11 kg and a mean height of 173 ± 10 cm. The subjects were recruited from the general population (neither patients nor coworkers) and received financial compensation. Before the investigation they received medical and physical examinations and routine biochemical analyses. All subjects were admitted twice (1 week apart) to the metabolic unit. Each volunteer was assigned to undergo in random order a 6-h multiple stable isotope infusion study (3 h fasted, 3 h dextrose infusion) either with or without epidural blockade.

**Epidural Blockade**

An epidural catheter was inserted at thoracic vertebral level T10–T11. Neural blockade was established with bupivacaine 0.5% to achieve a bilateral sensory block to ice and pin prick from thoracic dermatome level 7 (T7) to sacral dermatome level 1 (S1). The block was maintained with a constant infusion of bupivacaine 0.25% set at a rate of 8–12 ml/h.

**Dextrose Infusion**

After a 3-h period of fasting a solution of crystallized beet sugar (10% dextrose anhydrous, Avebe, Foxhol, Holland) was infused at 4 mg · kg⁻¹ · min⁻¹ for 3 h. The solution was prepared by the local pharmacy under sterile conditions and tested for sterility, stability, and absence of pyrogens before intravenous infusion. The beet dextrose solution was chosen because of its low ¹³C content and therefore the lack of significant perturbation of ¹³CO₂ enrichment in expired air.

**Experimental Protocol**

Plasma kinetics of leucine, glucose, and glycerol were determined by a primed constant infusion of tracer quantities of l-[¹-¹³C]leucine (99% ¹³C), [6,6-²H₂]-glucose (99% ²H), and [1,1,2,3,3-²H₅]-glycerol (99% ²H) obtained from Cambridge Isotope Laboratories (Cambridge, MA). Before each infusion study, sterile solutions of isotopes were prepared in the hospital pharmacy. The solution was passed through a 0.22-µm filter into injection bottles. The bottles were sealed, heat-sterilized at 121°C for 15 min, and kept at 4°C until administration. Each set of solutions was confirmed to be sterile and free of pyrogens (LAL Pyrogen test, Whittaker Bioproducts, Walkersville, MD).

All tests were performed in the fasted state beginning at 8 AM after a 12-h overnight fast. The subjects were studied in a temperature and humidity controlled environment (24°C, 35–42% relative humidity). Electrocardiogram, noninvasive systemic arterial pressure, and oxygen saturation were monitored during the whole study period. A superficial vein in the dorsum of the hand was cannulated and the cannula kept patent with saline 2 ml · kg⁻¹ · h⁻¹. This arm was warmed in a heated air box to achieve arterIALIZATION of venous blood. A second superficial vein in the contralateral arm was cannulated to provide access for the infusion of the stable isotopes. Blood and expired air samples were collected before the infusion to determine baseline enrichments. Priming doses of NaH¹³CO₃ 1 µmol/kg, l-[¹-¹³C]leucine 4 µmol/kg, [6,6-²H₂]-glucose 22 µmol/kg, and [1,1,2,3,3-²H₅]glycerol 1.2 µmol/kg were administered and followed immediately by continuous infusions of l-[¹-¹³C]leucine 0.06 µmol · kg⁻¹ · min⁻¹ and [1,1,2,3,3-²H₅]glycerol 0.09 µmol · kg⁻¹ · min⁻¹ lasting 6 h. [6,6-²H₂]-Glucose was infused at a rate of 0.22 µmol · kg⁻¹ · min⁻¹ during the first 3 h (fasted period) and then changed to 0.44 µmol · kg⁻¹ · min⁻¹ during the 3 h of dextrose administration. Isotope infusion was uninterrupted throughout the 6-h experimental period. Toward
the end of each 3-h study period four arterialized blood and expired breath samples were collected at 10-min intervals. Each blood sample was transferred immediately to a heparinized tube, centrifuged at 4°C (3,000 g, 15 min) and stored at −20°C. Breath samples were collected in a 2-l latex bag and transferred immediately to 20-ml vacutainers. A schematic representation of the protocol is shown in figure 1.

**Gaseous Exchange**

Indirect calorimetry (Datex Deltatrac, Helsinki, Finland) was performed in the last hour of the fasted state and of the dextrose infusion. The subjects were lying in a semirecumbent position (20 degrees), breathing room air in the ventilated hood, for 20 min on each occasion. Oxygen consumption (V\textsubscript{O\textsubscript{2}}) and carbon dioxide production (V\textsubscript{CO\textsubscript{2}}) were measured, and the respiratory quotient was calculated. An average value of V\textsubscript{O\textsubscript{2}}, V\textsubscript{CO\textsubscript{2}}, and the respiratory quotient was taken, with a coefficient of variation, 10%.

**Temperature Measurements**

Core body temperature was measured with a thermocouple probe (Mono-a-therm; Mallinckrodt Medical, St. Louis, MO) inserted in the aural canal and positioned adjacent to the tympanic membrane. Skin temperature was recorded at 15 skin sites located in the forehead, cheek, neck, nipple, midarm, midforearm, dorsum of the hand, umbilicus, iliac crest, medial thigh, lateral thigh, knee, medial calf, lateral calf, and dorsum of the foot with an infrared thermometer previously described.\textsuperscript{12} The mean unweighted skin temperature was calculated from the 15 sites. Tympanic (core) and skin temperatures were measured at isotopic plateau before and toward the end of dextrose infusion. Ambient temperature also was measured using a mercury in glass thermometer.

**Analytic Methods**

**Isotopic Enrichments.** Plasma [1-\textsuperscript{13}C]\textsubscript{6}-ketoisocaproate enrichment was determined by electron-impact selected-ion monitoring gas chromatography–mass spectrometry using the method previously described by Mamer and Montgomery,\textsuperscript{13} except that t-butyldimethylsilyl rather than trimethylsilyl derivatives were prepared. Expired [\textsuperscript{13}C]carbon dioxide enrichment was determined by isotope ratio mass spectrometry (Analytical Precision AP2,005, Manchester, United Kingdom). Plasma glucose was derivatized to its pentaacetate compound and the [6,6-\textsuperscript{2}H\textsubscript{2}]glucose enrichment determined by gas chromatography–mass spectrometry using electron-impact ionization.\textsuperscript{14} [1,1,2,3,3-\textsuperscript{2}H\textsubscript{5}]Glycerol was converted to its triacetylester derivative as recently described\textsuperscript{15} and analyzed by positive-ion chemical ionization. In each analysis run, duplicate injections were always performed and their means were taken to represent enrichment.

**Plasma Metabolites and Hormones.** Plasma glucose was measured by a glucose-oxidase method using a glucose analyzer 2 (Beckman Instruments, Fullerton, CA). Plasma lactate assay was based on lactate oxidase and was performed using the synchron CX 7 system (Beckman Instruments). The mean intraassay and interassay coefficients of variance were 3.0% and 4.5%, respectively. Plasma-free fatty acids and glycerol were analyzed by using the Boehringer Mannheim enzymatic colorimetric kit (Boehringer Mannheim, Laval, Quebec, Canada). The mean intraassay and interassay coefficients of variance for free fatty acids were 2.3% and 4.1% and for glycerol 3.1% and 4.0%, respectively. Circulating concentrations of insulin and glucagon were measured by a sensitive and specific double antibody radioimmunoassay (Amersham International, Amersham, Bucks, United Kingdom). Intraassay and interassay precisions for insulin were 5.6% and 7.3% and for glucagon were 5.4% and 6.0%, respectively.

**Calculations**

If a physiologic and isotopic steady state exists the rate of appearance (Ra) of unlabeled substrate in plasma can be derived from the plasma isotope enrichment (APE or atom percentage excess) calculated by:

\[
Ra = \left( \frac{APE_{\text{inf}}}{APE_{\text{pl}}} - 1 \right) \cdot F
\]

\textsuperscript{1}

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Fig. 1. Time course of the infusion of isotopes and collection of plasma and expired air samples (circles), indirect calorimetry (rectangles), and collection of plasma for the determination of metabolic substrates and hormones (squares) in the fasted state and during the infusion of dextrose.

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where F is the infusion rate of the labeled tracer (μmol·
kg\(^{-1}\)·min\(^{-1}\)), APE\(_{inf}\) is the tracer enrichment in the
infusate and APE\(_{pl}\) the tracer enrichment in plasma,
respectively. The APE used in this calculation were the
mean of the four APE determined during steady-state
conditions obtained at each phase of the studies. The
accuracy of the isotopic enrichments at isotopic plateau
was tested by evaluating the scatter of values above their
mean, expressed as coefficient of variation. A coefficient
of variation less than 5% was used as a confirmation of a
valid plateau.

Under steady-state conditions, leucine flux (Q) is de-

fined by the formula:

\[
Q = S + O = B = I
\]

where S is the rate at which leucine is incorporated into
body protein, O is the rate of oxidation of leucine, B is
the rate at which unlabeled leucine enters the free
amino acid pool from endogenous protein breakdown,
and I is the rate of leucine intake including tracer and
diet. In the postabsorptive state, the sole source of the
essential amino acid leucine for protein synthesis and
oxidation is that derived from the breakdown of endog-
enous proteins. Inspection of equation 2 indicates that,
when studies are conducted after absorption, leucine
flux is equal to leucine breakdown.\(^{16}\) Plasma enrichment
of \([1\text{-}^{13}\text{C}]\alpha\text{-ketoisocaproate}\) during infusion of \(\text{L-[1-}
\text{^{13}C]}\text{leucine}\) has been used as the basis for calculating
both flux and oxidation of leucine.\(^{17}\) This steady-state
reciprocal pool model is considered to provide a more
precise representation of intracellular precursor pool
enrichment than leucine itself.\(^{17}\) In the calculation of
oxidation, factors of 0.76 for the fasting state and 0.81
for the fed state were applied to account for the fraction
of \(^{13}\text{C}\)carbon dioxide released from leucine but retained
within slow turnover rate pools of the body.\(^{16}\)

In the fasted state \(R_a\) glucose was equal to the endog-
enous production of glucose. During the infusion of
dextrose, endogenous glucose production was calcu-
lated by subtracting the dextrose infusion rate from the
total \(R_a\) glucose.

The fractional plasma clearance rates of glucose and
glycerol were calculated as the \(R_a\) of glucose or glycerol
divided by the corresponding plasma substrate concen-
tration.

**Statistics**

All data are presented as mean ± SD. Comparisons for
each dependent variable were performed using two-
factorial analysis of variance with the two factors epidi-
4rul blockade and dextrose infusion. Analysis of vari-
ance for repeated measurements was applied to analyze
any significant change in the plasma concentrations of
metabolic substrates (glucose, lactate, glycerol, free fatty
acids) and hormones (insulin, glucagon) during dextrose
administration. If no significant change was detected the
average value of the two measurements obtained after
150 and 180 min of dextrose infusion was compared
with the corresponding fasting value. Statistical signifi-
cance was accepted at \(P < 0.05\).

**Results**

**Hemodynamics**

Volunteers’ hemodynamics (mean arterial pressure:
85 ± 8 mmHg, heart rate: 77 ± 9 beats/min) were not
significantly affected by epidural anesthetic before or
during dextrose infusion. Mean arterial pressure in the
epidural group was 84 ± 11 mmHg before and 79 ± 9
mmHg during dextrose administration; heart rate was
63 ± 10 beats/min before and 64 ± 5 beats/min there-
after. In subjects without epidural blockade postabsor-
tive mean arterial pressure at 81 ± 6 mmHg remained
unchanged at 79 ± 9 mmHg. Heart rate at 62 ± 7
beats/min also did not change during dextrose adminis-
tration (66 ± 6 beats/min).

**Kinetics**

In all experiments a plateau in the enrichments of plasma
\([1\text{-}^{13}\text{C}]\alpha\text{-ketoisocaproate}, [6,6\text{-}^{2}\text{H}_2]\text{glucose}, [1,1,2,3,3\text{-}^{2}\text{H}_5]\text{-}
glycerol, and expired \([^{13}\text{C}]\)carbon dioxide was achieved
before and after 3 h of dextrose infusion (coefficient of
variation < 5%), permitting the use of the steady-state
equation.

Epidural blockade had no significant effect upon
whole-body protein synthesis, breakdown, or leucine
oxidation; glucose production or clearance; or lipolysis
(table 1). Administration of dextrose did not affect the
kinetics of protein metabolism; total \(R_a\) glucose (\(P >
0.001\)) and glucose clearance (\(P < 0.05\)) increased in
both groups. Dextrose infusion decreased endogenous
\(R_a\) glucose (\(P < 0.001\)) and glycerol release (\(P < 0.05\)) to
a similar degree in the two groups.

**Metabolites and Hormones**

Plasma concentrations of metabolites and hormones
obtained after 150 and 180 min of dextrose infusion
were not significantly different. As shown in table 2
epidural blockade did not influence circulating concentrations of metabolic substrates and hormones in the fasted state. Dextrose administration increased plasma glucose and insulin concentration (P < 0.001) and decreased plasma concentrations of glycerol and free fatty acids (P < 0.05). These parameters were not affected by epidural blockade. Plasma concentrations of lactate and glucagon remained unchanged during the study period.

Gaseous Exchange and Temperature

Epidural blockade did not affect whole-body oxygen consumption, carbon dioxide production, or the respiratory quotient indicating unchanged substrate utilization. Dextrose infusion significantly stimulated whole-body carbon dioxide production (P < 0.05) in all subjects, resulting in a significant increase in the respiratory quotient (P < 0.05, table 3). Core and mean skin temperature showed no significant changes during dextrose administration and were not influenced by epidural blockade (table 3).

Discussion

The results of the present study demonstrate that epidural nerve blockade (T7–S1) with bupivacaine in healthy volunteers does not affect fasting leucine, glucose, or glycerol kinetics or the metabolic responses to dextrose infusion in healthy volunteers.

The metabolic impact of neural blockade with local anesthetics combined with surgery has been extensively

Table 1. Kinetics of Leucine, Glucose, and Glycerol Metabolism in Volunteers with and without Epidural Blockade in the Fasted State and during Dextrose Infusion

<table>
<thead>
<tr>
<th></th>
<th>Nonepidural Fasted</th>
<th>Nonepidural Dextrose Infusion</th>
<th>Epidural Fasted</th>
<th>Epidural Dextrose Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ra leucine (μmol · kg⁻¹ · min⁻¹)</td>
<td>2.11 ± 0.31</td>
<td>1.95 ± 0.39</td>
<td>2.10 ± 0.23</td>
<td>2.04 ± 0.28</td>
</tr>
<tr>
<td>Leucine oxidation (μmol · kg⁻¹ · min⁻¹)</td>
<td>0.38 ± 0.07</td>
<td>0.34 ± 0.08</td>
<td>0.43 ± 0.08</td>
<td>0.42 ± 0.08</td>
</tr>
<tr>
<td>Protein synthesis (μmol · kg⁻¹ · min⁻¹)</td>
<td>1.73 ± 0.31</td>
<td>1.61 ± 0.37</td>
<td>1.67 ± 0.22</td>
<td>1.62 ± 0.28</td>
</tr>
<tr>
<td>Ra glucose (μmol · kg⁻¹ · min⁻¹)</td>
<td>12.87 ± 2.23</td>
<td>24.85 ± 2.96*</td>
<td>12.63 ± 2.11</td>
<td>23.44 ± 1.21*</td>
</tr>
<tr>
<td>Endogenous Ra glucose (μmol · kg⁻¹ · min⁻¹)‡</td>
<td>12.87 ± 2.23</td>
<td>22.4 ± 2.28*</td>
<td>12.63 ± 2.11</td>
<td>1.26 ± 1.71*</td>
</tr>
<tr>
<td>Glucose clearance (ml · kg⁻¹ · min⁻¹)</td>
<td>2.54 ± 0.29</td>
<td>3.47 ± 0.74†</td>
<td>2.59 ± 0.36</td>
<td>3.50 ± 0.65†</td>
</tr>
<tr>
<td>Ra glycerol (μmol · kg⁻¹ · min⁻¹)</td>
<td>1.92 ± 0.82</td>
<td>0.98 ± 0.50†</td>
<td>1.95 ± 0.67</td>
<td>0.98 ± 0.15†</td>
</tr>
<tr>
<td>Glycerol clearance (ml · kg⁻¹ · min⁻¹)</td>
<td>20.47 ± 7.24</td>
<td>17.79 ± 9.82</td>
<td>21.88 ± 4.43</td>
<td>21.41 ± 6.31</td>
</tr>
</tbody>
</table>

Table 2. Plasma Concentrations of Circulating Metabolites and Hormones in Volunteers with and without Epidural Blockade in the Fasted State and during Dextrose Infusion

<table>
<thead>
<tr>
<th></th>
<th>Nonepidural Fasted</th>
<th>Nonepidural Dextrose Infusion</th>
<th>Epidural Fasted</th>
<th>Epidural Dextrose Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>5.1 ± 0.4</td>
<td>7.7 ± 1.2*</td>
<td>4.9 ± 0.3</td>
<td>7.4 ± 0.9*</td>
</tr>
<tr>
<td>Lactate (mg/dl)</td>
<td>1.0 ± 0.3</td>
<td>1.1 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>1.1 ± 0.1</td>
</tr>
<tr>
<td>Glycerol (μM)</td>
<td>92 ± 20</td>
<td>60 ± 21†</td>
<td>79 ± 20</td>
<td>50 ± 14†</td>
</tr>
<tr>
<td>FFA (μM)</td>
<td>0.37 ± 0.20</td>
<td>0.12 ± 0.02†</td>
<td>0.30 ± 0.09</td>
<td>0.13 ± 0.01†</td>
</tr>
<tr>
<td>Insulin (μU/ml)</td>
<td>7.2 ± 1.3</td>
<td>14.9 ± 3.1*</td>
<td>6.6 ± 1.4</td>
<td>13.8 ± 2.7*</td>
</tr>
<tr>
<td>Glucagon (pmol)</td>
<td>21 ± 11</td>
<td>17 ± 10</td>
<td>21 ± 11</td>
<td>17 ± 10</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

Ra = rate of appearance.

* P < 0.001 compared with fasted state.

† P < 0.05 compared with fasted state.

‡ Endogenous Ra glucose was calculated by subtracting the rate of exogenous glucose infusion from total Ra glucose.
studied. Epidural blockade, established before surgery, improved postoperative nitrogen balance,18 decreased the obligatory postoperative decrease in muscle fractional synthetic rate,3 and attenuated the rise in whole-body protein breakdown and leucine oxidation with minimal changes in protein synthesis.2 Epidural blockade with local anesthetics has been shown to ameliorate the hyperglycemic response to surgery,4 prevent the intraoperative impairment of glucose tolerance,5 and blunt the increases of the plasma concentrations of glycerol and free fatty acids during surgery.4,6 Few studies have addressed the independent metabolic effect of epidural blockade, and it has been suggested that epidural blockade in the absence of surgical stress exerts only minimal influence on metabolism. High thoracic or lumbar epidural blockade with bupivacaine for abdominal surgery produced no changes in circulating plasma concentrations of amino acids, glucose, glycerol, or free fatty acids and had no significant effect on splanchnic amino acid uptake and glucose release.1,4,6,7,19 These studies, however, have been performed exclusively in unpremedicated volunteers in a controlled environment after 12 h of fasting. In addition we applied stable isotopes to study the kinetics of protein, glucose, and lipid metabolism. Efforts were made to maintain the subjects normothermic throughout the study period, therefore limiting the possible effect of hypothermia on protein metabolism, which has been shown to occur in surgical patients.20

Whole-body protein breakdown, oxidation, and synthesis were not significantly altered by low thoracic epidural blockade with bupivacaine. Fasting endogenous glucose production, which was identical to values recently reported in healthy volunteers after 12 h of fasting,21 whole-body glucose clearance and lipolysis also were not affected, lending further support to the contention that neural blockade per se does not influence protein, glucose, and lipid metabolism. Epidural nerve blockade, however, by producing a neural blockade of the efferent adrenergic pathways to the pancreas, may contribute to a decrease in glucose tolerance and insulin release, as baseline adrenergic input is important in maintaining normal pancreatic islet function.22 Because the sympathetic innervation of the pancreas predominantly comes via the splanchnic nerves from thoracic cord segments T6–T10, the level of neural blockade plays an important role with regard to glucose metabolism. A recent study demonstrated that sympathetic efferent blockade established with high spinal anesthesia (T2) impaired the acute plasma insulin response to an intravenous glucose load in nonpremedicated patients before elective surgery.22 On the contrary patients receiving lower dermatome blockade (T9–T12)—similar to the block applied in our subjects—with minimal effect on sympathetic efferents exhibited no alteration of the insulin response to glucose.22 In the present study a sensory block from T7 to S1 also did not inhibit the plasma insulin and glucose response to dextrose infusion. The magnitude of increase of carbohydrate oxidation during dextrose infusion, reflected by the increase of the respiratory quotient caused by stimulated carbon dioxide production, also was not altered in the epidural group.

The nitrogen-sparing effect of dextrose is well documented in humans. Intravenous glucose administration in fasted volunteers has been reported to decrease nitro-
Because muscle protein is broken down to supply the amino acids that serve as precursors for the de novo glucose synthesis, gluconeogenesis occupies a central position in catabolic pathways. Urea is produced in the liver when these amino acids are deaminated, leaving the carbon skeleton for glucose production. It has therefore been hypothesized that by reducing gluconeogenesis urea formation and nitrogen, excretion can be diminished, resulting in a better preservation of whole-body protein. Animal studies demonstrating an inverse correlation between gluconeogenesis and hepatic protein synthesizing capacity document the interdependence between glucose and protein metabolism.29 Dextrose administration at 4 mg · kg⁻¹ · min⁻¹ significantly suppressed endogenous glucose production in all subjects. This finding is consistent with previous results revealing similar, almost complete reductions of endogenous glucose production in healthy postabsorptive volunteers.8 Although direct effects of increased glucose availability are difficult to separate from the effects of the increase in insulin that is induced by hyperglycemia, this response has been shown to occur independently of changes in plasma insulin concentration. Total glucose production and gluconeogenesis were all inhibited to the same degree if insulin secretion was inhibited by somatostatin as if insulin plasma concentration increased after 2 h of glucose infusion (4 mg · kg⁻¹ · min⁻¹).30 Whole-body glucose clearance also rose regardless of whether insulin was held at the basal level or was allowed to change spontaneously.30 Administration of dextrose caused a significant decrease of the Rₚ glycerol by 50%, indicating a direct inhibition of lipolysis, regardless of whether subjects received epidural bupivacaine or not. This finding is in line with previous observations reporting similar reductions of lipolysis during glucose administration in healthy postabsorptive volunteers.31,32 The decrease in free fatty acid plasma concentration was more pronounced than the decrease in plasma glycerol level in our study. This is in accordance with the results of a recent investigation showing that glucose infused at 4 mg · kg⁻¹ · min⁻¹ stimulated reesterification of fatty acids and triglyceride–fatty acid substrate cycling within adipose tissue.32 The suppressory effect of glucose on whole-body lipolysis could be explained on the basis of increased plasma insulin concentration and the antilipolytic action of insulin. From previous studies, however, it is apparent that a physiologic rise in plasma glucose per se without any concomitant rise in plasma insulin con-

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centration can decrease the release of glycerol from adipose tissue.\textsuperscript{55}

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References

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