Effect of Granulocyte Colony-Stimulating Factor on Sepsis-Induced Changes in Neutrophil Accumulation and Organ Glucose Uptake

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Neutropenia was seen in rats made septic by subcutaneous (sc) injection of *Escherichia coli*. The sepsis-induced increase in glucose uptake by tissues distant from the site of infection was not associated with increased myeloperoxidase (MPO) activity. Only the skin and muscle at the site of infection demonstrated an increase in both glucose uptake and MPO activity. Granulocyte colony-stimulating factor (G-CSF) attenuated the sepsis-induced decrease in circulating neutrophils. Both glucose uptake and MPO activity of skin and muscle adjacent to the infection site showed a smaller increase in G-CSF treated rats. In contrast, septic rats injected with G-CSF exhibited a greater number of leukocytes and a larger reduction in the number of bacteria in the sc lavage fluid. These results demonstrate that G-CSF is a potent immunomodulator that stimulates neutrophil function and also increases their recruitment to the site of infection, resulting in improved bacterial killing and host defense.

Neutrophils are essential for the initial stage of host defense against bacterial invasion, since they are the first phagocytic cell to migrate into a site of infection [1-3]. The number of neutrophils available for host defense depends on their production in bone marrow and hematopoietic organs. In part, this process is regulated by a class of growth factors called colony-stimulating factors (CSF). One member of this group, granulocyte (G)-CSF, stimulates proliferation and differentiation of hematopoietic progenitor cells and selectively increases the number of circulating neutrophils when administered to control subjects [4, 5]. G-CSF can also shorten the period of drug- or irradiation-induced neutropenia and amplify host resistance to infection [6, 7]. In addition, G-CSF stimulates the functional activity of mature neutrophils. The immunomodulatory actions of G-CSF include enhancing the rate of phagocytosis and superoxide anion generation and increasing chemotactic activity and antibody-dependent cell-mediated cytotoxicity of granulocytes [6, 8-11]. Elevations in serum G-CSF concentrations have been seen during infection and after administration of nonviable bacteria, bacterial products (e.g., lipopolysaccharide [LPS]), interleukin-1, and tumor necrosis factor [12-15]. Collectively these observations indicate that G-CSF is an important mediator of host defense against bacterial challenge.

Gram-negative infection is known to increase the rate of whole-body glucose utilization [16], which results primarily from the enhanced uptake of glucose by the liver, lung, skin, spleen, and intestine [17, 18]. After intravenous (iv) administration of LPS, the circulating number of neutrophils is markedly reduced, with many of these cells being sequestered in the liver and lung [19, 20]. The infiltration of activated neutrophils into these tissues may be related to the subsequent development of tissue damage and organ dysfunction and may, in part, be responsible for the increased glucose uptake observed. Meszaros et al. [20] have reported that after iv LPS, infiltrating neutrophils in the liver account for ~15% of the increase in total hepatic glucose uptake. However, for routes of bacterial challenge other than intravascular, the magnitude of neutrophil accumulation in various tissues and associated alterations in organ glucose uptake have not been determined. Moreover, it is not known whether G-CSF will promote a generalized neutrophil infiltration into all tissues or a more selective recruitment of cells into the focus of infection, nor is it known how this cytokine will modulate tissue glucose uptake. Therefore, we sought to determine whether in vivo administration of G-CSF modulates the accumulation of neutrophils and enhanced glucose uptake by individual tissues in response to a subcutaneous bacterial challenge.

Materials and Methods

Animal preparation. Male Sprague-Dawley rats (340-380 g; Charles River, Wilmington, MA) were housed in a controlled environment, exposed to a 12-h light-dark cycle, and provided with standard rodent chow and water ad libitum for at least 1 week before initiating experiments.

Animals were injected twice daily (10 A.M. and 10 P.M.) subcutaneously (sc) with human recombinant G-CSF (Amgen,
Thousand Oaks, CA) at a dose of 50 μg/kg for 2 days before the experiment. Time-matched control animals were injected sc with an equal volume (100 μL/100 g of body weight) of sterile isotonic saline. On the day before an experiment, animals were anesthetized with an intramuscular injection of ketamine and xylazine (90 and 9 mg/kg of body weight, respectively). By aseptic surgical techniques, catheters were placed in the arch of the aorta via the left carotid artery and in the right jugular vein. An additional catheter was passed down a subcutaneous tunnel located on the rat's dorsal surface, secured, and used for administration of live Escherichia coli [16]. This catheter was implanted to allow repeated injections of E. coli without anesthetizing or restraining the animal, thereby minimizing handling stress. A suspension of E. coli (E11775; American Type Culture Collection, Rockville, MD) containing ~5 × 10^10 cfu, was injected sc at noon and 5 p.m. on the day of surgery and at 6 a.m. the next day. Time-matched nonseptic animals received an equal volume (1 mL) of sterile saline. After surgery, animals were fasted to minimize gut absorption of nutrients and hepatic glycogen as contributors of substrate appearance. Multiple sc injections of live bacteria produce a hypermetabolic septic state, as evidenced by sustained elevation in body temperature and whole-body oxygen consumption [17]. In general, septic animals are hemodynamically and metabolically stable at the time experiments are done. The rats were conscious and unrestrained throughout the rest of the experiment.

Experimental protocol. Experiments were started at 6 a.m. the day after surgery, ~8 h after the final injection of G-CSF. At this time, whole-body glucose kinetics were measured using the primed, constant iv infusion of [3-3H]glucose (specific activity, 13.5 Ci/mmol; Du Pont, Boston) as previously described [16]. Blood samples for basal glucose kinetic determinations (0.3 and 1 mL) were withdrawn from the arterial catheter at 120 and 140 min after the start of the tracer infusion. Plasma glucose and lactate concentrations and glucose specific activity were determined for both samples; plasma concentrations of insulin and glucagon were determined only for the second sample. Total blood leukocyte counts were also determined for the second sample. Mean arterial blood pressure and heart rate were measured before the first blood sample by a pressure transducer (model 79E; Grass, Quincy, MA) attached to the arterial catheter.

After the second blood sample was collected, the [3H]glucose infusion was discontinued. Subsequently, in vivo glucose uptake by individual tissues was determined using [14C]-2-deoxyglucose (dGlc), a nonmetabolizable glucose analogue, as described [17, 18]. A tracer amount of 2-14C-deoxy-d-glucose (8 μCi/rat; specific activity, 328 mCi/mmoll; Amersham, Arlington Heights, IL) was injected iv, and tissues were obtained 40 min later. Serial blood samples (0.3 mL) were withdrawn, plasma was deproteinized, and radioactivity was determined (LS 7500; Beckman, Fullerton, CA). An aliquot of the supernatant for each sample was neutralized and the glucose concentration determined. Animals were anesthetized with sodium pentobarbital at the end of the 40-min in vivo labeling period, and selected tissues were excised to determine the intracellular accumulation of phosphorylated metabolites of dGlc (P-dGlc). At the end of the 2-dGlc experiment, a longitudinal incision was made through the skin on the dorsal surface of the rat overlying the injection site for the bacteria, and the subcutaneous space was lavaged with sterile isotonic saline. The number of leukocytes within the lavage fluid was subsequently determined.

In a second group of similarly treated rats, selected tissues were obtained for the determination of myeloperoxidase (MPO) activity. In this group of animals, the subcutaneous site of infection was also lavaged with saline and the number of viable bacteria recovered was determined. In a third group of similarly treated rats, epinephrine was administered to determine the size of the marinated leukocyte pool [21]. In these animals, the numbers of total leukocytes, neutrophils, and lymphocytes were determined under basal conditions in two arterial blood samples obtained 20 min apart. Thereafter, a bolus iv injection of epinephrine (5 μg/rat; Elkins-Sinn, Cherry Hill, NJ) was administered and blood samples collected at selected intervals up to 30 min.

Analytic procedures. Plasma glucose and lactate concentrations were determined enzymatically on neutralized supernatants of deproteinized plasma [22]. Plasma glucose specific activity was determined as previously described [16]. Rates of glucose appearance and disappearance were calculated using the steady-state equations of Steele [23]. The metabolic clearance rate for glucose, which measures the avidity of the tissues for glucose, was calculated by dividing the rate of glucose disappearance by the prevailing plasma glucose concentration. The in vivo rate of glucose uptake for each tissue examined was calculated on the basis of accumulation of P-dGlc by a respective tissue, the integrated dGlc-to-glucose ratio in plasma during the 40-min labeling period, and the lumped constant as described previously [17, 18]. Plasma immunoreactive insulin and glucagon concentrations were determined by radioimmunoassay using porcine standards (ICN, Irvine, CA). Tissue-associated MPO activity was determined by the method of Grisham et al. [24]. Serial dilutions of the lavage fluid were plated on tryptic soy agar for the quantitation of viable bacteria. Total white blood cells were counted in a hemocytometer (Fisher Scientific, Pittsburgh). Blood smears were stained with Wright's stain, and 100 cells were counted to determine the number of lymphocytes, neutrophils, and eosinophils.

Data were analyzed by analysis of variance followed by Newman-Keuls test to determine treatment effect. Statistical significance was set at P < .05.

Results

Alterations in leukocytes, body temperature, and hemodynamics. The twice-daily injection of G-CSF for 2 days increased the number of total leukocytes by >30,000 cells/μL of blood, which represents a 3.2-fold increase above basal nonseptic values (figure 1). Most (92%) of this increase was accounted for by the 7.0-fold increase in circulating neutrophils, although lymphocytes also tended to be elevated. In control animals, sepsis was associated with a 73% reduction in the number of circulating leukocytes, attributable to a decrease in both neutrophils and lymphocytes (26% and 79%, respectively). Pretreatment with G-CSF could not com-
G-CSF treatment and the presence of severe neutrophilia...
development of neutrophilia increased MPO activity in spleen and lung (95% and 72%). In septic animals pretreated with G-CSF, MPO activity of the liver, ileum, ventral skin, and gastrocnemius was not different from that in saline-treated septic rats. The sepsis-induced decrease in MPO activity seen in spleen and lung was slightly attenuated by G-CSF. Compared with untreated septic rats, infected animals injected with G-CSF showed a greatly attenuated increase in MPO activity in dorsal skin and skeletal muscle. This reduced MPO activity paralleled the diminished glucose uptake response of these two tissues.

Leukocyte number and bacterial counts in lavage fluid. In some animals, a longitudinal incision was made through the skin overlying the site of infection, the subcutaneous space was lavaged with saline, and the number of leukocytes or viable bacteria contained in the lavage fluid was quantitated. In the saline-injected nonseptic animals, the lavage fluid contained $0.9 \pm 1.1 \times 10^6$ leukocytes (mean ± SE). The

![Figure 3](https://academic.oup.com/jid/article-abstract/166/2/336/812789)  

**Figure 3.** Sepsis-induced changes in rate of in vivo glucose uptake of skin and muscle from saline (SAL) and G-CSF–treated rats (open bars, nonseptic rats; hatched bars, septic rats). Ventral and dorsal skin and gastrocnemius (Gastroc) and dorsal back muscles represent tissue and skeletal muscle distant from and adjacent to infection sites, respectively. Values are means ± SE; $n = 6–7$ rats/group. Means with same letter are not significantly different at $P < .05$.  

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Saline/ nonseptic</th>
<th>Saline/ septic</th>
<th>G-CSF/ nonseptic</th>
<th>G-CSF/ septic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diaphragm</td>
<td>80 ± 8</td>
<td>371 ± 4*</td>
<td>91 ± 7</td>
<td>214 ± 31*</td>
</tr>
<tr>
<td>Kidney</td>
<td>142 ± 8</td>
<td>200 ± 14*</td>
<td>131 ± 21</td>
<td>203 ± 15*</td>
</tr>
<tr>
<td>Fat</td>
<td>23 ± 6</td>
<td>45 ± 6*</td>
<td>21 ± 4</td>
<td>48 ± 4*</td>
</tr>
<tr>
<td>Ileum</td>
<td>228 ± 11</td>
<td>527 ± 41*</td>
<td>237 ± 22</td>
<td>569 ± 41*</td>
</tr>
<tr>
<td>Spleen</td>
<td>327 ± 32</td>
<td>796 ± 39*</td>
<td>351 ± 31</td>
<td>825 ± 58*</td>
</tr>
<tr>
<td>Liver</td>
<td>40 ± 4</td>
<td>141 ± 11*</td>
<td>38 ± 4</td>
<td>125 ± 3*</td>
</tr>
<tr>
<td>Lung</td>
<td>199 ± 20</td>
<td>358 ± 28*</td>
<td>184 ± 21</td>
<td>397 ± 37*</td>
</tr>
<tr>
<td>Brain</td>
<td>595 ± 80</td>
<td>623 ± 36</td>
<td>624 ± 31</td>
<td>613 ± 14</td>
</tr>
</tbody>
</table>

**NOTE.** Values are means ± SE; $n = 6–7$ animals/group. Data are nmol/min/g of tissue (wet weight).  
* $P < .05$ compared with same nonseptic group.  
† $P < .05$ compared with saline/septic group.  

G-CSF did not alter tissue glucose uptake in nonseptic rats (table 2, figure 3). Sepsis increased glucose uptake by the diaphragm (363%), kidney (41%), adipose tissue (96%), ileum (131%), spleen (143%), liver (252%), and lung (80%); it did not alter cerebral glucose uptake. G-CSF did not alter the sepsis-induced increases in glucose uptake by any tissue distant to the infection, except for diaphragm in which it attenuated the increase (table 2). G-CSF did influence the rate of glucose uptake of skin and muscle adjacent to the inflammatory locus (figure 3). Sepsis increased uptake of glucose by skin from the ventral surface of the rat by 91%. However, uptake was elevated by >200% in skin from the dorsal surface, which is adjacent to the site of infection. Sepsis did not produce a detectable change in uptake by the gastrocnemius muscle, which represents a muscle group distant from the focus of infection. In contrast, skeletal muscle obtained from the back of the animal, underlying the site of infection, demonstrated a 5.8-fold increase in glucose uptake. Unexpectedly, treatment with G-CSF reduced the increased glucose uptake of skin and muscle obtained from the focus of inflammation compared with that seen in saline-treated septic animals (21% and 72%, respectively).

**Tissue-associated myeloperoxidase (MPO) activity.** To better define the role of sequestered neutrophils in the sepsis-induced increases in glucose uptake, MPO activity was determined to assess the accumulation of neutrophils within specific tissues (figures 4 and 5). The septic insult produced an unexpected decrease in MPO activity in the spleen and lung (95% and 58%, respectively; figure 4); however, there was no detectable change in MPO activity in the liver, ileum, gastrocnemius muscle, or skin from the ventral surface (figures 4 and 5). In contrast, increased MPO activity was observed in tissues adjacent to the focus of infection: 7.0-fold in dorsal skin and 3.6-fold in the back muscles compared with that in nonseptic control animals (figure 5).

The twice-daily injection of G-CSF for 2 days and the development of neutrophilia increased MPO activity in spleen and lung (95% and 72%). In septic animals pretreated with G-CSF, MPO activity of the liver, ileum, ventral skin, and gastrocnemius was not different from that in saline-treated septic rats. The sepsis-induced decrease in MPO activity seen in spleen and lung was slightly attenuated by G-CSF. Compared with untreated septic rats, infected animals injected with G-CSF showed a greatly attenuated increase in MPO activity in dorsal skin and skeletal muscle. This reduced MPO activity paralleled the diminished glucose uptake response of these two tissues.
subcutaneous injection of live E. coli increased the lavaged leukocyte number by >25-fold to 23.5 ± 3.9 × 10^6 cells (P < .05 compared with control values). Nonseptic G-CSF–treated rats tended to have a higher number of leukocytes (1.4 ± 0.2 × 10^6 cells) than did nonseptic control animals, but this change was not statistically significant. However, in septic rats injected with G-CSF, the lavage leukocyte number was increased to 68.3 ± 7.9 × 10^6 cells, which is almost threefold greater than the increase seen in saline-injected septic animals.

Undiluted samples of the lavage fluid from nonseptic rats (either saline- or G-CSF-treated) contained no detectable bacteria. Serial dilutions of the lavage fluid obtained 12 h after the final sc injection of E. coli indicated the presence of 2.5 ± 0.8 × 10^8 cfu/mL. A significant reduction (>2 log units) was observed in the number of bacteria in the lavage fluid from G-CSF–treated septic rats (7.1 ± 3.5 × 10^5 cfu/mL; P < .05, n = 7 for all groups).

Epinephrine-stimulated leukocytosis. Administration of epinephrine produces leukocytosis, the magnitude of which provides an estimate of the marginated pool of leukocytes [21]. Therefore, studies were done to determine whether the sepsis-induced neutropenia was associated with a concurrent change in the number of epinephrine-releasable leukocytes and whether G-CSF modified this response. In all animals, maximum neutrophilia occurred 5–10 min after the injection of epinephrine, and blood neutrophil numbers returned to baseline by 20 min (data not shown). In nonseptic animals, epinephrine increased the total number of leukocytes by 4413 ± 522 cells/μL of blood (mean ± SE), which represents a 40% elevation above control levels (figure 6). Neutrophils were responsible for 55% of the leukocytosis in these animals. In contrast, septic rats (which were leukopenic and neutropenic compared with control animals) showed a much smaller elevation in leukocyte number (1125 ± 397 cells/μL; 33% above saline-injected septic animals) and no statistically significant change in blood neutrophils. As described earlier, G-CSF increased both leukocyte and neutrophil number. The injection of epinephrine increased leukocyte number by 18,350 ± 2970 cells/μL, which represents a 39% increase above control levels. About 65% of this increase was due to the elevation in circulating neutrophils. In G-CSF–treated septic rats, the number of leukocytes and neutrophils was lower than seen in nonseptic rats but elevated compared with saline-injected septic animals. These animals showed a 43% increase in leukocytes (3225 ± 389 cells/μL) above baseline values, which was primarily (80%) due to the epinephrine-stimulated neutrophilia.

**Discussion**

In the present study the twice-daily injection of G-CSF for 2 days produced a marked increase in circulating leukocytes, which resulted largely from selective elevation in number of neutrophils. These results are consistent with earlier reports on the ability of this growth factor to stimulate proliferation and differentiation of granulocyte progenitor cells [4]. Other investigators have demonstrated that the neutrophilia is primarily due to an increased number of structurally and functionally mature neutrophils [11, 25, 26]. G-CSF not only increases the circulating pool of neutrophils but also produces a proportional increase in the epinephrine-releasable pool of these cells. Previous studies have shown that epinephrine-induced neutrophilia results from a demargination of...
leukopenia that reflects a reduction in the circulating number of both neutrophils and lymphocytes. This sepsis-induced leukopenia (and neutropenia) could occur by several possible mechanisms, including a decreased rate of cell production, increased adhesion of cells to the vascular endothelium, and enhanced influx of cells into tissues. Of these possibilities, our present results indicate that the injection of bacteria produces a local inflammatory response accompanied by an influx of circulating neutrophils into the focus of infection. This is supported by the selective increase in MPO activity in both the overlying skin and underlying muscle. Because the epinephrine-releasable marginated pool of neutrophils is greatly reduced in septic animals, this suggests that these cells are not merely bound to the vascular endothelium but are sequestered within these tissues. The reduction in marginated neutrophils also has been documented under noninfectious leukopenic conditions [21] but has not previously been reported for the septic host. In addition, there is a massive influx of leukocytes into the subcutaneous space. This finding is similar to previous reports in which bacteria were injected intradermally [2], intramuscularly [28], or intratracheally [3], resulting in neutrophil immigration to these sites. In other studies, neutrophil sequestration has been seen in liver and lung after intravenous LPS administration [19, 20]. In the present study, as judged by MPO activity, no significant accumulation of neutrophils was detected in any tissue examined, including liver and lung, that was not at the site of infection. Indeed, the spleen and lung demonstrated a striking decrease in MPO activity in septic rats. The mechanism for this sepsis-induced demargination of neutrophils in these tissues is not known but could support neutrophil migration to the infection site.

Figure 5. Myeloperoxidase (MPO) activity in skin and skeletal muscle sampled from sites distal (ventral skin and gastrocnemius [gastrocj]) and proximal (dorsal skin and back muscles) to focus of infection (open bars, nonseptic rats; hatched bars, septic rats). Values are means ± SE; n = 6–7 rats/group. Means with same letter are not significantly different at P < .05.

Figure 6. Epinephrine-induced increases in blood leukocytes (entire bar) and neutrophils (hatched portion) in septic and nonseptic rats treated with G-CSF. B = basal value; E = epinephrine injected. *, P < .05 compared with basal leukocyte value from same group; †, P < .05 compared with basal neutrophil value from same group.
As a result of the large number of neutrophils leaving the circulation during the septic episode, these cells could theoretically contribute to the sepsis-induced increase in glucose uptake by individual tissues to which they migrate. A physiologically significant contribution of sequestered neutrophils to tissue glucose utilization is most likely to occur at the inflammatory locus. Indeed, our results indicate that the sepsis-induced increase in glucose uptake by the spleen, liver, lung, intestine, and ventral skin is not associated with an increase in MPO activity. However, neutrophil accumulation in skin and muscle adjacent to the infection site is accompanied by a corresponding increase in tissue glucose uptake. These results are consistent with, but do not prove, the conclusion that at least part of the increase in glucose uptake by tissues near the site of infection is dependent on neutrophil influx. It should also be emphasized that the enhanced rate of glucose uptake by all tissues represents an increased avidity of these tissues for glucose, since plasma glucose and insulin concentrations in septic animals are unchanged compared with control values.

G-CSF is a polyfunctional regulator of neutrophils and has been shown to protect animals from lethal infections produced by several types of bacteria [3, 28, 29]. However, for the most part, G-CSF has been administered to patients who already have a reduction in circulating neutrophils in an attempt to shorten the duration of the neutropenia [30]. In the present study G-CSF was administered prophylactically to animals before a septic challenge that was expected to reduce blood neutrophil numbers; we did this to modulate host defense. As described above, in control animals G-CSF increased the circulating number of neutrophils sevenfold. However, when G-CSF treatment was started before and continued throughout the septic challenge, no neutrophilia was observed. G-CSF did blunt the neutropenia seen in untreated septic animals. Furthermore, G-CSF more than doubled the margined pool of neutrophils in septic animals. Despite an increase in the circulating and margined pools of neutrophils in G-CSF-treated septic rats, none of the tissues examined showed a detectable influx of neutrophils. Importantly, administration of G-CSF did not appear to exert any adverse metabolic effects in tissues distant to the infection, since this cytokine did not alter the sepsis-induced increase in glucose uptake in these tissues.

Quite unexpectedly, samples of skin and muscle from the focus of infection in G-CSF-treated animals demonstrated a marked reduction in MPO activity compared with that in corresponding tissues from untreated septic animals. The ability of G-CSF to attenuate the accumulation of neutrophils in these tissues was associated with a corresponding reduction in their glucose uptake. Again, this suggests that some of the sepsis-induced increase in glucose uptake by tissues adjacent to the site of infection is dependent on neutrophil accumulation.

The exact reason for the reduction in infiltrating neutrophils in tissues adjacent to the infection site in G-CSF-treated septic rats is not known. We speculate that this response results from a priming of mature neutrophil functional activity by G-CSF. Numerous studies have demonstrated that G-CSF enhances neutrophil migration, phagocytosis, microbial killing, and production of superoxide anions [10, 11, 28]. The overall effect of these changes would be to rapidly enhance recruitment of neutrophils and other phagocytic cells from the blood into adjacent tissues and the subcutaneous space. According to Issekutz and Movat [2], nearly all of the neutrophil influx into tissues occurs during the first 4 h after injection of live bacteria. Therefore, in the present study, MPO activity should be elevated in the dorsal skin and muscle at this early time. As a result of this accumulation of neutrophils in G-CSF-treated rats, the number of viable bacteria present in the infected area would be expected to decrease over time. This is consistent with the finding of the present study in which the number of E. coli in the subcutaneous pocket was almost 3 log units lower in G-CSF-injected rats than in untreated septic animals. By increasing the magnitude of the neutrophil response to the site of infection, G-CSF effectively reduces the bacterial burden, limits the proliferation of these bacteria, and prevents their dissemination from the original focus. Thus, because the inflammatory stimulus diminishes over time and the infection is more effectively neutralized, the number of neutrophils within the adjacent skin and muscle would be expected to be lower in G-CSF-treated rats when tissues are sampled ~24 h after the initial injection of bacteria.

We cannot exclude the possibility that recruitment of neutrophils to the inflammatory focus may also be enhanced in G-CSF-treated rats because of the increased number of circulating neutrophils compared with numbers in saline-injected septic animals. However, because the magnitude of the increase is relatively small, this mechanism is probably less important than neutrophil activation. Similar results have been reported by Nelson et al. [3], who showed that G-CSF increased the number of neutrophils and decreased the number of viable bacteria in the bronchoalveolar lavage of rats injected intratracheally with Klebsiella pneumoniae [3].

In summary, the subcutaneous injection of bacteria increases glucose uptake by the skin and muscle surrounding the focus of infection, and this response appears to be dependent on neutrophil accumulation. However, the enhanced uptake of glucose by the liver, spleen, intestine, lung, and other tissues distant from the infection site cannot be explained by neutrophil influx. When G-CSF is administered to control animals it increases the number of circulating and margined neutrophils and, in the absence of a secondary stimulus, produces no sustained changes in hemodynamics or carbohydrate metabolism. G-CSF treatment of septic animals attenuates the neutropenia, enhances leukocyte recruit-
ment, and improves bacterial killing at the site of infection and thereby presumably improves host defense.

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References