Modulatory Activity of Chemotherapeutic Agents on Phagocytosis and Intracellular Bactericidal Activity of Human Polymorphonuclear and Mononuclear Phagocytes

Waldemar Pruzanski, Susan Saito, and Gerrit DeBoer

Immunology Diagnostic and Research Centre, Department of Medicine, The Wellesley Hospital [W. P., S. S.], and Department of Biostatistics, The Princess Margaret Hospital [G. D.], University of Toronto, Toronto, Ontario, Canada M4Y 1J3

ABSTRACT

Thirteen chemotherapeutic agents were tested for modulatory activity on phagocytosis by human granulocytes and monocytes. Phagocytosis, phagocytic index, and intracellular bactericidal activity were assessed using Staphylococcus aureus, smooth strain of Escherichia coli, and latex particles. Modulation of phagocytic activity depended on the type of particle used and the presence of serum in the medium. Testing granulocytes, only 1,3-bis(2-chloroethyl)-1-nitrosourea suppressed phagocytosis of all three types of particles used for ingestion. Other drugs suppressed either phagocytosis of E. coli and S. aureus or of one of the bacteria and latex particles. Three drugs enhanced ingestion of latex particles. The most pronounced modulation of phagocytosis was observed in conditions similar to those in vivo, namely, when serum was added to the medium and when the cells were exposed for longer time to the drugs. In the absence of serum, very little modulation of phagocytosis was observed, and only 1,3-bis(2-chloroethyl)-1-nitrosourea retained strong suppressive activity. Intracellular bactericidal activity was markedly suppressed by 7 of 13 drugs tested. Monocytes were less influenced by chemotherapeutic agents, their phagocytic activity being either suppressed or enhanced. The influence of chemotherapeutic agents on phagocytosis must be taken into consideration when assessing defense mechanisms and susceptibility to infection in patients with malignant diseases.

INTRODUCTION

Infection is one of the most common and serious complications in leukemia and some other malignant diseases. In the search for the mechanisms leading to increased susceptibility to infection, impairment of phagocytic activity (8, 12, 23) and abnormalities of humoral factors in patients' sera have been reported (20, 21). In many instances, the above studies were conducted while the patients were being treated with various chemotherapeutic agents. It has been reported that corticosteroids and vinblastine suppress chemotactic activity of PMN3 (24, 34). Vinblastine has also been shown to inhibit intracellular killing of staphylococci by phagocytes (14). Other reports describing the influence of various chemotherapeutic agents on limited aspects of phagocytosis have been published (2, 4, 5, 10, 11, 15-17, 26, 31, 32, 35), but no comprehensive study of the influence of chemotherapeutic agents on phagocytosis and intracellular bactericidal activity of human phagocytes has appeared in the literature.

In our previous report, bacteriolytic and bactericidal activities of normal human sera mixed with various chemotherapeutic agents and of sera of leukemic patients who received i.v. chemotherapeutic agents were tested (20, 21). Several drugs modulated in vitro antibacterial activity (22). This study describes the influence of various chemotherapeutic agents on normal human polymorphonuclear and mononuclear phagocytes. It may contribute to our understanding of the mechanisms leading to increased susceptibility to infection and should be considered when investigating phagocytosis in malignant diseases.

MATERIALS AND METHODS

Venous blood was drawn from healthy volunteers. The serum was separated and used either immediately or after a short storage at −70°.

Purification of PMN

PMN were separated as described previously (19, 29). Heparinized venous blood was diluted with 2 volumes of 0.15 M NaCl, layered over a mixture of 10 parts of 33.9% Hypaque (Winthrop Laboratories, Division of Sterling Drugs, Inc., New York, N. Y.) and 24 parts of 9% Ficoll (Pharmacia, Uppsala, Sweden), and centrifuged at 400 × g for 40 min at 4°. The mononuclear cell layer was removed, and 10% by volume of 3% dextran was added to the remaining blood: Hypaque:Ficoll. The PMN were allowed to settle for 45 to 60 min. The RBC were lysed with 0.84% ammonium chloride. The PMN-rich layer was removed and centrifuged for 10 min at 200 × g, and the resulting pellet was washed twice in HBSS (Grand Island Biological Co., Grand Island, N. Y.). Wright's, myeloperoxidase (13), and nonspecific esterase (36) stains were used for evaluation of contaminating cells. The purity of PMN suspensions was 92%, and the viability was 98 to 100%.

Purification of Monocytes

Monocytes were purified as described previously (18). Forty to 60 ml of venous blood were taken in heparinized tubes. The blood was placed in 50-ml plastic tubes and centrifuged at 650 × g for 10 min. The supernatant plasma was removed and left for later use. A cell suspension was prepared by diluting and mixing the infranatant buffy coat and RBC layer with 2 volumes of phosphate-buffered saline, pH 7.2. Ten-ml aliquots of a mixture of 10 parts of 33.9% Hypaque with 24 parts of 9% Ficoll were placed in 50-ml centrifuge tubes, and the cell suspension was layered on top (25 ml/tube) and centrifuged at 400 × g for 20 min. The mononuclear cell layer was carefully removed. The cells were washed twice with 0.1 M phosphate-buffered saline and centrifuged at 200 × g for 15 min. The supernatant was aspirated, and the sedimented cells were combined, washed, centrifuged again, and...
Chemotherapeutic Agents and Phagocytosis

Phagocytic Assays

PMN. These were mixed with microorganisms or with latex particles in the ratio of 10 to 20 particles to 1 PMN. Chemotherapeutic agents were mixed with the PMN 1 hr before start of phagocytosis. The incubation was conducted in a shaker water bath at 37° for 60 min. After spinning, phagocytosis, i.e., the number of cells that ingested microorganisms or latex particles as a percentage of the total number of PMN, was estimated by counting 200 cells. Phagocytic index, i.e., the average number of particles per phagocytizing cell, was also estimated. The viability of the PMN was tested by the trypan blue exclusion test at the end of incubation and by lactate dehydrogenase estimation in the supernatant. Each experiment was performed with and without addition of normal AB human serum. Normal values for phagocytosis were: S. aureus without serum, phagocytosis 58 ± 4.4% (S.D.), phagocytic index 3.4 ± 0.95; S. aureus with serum, phagocytosis 97 ± 1.3%, phagocytic index 15.8 ± 1.3; E. coli without serum, phagocytosis 54 ± 6.5%, phagocytic index 4.0 ± 1.2; E. coli with serum, phagocytosis 90 ± 9.0%, phagocytic index 13.5 ± 3.9; latex particles without serum, phagocytosis 58 ± 7.0%, phagocytic index 3.4 ± 0.4; latex particles with serum, phagocytosis 88 ± 3.0%, phagocytic index 10.6 ± 1.8.

Intracellular Survival of Microorganisms

Survival was estimated by the lysostaphin method using viable S. aureus (30). Polymorphonuclear phagocytes were incubated with S. aureus for 1 hr, and then lysostaphin (20 units/ml) was added, and the mixture was incubated for 20 min. The reaction was stopped by addition of 2.5% trypsin solution. The mixture was appropriately diluted

Table 1

<table>
<thead>
<tr>
<th>Chemotherapeutic agent</th>
<th>Therapeutic dose (mg)</th>
<th>Total dose (mg)</th>
<th>Concentration used (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCNU (carmustine; Ben Venue Laboratories, Bedford, Ohio)</td>
<td>250 mg/sq m</td>
<td>432.5</td>
<td>20.0</td>
</tr>
<tr>
<td>Cephalosporin (cefazolin; Poulenc, Montreal, Quebec, Canada)</td>
<td>60 mg/sq m</td>
<td>103.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Adriamycin (doxorubicin HCl; Farmitalia, Milan, Italy)</td>
<td>0.5 mg/kg</td>
<td>30–40</td>
<td>1.0</td>
</tr>
<tr>
<td>Cytosor (cytarabine; The Upjohn Co., Kalamazoo, Mich.)</td>
<td>40 mg/sq m</td>
<td>70.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Biloxane (bleomycin sulfate; Bristol Laboratories, Canada)</td>
<td>10 units/sq m</td>
<td>15 units</td>
<td>0.003 unit/ml</td>
</tr>
<tr>
<td>E. coli (S-FU; Hoffman-La Roche Inc., Nutley, N.J.)</td>
<td>15 mg/kg</td>
<td>1050</td>
<td>50.0</td>
</tr>
<tr>
<td>Oncovin (vincristine sulfate; Eli Lilly, Indianapolis, Ind.)</td>
<td>2 mg/dose</td>
<td>2</td>
<td>0.1</td>
</tr>
<tr>
<td>Velbe (vinblastine sulfate; Eli Lilly)</td>
<td>10 mg/day</td>
<td>10</td>
<td>0.5</td>
</tr>
<tr>
<td>Leukeran (chlorambucil; Burroughs Wellcome, Tuckahoe, N.Y.)</td>
<td>14 mg/day</td>
<td>14</td>
<td>0.7</td>
</tr>
<tr>
<td>Mustine (melphalan HCl, U.S.P.; Boots, Nottingham, England)</td>
<td>30 mg/day</td>
<td>30</td>
<td>1.5</td>
</tr>
<tr>
<td>Methotrexate (amethopterin; Lederle, Pearl River, N.Y.)</td>
<td>1 g/dose</td>
<td>1000</td>
<td>50.0</td>
</tr>
<tr>
<td>Myleran (busulfan; Burroughs Wellcome)</td>
<td>6 mg/day</td>
<td>6</td>
<td>0.3</td>
</tr>
<tr>
<td>Prednisone (U.S.P. Organon, Canada)</td>
<td>40 mg/day</td>
<td>40</td>
<td>2.0</td>
</tr>
</tbody>
</table>

a Therapeutic dose calculated per 70 kg body weight and 1.73 sq m body surface.
b Calculated "maximal momentary concentration of the drug in the extracellular fluid" (see "Materials and Methods").

smooth strain of Escherichia coli, and latex particles (diameter, 1.101 µ; Dow Diagnostic, Ind.) were used for phagocytic assays.
(10^{-3}, 10^{-4}, or 10^{-5}), and culture plates were poured. The proportion of surviving intracellular bacteria with addition of drugs to the control intracellular bacterial counts was estimated and related to phagocytosis. At the end of incubation, an aliquot was taken from each tube, and the total number of bacteria was counted in 100 cells. (Since lyso-

staphin was used, there were no extracellular bacteria.) The number of colonies obtained from each sample was divided by the number of ingested bacteria in the sample and was expressed as percentage. Then, the values obtained from samples with drugs were divided by the values obtained from appropriate controls and again expressed as a percentage. This was called the intracellular bactericidal activity index. An index higher than 100 signified more residual bacteria, i.e., impaired bactericidal activity, whereas an index lower than 100 signified enhanced bactericidal activity.

Each experiment with phagocytosis was performed twice using PMN or monocytes from 2 healthy individuals, and each assay was done in duplicate. The results of all experiments were assessed by the method described below. Little variation was detected within control samples run on the same day. However, larger variations were observed between samples run on different dates. To test the significance of differences between samples run on the same day, the within-group variance using all controls was calculated. When k samples of n readings for a total of nk observations were assessed, the difference of each reading was taken from its respective mean.

\[ d_i = x_i - \bar{x} \]

These differences were used to calculate the within-group variance, \( S_w^2 \).

\[ S_w^2 = \frac{1}{(n-1)k} \sum d_i^2 \]

Then the standard error of difference between means of 2 samples run on the same day was estimated.

\[ S_{om} = \sqrt{\frac{S_w^2}{n_1} + \frac{1}{n_2}} \]

where \( n_1 \) and \( n_2 \) were the sample sizes. The Student t ratio then was calculated as

\[ t = \frac{\bar{x}_1 - \bar{x}_2}{S_{om}} \]

RESULTS

Before the experiments with phagocytosis were conducted, the influence of drugs on microorganisms and on PMN was investigated. It was found that after incubation for 1 hr BCNU and mustine killed up to 20% of the S. aureus and up to 60% of E. coli. Other drugs did not significantly influence microorganisms. Some, but not significant (10% or less), kill of PMN was observed when BCNU, mustine, Cerubidine, Myleran, or chlorambucil was added to the medium for 1 hr. Kill of bacteria and/or of PMN was taken into account and corrected by an appropriate increase in the number of microorganisms and/or PMN when phagocytic assays were performed. The drugs had no influence on survival of monocytes, which after incubation were 90 to 99% viable (mean, 95%).

Granulocytes. Nine drugs reduced significantly the phagocytic index of S. aureus (Table 2; Chart 1). Only 2 of these 9 drugs, vinblastine and Cytosar, suppressed significantly phagocytosis as well. BCNU suppressed phagocytosis but not phagocytic index. The results as shown include only statistically significant values. In several instances, phagocytosis was suppressed, but the suppression did not reach statistical significance.

Ten drugs suppressed phagocytosis of E. coli (Chart 2). All of them with the exception of bleomycin also suppressed phagocytic index.

Phagocytosis of latex particles is shown in Chart 3. Seven drugs suppressed phagocytosis, and 2 from this group also suppressed the phagocytic index. Two drugs, mustine and Cerubidine, enhanced phagocytosis; and vincristine enhanced phagocytic index of latex particles.

Investigation of intracellular bactericidal activity against S. aureus has shown that 7 drugs significantly enhanced the intracellular bactericidal activity index, i.e., impaired bactericidal activity of granulocytes (Chart 4). All these drugs also suppressed phagocytic index and/or phagocytosis of staphy-

| Table 2 |
| Influence of chemotherapeutic agents on phagocytosis and intracellular bactericidal activity |
| Granulocytes | Monocytes |
| | E. coli (smooth) | S. aureus | Latex | E. coli (smooth) | S. aureus | Latex |
| **Drugs** | **PH** | **PI** | **ICBA index** | **PH** | **PI** | **PH** | **PI** | **PH** | **PI** | **PH** | **PI** |
| 5-Fluorouracil | - | - | - | - | - | - | - | - | - | - | - |
| Methotrexate | - | - | - | - | - | - | - | - | - | - | - |
| Mustine | - | - | - | - | - | - | - | - | - | - | - |
| BCNU | - | - | - | - | - | - | - | - | - | - | - |
| Adriamycin | - | - | - | - | - | - | - | - | - | - | - |
| Bleomycin | - | - | - | - | - | - | - | - | - | - | - |
| Chlorambucil | - | - | - | - | - | - | - | - | - | - | - |
| Vinblastine | - | - | - | - | - | - | - | - | - | - | - |
| Vincristine | - | - | - | - | - | - | - | - | - | - | - |
| Myleran | - | - | - | - | - | - | - | - | - | - | - |
| Cerubidine | - | - | - | - | - | - | - | - | - | - | - |
| Cytosar | - | - | - | - | - | - | - | - | - | - | - |
| Prednisone | - | - | - | - | - | - | - | - | - | - | - |
| **Note:** PH, phagocytosis; PI, phagocytic index; ICBA, intracellular bactericidal activity; - , no significant influence; ↓, suppression of phagocytosis, phagocytic index, or ICBA index (i.e., increased kill of bacteria) \((p < 0.01)\); ↑, enhancement of phagocytosis, phagocytic index, or ICBA index (i.e., suppressed kill of bacteria) \((p < 0.01)\).
Chemotherapeutic Agents and Phagocytosis

Chart 1. Influence of chemotherapeutic agents on phagocytic index of PMN ingesting S. aureus in the presence of serum. ⊗, suppression significant at $p < 0.005$; Δ, suppression significant at $p = 0.01$ to 0.005. MX, methotrexate; MU, mustine; FU, 5-fluorouracil; VC, vincristine; CE, Cerubidine; CY, Cytosar; VB, vinblastine; CB, chlorambucil; PR, prednisone; MY, Myleran; AD, Adriamycin; BC, BCNU; BL, bleomycin.

Chart 2. Influence of chemotherapeutic agents on phagocytosis of E. coli by PMN in the presence of serum. ⊗, suppression significant at $p < 0.005$. Abbreviations as in Chart 1.

Chart 3. Influence of chemotherapeutic agents on phagocytosis of latex particles by PMN in the presence of serum. ⊗, suppression significant at $p < 0.005$; Δ, enhancement significant at $p = 0.01$ to 0.005. Abbreviations as in Chart 1.

lococci. BCNU had the most potent suppressing activity reducing phagocytosis of all 3 types of particles and inhibiting intracellular bactericidal activity.

Monocytes. Phagocytosis of S. aureus by monocytes was suppressed by methotrexate and vincristine (Table 2). Ingestion of latex particles was either not influenced or enhanced.

Bleomycin, vinblastine, and Cerubidine enhanced the phagocytic index of latex particles.

When phagocytic assays were performed without addition of human serum or when the incubation time was reduced, the majority of drugs did not influence phagocytosis at all. Without human serum, phagocytosis of S. aureus was suppressed by BCNU and prednisone and enhanced by 5-fluorouracil and Cerubidine. Phagocytosis of E. coli was suppressed by BCNU and was not influenced by other drugs.

DISCUSSION

Phagocytosis of microorganisms by polymorphonuclear and mononuclear phagocytes is a complex process. Thus, investigation of phagocytic activity usually has concerned one or only a few of its aspects, and only rarely has more than one type of particle been used. The results of in vitro experiments varied depending on the experimental conditions, especially on the period of incubation, proportion of particles to phagocytes, and presence of serum in the medium (1, 9). It does not come as a surprise, therefore, that the results obtained in various laboratories have often been confusing and contradictory.

The influence of vinblastine on phagocytosis was observed by Malawista (14), who found that engulfment of S. aureus by human granulocytes was normal, whereas intracellular kill was reduced. To the contrary, others reported that the phagocytic index of human granulocytes for Candida was reduced by vinblastine or other drugs such as vincristine, methotrexate, mustine, cyclophosphamide, busulfan, daunorubicin, or Cytosar, but not by procarbazine (5, 35). Statistically, some of these results were certainly insignificant since reduction was often less than 1 S.D. from the normal mean and very rarely less than 2 S.D.s (5). Peritoneal PMN in rats showed reduced phagocytic index against S. aureus, but no suppression of intracellular kill when the animals were pretreated with cyclophosphamide (26). Addition of cyclophosphamide to human monocytes did not influence phagocytosis or intracellular kill of S. aureus, but there was reduction of chemotaxis. Reduction
of phagocytosis and of chemotaxis but not of intracellular kill was observed with methotrexate and vinblastine. The purity of monocytes in this study was only 20 to 40% (16). Dual, dose-dependent action of drugs was noted, phagocytosis being suppressed by high concentrations and enhanced by low concentrations of vinblastine and 6-mercaptopurine (16).

Variable results were obtained when the influence of steroids on phagocytic activity was studied. Normal phagocytosis and intracellular kill of Gram-positive bacteria and reduced intracellular kill of some Gram-negative bacteria were observed when peritoneal macrophages were tested in mice treated with steroids (31, 32). Reduced engulfment of E. coli and weak opsonization were noted when rat peritoneal PMN were studied (2). Steroids made PMN insensitive to opsonins, since addition of serum to the medium did not improve completely the uptake of E. coli (2). Stabilization of lysosomes was observed when guinea pig or rabbit PMN were tested for enzyme release (10, 11). Human PMN showed impairment of nitroblue tetrazolium reduction but normal engulfment of latex particles (4, 15). Normal intracellular kill of microorganisms (31) and normal phagocytic index using killed yeast particles (17) were reported. Human monocytes exposed to dexamethasone showed normal phagocytosis and intracellular kill of S. aureus (16). The effect of steroids on phagocytosis is thought to be biphasic, low concentrations stimulating and high concentrations suppressing it (28, 34). Reduction of bactericidal capacity without impairment of phagocytosis has also been observed (27).

We have tried to reduce the experimental error to a minimum by using the same reagents, particles, and phagocytizing cells in all experiments and by choosing optimal proportion of particles to cells and incubation time. At the same time, we have attempted to cover several aspects of phagocytosis, testing granulocytes and monocytes, using 3 kinds of ingestible particles, and assessing 3 aspects of phagocytic activity simultaneously. The concentration of the drugs that we used may not always be identical to that used by other investigators; however, the variation could not be too great. The choice of the final concentration in vitro is often arbitrary, since there is no sufficient information about blood levels of therapeutic agents in humans (22). Schabel et al. (25) elected to use in vitro experiments a concentration that would be obtained if a maximal given dose was distributed momentarily and equally in the total free body fluid, including the intracellular unbound fluid. We chose higher concentrations because the maximal blood concentration of a drug is apparently achieved before the drug mixes with the intracellular fluid. Rigorous statistical assessment was used, and no "slight" differences were taken into consideration. In assays with granulocytes, motulatory activity was much more obvious when the conditions were similar to those encountered in vivo, namely, when fresh human serum was added to the medium and when the cells were exposed to drugs for longer periods of time. The importance of serum in the phagocytic system depends on the availability of opsonins and binding to the specific receptor sites on the surface of the phagocytic cells (3). The membrane of phagocytizing cell undergoes marked organizational change during phagocytosis. Perhaps certain drugs which exert their influence on the membrane by affecting the microtubuli such as vinblastine (3), or by affecting other structures, act better when serum is added because of serum-induced membranous changes. On the other hand, other factors such as tonicity of the medium and availability of divalent cations may play a role.

The majority of drugs markedly suppressed phagocytosis of Staphylococcus and/or of E. coli, but only BCNU inhibited phagocytic activity against all 3 particles used. Three drugs enhanced phagocytosis of latex particles. BCNU remained the most potent inhibitor of phagocytosis regardless of the conditions of the assays. Perhaps the most marked influence of the chemotherapeutic agents was observed in testing intracellular bactericidal activity. Seven drugs markedly inhibited intracellular kill of microorganisms, BCNU and Cerubidine being the most potent inhibitors. The influence of chemotherapeutic agents on monocytes was more complex. Whereas 2 drugs suppressed their phagocytic activity, 5 others enhanced phagocytosis of Staphylococcus or of latex particles.

Whereas the mechanisms of suppressive activity of various drugs have been analyzed (4, 10, 11, 15), enhancing activity is difficult to explain. Dose-dependent modulation of phagocytosis was noted when vinblastine and 6-mercaptopurine (16) or steroids (28, 33) were used. In our study, only one concentration of drugs was used; therefore, we could not estimate whether any change in phagocytosis would occur if different concentrations were used. However, the dose-dependent dual action of drugs may have relevance to the fact that some of the drugs that we were testing inhibited phagocytosis of one particle and enhanced it when another particle was used. It is possible that the concentration of a drug necessary to suppress (or to enhance) phagocytosis varies depending on the type of ingestible particle. Regardless of the mechanisms of modulatory activity, our results show that chemotherapeutic agents may exert a profound influence on various aspects of phagocytic activity. This should be taken into consideration while investigating phagocytosis and resistance to infections in patients treated with these drugs.

REFERENCES

4. Chretien, J. H., and Garagusi, V. F. Corticosteroid effect on phagocytosis and bacterial kill of some Gram-negative bacteria were observed. Perhaps certain drugs which exert their influence on the membrane by affecting the microtubuli such as vinblastine (3), or by affecting other structures, act better when serum is added because of serum-induced membranous changes. On the other hand, other factors such as tonicity of the medium and availability of divalent cations may play a role.

The majority of drugs markedly suppressed phagocytosis of Staphylococcus and/or of E. coli, but only BCNU inhibited phagocytic activity against all 3 particles used. Three drugs enhanced phagocytosis of latex particles. BCNU remained the most potent inhibitor of phagocytosis regardless of the conditions of the assays. Perhaps the most marked influence of the chemotherapeutic agents was observed in testing intracellular bactericidal activity. Seven drugs markedly inhibited intracellular kill of microorganisms, BCNU and Cerubidine being the most potent inhibitors. The influence of chemotherapeutic agents on monocytes was more complex. Whereas 2 drugs suppressed their phagocytic activity, 5 others enhanced phagocytosis of Staphylococcus or of latex particles.

Whereas the mechanisms of suppressive activity of various drugs have been analyzed (4, 10, 11, 15), enhancing activity is difficult to explain. Dose-dependent modulation of phagocytosis was noted when vinblastine and 6-mercaptopurine (16) or steroids (28, 33) were used. In our study, only one concentration of drugs was used; therefore, we could not estimate whether any change in phagocytosis would occur if different concentrations were used. However, the dose-dependent dual action of drugs may have relevance to the fact that some of the drugs that we were testing inhibited phagocytosis of one particle and enhanced it when another particle was used. It is possible that the concentration of a drug necessary to suppress (or to enhance) phagocytosis varies depending on the type of ingestible particle. Regardless of the mechanisms of modulatory activity, our results show that chemotherapeutic agents may exert a profound influence on various aspects of phagocytic activity. This should be taken into consideration while investigating phagocytosis and resistance to infections in patients treated with these drugs.

REFERENCES

Chemotherapeutic Agents and Phagocytosis


Modulatory Activity of Chemotherapeutic Agents on Phagocytosis and Intracellular Bactericidal Activity of Human Polymorphonuclear and Mononuclear Phagocytes

Waldemar Pruzanski, Susan Saito and Gerrit DeBoer


Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/43/3/1420

Sign up to receive free email-alerts related to this article or journal.

To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.