Chemotactic peptide uptake in acute pancreatitis: correlation with tissue accumulation of leukocytes

WERNER HARTWIG, EDWARD A. CARTER, RAMON E. JIMENEZ, JENS WERNER, ALAN J. FISCHMAN, CARLOS FERNANDEZ-DEL CASTILLO, AND ANDREW L. WARSHAW

Departments of Surgery and Pediatric Gastroenterology, and Division of Nuclear Medicine, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts 02114

Hartwig, Werner, Edward A. Carter, Ramon E. Jimenez, Jens Werner, Alan J. Fischman, Carlos Fernandez-del Castillo, and Andrew L. Warshaw. Chemotactic peptide uptake in acute pancreatitis: correlation with tissue accumulation of leukocytes. J. Appl. Physiol. 87(2): 743-749, 1999.—Chemotactic peptides bind specifically to receptors on leukocyte membranes. This property makes them prospective vehicles to evaluate inflammation and infection. We used two well-established models of acute pancreatitis to quantitate the binding of the chemotactic peptide N-formyl-methionyl-leucyl-phenylalanine-lysine (fMLFK) to leukocytes and its correlation to degree of organ inflammation. Uptake of the 99mTc-labeled nicotinyl hydrazine-derivatized chemotactic peptide analog fMLFK-HYNIC was measured in blood, pancreas, lung, and muscle specimens in rats with edematous or necrotizing pancreatitis and was compared with neutrophil sequestration assessed by myeloperoxidase activity and histology. Chemotactic peptide uptake in the pancreas was increased in mild and severe pancreatitis compared with controls, with higher levels in severe than in mild disease, and correlated with tissue myeloperoxidase activity (r = 0.7395, P < 0.001). Increased pulmonary uptake only in severe pancreatitis reflected pancreatitis-induced neutrophil sequestration in the lungs. Muscle uptake was unchanged compared with controls. Edema formation did not affect chemotactic peptide uptake. The data suggest that uptake of chemotactic peptides can contribute to quantitative assessment of neutrophils in localized inflammatory processes and is independent of associated edema formation or microcirculatory compromise.

chemotactic factors; inflammation; leukocytes; N-formylmethionyl-leucyl-phenylalanine

RADIOLABELED CHEMOTACTIC peptides are promising tools for the imaging of inflammation and infection (4, 7). Chemotactic peptides are naturally released by bacteria and initiate leukocyte chemotaxis by binding to high-affinity receptors on the white blood cell membrane (21, 26). These receptors are present on polymorphonuclear neutrophils and monocytes. N-formylmethionyl-leucyl-phenylalanine-lysine (fMLFK) is one of the most potent synthetic chemoattractants, is readily synthesized and radiolabeled, and has been shown to be an effective means for the rapid localization of focal sites of inflammation or infection (2). Specific binding of fMLFK to leukocyte receptors in vivo has not been definitely proved, but decreased uptake after application of an antagonist and high target-to-background ratios in inflamed tissue suggest leukocyte targeting (3, 8).

Previous studies evaluating the in vivo behavior and biodistribution of chemotactic peptides used models of bacterially or chemically induced muscular inflammation (2, 3, 6, 8, 24). These studies, however, did not document leukocyte infiltration histologically or otherwise and thus did not provide evidence that chemotactic peptide localization correlates with leukocyte infiltration. To address this issue, two well-established models of acute pancreatitis in rats have been applied in the present study. The first model produces mild pancreatitis, which is predominantly characterized by interstitial edema and increased capillary blood flow (14, 15). Leukocyte infiltration in the pancreas is limited. In contrast, the second model produces severe pancreatitis, characterized by large areas of necrosis, less pronounced edema, extensive leukocyte infiltration, and decreased microcirculatory perfusion and ischemia in the pancreas (12, 23).

Recently, our laboratory described the local and systemic distribution patterns of leukocytes in identical models of acute pancreatitis by using in vitro radiolabeled white blood cells (25). In the present study we evaluated the biodistribution of the nicotinyl hydrazine-derivatized chemotactic peptide analog 99mTc-fMLFK-HYNIC in these two models and compared the results with data obtained by the technique established in the previous study. Because nonspecific inflammatory reactions, such as edema formation and alterations in tissue perfusion, may affect the tissue uptake of various radiopharmaceuticals, the combination of well-described specific and nonspecific inflammatory reactions in our models of mild and severe pancreatitis makes them appropriate for evaluating the in vivo behavior of chemotactic peptides.

MATERIALS AND METHODS

Animals and catheter placement. Experiments were performed in male Sprague-Dawley rats weighing 300–350 g. Care was provided in accordance with the procedures outlined in the Guide for Care and Use of Laboratory Animals [DHHS Publication No. (NIH) 85-23, revised 1985. Office of Science and Health Reports, Bethesda, MD 20892]. Animals were fasted overnight before the experiments but allowed free access to water.

Surgical anesthesia was induced with vaporized ether and maintained by an intramuscular injection of pentobarbital sodium (20 mg/kg; Anthony Products, Arcadia, CA) and ketamine (40 mg/kg; Ketalar, Parke-Davis, Morris Plains,
N.). Two polyethylene catheters (0.5 mm ID) were inserted into the left carotid artery and the right internal jugular vein, respectively, tunnelled subcutaneously to the suprascapular area, and exited through a steel tether that allowed the animals free movement.

Study design. Animals were randomly allocated to a control group or two groups of acute pancreatitis: mild edematous or severe necrotizing disease. Mild pancreatitis was induced by intravenous infusion of cerulein (5 µg·kg⁻¹·h⁻¹; Takus, Farmitalia, Carlo Erba, Freiburg, Germany) for 6 h (15). Cerulein was reconstituted in normal saline and infused at 3 ml·kg⁻¹·h⁻¹. Necrotizing pancreatitis was induced as follows and as described in detail elsewhere (23). The biliopancreatic duct was cannulated with a 24-gauge Teflon catheter (Critikon, Tampa, FL), and bile and pancreatic juice were drained by gravity for 5 min with the common hepatic duct clamped at the porta hepatitis. Glycylglycine-NaOH-buffered solution (pH 8.0, room temperature) was infused retrogradely into the biliopancreatic duct at a concentration of 10 mmol/l in a volume (1.2 ml/kg)-, time (10 min)-, and pressure (30 mmHg)-controlled fashion, followed by the intravenous infusion of cerulein over 6 h. Control animals received saline infusions alone.

Animals (n = 6/group) were killed at 6 h, when infusions were completed (Fig. 1A). One additional group of animals with necrotizing pancreatitis (n = 5) received saline after completion of cerulein infusions and was euthanized at 12 h (Fig. 1B). Ninety-nine mTc-labeled fMLFK (~25 µCi) was injected intravenously into the rats 3 h before they were killed to simulate clinical conditions for imaging human diseases. Blood was collected at the time the animals were killed for measurement of trypsinogen activation peptide (TAP) and radioactivity. Tissue samples of the pancreatic head, the right middle lobe of the lung, and the inferior part of the right trapezius muscle were excised, rinsed with saline, blotted dry, and weighed before measurement of radioactivity. Leukocyte sequestration in the pancreas and lungs was quantitated by assay of myeloperoxidase activity and tissue edema by determination of wet-to-dry weight ratio. Gamma camera imaging and histopathology of the pancreas were performed in additional animals. Because the pancreas of rodents is a thin organ that cannot be visualized in whole body scintigraphy because of its proximity to the relatively large liver, we excised the pancreas en bloc for imaging. Duodenum and spleen serve as anatomic landmarks and represent organs with relatively low and high chemotactic peptide uptake, respectively.

Ninety-nine mTc-labeled chemotactic peptide. N-formyl-methionyl-leucyl-phenylalanine (fMLF) was purchased from Sigma Chemical. Ninety-nine mTcO₄⁻ (99Mo/99Tc generator) and stannous glucohepatonate (Glucosan) were obtained from DuPont (Bilerica, MA). Hank’s balanced salt solution was purchased from Gibco (Grand Island, NY). Dimethylformamide (DMF), trifluoroacetic acid (TFA), ether, petroleum ether, ethyl acetate, and p-cresol were obtained from Fisher Scientific (St. Louis, MO). Instant thin-layer silica gel chromatographic strips were obtained from Gelman Laboratories (Ann Arbor, MI).

Peptide synthesis. fMLFK was synthesized and purified by standard solid-phase techniques (16), as previously described (18). The nicotinyl hydrazine-derivatized chemotactic peptide analog 99mTc-HYNIC was prepared as described below.

DMF (2 ml) and 60 µl of disopropylethylamine were added to 186 mg of fMLF-diaminohexyl amide and then 154 mg of succinimidyl-6-t-Boc-hydrazinopyridine-3-carboxylic acid in 1 ml of DMF were added. The peptide dissolved within a short time. After 2 h, ether-petroleum ether was added to the reaction mixture, and the upper layer was discarded. Water was added to the oily residue, causing a solid to form. The solid was washed with 5% sodium bicarbonate, water, and ethyl acetate, and the yield of crude product was 183 mg. The t-Boc-protecting group was removed by stirring the product with 5 ml of TFA containing 0.1 ml of p-cresol for 15 min at 20°C. The TFA was removed by rotary evaporation, and the ether was added to the residue to precipitate the deprotected peptide. The product was purified by reverse-phase HPLC on a 2.5 × 50 cm Whatman ODS-3 column eluted with a gradient of water-acetonitrile in 0.1% TFA. Chemical purity was evaluated by TLC, HPLC, ultraviolet spectroscopy, mass spectroscopy, and amino acid analysis.

Radio-labeling with 99Tc. A 99Tc generator was eluted ~5 h after a previous elution to yield ~500 mCi of 99TcO₄⁻. A typical elution contained ~3 nmoles of 99Tc; the 99Tc-to-99mTc ratio was ~1.5:1, and specific activity was >100,000 mCi/mmol. Ninety-nine mTc-glucopheratonate (99Tc-Gluco) was used to provide the Tc(V) oxo species for radio-labeling the HYNIC-conjugated peptide (1, 7). Ninety-nine mTc-Gluco was prepared by adding ~300 mCi of 99TcO₄⁻ in saline (~2.5 ml) to freeze-dried kits. The radiochemical purity of the product was >95% by instant thin-layer silica gel chromatography with acetonitrile and saline as mobile phase solvents.

The HYNIC-derivatized chemotactic peptide (200 µg) was dissolved in 200 µl of DMSO and diluted to 20 µg/ml with acetate buffer, pH 5.2. The peptide solution (0.5 ml) was placed in a clean glass vial, 99mTc-Gluco (0.5 ml, ~75 mCi) was added, and the mixture was vortexed and allowed to stand at room temperature for 1 h. Peptide labeling was monitored by instant thin-layer silica gel chromatography with three solvent systems: acetone, saline, and acetone-water (9:1). Radiolabeled peptide was purified by reverse-phase HPLC on a C₁₈ column (5 µm, 4.5 × 46 mm) eluted with a binary gradient (solvent A: 0.1% TFA in water; solvent B, 0.1% TFA in acetonitrile; gradient, 0%-100% solvent B over 20 min).

Radioactivity in tissue and blood was measured using a well-type gamma counter (LKB model 1282, Wallac). The data are presented as the percentage of injected dose per gram of tissue or as tissue-to-blood ratios of 99Tc radioactivity. Gamma camera images of the pancreas were acquired using a large-field-of-view gamma camera equipped with a parallel-hole medium-energy collimator.

Myeloperoxidase activity. Excised pancreatic and pulmonary tissues were rinsed with saline, blotted dry, snap frozen in liquid nitrogen, and stored at −80°C until they were...
Absolute uptake of $^{99m}$Tc in the pancreas (percent injected dose/g) increased in proportion to the severity of pancreatitis (Fig. 2A). Uptake was increased in edematous ($P = 0.04$) and necrotizing ($P < 0.001$) pancreatitis compared with controls, with significantly higher levels in necrotizing than in edematous pancreatitis ($P = 0.001$). To assess whether the pancreatic uptake was affected by intravascularly retained $^{99m}$Tc-fMLFK-HYNIC, pancreas-to-blood ratios of $^{99m}$Tc activity were calculated. Pancreas-to-blood ratios were significantly increased in severe pancreatitis ($P < 0.001$ vs. control, $P = 0.002$ vs. cerulein) but showed only a trend in mild pancreatitis (Table 1). Pancreas-to-blood ratios were similar in animals with severe pancreatitis killed at 6 and 12 h (Table 1).

**RESULTS**

Table 1. Tissue-to-blood ratios of $^{99m}$Tc-fMLFK-HYNIC activity in controls and edematous (cerulein) and necrotizing (GDOC) pancreatitis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Cerulein</th>
<th>GDOC 6 h</th>
<th>GDOC 12 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>0.37 ± 0.09</td>
<td>0.56 ± 0.06</td>
<td>1.10 ± 0.10‡</td>
<td>1.16 ± 0.20*</td>
</tr>
<tr>
<td>Lungs</td>
<td>6.67 ± 1.03</td>
<td>5.49 ± 1.04</td>
<td>8.40 ± 1.17</td>
<td>6.54 ± 0.63</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.18 ± 0.02</td>
<td>0.17 ± 0.03</td>
<td>0.16 ± 0.01</td>
<td>0.13 ± 0.02</td>
</tr>
</tbody>
</table>

Values are means ± SE. GDOC, glycodeloxycholic acid; fMLFK-HYNIC, nicotinyl hydrazine-derivatized analog of N-formyl-methionyl-leucyl-phenylalanine-lysine. Data were calculated by dividing percent injected dose per gram in excised tissue by corresponding value in blood. Pancreas-to-blood ratios were increased in necrotizing pancreatitis, but no significant differences were found in lung-to-blood or muscle-to-blood ratios. *$P = 0.03$, †$P < 0.001$ vs. control; ‡$P = 0.002$, GDOC vs. cerulein.

Histopathological evaluation. For histological evaluation the pancreas was fixed in 10% phosphate-buffered Formalin and embedded in paraffin. One coronal section was made in the plane of the flattened pancreas and stained with hematoxylin-eosin.

Myeloperoxidase activity in the pancreas demonstrated increased leukocyte sequestration with worsening of pancreatitis (Fig. 2B). Although there was a moderate increase in cerulein pancreatitis ($P < 0.001$ vs. control), a major increase of leukocyte sequestration was found in necrotizing pancreatitis ($P < 0.001$ vs. control, $P = 0.03$ vs. cerulein). Myeloperoxidase activity in the pancreas specifically reflects the conversion of tryptosnogin to trypsin by cleavage of the TAP fragment (11). Blood samples (0.5 ml) for the measurement of TAP were collected in 0.2 mol/l EDTA to inactivate peptidases. After centrifugation of the samples (500 g, 10 min, 4°C) the remaining serum was coded and stored at −20°C until assayed.

TAP concentrations were measured in a blinded fashion by an ELISA (5). Synthetic TAP (YD4K), a conjugate of rabbit serum albumin with YD4K, and rabbit anti-TAP antiserum containing calcium-independent anti-TAP antibodies were provided by Professor J. Hermon-Taylor (St. George's Hospital Medical School, London, UK). Biotin-conjugated goat anti-rabbit IgG antibody and alkaline phosphatase-labeled streptavidin were purchased from Sigma Chemical. This assay has a very close correlation to the previously reported RIA described by Hurley et al. (11). TAP concentrations in blood are expressed as nanomoles per liter.

Statistical analysis. Values are means ± SE. ANOVA was used to show an overall difference between groups, Student's t-test to make pairwise comparisons of normal distributed parameters, and regression analysis to evaluate the correlation between $^{99m}$Tc radioactivity and myeloperoxidase activity in pancreatic tissue. $P < 0.05$ was considered to be statistically significant.

**RESULTS**

Table 1. Tissue-to-blood ratios of $^{99m}$Tc-fMLFK-HYNIC activity in controls and edematous (cerulein) and necrotizing (GDOC) pancreatitis
in the pancreas of animals with severe pancreatitis that were killed at 12 h showed no significant difference from levels in animals killed at 6 h (18.7 ± 1.4 and 15.9 ± 1.6, respectively).

Pancreatitis-associated inflammatory response in the lungs, as reflected by pulmonary myeloperoxidase activity, was present in severe pancreatitis (P < 0.001 vs. control, P = 0.03 vs. cerulein) and to a lesser degree in mild pancreatitis (P = 0.02 vs. control; Fig. 3A). Absolute uptake of 99mTc-labeled chemotactic peptide in the lungs showed similar patterns, with increased levels in animals with severe pancreatitis (P = 0.04 vs. control, P = 0.03 vs. cerulein; Fig. 3B). Lung-to-blood ratios of 99mTc activity were only slightly higher in severe pancreatitis than in mild pancreatitis or controls (Table 1).

No significant differences were found in chemotactic peptide uptake in muscle or muscle-to-blood ratio between the two groups of pancreatitis and controls (Table 1), indicating that the uptake of chemotactic peptide in pancreas and lungs is organ specific and not due to nonspecific processes. Slightly higher levels of uptake of 99mTc in blood were found in animals with mild and severe pancreatitis than in controls (controls: 0.36 ± 0.07% injected dose/ml; cerulein: 0.41 ± 0.04% injected dose/ml; glycodeoxycholic acid: 0.50 ± 0.05% injected dose/ml; differences not statistically significant).

Figure 4 assesses the correlation between tissue uptake of chemotactic peptide and leukocyte sequestration and demonstrates a highly significant positive correlation (r = 0.7395, P < 0.001) between 99mTc-labeled FMLFK uptake and myeloperoxidase activity in pancreatic tissue. Solid line, curve of best fit; dashed lines, 95% confidence limits.

---

**Fig. 3.** Myeloperoxidase activity (A) and chemotactic peptide uptake (B) in lung. Similar to myeloperoxidase activity in pancreatic tissue, myeloperoxidase activity in lung tissue was increased in mild (cerulein) and severe (GDOC) pancreatitis (*P = 0.02; †P < 0.001 vs. control). Levels were higher in severe than in mild disease (‡P = 0.03). Uptake of chemotactic peptide in lung showed increased levels only in severe pancreatitis (*P = 0.04 vs. control; †P = 0.03 vs. cerulein).

**Fig. 4.** Correlation between chemotactic peptide uptake and myeloperoxidase activity: regression analysis between uptake of chemotactic peptide and leukocyte sequestration as assessed by myeloperoxidase activity in pancreatic tissue. Solid line, curve of best fit; dashed lines, 95% confidence limits.

---

The concentration of TAP in plasma, reflecting trypsinogen activation to active trypsin, was increased in all animals with acute pancreatitis compared with...
controls (Table 2). TAP concentrations were higher in necrotizing than in edematous pancreatitis \((P < 0.001)\), confirming the severity of pancreatitis.

**DISCUSSION**

Radiolabeled chemotactic peptides have been proposed as localizing agents for inflammation and infection (8, 24), but there is only indirect evidence that they are retained in inflamed tissue by high-affinity binding to fMLF receptors on the membranes of leukocytes (polymorphonuclear neutrophils and mononuclear phagocytes). Previous studies have shown that the chemotactic peptide \(^{99m}\text{Tc-fMLFK-HYNIC}\) localizes with high target-to-background ratios in bacterially or chemically induced muscle inflammation (3, 6, 24). Coinjection of a cold peptide (moderate antagonist) (3) or injection of a control peptide with low receptor-binding affinity (24) resulted in significantly lower target-to-background ratios, suggesting that the retention of the high-affinity peptide fMLFK is due to receptor-specific binding at the inflammatory site. However, receptor specificity and leukocyte binding have not been completely established, and significant amounts of peptide accumulation may be due to nonspecific interactions or leakage into the inflammatory site coincident with edema formation.

In the present study we have used two well-established experimental models of acute pancreatitis to evaluate the characteristics of \(^{99m}\text{Tc-labeled chemotactic peptide fMLFK}\) in localizing inflammatory sites. The first model is one of mild edematous pancreatitis, characterized by hyperemia, pronounced edema, hyperamylasemia, and moderate trypsinogen activation (14, 15, 19), findings confirmed in this study. In contrast,
the second model results in necrotizing pancreatitis with markedly impaired pancreatic microcirculatory perfusion, significantly less tissue edema, more tryptase, and concomitant development of lung injury, reflecting a systemic inflammatory response (10, 12, 22). Pancreatic leukocyte infiltration occurs in both models, but to a much greater degree in severe than in mild pancreatitis. Pulmonary leukocyte sequestration reminiscent of acute respiratory distress syndrome-related lung injury (9) is also greater in necrotizing than in edematous pancreatitis (10). A recent study from our laboratory confirmed this leukocyte distribution pattern by using in vitro radiolabeled white blood cells (25).

The present study demonstrates that pancreatic uptake of the chemotactic peptide \(^{99m}\text{Tc}}\)-fMLFK-HYNIC quantitatively correlates with leukocyte infiltration in acute pancreatitis. Leukocyte infiltration was quantified by measurement of myeloperoxidase activity, an enzyme stored in the azurophilic granules of polymorphonuclear leukocytes (13), and confirmed by histology. With leukocyte infiltration being more pronounced in severe than in mild pancreatitis, our data provide strong evidence that chemotactic peptides can be used to differentiate between different severities of this disease. This is also the first study showing that chemotactic peptides localize at an acute intra-abdominal inflammatory site. However, and more importantly, significantly increased pancreas-to-blood ratios in severe pancreatitis indicate high target-to-background ratios necessary for using chemotactic peptides in external imaging.

Other microcirculatory phenomena that may influence the trafficking of chemotactic peptides to leukocytes, such as alterations in endothelial permeability or capillary perfusion, may affect the uptake or concentration of chemotactic peptides at sites of inflammation. In our models, pancreatic edema formation was more prominent in edematous than in severe pancreatitis (25). Nonetheless, there was greater uptake of chemotactic peptide in the pancreas in severe than in mild pancreatitis, correlating with the greater myeloperoxidase activity. The finding confirms that leukocyte accumulation is more important than plasma leakage in chemotactic peptide localization (24). Although the study does not directly address whether alterations of tissue perfusion at the inflammatory site may affect chemotactic peptide uptake, the two models of pancreatitis used in this study have been well characterized previously using intravital microscopy and diffuse reflectance spectroscopy (12, 14). In mild edematous pancreatitis, pancreatic blood flow is temporarily increased, whereas capillary perfusion is markedly reduced and even shut down in severe pancreatitis. Inasmuch as these perfusion abnormalities are discordant with the relative uptake of chemotactic peptide observed in these experiments, we infer that they cannot account for the findings. The combined weight of evidence and each of its elements are consistent with a specific quantitating link between chemotactic peptide concentration and leukocyte sequestration.

The results obtained by using chemotactic peptides to localize pancreatic inflammation are similar to those of a previous study using in vitro radiolabeled white blood cells (25). Such labeled white blood cells accumulate in an inflammatory locus only after replacement in the circulation and subsequent migration to the extravascular destination. As a consequence, radiolabeled white blood cells required injection before induction of pancreatitis in the previous study. Because chemotactic peptides are very small molecules that can diffuse rapidly through tissues, they will bind to circulating leukocytes and to extravascular cells that have already localized at a site of inflammation (2, 7). In the present study, chemotactic peptides were injected well after the induction of the disease and still localized successfully in the pancreas and the lungs. Myeloperoxidase levels had reached a plateau by 6 h after induction of severe pancreatitis and remained stable for the next 6 h, suggesting that leukocyte migration was at its maximum in this time frame; chemotactic peptide levels mirrored the finding.

Unlike in vitro radiolabeled white blood cells, chemotactic peptides can be readily synthesized and radiolabeled, and the technique does not involve the potential hazards associated with handling of blood and reinjection of labeled cells. Additionally, special care must be taken to avoid damage and activation of the cells in the processing of in vitro radiolabeled leukocytes. Cell damage and activation induced by in vitro procedures lead to initial entrapment of labeled cells in the lungs after their injection, with their subsequent delayed release into the systemic circulation (20).

Chemotactic peptides have been investigated principally for imaging local inflammatory processes but not associated remote organ injury. The systemic inflammatory response to severe local inflammation may produce other sites of leukocyte accumulation, as illustrated in the lungs in our model of necrotizing pancreatitis. Chemotactic peptide uptake and myeloperoxidase activity in the lungs were significantly increased in severe pancreatitis. Uptake of chemotactic peptide in the lungs was not caused by the development of vascular leakage, inasmuch as no significant pulmonary edema formation was detected in any group at 6 h. The absence of increased chemotactic peptide uptake into muscle in animals with severe acute pancreatitis indicates that the pulmonary uptake is organ specific and not due to generalized systemic leukocyte sequestration.

This study thus demonstrates that the uptake of \(^{99m}\text{Tc}}\)-labeled chemotactic peptide fMLFK correlates quantitatively with leukocyte sequestration at specific inflammatory sites and is unaffected by nonspecific microcirculatory events. Their localization in acute experimental pancreatitis and associated lung injury suggests that chemotactic peptides have potential use in demonstrating and perhaps assessing the degree of injury in intra-abdominal inflammatory processes and distant organs. Future studies are needed to validate the application of chemotactic peptides for external imaging.
imaging in human pancreatitis and other intra-abdominal inflammatory processes.

We thank Shawn Hillier for help in peptide labeling and gamma camera imaging.

This study was supported by Deutsche Akademie der Naturforscher Leopoldina Grant BMBF-LPD 9801-14. Preliminary results were presented at the 1998 Meeting of the Pancreas Club (Tokyo, Japan) and the 1998 Meeting of the Pancreas Club (New Orleans, LA). Address for reprint requests and other correspondence: A. L. Warshaw, WHT 506, Massachusetts General Hospital, Boston, MA 02114 (E-mail: awarshaw@partners.org).

Received 24 November 1998; accepted in final form 21 April 1999.

REFERENCES


