A Comparison of Nitrogen Content of Lymph Nodes from Cancer and Noncancer Patients*

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Cancer patients, even when maintained in positive nitrogen balance, may show progressive decrease in serum protein and lack of clinical improvement (3). When weight gain occurs in such individuals, it does not account for all nitrogen retained (1). Increase in nitrogen content as well as hyperplasia of lymphatic tissue has been observed in mice bearing transplanted sarcomas and adenocarcinomas (2). Conversely, lymph nodes of tumor-bearing rats (Walker carcinoma 256) were found to contain less nitrogen than did the same tissues from pair-fed controls (5). This study was undertaken in an attempt to determine whether lymphatic tissue in human cancer patients acts as a possible source of nitrogen or competes with the growing tumor in consumption of nitrogen.

MATERIALS AND METHODS

Lymph nodes were obtained from cancer and noncancer patients, either at operation or post mortem examination. The nodes were immediately dissected free of fat and divided into two portions. One portion of each node was carefully weighed and then dissolved in equal parts of nitrogen-free sulfuric acid and water. A micro-Kjeldahl Nesslerization method was used for nitrogen determination, and readings were made on a Coleman junior spectrophotometer. The second portion was fixed in 10 per cent formalin, imbedded in paraffin, cut, and stained routinely with hematoxylin and eosin. Pathological examination was done to verify the type of tissue and to determine the presence or absence of cancer. Nodes showing fatty replacement on microscopic examination were not included in this study.

A limited number of blocks of tissue from various organs (liver, spleen, kidney, lung, and thyroid), as well as from tumors, was obtained at post mortem examinations. These were analyzed for nitrogen content by the same method employed in the examination of lymph nodes.

RESULTS

Two hundred and ten nodes were obtained from 41 patients (28 surgical and 13 post mortem). Sex and age distribution were as follows:

<table>
<thead>
<tr>
<th>Type</th>
<th>Case</th>
<th>Age Range</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>9</td>
<td>28-73 years</td>
<td>51.5 years</td>
</tr>
<tr>
<td>Noncancer</td>
<td>5</td>
<td>25-68</td>
<td>51.1</td>
</tr>
</tbody>
</table>

The diagnoses were as follows:

<table>
<thead>
<tr>
<th>Cancer Cases</th>
<th>Noncancer Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td>Surgical</td>
</tr>
<tr>
<td>Breast</td>
<td>Heart disease</td>
</tr>
<tr>
<td>Skin</td>
<td>Nephritis</td>
</tr>
<tr>
<td>Tongue</td>
<td>Adenofibroma</td>
</tr>
<tr>
<td>Mouth</td>
<td>Breast</td>
</tr>
<tr>
<td>Metastatic to neck*</td>
<td>Intracranial hemorrhage</td>
</tr>
<tr>
<td>Bronchus</td>
<td>Peptic ulcer</td>
</tr>
<tr>
<td>Cervix</td>
<td>Saphenous vein</td>
</tr>
<tr>
<td>Vulva</td>
<td>Ligation</td>
</tr>
<tr>
<td>Stomach</td>
<td>Intestinal perforation</td>
</tr>
<tr>
<td>Duodenum</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
</tr>
</tbody>
</table>

*Primary site unknown.

Nodes were classified in three groups: (a) nodes from noncancer patients, (b) nodes from cancer patients which on pathological examination showed the presence of neoplastic cells, and (c) nodes from cancer patients which on pathological examination were free of neoplastic cells. The range of nitrogen content, as well as the average for each group, is given in Table 1. The range is

<table>
<thead>
<tr>
<th>Table 1: Nitrogen Content of Nodes from Cancer and Noncancer Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type Case</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Noncancer</td>
</tr>
<tr>
<td>Cancer</td>
</tr>
<tr>
<td>Neg. nodes</td>
</tr>
<tr>
<td>Pos. nodes</td>
</tr>
</tbody>
</table>
similar in nodes from noncancer patients and in
noncancerous nodes from cancer patients and
overlaps at both ends the range of nitrogen con-
tent of cancer nodes. There is no significant differ-
ence between the averages of the three groups at
the 0.05 level of probability.

The nodes were further divided according to
site as well as source. The range and average ni-
trogen content of each group are given in Table 2.

| TABLE 2 |
| NITROGEN CONTENT OF NODES GROUPED | ACCORDING TO SITE |

<table>
<thead>
<tr>
<th>SITE</th>
<th>SOURCE</th>
<th>No. NODES</th>
<th>Range (gm/100 gm)</th>
<th>Av. (gm/100 gm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axillary</td>
<td>Non-ca. pts.*</td>
<td>16</td>
<td>1.52–3.07</td>
<td>1.97</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. neg.</td>
<td>54</td>
<td>1.52–3.95</td>
<td>2.08</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>14</td>
<td>1.42–2.53</td>
<td>2.00</td>
</tr>
<tr>
<td>Cervical</td>
<td>Non-ca. pts.*</td>
<td>8</td>
<td>2.50–2.67</td>
<td>2.55</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. neg.</td>
<td>28</td>
<td>2.55–3.00</td>
<td>2.77</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>2</td>
<td>2.40–2.65</td>
<td>2.45</td>
</tr>
<tr>
<td>Hilar</td>
<td>Non-ca. pts.*</td>
<td>12</td>
<td>1.61–2.15</td>
<td>1.96</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>2</td>
<td>2.22–2.40</td>
<td>2.31</td>
</tr>
<tr>
<td>Inguinal</td>
<td>Non-ca. pts.*</td>
<td>8</td>
<td>0.98–2.14</td>
<td>1.68</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. neg.</td>
<td>8</td>
<td>1.43–2.56</td>
<td>1.80</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>1</td>
<td>1.68</td>
<td></td>
</tr>
<tr>
<td>Mesenteric</td>
<td>Non-ca. pts.*</td>
<td>14</td>
<td>1.27–3.19</td>
<td>1.91</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. neg.</td>
<td>28</td>
<td>0.99–2.55</td>
<td>1.37</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>5</td>
<td>1.45–2.65</td>
<td>2.22</td>
</tr>
<tr>
<td>Periaortic</td>
<td>Non-ca. pts.*</td>
<td>7</td>
<td>1.61–2.50</td>
<td>1.86</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. neg.</td>
<td>3</td>
<td>1.67–1.83</td>
<td>1.72</td>
</tr>
<tr>
<td></td>
<td>Ca. pts. pos.</td>
<td>5</td>
<td>1.85–2.19</td>
<td>2.04</td>
</tr>
</tbody>
</table>

* Pts. = patients.

The average nitrogen content was highest in nodes
from the cervical region in all groups and lowest
in nodes from the inguinal region, except for the
periaortic negative nodes from cancer patients.
When these statistics were analyzed, more varia-
tion was found among the different sites than
should have been expected from the variation that
existed within any one group. As a result, it can
be said that there was a significant difference in
nitrogen content between nodes from various
sites.

In an attempt to correlate tumor size with
total number of regional nodes, as well as percent-
age of metastatic nodes, nine cases of breast can-
cer are compared (Table 3).

| TABLE 3 |
| SIZE OF TUMOR AND NO. OF REGIONAL LYMPH NODES IN NINE CASES OF RADICAL MASTECTOMY |

<table>
<thead>
<tr>
<th>TUMOR SIZE</th>
<th>REGIONAL LYMPH NODES</th>
</tr>
</thead>
<tbody>
<tr>
<td>(cm.)</td>
<td>Total</td>
</tr>
<tr>
<td>C</td>
<td>Metastatic</td>
</tr>
<tr>
<td>Liver</td>
<td>10</td>
</tr>
<tr>
<td>Kidney</td>
<td>4</td>
</tr>
<tr>
<td>Spleen</td>
<td>5</td>
</tr>
<tr>
<td>Lung</td>
<td>5</td>
</tr>
<tr>
<td>Muscle</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2</td>
</tr>
<tr>
<td>Fat conn.</td>
<td>2</td>
</tr>
<tr>
<td>Tumor</td>
<td>7</td>
</tr>
</tbody>
</table>

* This specimen was obtained from a liver showing gross fatty change.
† Does not include single specimen from fatty liver.

DISCUSSION

In a careful study of the parametrium in 27
cases of carcinoma of the cervix, Sampson (4)
found not only newly formed nodes projecting
into lymph channels to which cancer could metas-
tasize but also newly formed lymph nodes which
apparently bore no relation to the lymph channels
and in which cancer metastases were never seen.
That growing tumor is associated with lymph
node hyperplasia, even in the absence of meta-
static involvement, was particularly apparent in
the cases of carcinoma of the breast observed in

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in nodes from the inguinal region, except for the
periaortic negative nodes from cancer patients.
When these statistics were analyzed, more varia-
tion was found among the different sites than
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In an attempt to correlate tumor size with
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The tumor specimens as well as the regional lymph nodes were obtained at surgery, since all
the patients had radical mastectomies. None of
these patients presented the extreme cachexia and
malnutrition so frequently seen in far advanced
neoplastic disease, so that this was a roughly
homogeneous group as to site of disease and state
of nutrition. As can be seen there was much
greater variance in percentage of positive nodes
than there was in total number of regional lymph
nodes present. The size of the tumor did not seem
to be related to either the total number or percent
positive regional lymph nodes present.

Nitrogen content of blocks of tissues from vari-
ous sites from cancer and noncancer patients
showed no appreciable difference, although the
total number of specimens analyzed is small. The
type of tissue, number of specimens, range of ni-
trogen, and average nitrogen content are given in
Table 4. Tumor metastases in liver contained less

TABLE 4 |
| NITROGEN CONTENTS OF BLOCKS OF TISSUE OTHER THAN LYMPH NODES |

<table>
<thead>
<tr>
<th>TISSUE</th>
<th>No. SPECIMENS</th>
<th>Range (gm/100 gm)</th>
<th>Av.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>10</td>
<td>2.16–3.57</td>
<td>2.90†</td>
</tr>
<tr>
<td>Kidney</td>
<td>4</td>
<td>2.10–2.67</td>
<td>2.35</td>
</tr>
<tr>
<td>Spleen</td>
<td>5</td>
<td>2.64–3.26</td>
<td>3.02</td>
</tr>
<tr>
<td>Lung</td>
<td>5</td>
<td>2.62–2.59</td>
<td>2.59</td>
</tr>
<tr>
<td>Muscle</td>
<td>2</td>
<td>2.46–3.43</td>
<td>2.94</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2</td>
<td>2.18–3.22</td>
<td>2.20</td>
</tr>
<tr>
<td>Fat conn.</td>
<td>2</td>
<td>0.40–0.77</td>
<td>0.59</td>
</tr>
<tr>
<td>Tumor</td>
<td>7</td>
<td>2.36–3.72</td>
<td>2.54</td>
</tr>
</tbody>
</table>

* This specimen was obtained from a liver showing gross fatty change.
† Does not include single specimen from fatty liver.
this study. Only a few small axillary nodes were
obtainable from noncancer patients. In the pre-

cence of malignant neoplasm of the breast, large
nodes were found in which no neoplastic cells were
seen microscopically, and such cancer-free nodes
greatly outnumbered those in which metastatic
cancer was found.

Although serial sections were not done and the
presence of a few neoplastic cells in some of these
nodes may have been missed, the general increase
in lymphoid tissue in the presence of cancer was
striking. The masses of hyperplastic lymphoid tis-

eue were found frequently as cords or even flat
sheets between fat lobules. Occasionally in section
a fat lobule was revealed, sheathed in an envelope
of lymphoid tissue. Homburger (2) observed en-

largement of lymph nodes, which was due to sim-
ple hyperplasia in mice bearing transplanted
tumors. This increase in weight of lymphoid tissue
was accompanied by a rise in nitrogen content.
Sherman et al. (5) demonstrated a striking de-
crease in nitrogen content of lymph nodes, which
in some cases was as great as 70—90 per cent in rats
with transplanted Walker carcinoma 256, and
postulated this tissue as one of the nitrogen
sources for the growing tumor.

This study shows no significant difference in
nitrogen content of nodes from noncancer and can-

cer patients. However, the increase in total lym-
phatic tissue in the region of the tumor suggests
that, rather than being a source of nitrogen for
the tumor, such tissue is a site of nitrogen shunt.
The differences reported in lymphatic nitrogen
in tumor-bearing animals may be attributed to
species differences. Although we did not observe
a significant absolute increase in lymph node ni-

trogen, the apparent increase in lymphatic tissue
resembled that seen in tumor-bearing mice.

It is beyond the scope of this paper to discuss
the mechanism of lymphoid hyperplasia asso-
ciated with tumor growth. Willis (6) attributes
these changes to mild bacterial infection in super-

ficial growths, to degenerative changes in tumor
or to blockage of ducts and retention of secretions
in glandular organs. The observations in our study
indicate that lymphoid tissue in human cancer pa-

tients does not act as a source of nitrogen and
probably shares to a small extent with growing
tumors in deviating nitrogen from its normal met-
bolic pathways.

SUMMARY

1. Two hundred and ten lymph nodes were ob-
tained from 28 surgical and 13 post mortem exami-
nations. These nodes were examined biochemically
for nitrogen content and histologically for verifica-
tion of type tissue and presence of cancer.
2. There was no significant difference between
the nitrogen content of metastatic and nonmeta-
static nodes from cancer patients and that of nodes
obtained from noncancer patients.
3. A consistent hyperplasia of lymphoid tissue
observed in cancer patients suggests that this tis-

ue shares to some extent with growing tumor the
role of depleting other body tissues of their nitro-
gen stores.
4. Significant differences of nitrogen content
were observed in lymph nodes from various sites.

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her help in pathological examination of tissues, to Mr. Marvin
Schneiderman for statistical analysis of data, and to Dr.
Robert Hill for help in obtaining the specimens examined.

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