In human medicine, critical care patients frequently require dextrose administration as a component of supportive treatment and care. An insulin infusion is often required in conjunction with the infusion of dextrose solutions to effectively manage the blood glucose concentration. Conventional glycemic control has been directed at maintaining the blood glucose concentration at \( < 180 \) to \( 200 \) mg/dL, but an increasingly prevalent trend has been strict maintenance of blood glucose concentrations within the reference range.\(^1\) Several studies\(^2\) to\(^5\) in human patients have revealed numerous benefits associated with the use of intensive insulin administration to maintain strict glycemic control. A prospective study\(^6\) of 1,548 humans in a surgical critical care unit revealed a 34% reduction in mortality rate when blood glucose concentration was maintained between 80 and 110 mg/dL. Further benefits included a significant decrease in critical care complications, including reductions in bacteremia, prolonged inflammation, acute renal failure requiring dialysis or hemofiltration, and dependence on mechanical ventilation. Furthermore, comparable benefits have been reported\(^6\) with more moderate glycemic control, including a 29.3% decrease in hospital mortality rate and a 10.8% decrease in duration of hospital stay in critically ill humans in an intensive care unit when blood glucose concentration was maintained at \( < 140 \) mg/dL.

### Objective
To investigate the effects of a continuous rate infusion (CRI) of dextrose solution or dextrose solution and insulin on glucose and insulin concentrations in healthy and endotoxin-exposed horses.

### Animals
9 adult mares.

### Procedures
During phase 1, treatments consisted of saline (0.9% NaCl) solution (control group; \( n = 4 \)) or 20% dextrose solution (group 1; 4) administered IV as a 360-minute CRI. During phase 2, treatments consisted of 360-minute CRIs of 20% dextrose solution and insulin administered simultaneously at 367.6 mg/kg/h (30 kcal/kg/d) and 0.07 U/kg/h, respectively, in healthy horses (group 2; \( n = 4 \)) or horses administered 35 ng of lipopolysaccharide/kg IV, 24 hours before starting the dextrose solution and insulin CRIs (group 3; 4). A balanced crossover study design was used in both phases. Blood samples were collected for measurement of plasma glucose and insulin concentrations.

### Results
Infusion of dextrose solution alone resulted in hyperglycemia for most of the 360-minute CRI. Insulin concentration increased significantly in group 1, compared with that in the control group. Mean insulin concentration of group 2 was significantly higher throughout most of the infusion period, compared with concentrations of the control group and group 1. Mean glucose concentration did not differ significantly between groups 2 and 3.

### Conclusions and Clinical Relevance
Insulin infusion at a rate of 0.07 U/kg/h was found to be effective for the prevention of hyperglycemia when administered concurrently with dextrose solution. This rate was considered to be safe because horses did not become hypoglycemic during infusions of dextrose solution. (Am J Vet Res 2011;72:522–529)
Similar to the situation in humans, horses in a hospital setting may require nutritional supplementation in the form of parenteral administration of nutrients (ie, parenteral nutrition) to prevent malnutrition and catabolism, which can deleteriously affect immune function and wound healing. In human medicine, malnutrition has been reported to increase the risk of morbidity in hospitalized patients, whereas parenteral nutrition has in turn been found to reduce the morbidity rate for malnourished patients. Hyperglycemia can develop when parenteral nutrition is provided to humans, and horses can similarly become insulin resistant when provided with parenteral nutrition. The administration of exogenous insulin, often via CRI, has been used under these circumstances to prevent the development of hyperglycemia. In human medicine, CRI of insulin has been reported to result in more effective glycemic control and reduced mortality rates when compared with results for intermittent SC administration of insulin. The increasing recognition of the numerous benefits of preventing hyperglycemia through the use of intensive insulin administration in human medicine suggests that there may be benefit in the use of a similar protocol in horses. However, there is a paucity of information regarding appropriate insulin dosages to prevent hyperglycemia in horses, particularly with regard to the use of a CRI. The purpose of the study reported here was to investigate and characterize the effects of a CRI of dextrose solution or dextrose solution and insulin on glucose and insulin dynamics (concentrations) in healthy and endotoxin-exposed horses. Our hypothesis was that a CRI of 0.07 U of insulin/kg/h would maintain blood glucose concentrations < 180 mg/dL in both healthy and endotoxin-exposed horses when hyperglycemia was induced by the IV administration of dextrose solution.

Materials and Methods

Horses—Nine healthy adult Thoroughbred mares that ranged from 4 to 18 years of age (mean ± SD, 11 ± 4.81 years) and weighed from 457 to 601 kg (mean ± SD, 531 ± 43 kg) were used in the study. Body condition was not directly assessed by determination of a body condition score; however, horses were subjectively assessed to have similar body condition. No clinical evidence of metabolic disease was apparent as determined on the basis of results of physical examination. During washout periods, horses were maintained in a single group on pasture. Horses had access to fresh water at all times but did not receive any grain. However, horses were individually housed in box stalls in preparation for and during each CRI and provided free-choice access to grass hay and water. The study was conducted at the Middleburg Agricultural Research and Extension Center and approved by the Virginia Tech Institutional Animal Care and Use Committee.

Study design—The study comprised 2 phases. During phase 1, effects of a CRI of dextrose solution or saline (0.9% NaCl) solution on plasma glucose and insulin concentrations were investigated. After a washout period, phase 2 involved the investigation of the effects of administration of dextrose solution and insulin CRI on plasma glucose and insulin concentrations in healthy and endotoxin-exposed horses.

Phase 1: Effects of dextrose solution or saline solution CRI on plasma glucose and insulin concentrations in healthy horses

Eight mares were selected for use in a balanced crossover study. Treatments consisted of saline solution (control treatment group; n = 4 horses) or 20% dextrose solution (group 1; 4) administered IV as a CRI by use of a volumetric delivery pump during a 360-minute period. The 20% dextrose solution was administered to horses in group 1 at a rate calculated to deliver 30 kcal/kg/d, which was equivalent to 367.6 mg/kg/h. Similarly, saline solution was administered to horses in the control group at a rate equivalent to that of group 1. After a 3- to 4-day washout period, horses were administered the other treatment. A handheld glucometer was used to monitor blood glucose concentration of each horse every 30 minutes on a real-time basis during the administration of CRIs to detect instances of severe hypoglycemia or hyperglycemia.

Phase 2: Effects of a dextrose solution and insulin CRI on plasma glucose and insulin concentrations in healthy and endotoxin-exposed horses

After the completion of phase 1, horses were maintained on pasture during a 1-week washout period. Subsequently, 8 mares were selected for use in a balanced crossover study to investigate the effects of the coadministration of dextrose solution and insulin as a CRI on glucose and insulin concentrations in healthy and endotoxin-exposed horses. Treatments consisted of 360-minute CRIs of 20% dextrose solution and insulin administered simultaneously into an IV catheter at rates calculated to deliver 30 kcal/kg/d (367.6 mg/kg/h) and 0.07 U/kg/h, respectively, in healthy horses (group 2) or horses administered a low dose of endotoxin (LPS) 24 hours prior to the start of the dextrose solution and insulin CRIs (group 3). After a 5- to 8-day washout period, horses were administered the other treatment. Real-time monitoring of blood glucose concentrations was performed as described in phase 1.

Catheterization—On the day prior to the start of each CRI or LPS administration, skin overlying each jugular vein was aseptically prepared and a catheter was inserted into each jugular vein and secured to the skin with cyanoacrylate. One catheter was used for the administration of the dextrose solution, dextrose solution and insulin, or saline solution, and the other catheter was used for collection of blood samples for a CBC and measurement of glucose, insulin, and TNF-α plasma concentrations. The LPS was administered in the catheter not used for blood sample collection.

Insulin preparation—Insulin has an affinity for binding to fluid administration lines. Therefore, an insulin solution was prepared in saline solution that had been pretreated with 3 mL of autologous serum/L for use in this study to help prevent adherence to the administration line.

LPS preparation and administration—An LPS solution was formulated by adding 1 mL of 5 µg of ly...
ophihized Escherichia coli O55:B5 LPS/mL to 999 mL of saline solution. The dose of LPS to be administered was 35 ng/kg. The calculated dose of LPS for each horse was prepared and added to saline solution to achieve a final volume of 1 L. The 1-L LPS solution was administered IV during a 30-minute CRI by use of a volumetric delivery pump 24 hours prior to the start of the dextrose and insulin CRIs administered in phase 2. Horses were housed in box stalls during LPS CRIs and provided free-choice access to grass hay and water. Assessment of clinical signs and other variables associated with LPS administration, including attitude, colic, heart and respiratory rates, rectal temperature, and trembling, was conducted once 15 minutes before and every 15 minutes for 6 hours after LPS infusion.

Sample collection and analysis—Fifteen and 5 minutes before and 1, 2, 5, 10, 15, 30, 45, 60, 90, 120, 150, 180, 240, 300, and 360 minutes after the initiation of each CRI, 10 mL of blood was collected into evacuated tubes that contained lithium heparin and used for measurement of plasma glucose and insulin concentrations; tubes were immediately placed in an ice bath after collection. Within 30 minutes after collection, cooled samples were centrifuged for 10 minutes at 3,000×g, and plasma was harvested and transferred to storage containers. Plasma samples were initially stored at –20°C for 24 hours and then at –80°C until analysis. Plasma glucose concentrations were measured via an automated analyzer. Plasma insulin concentrations were measured by use of a commercially available radioimmunoassay, which has been validated for the quantification of insulin concentration in equine plasma and serum. Ten milliliters of blood was collected immediately before each CRI of LPS (0 hours) and 3 and 24 hours after LPS infusion for a CBC and measurement of serum TNF-α concentration. Samples for CBCs were collected into evacuated tubes containing EDTA and immediately processed; counts were determined by use of an automated analyzer. Blood samples for the measurement of TNF-α concentration were collected into evacuated glass tubes that contained no additives. Samples were allowed to clot at 4°C overnight, and serum was harvested and stored at –20°C until analysis; concentrations were measured by use of a commercially available equine-specific ELISA.

Statistical analysis—Values were reported as mean ± SD. Data for plasma glucose and insulin concentrations were logarithmically (log 10) transformed to achieve normal distributions. A 2-way repeated-measures ANOVA was used to compare blood glucose and plasma insulin concentrations among all treatments (control group and groups 1, 2, and 3); post hoc analysis was performed by use of the Tukey honestly significant difference test. A 2-way repeated-measures ANOVA was used to compare temperature, heart rate, and respiratory rate over time during the LPS infusion; post hoc testing was performed by use of the Tukey honestly significant difference test. Serum TNF-α concentra-
Blood glucose monitoring via the handheld glucometer—Measurements obtained during the experimental phases by use of the handheld glucometer were only for monitoring purposes to ensure that none of the horses were developing profound hypoglycemia or hyperglycemia. The values for blood glucose concentration obtained from the automated analyzer were used for statistical analysis.

Plasma glucose concentrations—Saline solution was administered as a CRI to horses in the control group to determine the potential effects of environment, fluid infusion protocol, and sample collection protocol on the endogenous production of insulin and regulation of euglycemia. Saline solution infusion resulted in no significant changes in plasma glucose or insulin concentrations at any time point. Infusion of dextrose solution alone resulted in a significant increase in plasma glucose concentration (> 180 mg/dL) from 30 to 300 minutes during the infusion period. Although plasma glucose concentration increased significantly over time in groups 1, 2, and 3, hyperglycemia (> 180 mg/dL) was detected only in group 1. Plasma glucose concentrations in group 1 were significantly higher than those in group 2 at 45 minutes through 240 minutes (Figure 1). Plasma glucose concentrations in group 3 were not significantly different from those in group 2.

Insulin concentration—Insulin concentration increased significantly in groups 1, 2, and 3 over time, compared with insulin concentration in the control group. When compared with results for the control group, plasma insulin concentrations were significantly higher in group 1 at 10 minutes and from 45 to 360 minutes after the start of the infusion, with a peak mean ± SD concentration of 88.0 ± 25.6 mU/L measured at 300 minutes. Insulin concentrations were higher in group 2 than in group 1 at 15, 30, and 45 minutes after the start of the infusion, but were not significantly different from concentrations measured in group 3 at any time point during the infusion (Figure 2). When group 1 was compared with group 3, the insulin concentration was significantly greater in group 3 from 10 to 360 minutes after the start of the insulin infusion.

LPS infusion, CBC, and serum TNF-α concentration—The purpose of the infusion of a low dose of LPS was to induce a low-grade proinflammatory state and an associated transient state of insulin resistance. Seven mares used in phase 1 were also included in phase 2. However, the remaining mare used during phase 1 was found to be pregnant and was replaced by another mare during phase 2. Clinical signs associated with LPS infusion were fairly mild and included an increase in rectal temperature.
temperature, mild tachycardia, trembling, mild signs of colic, and the passing of soft feces; furthermore, these resolved by the end of the 6-hour monitoring period. At least one of these clinical signs was observed in each horse after the start of the LPS infusion. Rectal temperature, heart rate, and respiratory rate after LPS infusion were all significantly different over time, compared with results for these variables obtained before LPS infusion. However, when rectal temperatures before and after LPS infusion were compared, rectal temperature was found to be significantly different only from 150 to 345 minutes after the start of the LPS infusion (Table 1). Mean ± SD WBC count (×10³ WBCs/µL) was significantly decreased 3 hours after the start of the LPS infusion, compared with the WBC count (7.4 × 10³ WBCs/µL ± 1.0 × 10³ WBCs/µL) before the infusion in group 3 horses. Serum TNF-α concentrations (median, 229 pg/mL [range, 103 to 2,380 pg/mL]) were significantly increased 3 hours after the start of the LPS infusion, compared with concentrations (median, 65 pg/mL [range, 0 to 933 pg/mL]) before LPS infusion.

Discussion

In the study reported here, a 360-minute CRI of insulin (rate, 0.07 U/kg/h) when administered concurrently with infusion of 20% dextrose solution in healthy horses and endotoxin-exposed horses maintained plasma glucose concentration at < 180 mg/dL. A dextrose infusion rate (367.6 mg/kg/h) equivalent to the administration of 30 kcal/kg/d was selected for the present study. The mean daily digestible maintenance energy requirement for horses is estimated to be 30.3 kcal/kg; therefore, we chose to use this as the basis for the infusion rate used during phases 1 and 2. However, it should be recognized that the energy requirements of hospitalized horses may be reduced as a result of decreased energy consumption, for example, because of reduced physical activity. It is estimated that the daily digestible energy requirement for horses maintained in a stall is 22 to 23 kcal/kg. Alternatively, energy requirements may actually be increased in instances of critical illness and disease states (eg, sepsis). In human medicine, the relationship between severity of illness and energy expenditure is not completely understood. In a review, it was indicated that energy expenditure may be slightly higher with more severe illness; however, results were not consistent. Furthermore, head trauma, burns, and fever were excluded from that review because those conditions have been repeatedly associated with increased energy expenditure in humans. In contrast to human medicine, the relationship between illness and energy requirements in horses is not as clearly delineated.

Development of hyperglycemia has been reported as the most common complication associated with provision of parenteral nutrition in hospitalized adult horses and foals, with concurrent insulin infusion being required in some instances for control of hyperglycemia. There is a paucity of information, particularly in adult horses, in the literature regarding an appropriate initial insulin infusion rate. In foals, insulin infusion rates of 0.01 to 0.02 U/kg/h, 0.014 to 0.2 U/kg/h, and 0.07 U/kg/h have been reported. We chose an insulin infusion rate of 0.07 U/kg/h on the basis of our clinical observations that this dose appeared to be generally well tolerated in both adult horses and foals. An insulin infusion rate of 0.07 U/kg/h administered concurrently with dextrose solution (infusion rate, 367 mg/kg/h) was effective in maintaining plasma glucose concentrations at < 180 mg/dL, even after the induction of systemic inflammation by LPS infusion. When compared with infusion of dextrose solution alone (group 1), plasma insulin concentrations were significantly higher when insulin was infused concurrently with dextrose solution (group 2), most likely because of the exogenous administration of insulin. In contrast to the persistent hyperglycemia that developed in group 1, the increased plasma insulin concentrations in group 2 were associated with maintenance of blood glucose concentrations < 180 mg/dL, which lend support for the use of 0.07 U of insulin/kg/h as a valid CRI. This CRI of insulin was also considered to be safe because none of the horses administered concurrent infusions of dextrose solution and insulin became hypoglycemic. These findings provide a useful starting point for the determination of appropriate insulin infusion regimens for use in horses being administered dextrose solutions.

When LPS was administered as a CRI 24 hours prior to the infusion of dextrose solution and insulin in the horses of group 3, plasma insulin concentrations typically were higher (although not significantly different) 10 to 360 minutes after the start of infusion.

Table 1—Mean ± SD values for several variables measured before (0 hours) and 3, 6, and 24 hours after the start of a 30-minute CRI of an LPS solution in 8 horses.

<table>
<thead>
<tr>
<th>Variable</th>
<th>0*</th>
<th>3</th>
<th>6</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>16.5 ± 3.3</td>
<td>12.5 ± 1.4</td>
<td>14.5 ± 3.0</td>
<td>—</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>42.0 ± 4.8</td>
<td>42.5 ± 4.8</td>
<td>43.0 ± 4.7</td>
<td>—</td>
</tr>
<tr>
<td>Rectal temperature (°F)</td>
<td>98.3 ± 0.8</td>
<td>102.1 ± 0.8</td>
<td>100.3 ± 0.6</td>
<td>—</td>
</tr>
<tr>
<td>WBCs (×10³/µL)</td>
<td>7.4 ± 1.0</td>
<td>7.4 ± 0.5</td>
<td>7.3 ± 1.5</td>
<td>—</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>65.0 (0–933.0)</td>
<td>229.0 (103.0–2,380.0)</td>
<td>—</td>
<td>170.8 (34.5–3,240.0)</td>
</tr>
</tbody>
</table>

*An LPS solution was formulated by adding 1 mL of 5 µg of lyophilized Escherichia coli O55:B5 LPS/mL to 999 mL of saline (0.9% NaCl) solution. The administered dose of LPS was 35 ng/kg. The calculated dose of LPS for each horse was prepared and added to saline solution to achieve a final volume of 1 L, which was administered during the CRI. Rectal temperature and heart and respiratory rates were monitored once 15 minutes before and every 15 minutes for 6 hours after LPS infusion; however, results are only reported at 0, 3, and 6 hours to indicate patterns over time. Within a row, value is significantly (P < 0.05) different from the value reported at 0 hours. ÆData are reported as mean (range). — Not determined because a measurement was not obtained at this time point.
compared with concentrations in group 2 horses. In addition, mean plasma glucose concentrations of group 3 horses typically were higher (although not significantly different) 15 to 360 minutes after the start of the infusion, compared with the mean concentration of group 2 horses. Despite this pattern of higher plasma glucose concentrations in group 3 horses, the selected infusion rate of insulin was sufficient to maintain blood glucose concentrations between 140 and 180 mg/dl.

Administration of a low dose of endotoxin (LPS) has been used in horses to mimic the clinicopathologic changes observed with endotoxemia, including the development of an inflammatory response and a transient state of insulin resistance.\(^{9,20}\) This low-dose endotoxin method has been used extensively in horses and results in fairly consistent and reproducible changes in clinical, hematologic, and hemodynamic variables.\(^{21-28}\) Investigators in other studies\(^{19,21-28}\) have administered a low-dose infusion of endotoxin (20 to 35 mg/kg) in horses and have observed increases in heart rate, respiratory rate, and rectal temperature as well as mild signs of depression and colic. Hematologic changes after endotoxin administration include leukopenia with or without neutropenia as well as rebound leukocytosis and neutrophilia\(^{21-26}\); furthermore, an increase in serum interleukin-6 and TNF-\(\alpha\) concentrations has also been reported.\(^{23}\) Changes observed after endotoxin infusion in the horses in the present study, including changes in rectal temperature, WBC counts, and serum TNF-\(\alpha\) concentration, were consistent with changes reported in another study\(^{19}\) and, as expected, were transient in nature. Therefore, successful induction of a temporary state of inflammation and insulin resistance in these horses was assumed.

Reported\(^{19,20}\) changes in glucose and insulin concentrations in response to a low-dose endotoxin infusion have varied slightly between studies. Investigators in 1 study\(^{19}\) reported a reduction in insulin sensitivity at a time point 24 hours after endotoxin challenge, whereas investigators in another study\(^{20}\) reported a transient increase in insulin sensitivity followed by a decrease in insulin sensitivity at time points 6 and 24 hours after LPS administration, respectively. Despite differences reported in these studies,\(^{19,20}\) a decrease in insulin sensitivity was consistently observed 24 hours after LPS administration, and this response was anticipated in the horses of the study reported here. However, the observed changes in plasma glucose and insulin concentrations in the present study were of a lesser magnitude than expected when compared with results for the aforementioned studies.\(^{19,20}\) It is possible that administration of LPS did not result in a state of inflammation and insulin resistance of sufficient magnitude, duration, or both to result in hyperglycemia. This is a possibility that could have been further evaluated by having included additional treatment groups; for example, 2 additional treatment groups could have been included in which 1 group was administered LPS without a subsequent dextrose solution or insulin infusion and another group in which LPS was administered followed by dextrose solution infusion without concurrent insulin infusion.

In addition, it is possible that insulin resistance was not induced at all. The clinical and laboratory changes in the horses of the present study were consistent with those reported in other studies.\(^{16-28}\) Therefore, we assumed that LPS administration had successfully induced a state of insulin resistance. However, specific testing for insulin resistance, such as via a euglycemic-hyperinsulinemic clamp technique or minimal model analysis of a frequently sampled IV glucose tolerance test, was not performed.

The insulin dose used in the study reported here proved to be effective in the prevention of hyperglycemia when administered concurrently with infusion of dextrose solution. However, healthy horses were used in this study, and further research would be needed to enable investigation of the use of an insulin CRI in ill horses. It is likely that the response to insulin would be altered in a clinical setting, for example, because of derangements of glucose metabolism that are not uncommon in critically ill horses. In human medicine, hyperglycemia is a frequent condition in critically ill patients and has been associated with increased mortality rates and morbidity\(^{20,21}\); furthermore, hyperglycemia observed under these circumstances is referred to as stress hyperglycemia and is caused by insulin resistance and impaired glucose metabolism, a development that is mediated by increased amounts of catecholamines, cortisol, growth hormone, glucagon, and inflammatory cytokines. Therefore, the processes of glucose production outweigh the processes of glucose clearance, and the end result is hyperglycemia.\(^{1}\) The presence and detrimental effects of hyperglycemia have not been thoroughly explored in critically ill horses, but higher blood glucose concentrations have been reported to be associated with nonsurvival in horses with colic\(^{35}\) and with acute abdominal disease.\(^{36}\) In addition, abnormal blood glucose regulation is associated with increased mortality rates in critically ill foals, with both hypoglycemia and hyperglycemia at the time of admission being associated with a decreased likelihood of survival, similar to the decreased likelihood of survival for hospitalized humans with hyperglycemia.\(^{37}\)

Other factors could also contribute to an altered response to an insulin CRI in a clinical setting and similarly require further investigation. These include body condition, age, breed, diet, and reproductive status. For example, obesity in horses has been reported\(^{20,28}\) to be associated with development of insulin resistance. As reported by investigators in a study\(^{39}\) that found deficient clearance of glucose in response to exogenous glucose administration, age is also a factor in glucose regulation, with newborn foals potentially being slightly insulin resistant. Diseases that result in insulin resistance, specifically equine metabolic syndrome and hyperadrenocorticism, are more likely to be diagnosed as a horse increases in age.\(^{40-43}\) Furthermore, certain breeds of horses may be at a higher risk for development of these diseases. Diet is another factor that can lead to insulin resistance. Horses fed diets rich in fat and insoluble carbohydrates (eg, starches and sugars) have decreased insulin sensitivity, compared with that for horses fed diets rich in fat and insoluble carbohydrates (eg, fiber).\(^{39,42}\)

Pregnancy in mares has been associated with increased sensitivity of pancreatic beta cells to endogenous and exogenous glucose, increased insulin degra-
dation, and insulin resistance. In fact, a possible confounding factor during phase 1 of the study reported here was that one of the mares was pregnant but was not identified as such until prior to the start of phase 2. However, plasma glucose and insulin concentrations in this pregnant mare measured before and after the start of CRIs of saline solution and dextrose solution were not significantly different from those reported for the 7 other mares in the control group and group 1. The pregnant mare was replaced in phase 2 of the study because of concerns regarding the safety of the fetus related to the experimental induction of endotoxemia.

Analysis of results of the present study indicated that infusion of a concentrated (20%) dextrose solution without concurrent administration of insulin will rapidly increase blood glucose concentrations, even in healthy horses, with concentrations exceeding 180 mg/dL only 30 minutes after the start of a CRI of dextrose solution. In critically ill human patients, the prevention of hyperglycemia, rather than the infused insulin dose per se, appears to be largely responsible for reports of reductions in mortality rates and morbidity and may be equally important in critically ill horses.

The increase in endogenous insulin secretion in response to a glucose challenge in horses differs from results reported in humans. For example, when the hyperglycemic clamp technique, which assesses beta-cell sensitivity to exogenous glucose administration, was used in horses, the mean amount of glucose metabolized was lower in horses than in humans. This was attributed to lower secretion of insulin by beta cells in horses in response to hyperglycemia. When a modified frequent sampling IV glucose tolerance test was used in horses, endogenous insulin secretion initially increased and then reached a plateau 1 minute after IV glucose administration. This differs from the pattern of endogenous insulin secretion observed in both humans and sheep, in which insulin secretion reaches a peak within minutes and then begins to decrease concurrently with decreasing plasma glucose concentrations. Therefore, horses appear to differ, at least to some extent, from other species in terms of response to a glucose load and overall glucose regulation. In the present study, infusion of dextrose solution into healthy horses rapidly resulted in hyperglycemia (plasma glucose concentration, > 180 mg/dL). Concurrent administration of a CRI of insulin (rate, 0.07 U/kg/h) prevented hyperglycemia. Additional studies should be conducted to include investigation of a more strict glycemic regulation protocol because many of the benefits of insulin administration in human medicine have involved stricter regulation of blood glucose concentration than was achieved in the study reported here.

References

5. Grey NJ, Perdrizet GA. Reduction of nosocomial infections in the surgical intensive-care unit by strict glycemic control. En
22. Clark ES, Moore JN. The effects of slow infusion of a low


