Studies in Experimental Eosinophilia. I. Repeated Quantitation of Peritoneal Eosinophilia in Guinea Pigs by a Method of Peritoneal Lavage

By Mortimer Litt

The eosinophil is so intimately related to hypersensitivity that its presence in tissues in increased numbers strongly suggests that an allergic reaction has occurred. In spite of considerable research concerning the eosinophil, several fundamental aspects of its life history remain unknown: (a) the stimuli which direct the bone marrow to increase the production of eosinophils and to release them into the blood stream, (b) the stimuli which direct eosinophils to leave the blood stream and to infiltrate tissues, (c) the reactions of the cells at tissue sites where they accumulate, and (d) the fate of the cell after its reaction in tissue.

Eosinophilia is readily induced in laboratory animals by repeated injection of foreign protein. Though previous studies have focussed predominantly on eosinophilia of the blood stream, the major stimulus to the accumulation of eosinophils probably arises at extravascular sites, in which these cells usually reach higher levels and persist longer than in blood. Weinberg and Séguin found that the peritoneal cavity was a suitable site for investigating the tissue eosinophil response; and more recently Speirs and Speirs and Dreisbach have extended this approach with the use of modified hematologic technics to determine the concentration of eosinophils in peritoneal fluid of mice.

Guinea pigs seem to be particularly suitable for studies in eosinophilia, since their hypersensitive reactions resemble some human counterparts more closely than do those of other laboratory animals. The present paper describes a method of peritoneal lavage in guinea pigs whereby the total number of peritoneal eosinophils may be determined repeatedly in the same animal. This method has been used to explore the phenomenon of extravascular eosinophilia, and the findings are given in this and subsequent papers.

Materials and Methods

Guinea pigs.—English short-haired guinea pigs, weighing 150 to 180 Gm. at the start of the experiments, were caged in groups of six and given a diet of Rockland rabbit pellets, water and twice weekly cabbage. No differences in experimental results were noted between the sexes.

Materials.—Normal horse serum was obtained from the Commonwealth of Massachusetts.

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Department of Public Health Antitoxin and Vaccine Laboratory, Boston, Mass. Hemocyanin was obtained from Limulus polyphemus blood by three times repeated precipitation at the isoelectric point (pH 6.4). The precipitate obtained the third time was dissolved in 0.85 per cent NaCl and stored at 4° C. under a layer of toluene. Normal human serum albumin was obtained in 25 per cent solution (Armour) and diluted to 5 per cent with 0.85 per cent NaCl. Asbestos was prepared by shredding ½ inch Seitz filter discs (Becton Dickinson and Company, Rutherford, N.J.) and suspending (0.1 per cent) in 0.85 per cent NaCl. Diphenhydramine hydrochloride (Benadryl, Parke-Davis and Company) was obtained as a 10 mg./ml. solution. A modified Tyrode's solution containing (Gn./l.): NaCl, 8.0; KCl, 0.2; NaH₂PO₄.H₂O, 0.058; NaHCO₃, 0.3; and ethylene diamine tetraacetic acid, 1.27, was prepared and sterilized by autoclaving.

Injections.—Injections were made into the ventral abdomen through 21 gage needles. Unless otherwise stated, guinea pigs prepared with horse serum were injected with 1.5 ml. of undiluted serum; those prepared with hemocyanin were injected with 1 ml. of 1 per cent solution.

Collection of exudates.—The guinea pig was immobilized on its back. A special needle with stylet was introduced at an acute angle into the peritoneal cavity at the ventral midline, and 15 ml. of modified Tyrode's solution was injected. The abdomen was massaged for about 15 seconds, and then, while the animal-board was supported so that the abdominal wall of the guinea pig was dependent, the stylet was removed and the effluent fluid was received in an ice-cold, siliconed, 15 ml. graduated centrifuge tube. Omentum occasionally plugged the needle. Flow resumed if the withdrawn needle were freed of omentum, or if it was inserted at another site. Massage of the abdomen contributed to larger yields. Of the 15 ml. of fluid injected, 10 to 15 ml. were recovered generally, 12 to 14 ml. in most cases. Needle wounds healed rapidly; no fluid leaked from them when the peritoneal cavity was lavaged again within 24 hours.

This procedure could be repeated without apparent ill effects. One group of animals was lavaged 25 times in the course of 35 days; another, 61 times in the course of 16 months. Of 3434 paracenteses, 50 (1.5 per cent) resulted in perforation of bowel.

Counting of cells.—Hemocytometer counts were made on samples of peritoneal exudate, using phloxine-acetone-Alconox diluent. With propylene glycol diluent the counts were essentially the same. All figures given are based on the average of two values, which rarely differed by more than 5 per cent. The total number of eosinophils in a lavage was calculated by multiplying the concentration (determined by hemocytometer count) by the volume of the fluid removed.

Determination of the total number of eosinophils in the peritoneal cavity.—In order to remove all contained cells, it was necessary to wash out the peritoneal cavity more than once. A single lavage removed only about two-thirds of the cells. Three additional lavages removed 26, 12 and 8 per cent, respectively, as much as the first lavage; further washing removed still fewer cells. Lavaging was continued routinely until either (a) the total number of eosinophils removed in a wash was less than 10 per cent of the number present in the first wash (the maximum error involved in the usual counting technic); or, (b) the number of eosinophils removed was five million or less (an amount which may be found in a normal animal).

Identifying cells in exudates and bone marrow.—Preparations were Wright-stained. One hundred leukocytes were identified in cover slip smears of exudate; the values given...

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*14 gage, 1 ½ inches long. The distal one inch of the needle was perforated by 12 holes, 0.35 inches in diameter.

*Omentum was seen wrapped around the needle when the needle was withdrawn. Autopsy of animals which had experienced multiple paracenteses usually revealed omentum adherent to the abdominal wall at sites where injections had occurred.

†These figures are based on 633 determinations of the total peritoneal eosinophil count.
RESULTS

Peritoneal Eosinophilia

Occurrence following injections of foreign protein.—Eosinophils were found in the peritoneal cavity of 108 of 116 normal guinea pigs examined. The average number was \(2.7 \pm 1.0\) million; only five animals had more than five million, the highest number being eight million. A single intraperitoneal injection of either horse serum or hemocyanin in normal guinea pigs produced no detectable effect on the number of peritoneal eosinophils either 24 hours or two weeks later; nor did a second injection of hemocyanin given nine days after the first result in eosinophilia. If, however, the injection was repeated at weekly intervals, peritoneal eosinophilia resulted. The number of eosinophils found one to two days after a particular injection increased over the course of several months (table 1).* On discontinuing the injections, the number of peritoneal eosinophils fell to normal levels within a week and remained so for as long as followed. With one group of animals, when the injections were resumed after a six month rest, a high degree of peritoneal eosinophilia (60 to 80 million) resulted after only three injections given at weekly intervals (see also figure 1). This is in marked contrast to the lesser and much slower rise seen during the first course of injections.

All the normal blood cell types were seen in peritoneal exudates.† The highest percentage of eosinophils was found on the first day following a reinjection of protein; thus, during the first three days, the percentage was 34, 17 and 6, respectively.† Neutrophils were seen in the smears in large numbers on the day following lavage (whether with modified Tyrode's solution or 0.85 per cent NaCl), irrespective of how much time (between 1 and 150 days) had elapsed since the last injection of protein solution (table 2 gives the results when daily lavage was commenced on the first day following injection; when lavage was commenced, for example, on the fifth day, the number of neutrophils increased on the sixth day, and so forth). The injection of foreign protein did not provoke neutrophilia. Since the act of lavage altered the composition of the leukocyte population, this method precluded the collection of neutrophil-free exudates on successive days. Mononuclears (monocytes, lymphocytes and macrophages) usually constituted the major proportion of the cells seen at any time. Phagocytes containing eosinophils or neutrophils constituted 1.5 per cent of the cells in the exudates. Eighty-one per cent of the smears contained between zero and two per cent of this type of cell. Phagocytized eosinophils were seen

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*The third injection of hemocyanin (14 days after the first) resulted in 27/48 anaphylactic deaths. Injection of the antihistaminic, Diphenhydramine hydrochloride (10 mg./Kg.), ½ hour before the third injection, resulted in a much reduced incidence (5/120) of anaphylactic deaths. Intraperitoneal horse serum injections gave less anaphylaxis, but antihistamine was routinely administered with the third injection. In some guinea pigs, antihistamine was given with every hemocyanin injection; the eosinophil response was essentially the same, over the course of five months, as in guinea pigs that had received no antihistamine.

†The results in this section are based on identification of 260,000 leukocytes in 816 smears.

‡These figures are based on determinations in 85 guinea pigs.
ONE WEEK

UANTI1A'llON 01" PERITONEAL

EOSINOPH1LIA

Fig. 1.—Effect of resumption of treatment with horse serum on magnitude of peritoneal eosinophil response in a guinea pig prepared by weekly injections of horse serum for eight months and subsequently rested without injections for one month.

The number of eosinophils shown represents those found 24 hours following each injection. The size of the injected dose apparently had little effect on the magnitude of the cellular response.

in various degrees of intactness. They occurred in similar numbers during each of the first three days of the reaction. Basophils were seen rarely; they constituted 0.003 per cent of the total leukocytes examined. Mitotic figures and cells containing Kurlf bodies were seen rarely, constituting 0.004 per cent and 0.007 per cent, respectively, of the total leukocytes in the smears. Erythrocytes, when present, ranged from one per white cell to one per 100 white cells. They seemed to appear as a consequence of skin trauma.

Specificity of eosinophil response.—The eosinophil response occurred after reinjection of the protein used to prepare the animals but not in response to

Table 1.—Peritoneal Eosinophilia after Repeated Weekly Injections

<table>
<thead>
<tr>
<th>Protein injected</th>
<th>No. of determinations</th>
<th>Duration of injections in months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horse serum</td>
<td>15</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12</td>
</tr>
<tr>
<td>Hemocyanin</td>
<td>12</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12</td>
</tr>
<tr>
<td>Human serum albumin</td>
<td>10</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12</td>
</tr>
</tbody>
</table>

The figures represent the average number of eosinophils in millions in the peritoneal cavity 24 hours following the last injection.

*Except months 1–4, in which the data are based on 36, 69, 73 and 58 determinations, respectively.

†Except months 3 and 4, in which the data are based on 50 and 41 determinations, respectively.
Table 2.—Types of Leucocytes in Peritoneal Exudates

<table>
<thead>
<tr>
<th>Days after last injection</th>
<th>Total cells</th>
<th>Eosinophils</th>
<th>Mononuclears</th>
<th>Neutrophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>131</td>
<td>49</td>
<td>80</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>95</td>
<td>16</td>
<td>59</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>95</td>
<td>6</td>
<td>65</td>
<td>24</td>
</tr>
</tbody>
</table>

The figures give the average number of cells in millions found in 75 guinea pigs prepared by 5 to 6 months of weekly horse serum injections.

Table 3.—Specificity of Eosinophil Response to Foreign Protein

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Response* to test doses of</th>
<th>No. of determinations</th>
<th>heterologous protein</th>
<th>homologous protein</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>range</td>
<td>mean</td>
</tr>
<tr>
<td>Horse serum</td>
<td></td>
<td>17</td>
<td>0–8</td>
<td>3</td>
</tr>
<tr>
<td>Hemocyanin</td>
<td></td>
<td>14</td>
<td>0–8</td>
<td>3</td>
</tr>
</tbody>
</table>

*Total number of peritoneal eosinophils in millions 24 hours after the injection of protein. The response to heterologous protein was tested 24 hours before the homologous.

another protein (table 3). However, the cellular response was not restricted to eosinophils; mononuclears were actually the predominant cells usually found and must be considered as part of the response to reinjection of foreign protein, since they did not appear in response to the first injection.

Time course of the eosinophil response following reinjection of foreign protein.—When daily lavage was carried out following a reinjection of horse serum, the greatest number of peritoneal eosinophils was found one day after injection; two and three days after injection, the number was 31 and 14 per cent, respectively, of the number found on the first day.* Figure 2 gives the results in detail for one group of guinea pigs. New cells continued to enter on the second and third days. In most instances, by the third day, the number of eosinophils was little more than may be found in a normal animal. Replacement of the fluid after each lavage did not alter the pattern of response (fig. 3). If the peritoneal cavity was not lavaged daily, the number of eosinophils did not return to resting levels until the seventh to the twelfth day. When the response on the first day was relatively large, the number of eosinophils tended to persist at a fairly high level several days longer than in the more average responders.

Individuality of the eosinophil response.—The magnitude of the eosinophil response varied considerably among the members of a group (and hence the calculated standard deviation from the group mean was very large). But a particular guinea pig tended to maintain its relative standing from day to day (fig. 2) and from week to week (table 4), and hence the trend of the group average reflects fairly well the behavior of individual guinea pigs. Differences among animals often persisted for the entire period during which studies were made, in one group for as long as 16 months. Of 310 guinea pigs studied, three consistently showed negligible responses, not exceeding 0, 9 and 5 mil-
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Fig. 2.—Number of eosinophils obtained by daily peritoneal lavage following intraperitoneal injection of horse serum in guinea pigs prepared by similar injections during a period of nine months.

Of the 15 ml. injected into guinea pig 5 on day 1, only 5.5 ml. were recovered. (From the other guinea pigs, at least 10 ml. were recovered in each of two or more lavages.) It seems likely that the cells which were not washed out of guinea pig 5 on the first day persisted and were tallied on the second.

Fig. 3.—Effect of replacing lavage fluid on the number and types of peritoneal leukocytes in guinea pigs prepared by weekly horse serum injections for three months.

The number of peritoneal eosinophils was determined on six successive days (days 2–7) following the last preparatory injection. On day 3, each guinea pig was given an injection of horse serum immediately after lavage. In two of the four guinea pigs, the fluid removed from the peritoneal cavity was returned to it, after the cells were removed by centrifugation.
Table 4.—Consistency of the Relative Eosinophil Response in Individual Guinea Pigs

<table>
<thead>
<tr>
<th>Guinea pig</th>
<th>Type of response</th>
<th>Number of weekly injections of horse serum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>8-2</td>
<td>Average</td>
<td>6</td>
</tr>
<tr>
<td>8-3</td>
<td>High</td>
<td>21</td>
</tr>
<tr>
<td>8-5</td>
<td>Low</td>
<td>4</td>
</tr>
</tbody>
</table>

The figures give the total number of eosinophils in millions in the peritoneal cavity 24 hours following each injection.

Over a period of 16 months, guinea pig 8-3 remained the highest responder of a group of 10 guinea pigs, while 8-5 never yielded more than 5 million eosinophils at any time.

The repeated injection of horse serum resulted in an increased percentage of eosinophils in the femoral marrow of guinea pigs (fig. 4'), regardless of the

Table 5.—Effect of Dose of Horse Serum on the Peritoneal Eosinophil Response

<table>
<thead>
<tr>
<th>In guinea pigs prepared by 1.5 ml. horse serum injections weekly for 4 months</th>
<th>9 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of guinea pigs</td>
<td>6</td>
</tr>
<tr>
<td>Dose of horse serum (ml.)</td>
<td>0.03</td>
</tr>
<tr>
<td>Average number of peritoneal eosinophils in millions</td>
<td>8</td>
</tr>
</tbody>
</table>

*The two doses were given one week apart to the same animals.

**Twenty-four hours after the test dose; the test dose was administered seven days after the last preparatory injection.
QUANTITATION OF PERITONEAL EOSINOPHILIA

Fig. 4.—Bone marrow eosinophilia at various times following an injection of horse serum, one week after the last preparatory injection.

The values given for peritoneal eosinophils were obtained 24 hours after this last injection. A different guinea pig was the source of the marrow for each determination. The data plotted for normal guinea pig bone marrow represents the average of values obtained in 12 guinea pigs; the standard deviation of the mean was ± 0.7 million.

interval since the last injection. There was no consistent change in numbers among the different types of eosinophils, nor were there any consistent changes in the relative numbers of other cell types in the bone marrow. Furthermore, the degree of bone marrow eosinophilia did not correlate with individual variations in peritoneal response.

Blood Eosinophilia

Isolated determinations on various days following a reinjection of horse serum failed to reveal any parallel between the degree of eosinophilia in the blood stream and that in the peritoneal cavity. However, with repeated sampling of the blood of 12 individual guinea pigs (hourly for 12 hours and daily thereafter), the following general pattern emerged after injection: there was an increase in the concentration of eosinophils in the blood starting at two to four hours, reaching peak values (500 ± 210/cu.mm.) at four to nine hours, and returning to lower values by 12 hours. Less frequent sampling would have missed some of the peak values and, in some instances, even the rise. There was, in 10/12 cases, a second and often greater rise (to concentrations as high as 2450/cu.mm.) between the first and fifth days, and a return to resting values by the sixth day. Thus at a time when the number of eosinophils in the peritoneal cavity is increasing, the concentration of eosinophils in
the blood may be anywhere from normal (34 ± 27/cu.mm.; 18 determinations) to substantially increased.

**DISCUSSION**

In tissues such as lung, only crude estimates of the degree of eosinophilia can be arrived at by counting the number of cells per microscopic field. The quantitation of eosinophilia in exudates is easier, but it is important to determine the total number of cells involved because values expressed as per cent are affected by changes in numbers of other cells, and values expressed as concentration are affected by changes in fluid volume. It also seems important to use the same animal to compare various stimuli, since individual variation is so great. In the method described here, virtually all the cells may be removed from a particular extravascular area and counted precisely.

The method of peritoneal lavage described in this paper offers major advantages for the study of extravascular eosinophilia. Since the procedure can be repeated indefinitely, long-term follow-up of individual animals is possible. One can also determine the number of eosinophils entering the peritoneal cavity on successive days.* Thus, it was established for the first time (fig. 2) that new eosinophils continue to enter the peritoneal cavity during at least the first few days following reinjection of foreign protein; in some instances, the influx continues for longer than a week. The method of peritoneal lavage is particularly suited for study of the eosinophilotactic potency of various materials. The blood stream is a less satisfactory site for such studies since its concentration of eosinophils fluctuates and the time of assay may affect the results, while various stresses, including surgery, depress blood eosinophilia. In the peritoneal cavity, cells continue to accumulate during the first few days' response to a suitable stimulus, making the time of assay not so critical; moreover peritoneal eosinophilia occurs in spite of the stress of surgery. The present paper describes the magnitude and timing of the response which one may expect following a protein reinjection and furnishes the essential background for studies of eosinophilotaxis to be reported in subsequent papers of this series. Finally, the method of peritoneal lavage enables one to obtain regularly relatively large numbers of eosinophils. Most guinea pigs yield, after four months of weekly injections of horse serum or hemocyanin, about 40 to 50 million eosinophils on the first day following reinjection. With strong responders, as many as 400 million eosinophils have been obtained at one time. Such exudates, in which the eosinophils usually comprise about 30 to 40 per cent of the population, might after fractionation serve as a suitable material for the chemical study of eosinophils.

A consideration of the quantitative aspects of peritoneal eosinophilia must take into account the large variation in responsiveness among different guinea pigs (see also reference 13). The differences are actually so large that

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*The technic of determining the concentration of cells in samples of exudate removed on various days is unsatisfactory for this purpose, since almost all the cells remain in the cavity after sampling.
isons of different experimental conditions are best made only in the same animal; the method described in the present paper makes this feasible. A lesser variation was noted during similar studies in mice.

The bone marrow, probably the major source of eosinophils, showed an increased concentration of these cells in guinea pigs which had received repeated injections of horse serum (fig. 4). This observation agrees with the findings of Biggart, Hajos and Homma. Samter gave evidence of a slight to marked increase in the average concentration of eosinophils in the bone marrow of anaphylactically shocked guinea pigs, but felt that the variation in the distribution of cells in the bone marrow of individual animals was too marked to permit any conclusion regarding differences between normal and shocked guinea pigs. While the irregular arrangement of cells in bone marrow makes interpretation difficult, our study showed a definite difference in the two marrows: the percentage of eosinophils in the bone marrow of 11/13 sensitized and challenged guinea pigs was more than twice that of normal bone marrow. No consistent short-term alterations were noted during the time when eosinophils were accumulating in the peritoneal cavity (when samples were obtained from different animals). However, for information about cell turnover, additional technics are needed, such as the use of radioactive tracers, total marrow counts and a method for obtaining repeated marrow samples from the same animal.

Cells arising in the bone marrow presumably travel via the blood stream to reach tissue sites at which they accumulate. During the time when eosinophils were accumulating in the peritoneal cavity of the guinea pigs studied, there occurred an early transient rise in the concentration of eosinophils in the blood, and in most cases, a delayed rise. The blood level of eosinophils fluctuates much more than the peritoneal level, and frequent counts are necessary to detect the response. As in bone marrow studies, other methods are needed to determine the total number of cells entering and leaving the blood.

Tissue eosinophils probably derive from the blood stream, but the site at which foreign protein reacts to initiate tissue eosinophilia has remained unknown. Experiments reported in a subsequent paper of this series show that under certain conditions the peritoneal lining can act as a source of an eosinophilotactic substance.

**Summary**

A method is described for studying peritoneal eosinophilia quantitatively in guinea pigs. With repeated lavaging of the peritoneal cavity, the total number of eosinophils accumulating locally each day can be precisely measured. This procedure can be repeated indefinitely in individual animals.

Peritoneal eosinophilia was induced by prolonged series of weekly intraperitoneal injections of horse serum, Limulus hemocyanin or human serum albumin. The response was evident during the first three days following reinjection of foreign protein and ceased by the fourth to the twelfth day. The response was specific, occurring only after reinjection of the same protein used to prepare the animals. With continued injections, the magnitude of the eosin-
ophil response became greater. While the total cell values attained varied considerably from animal to animal, the relative responsiveness of an individual guinea pig remained fairly consistent for months.

In the bone marrow, an increased concentration of eosinophils was found in guinea pigs in which peritoneal eosinophilia could be elicited.

In the blood stream, the reinjection of horse serum resulted in a biphasic response: there was an increase in the concentration of eosinophils during the first 12 hours and again at various times during the next seven days.

Peritoneal exudates were obtained frequently in which as many as 40 per cent of the cells were eosinophils: such exudates commonly contained as many as 50 million eosinophils.

**SUMMARY IN INTERLINGUA**

Es describite un metodo pro studiar eosinophilia peritoneal in porcos de India quantitativamente. Per medio de repetite lavages del cavitate peritoneal, le numero total del eosinophilos que se accumula omne die pote esser mesurate precisemente. Le manovra pote esser repetite irrestringitemente in le mesme animales.

Eosinophilia peritoneal esseva inducite per prolongate series de injectiones septimanal intraperitoneal de sero equin, de hematocyanina de Limulus, o de albumina de sero human. Le responsa esseva evidente durante le prime tres dies post le reinjection de proteina alien e cessava inter le quart e le dece-secunde die. Le responsa esseva specific: Illo occurreva solmente pos le reinjection del mesme proteina que habeva essite usate pro preparar le animales. Con le continuation del injectiones, le magnitude del responsa eosinophilic deveniva plus marcate. Durante que le valores total de cellulas variava considerabilemente ab un animal al altere, le responsivitate relative de un porco de India individual remaneva satis stabile durante un periodo de menses.

In le medulla ossee, un augmento del concentration de eosinophilos esseva trovate in le caso de porcos de India in que eosinophilia peritoneal poteva esser evocate.

In le circulation del sanguine, le re-injection de sero equin resultava in un responsa biphasic: Il occurreva un augmento del concentration de eosinophilos durante le prime 12 horas e de novo a varie tempores in le curso del sequente septe dies.

In le exsudatos peritoneal obtenite, frequentemente usque a 40 pro cento del cellulas esseva eosinophilos. Communmente tal exsudatos contineva usque a 50 milliones de eosinophilos.

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QUANTITATION OF PERITONEAL EOSINOPHILIA

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Medullary fat was studied in vital preparations by means of phase contrast microscopy and in polarized light in 34 cases of nephrotic syndrome and in a miscellaneous group of 200 control cases. In nephrotic subjects the presence of anisotropic birefringent fat droplets, either isolated or ingested by phagocytic histiocytes was a constant finding. Among control cases, this finding was observed only in some elderly patients with atherosclerosis, hypercholesterolemia and with a large fatty component in the bone marrow.
—P. d. N.
Studies in Experimental Eosinophilia. I. Repeated Quantitation of Peritoneal Eosinophilia in Guinea Pigs by a Method of Peritoneal Lavage

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