Retention of Lymphocytes in the Subcapsular Sinus of Lymph Nodes: A Physiological Event

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Summary. This study examined the lymphocyte content of the subcapsular sinus of lymph nodes of diverse anatomical sites, from euthymic and athymic animals of various ages. One unusual feature which prevailed in young euthymic animals consisted of the accumulation of lymphocytes on the outer wall of the subcapsular sinus, following differential patterns with respect to diverse domains or areas of the subcapsular sinus of a node compartment. It is concluded that such an accumulation is due to the retention of lymphocytes on the sinus outer wall. Whether the retention reflects a step in unspecific defence mechanisms, in an immunological reaction pathway, or a transient state of the misfunctioning of lymph-carried cells, is considered. Some findings favor the latter possibility. In this case, retention would be due to a mild form of lymphocyte alteration caused by the emergence of an abnormal milieu in a drained tissue, and conceivably involving mast cell products. Whatever the case, the retention on the outer wall of the subcapsular sinus, instead of on its inner wall, would prevent any hindering of the usual activity of the latter wall.

The present work analyzed the lymphocyte content of the subcapsular sinus in nodes of various sites, from euthymic and athymic animals of various ages. We observed an unusual feature, predominating in young euthymic animals, which consisted of the differential accumulation of generally normal-looking lymphocytes on the outer wall of the subcapsular sinus of one or more compartments of a node. Figure 1 schematizes a node compartment and defines the present terms.

MATERIALS AND METHODS

Nodes from 16 normal Sprague-Dawley rats aged 2 or 12 months, eight 2-month-old germ-free CD rats and six 12-month-old gnotobiotic rats were analyzed. We also analyzed nodes from sixteen athymic rats, aged 2 or 12 months, which were born from heterozygous nude females and homozygous nude males. For comparison, we examined nodes from twelve normal CD-mice, aged 2 or 12 months. The animals were sacrificed with chloroform, and cervical, parathymic, mesenteric, brachial, axillary, inguinal and popliteal nodes were removed from each. The nodes were fixed in a solution of Bouin-Hollande for 48 h and embedded in paraffin. Each node was cut serially at 7 μm; one out of every 15 rat node sections, and one of every ten mouse node sections, was mounted and stained with the technique by Dominici.

We estimated the usual concentration of lymphocytes in the subcapsular sinus of a randomly chosen node in eight different locations, from six or eight rats of each of the three types examined, aged 2 or 12 months. In each node, we analyzed 40 surface units of the subcapsular sinus. A surface unit was a square with 22 μm sides, determined from a grid placed in one eyepiece of the microscope. Counts were carried out at a magnification of 320×.

RESULTS

Lymphocytes showed no obvious distribution pattern in any subcapsular sinus, and their concentration varied. In a given animal, the concentration varied mostly with the site of a node; commonly, cervical and caecal nodes showed the highest concentrations (Table 1). Moreover, the concentration was about half in athymic than in euthymic animals. Age did not appear to be very influential, except in the case of aged gnotobiotic animals in which the concentration was markedly greater than in younger normal or germ-free euthymic animals.
Unusual situations

Unusually, lymphocytes accumulated to variable extents in the subcapsular sinuses of nodes from mice and rats, a feature which we will term "lymphocyte accumulation". However, even in extreme cases of accumulation in the subcapsular sinus of a node, lymphocyte concentration remained within the normal range in the medullary sinuses. In mesenteric nodes mostly, blasts were present among the accumulated lymphocytes, along with intermediate cell forms (Fig. 7). Mast cells could also show unusual accumulations on the outer wall of the subcapsular sinus; in rare cases they were relatively abundant (Fig. 11). Below a site of heavy lymphocyte accumulation, the "subsinus layer", which underlies the subcapsular sinus and is commonly 25-40 μm thick, was often unusually lymphocyte-depleted. At times, depletion extended in the extrafollicular zone (Fig. 10).

Lymphocyte accumulation was much more frequent in euthymic than in athymic animals, and was more frequent in young than in aged euthymic animals (Table 2). In a given node, accumulation occurred in one or more compartments (Figs. 2, 3). Accumulation in the subcapsular sinus of a compartment followed one of three basic, albeit somewhat variable, patterns. These patterns are defined in relation to the "deep cortex unit" (or "unit") of the node compartment, and to the center and periphery of the unit. Hence, lymphocyte accumulation occurred: 1) exclusively, or almost exclusively, in the subcapsular sinus above peripheral cortex extending beyond the unit center; 2) in the subcapsular sinus above the unit center; or 3) in the whole subcapsular sinus of a compartment.

### Table 1. Numbers (±S.E.) of lymphocytes, per surface unit of subcapsular sinus, in lymph nodes of various sites from euthymic or athymic rats, aged 2 or 12 months

<table>
<thead>
<tr>
<th>Location of nodes</th>
<th>Euthymic</th>
<th>Athymic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal 2 months (n=8)</td>
<td>12 months (n=8)</td>
</tr>
<tr>
<td>Cervical</td>
<td>3.3 (±0.3)</td>
<td>3.7 (±0.5)</td>
</tr>
<tr>
<td>Jejunal</td>
<td>1.9 (±0.1)</td>
<td>2.1 (±0.5)</td>
</tr>
<tr>
<td>Caecal</td>
<td>3.1 (±0.3)</td>
<td>3.5 (±0.6)</td>
</tr>
<tr>
<td>Parathympic</td>
<td>2.7 (±0.2)</td>
<td>2.6 (±0.5)</td>
</tr>
<tr>
<td>Brachial</td>
<td>2.2 (±0.2)</td>
<td>2.4 (±0.3)</td>
</tr>
<tr>
<td>Axillary</td>
<td>3.2 (±0.3)</td>
<td>3.3 (±0.4)</td>
</tr>
<tr>
<td>Popliteal</td>
<td>2.4 (±0.3)</td>
<td>2.6 (±0.2)</td>
</tr>
<tr>
<td>Inguinal</td>
<td>2.3 (±0.2)</td>
<td>3.1 (±0.3)</td>
</tr>
<tr>
<td>Means</td>
<td>2.6 (±0.2)</td>
<td>2.9 (±0.2)</td>
</tr>
</tbody>
</table>

Lymphocyte accumulation in subcapsular sinus extending beyond the center of the deep cortex unit (Pattern I)

In this most common pattern (Table 2), accumulation was generally rather even on either side of the unit of a compartment (Fig. 4). Uneven distribution was observed mostly in compartments neighbouring a node's hilus: accumulation prevailed in the area of the subcapsular sinus which extended from the compartment's unit to the perihilar parts of the compartment's margin.

Stages could be distinguished by the degree of development of lymphocyte accumulation. In place, small numbers of lymphocytes accumulated just beneath the outer wall of the subcapsular sinus, forming a row or a series of tiny clumps (Figs. 7, 8). By contrast, the lymphocytes present in a nearby lymphatic vessel, running parallel to a node capsule, had sedimented towards the inner wall of the subcapsular sinus (Fig. 14). Elsewhere, more lymphocytes stuck together, forming up to several faint rows of more or less crowded cells which hung from the outer sinus wall (Fig. 9). In fewer places, lymphocytes filled the sinus depth (Fig. 10). Here, lymphocyte concentration reached up to 21 cells per surface unit of sinus, instead of 1.1 to 4.8 under usual conditions (Table 1).

In some cases, accumulation took place solely in small areas at the compartment margin (Fig. 5). Such
Fig. 1. Diagram showing a rat lymph node “compartment” centered on the related opening of an afferent lymphatic vessel abutting the subcapsular sinus. At the margin of the compartment, there occur gaps where the subcapsular sinus connects directly with medullary sinuses. The peripheral cortex has an extrafollicular zone (e) and folliculo-nodules (f), i.e., a follicle having a nodule (or germinal center). It also has a deep cortex unit (or “unit”), with a center (c) and periphery (p). Note that the peripheral cortex may extend variably beyond the deep cortex unit. Medullary cords stretch from the deep, or the peripheral, cortex.

Table 2. Numbers of animals and lymph nodes with lymphocyte accumulation in the subcapsular sinus (W.L.A. I.S.S.), and percentages of patterns I-III of accumulation, in euthymic or athymic rats, aged 2 or 12 months

<table>
<thead>
<tr>
<th></th>
<th>Analyzed animals</th>
<th>Analyzed nodes</th>
<th>Lymphocyte accumulation*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No.</td>
<td>No.</td>
</tr>
<tr>
<td>Euthymic</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td>8</td>
<td>8</td>
<td>280</td>
</tr>
<tr>
<td>12 months</td>
<td>8</td>
<td>6</td>
<td>238</td>
</tr>
<tr>
<td>Germ-free</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td>8</td>
<td>8</td>
<td>187</td>
</tr>
<tr>
<td>12 months</td>
<td>6</td>
<td>6</td>
<td>173</td>
</tr>
<tr>
<td>Gnotobiotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>6</td>
<td>6</td>
<td>173</td>
</tr>
<tr>
<td>Athymic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td>8</td>
<td>2</td>
<td>214</td>
</tr>
<tr>
<td>12 months</td>
<td>8</td>
<td>6</td>
<td>218</td>
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<tr>
<td>Totals</td>
<td>1310</td>
<td>283</td>
<td>85</td>
</tr>
</tbody>
</table>

*Pattern I: accumulation beyond the center of the deep cortex unit of a compartment
Pattern II: accumulation above the center of the deep cortex unit of a compartment
Pattern III: accumulation above the whole compartment
Figs. 2-23. The micrographs are lymph nodes of normal or athymic nude rats, aged 2-12 months. The sections, 7 μm thick, are stained with the technique of Dominici.

Fig. 2. Mesenteric node in a 2-month-old normal rat. Two deep cortex units (u) almost touch one another. Lymphocyte accumulation (arrow) occurs above the center of the left unit only. ×30

Fig. 3. Mesenteric node in a 2-month-old normal rat. Lymphocyte accumulation in the subcapsular sinus occurs above the left compartment only. Accumulation shows as a dark band covering the compartment’s parenchyma. The arrow points to the related afferent lymphatic with an unusually high lymphocyte content. ×30

Fig. 4. Cervical node in a 2-month-old normal rat. Lymphocyte accumulation (arrows) takes place in the subcapsular sinus of a compartment, except for above its hemispheric deep cortex unit (u). ×30

Figs. 5 and 6. Legends on the opposite page.
a small area of accumulation was observable in as few as three consecutive sections, 105 µm apart one from another, but several such small areas of accumulation could be found in the same compartment. In some compartments, in which lymphocyte accumulation took place only at their perihilar margin, the area of subsinus layer beneath the site of accumulation was lymphocyte-depleted, fibrotic, and underlined by mast cells (Figs. 19, 20). Otherwise, accumulation extended variably from the margin towards the unit of a compartment. Where heavy accumulation occurred, lymphocytes concentrated above the unit periphery as well, then occurring throughout, or almost throughout, the domain of the subsinus layer extending beyond the unit center. In these cases, the thickness of the mass of accumulated lymphocytes often grossly decreased from the margin toward the unit of a compartment.

In other respects, lymphocyte accumulation most often prevailed above the extrafollicular zone (Fig. 15). A large mass of lymphocytes accumulating there at times expanded above the nearby folliculo-nodules or follicles, decreasing in thickness with distance from that zone (Fig. 16). As the nodes of athymic animals lack nodules (germinal centers), they have "follicles" instead of the usual "folliculo-nodules" (follicles with a nodule) of normal animals. In some cases, accumulation took place exclusively, or almost exclusively, above these folliculo-nodules or follicles (Fig. 17). This variant of accumulation was observed mostly above much hypertrophied follicles, common in athymic animals (Fig. 18). Very occasionally, lymphocytes further lined the inner wall of the subsinus above the folliculo-nodules or follicles, while the subsinus layer beneath was more or less lymphocyte-depleted (Figs. 12, 13).

Lymphocyte accumulation in subcapsular sinus above the center of the deep cortex unit (Pattern II)

This pattern was rare (Table 2) and best developed in caecal or cervical nodes of aged athymic, and to a lesser degree of aged euthymic, animals. In this pattern, accumulation was observed above the unit center, at times expanding above the unit periphery (Fig. 2). Where present, the related afferent lymphatic vessel was often dilated and had a markedly increased lymphocyte content. Generally, accumulation was dense and the thickness of the mass of accumulated lymphocytes decreased with distance from the afferent lymphatic opening (Fig. 21). Again, accumulation appeared to initially occur on the outer wall of the sinus, and predominantly above the extrafollicular zone (Fig. 15). In some compartments, lymphocytes loaded the afferent lymphatic and the sinus as well. Such loading of the sinus could greatly prevail on one side of the lymphatic opening, stopping on the opposite side at the edge of a greatly hypertrophied follicle (Fig. 22). It is to be noted that the lymphocytes, loading an afferent lymphatic and the surrounding area of subcapsular sinus, often assumed an obviously darker aspect than usual (Figs. 21-23).

Lymphocyte accumulation in the entire subcapsular sinus (Pattern III)

In this relatively unfrequent pattern (Table 3), lymphocyte accumulation took place in the entire subcapsular sinus of a compartment (Fig. 6) while it could be more pronounced above than beyond the unit center, or vice versa. This pattern represented a combination of patterns I and II, and its features resembled those described above.

DISCUSSION

Usual lymphocyte concentration in the subcapsular sinus was commonly site-influenced, likely reflecting local variations in the intensity of lymphocyte traffic in a drained tissue. As expected, the concentration was lower in athymic than in euthymic animals. Surprisingly, however, it was about equal in young germ-free as in normal euthymic animals, while being greater in aged gnotobiotic animals. This does not necessarily mean that the lymphocyte traffic was equal or more intense in these than in control animals; there could be a lesser formation of lymph fluid, for instance.

One may seek physical explanations for the occurrence of "lymphocyte accumulation" in the subcapsular sinus. Transient changes in the cell content and the rate of flow of the afferent lymph, or flow patterns in this sinus, are likely. Hence, accumulation

Fig. 5. Cervical node in a 2-month-old normal rat. Lymphocyte accumulation (arrow) in the subcapsular sinus occurs only at the perihilar margin of a compartment. ×65

Fig. 6. Mesenteric node in a 2-month-old normal rat. Lymphocyte accumulation occurs in the whole subcapsular sinus of a compartment. At right, the thick accumulation ends at the edge of a large protruding folliculo-nodule (f). ×40
Figs. 7-15. Legends on the opposite page.
Table 3. Numbers and percentages of lymph nodes in various locations, with lymphocyte accumulation in the subcapsular sinus, from euthymic or athymic rats, aged 2 or 12 months

<table>
<thead>
<tr>
<th>Location of nodes</th>
<th>Euthymic</th>
<th>Athymic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Germ-free</td>
</tr>
<tr>
<td></td>
<td>2 months (n=8)</td>
<td>12 months (n=8)</td>
</tr>
<tr>
<td></td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>Cervical</td>
<td>44/86</td>
<td>51/22</td>
</tr>
<tr>
<td></td>
<td>5/13/38</td>
<td>3/19</td>
</tr>
<tr>
<td>Jejunal</td>
<td>32/44</td>
<td>73/5</td>
</tr>
<tr>
<td>Caecal</td>
<td>8/39/21</td>
<td>2/13</td>
</tr>
<tr>
<td>Parathympic</td>
<td>7/29/24</td>
<td>4/33</td>
</tr>
<tr>
<td>Brachial</td>
<td>0/17/19</td>
<td>7/8</td>
</tr>
<tr>
<td>Axillary</td>
<td>4/15/27</td>
<td>3/17</td>
</tr>
<tr>
<td>Popliteal</td>
<td>3/27/11</td>
<td>3/36</td>
</tr>
<tr>
<td>Inguinal</td>
<td>0/18/20</td>
<td>0/18</td>
</tr>
<tr>
<td>Totals</td>
<td>122/280</td>
<td>44</td>
</tr>
</tbody>
</table>

Fig. 7. Mesenteric node in a 2-month-old normal rat. Lymphocytes and a few blasts adhere, in a row, to the outer wall of the pale subcapsular sinus. ×380

Fig. 8. Cervical node in a 2-month-old normal rat. Lymphocytes form a series of tiny clumps on the outer wall of the subcapsular sinus. ×380

Fig. 9. Cervical node in a 2-month-old normal rat. Thick lymphocyte accumulation occurs beneath the outer wall of the subcapsular sinus. A thin stratum of pale lymph is present between the accumulation and the much lymphocyte-depleted "subsinus layer" (above arrow). ×380

Fig. 10. Mesenteric node in a 2-month-old normal rat. The accumulated lymphocytes fill the subcapsular sinus (above arrow), above the much lymphocyte-depleted peripheral cortex. ×380

Fig. 11. Parathympic node in a 12-month-old gnotobiotic rat. Two mast cells adhere together on outer wall of the subcapsular sinus at a site of moderate lymphocyte accumulation. ×380

Fig. 12. Cervical node in a 12-month-old normal rat. Lymphocytes adhere to the inner wall of the subcapsular sinus (s), forming a dark row above a bulging folliculo-nodule. ×230

Fig. 13. Cervical node in a 12-month-old normal rat. The subsinus layer (between arrows) is much lymphocyte-depleted beneath lymphocyte accumulation on the inner wall of the subcapsular sinus (s). Note that the lymphocyte at the right of the tip of the upper arrow has a shape indicating migration across the inner wall of the sinus. ×760

Fig. 14. Parathympic node in a 12-month-old normal rat. Lymphocytes are accumulated on the upper wall of the subcapsular sinus. In the above lymphatic vessel (v), the lymphocytes are sedimented on the lower wall of the vessel. ×170

Fig. 15. Parathympic node in a 2-month-old normal rat. Lymphocyte accumulation is observed mainly above depressed areas of the extrafollicular zone (arrows) of one compartment. ×25
Figs. 16-23. Legends on the opposite page.
often did not occur symmetrically in the subcapsular sinus of a compartment with respect to its afferent lymphatic opening. This can be explained by the fact that the amount of lymph flowing in a given part of the subcapsular sinus of a compartment is influenced by the width of the gaps at the compartment margin where this sinus connects with medullary sinuses, because lymph flows more via broad than narrow gaps (SAINTE-MARIE et al., 1982). For the same reason, the lymph flow is most important in the perihilar parts of the subcapsular sinus, which connects widely with medullary sinuses at its perihilar outline. Accordingly, accumulation was commonly more pronounced in perihilar parts of the subcapsular sinus which receive more lymph-carried cells. Moreover, the outward protrusion of greatly hypertrophied follicles can sharply decrease lymph flow above them and thus influence the flow in the neighbouring sinus area.

In our view, and for a number of reasons, such physical parameters do not constitute the initial cause of lymphocyte accumulation, hypothetically by producing sites of passive lymphocyte margination. For example, why would passive cell margination start at a compartment margin, where the subcapsular sinus becomes wider and the afferent lymph enters still wider medullary sinuses in which it carries free lymphocytes? And how could cells, if passively marginated, accumulate there to the extent of filling the sinus? Moreover, why would cells passively marginated on the outer wall of the subcapsular sinus not sediment, after node removal, in half of the cases on either wall of this sinus as was observed with cells in lymphatic vessels? Hence, it appears that accumulation reflects lymphocyte retention on the outer sinus wall rather than passive cell margination. This is supported by the fact that, where accumulation was heavy, the underlying sub-sinus layer and extrafollicular zone were lymphocyte-depleted. This depletion indeed indicates that sinus lymphocytes had almost ceased to enter the underlying components due to retention in the sinus, which agrees with the finding that lymphocytes carried by the afferent lymph can contribute substantially to the lymphocyte populations of these components (SAINTE-MARIE et al., 1975). In another respect, the comparison of data in Tables 1 and 3 reveals that accumulation tended to co-occur with a greater lymphocyte concentration in a subcapsular sinus. However, this greater concentration was not necessarily accompanied by accumulation, so that greater

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**Fig. 16.** Mesenteric node in a 2-month-old normal rat. Lymphocyte accumulation in the subcapsular sinus is more pronounced above the extrafollicular zone (e) than above the nearby folliculo-nodule (F). ×100

**Fig. 17.** Axillary node in a 12-month-old normal rat. Above the folliculo-nodule (f) outlined by arrows, the accumulated lymphocytes almost fill the subcapsular sinus. The outermost stratum of the folliculo-nodule is partly lymphocyte-depleted. ×100

**Fig. 18.** Inguinal node in a 12-month-old normal mouse. The transversely cut deep cortex units (u) of two compartments touch one another. Lymphocyte accumulation (arrows) takes place above the much hypertrophied folliculo-nodules of the right compartment. The follicle below the left arrow lays on the medulla. ×40

**Fig. 19.** Inguinal node in a 12-month-old normal rat. Lymphocyte accumulation (arrows) occurs in the perihilar part of the subcapsular sinus. The pale underlying sub-sinus layer is lymphocyte-depleted, fibrotic, and underlined by numerous mast cells. ×95. Inset: Site delimited by the arrows. ×230

**Fig. 20.** Same as Figure 18. Lymphocyte accumulation is observed in the subcapsular sinus above an area of pale and fibrotic sub-sinus layer, overlying the depressed extrafollicular zone but not the protruding folliculo-nodule (F). Fibrosis expands slightly in the extrafollicular zone below. Note the presence of lymphocytes between the fibrotic fibers, and of mast cells (arrows) beneath the fibrotic area. ×230

**Fig. 21.** Mesenteric node in a 12-month-old normal rat. An afferent lymphatic opening (arrow) is loaded with lymphocytes. Lymphocyte accumulation in the subcapsular sinus shows rough gradient of decreasing density away from the opening. ×30

**Fig. 22.** Mesenteric node in a 5-month-old athymic rat. Lymphocyte accumulation occurs in the subcapsular sinus, mostly at the left of the afferent lymphatic opening (arrow), not expanding above the much-protruding follicle at right. ×20

**Fig. 23.** Mesenteric node in a 4-month-old athymic rat. An afferent lymphatic (arrow) is loaded with lymphocytes. Lymphocytes are accumulated on the outer wall of the subcapsular sinus above a bulging follicle (f). Most lymphocytes present in the afferent lymphatic and the sinus are much darker than those in the follicle. ×320.
concentration *per se* does not appear to cause accu-

mulation. Indeed, under the euthymic state, accu-
mulation was about twice more frequent in youn-
ger than in older animals, albeit the concentra-
tion was similar. The frequent co-occurrence of both
features could be due to the fact that certain tissue
conditions, which increase local lymphocyte traffic,
also modify lymphocytes such as to cause their reten-
tion on the outer wall of the draining subcapsular
sinus (see below).

Because accumulation according to the most fre-
quent Pattern I prevailed in young normal animals, it
could conceivably reflect a step in unspecified defence
mechanisms or in an immunological reaction path-
way related mostly to a newly challenging antigen.
Alternatively—or in some cases—it could instead
reflect a transient misfunctioning, or a mildly altered
state, of the retained cells. This second possibility is
suggested by a recently described anomaly consisting
of the accumulation of “dark lymphocytes” in the
subcapsular sinus (SAINTE-MARIE and PENG, 1990b).
We concluded that these cells were lethally altered
due to the emergence of a very abnormal milieu in the

tissue in which they had circulated prior to being

lymph-carried to a subcapsular sinus, where they also
initially accumulated on the outer wall. We proposed
that their retention on the outer sinus wall postpones
the loading of the inner sinus wall with altered cells,
thus allowing the inner wall to continue its activities
of the selection of lymph-carried elements to enter

underlying structures. Therefore, it is conceivable
that a slight alteration of circulating lymphocytes in
a drained tissue could cause their transient retention
by the outer wall of a subcapsular sinus, thus not
hindering the essential activities of its inner wall.
Variations in the extent of the accumulation in a
sinus could result from variations in the duration of
accumulation, conceivably due to variations in the
degree of lymphocyte alteration.

Lethal alteration of tissue lymphocytes was
proposed to involve excessive amounts of certain

mast cell products (SAINTE-MARIE and PENG, 1990b).
One may therefore wonder whether a mild effect of
the same products could not contribute to a slight
alteration of tissue lymphocytes, possibly causing
their accumulation in the draining subcapsular sinus.
Some mast cell products indeed affect cell adherence
(HAYASHI and YAMADA, 1982) or alter cell surface
receptors (HUBBARD and KALIMI, 1983). It might not
be coincidental that lymphocyte accumulation in the
subcapsular sinus extending beyond a unit center and

mast cell distribution in the peripheral cortex
(SAINTE-MARIE and PENG, 1990a) follow a similar
topographical pattern. Indeed, both features start at
a compartment margin. Moreover, we observed cases
in which lymphocyte accumulation and mast cell
concentration took place together at the same com-
partement margin. Thus, there likely exists relation-
ships between these features.

Lymphocyte loading of the subcapsular sinus above
a unit center, observed in Patterns II and III, could
have a somewhat different meaning than the gener-
ally light accumulation of normal-looking lympho-
cytes on the outer sinus wall, as discussed above.
This is because the concerned lymphocytes were
unusually dark, such dark lymphocytes being respon-
sible for the development of the recently described
nodal anomaly (SAINTE-MARIE and PENG, 1990b).
The loading of the sinus next to an afferent lymphatic
opening likely results from the emergence of a pro-
nounced abnormality of the milieu in the drained site,

much enhancing local lymphocyte traffic and the
lymphocyte content in the draining lymphatic. When
such a pronounced abnormal milieu acutely emerges
in a tissue, it could produce the formation of the rare
Pattern II, if not preceeded by lymphocyte accumu-
lation according to Pattern I. The present cases of the

heavy accumulation of dark lymphocytes, above a

unit center, thus appear to represent initial stages in
the development of the nodal anomaly studied in our
preceeding work and involving the arrival of lethally
altered lymphocytes in a subcapsular sinus. This can
explain why the latter anomaly, together with the

present accumulation of dark lymphocytes around an

afferent lymphatic opening, were both encountered
mostly in caecal nodes of athymic or some aged

euthymic animals.

Previous observations, made mostly in athymic
animals, revealed that cells carried by the afferent

lymph may or may not enter the diverse domains or
components of the peripheral cortex of a com-
partment. Hence, giant cells enter only the domain of
the peripheral cortex above the unit center (SAINTE-
MARIE and PENG, 1983). Mast cells selectively enter
the peripheral cortex present beyond a unit center and
moreover, like most sinus lymphocytes, mast
cells enter only the extrafollicular zone of the periph-

eral cortex (SAINTE-MARIE and PENG, 1990a). These
findings indicate that the subcapsular sinus selects
lymph-carried cells to enter the different underlying
domains or components. The present findings indicate
that such a selection takes place in euthymic animals
as well; they also show that, under certain conditions,
cells selected by a given sinus site unusually adhere to
its outer wall. Accordingly, lymphocyte accumulation
prevailed above the extrafollicular zone which most
sinus lymphocytes enter.

The present observations further indicate that the subcapsular sinus areas above the follicles can also select and retain lymphocytes. This is in line with reports that macrophages (Kotani et al., 1977), dendritic cells (Szakal et al., 1983) and transferred nodulocytes (germinal center cells) (Deenen et al., 1984) may enter folliculo-nodules from the subcapsular sinus. An entry of sinus lymphocytes into follicles was indicated by the occasional lining of the inner sinus wall above the follicles by normal-looking lymphocytes, accompanied by a lymphocyte depletion of the underlying subsinus layer. Both features indeed appear to result from a certain temporary impairment of the entry of sinus cells into the follicles. Lymphocyte accumulation, prevailing above the follicles, occurred mainly in intensely stimulated nodes of athymic animals. Their follicles are commonly much hypertrophied, a lack of helper T-cells or overstimulation provoking an overdevelopment of their B-cell populations (Sainte-Marie and Peng, 1983). This must increase the entry of lymphocytes in hypertrophying follicles. Under conditions further inducing lymphocyte accumulation in the subcapsular sinus, this increased entry would allow more frequent or marked accumulations above the follicles—as was the case.

To conclude, an occasional retention of most generally normal-looking lymphocytes can occur on the outer wall of the subcapsular sinus, following differential patterns with respect to the diverse domains or areas of the subcapsular sinus of a node compartment. Whatever the cause, the observations were interpreted as indicating that these diverse domains or areas of the subcapsular sinus exert a selective activity with respect to the lymphocytes carried by the afferent lymph.

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REFERENCES


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