The Weight and Lipid Content of the Intestines in Rats with Walker Carcinoma 256*

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Patients with severe cancer lose weight and often die of what is essentially starvation. Similarly, in our work on rats with Walker carcinoma 256 we have observed that the rats ate well until the tumor reached a certain size (generally 40–50 per cent of the body weight); then they ceased to eat and died in a day or two. Blood taken during the active growth of the tumor was generally lipemic owing to mobilization of fat from the stores. The lipemia subsided terminally, and it was found that the fat stores were then empty.

In these animals, as in human cancer patients, the needs of the animal are no longer supplied by the food. Since food is available at all times, the digestive tract is a logical place to look for nutritional failure. A study was accordingly undertaken of the intestinal tract and constituent lipids in rats near death from large tumors, as compared with the intestines in normal rats of approximately the same age and weight. In a study of the effects of this tumor on the lipid composition of body tissues, Boyd et al. (3) found in agreement with Greenstein (6) that the composition of the body tissues approached the composition of the tumor. Boyd et al. (8) used only the duodenum as representative of the intestine. In the present work the whole intestine from stomach to anus was used.

METHODS

Male albino rats of the Wistar strain and Walker carcinoma 256 grown subcutaneously were used throughout the experiments. The rats, which weighed from 70 to 100 gm. at the time of transplantation of the tumor, had access to a diet of Purina Fox Chow meal. The tumor was allowed to grow for 4–6 weeks (average = 37 days) after transplantation.

The rats were killed by decapitation; the whole intestine from stomach to anus was removed, slit throughout its length, washed out with warm wa-
for phosphorus multiplied by \(25\) was called the phospholipid (PL). The value for neutral fat was obtained by subtracting from the total lipid the sum of the unsaponifiable and two-thirds of the weight of the phospholipid (the fatty acid content).

RESULTS AND DISCUSSION

The results of the examination of the lipids of the intestine of tumor-bearing as compared with normal rats are given in Table 1. The following outstanding similarities and differences may be noted.

<table>
<thead>
<tr>
<th>WEIGHT OF INTESTINE</th>
<th>PER CENT OF DRY AND FAT-FREE INTESTINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moist</td>
<td>Dry</td>
</tr>
<tr>
<td>No. Av. WT. (Gm.)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Per cent of B.W.*</td>
</tr>
<tr>
<td>26 200</td>
<td>3.09</td>
</tr>
<tr>
<td>26 200</td>
<td>2.04</td>
</tr>
<tr>
<td>P value†</td>
<td>.01</td>
</tr>
<tr>
<td>Significance</td>
<td>H.S.‡</td>
</tr>
</tbody>
</table>

† Significance of the difference between the averages for normal and for tumor-bearing rats.
‡ Highly significant.
§ Not significant.

a) In terms of final body weight (including the tumor), the percentage of intestine is much lower in tumor-bearing animals (2 per cent) as compared with the normal controls (3 per cent). The same is shown for the value of dry and fat-free intestine as percentage of body weight (0.49 for controls as compared with 0.36 for tumor-bearing animals).

b) The percentage of cholesterol is the same in the intestines of both tumor-bearing and normal rats. The percentage of phospholipid is significantly higher in the intestine of the tumor-bearing animals.

c) The neutral fat content of the intestines of the animals bearing tumors is much below that of the controls (1.1 per cent of the dry and fat-free intestine weight as compared with 10 per cent in the controls).

d) The value for unsaponifiable matter other than cholesterol is much lower in the tumor animals, namely, 1.1 per cent of the dry and fat-free intestine, as compared with 1.9 per cent in the controls.

The significance of the differences in (a) is brought out when a comparison is made between the dry extracted intestines, expressed as percentage of the body weight, for the last samples in the normal series, and the same values expressed as percentage carcass weight (body weight less tumor) for the last samples in the tumor series (Table 2). For the normals, the average is 0.50 per cent of body weight and for the tumor animals 0.52 per cent of carcass weight, values which do not differ statistically. Thus, the intestine in the tumor-bearing animals has not grown with the tumor but has remained parallel in weight with the carcass (body weight less tumor weight).

The dry weight of the intestine as the percentage of moist weight is significantly lower in the tumor-bearing than in the normal animals. The enhanced water content of the tissues of the tumor-bearing animal has been noted previously for liver (10) and for other tissues (6).

The significantly higher values for phospholipid in (b) in the intestines of the tumor-bearing
animals may mean, first, an increased activity of
the intestine similar to that found in earlier work
with muscle (1); second, a greater production of
phospholipid for use in the tumor where lipid phos-
phorus has been shown to be concentrated (7); or,
third, a shift in the metabolism of the tissues to-
ward that of the tumor as indicated by Boyd et al.
(9) and earlier workers (6).

The lower values for neutral fat in (c) mean
merely that the fat of the intestine, like that of the
rest of the body, has been mobilized for energy in
the starving animal. The very low values for the
fraction in (d) consisting of total unsaponifiable fat
less cholesterol, also found to be low in earlier
work with adrenals and blood (8), indicate that
this fraction is important in connection with the
growing tumor. It may be simply stored energy
like the neutral fat but is more probably concerned
with growth, either of the tumor or of the host
body.

In these young animals the intestine seems to
grow along with the rest of the body until the tu-
mor becomes established. Then the tumor presum-
ably takes the material needed for growth of the
intestine, which then stops growing. Some interest-
ing light on this problem is obtained by exami-
nation of Donaldson's (4) charts on the rat. Thus,
our tumor-bearing animals at 250–300 gm. body
weight have intestinal weights of only 4–5 gm.,
values which correspond to a body weight in the
normal animal of about 100 gm. On the other
hand, the control rats of the same weight have an
intestinal weight of 6–7 gm., which corresponds to
their body weight in the Donaldson chart. The in-
ference is that the intestines of the tumor-bearing
rats do not grow after the tumor has become es-

dblished or after the weight of the carcass less the
tumor has reached 100–125 gm. The following cal-
culation may then be made: in a tumor-bearing
animal of 250 gm. in which 40 per cent of the
weight is tumor, the weight of the carcass less the
weight would be 150 gm. The tumor of 100 gm. is
growing fast and therefore requires more food—
perhaps twice as much as would be required for
maintenance. At death, then, the tumor animal
consists of a slowly growing or stationary host body
of about 150 gm. and a fast-growing 100-gm. tu-
mor. The total energy requirement would then be
that of an animal of more than 350 gm. (body re-
quirement of 150 gm. and a tumor requirement of
200 gm.). Another factor is the possibly increased
basal metabolic rate in tumor animals as discussed
by Fenninger and Mider (5). To meet these re-
quirements there is intestine enough to supply the
unsaponifiable fraction (unsaponifiable other
than cholesterol). These results indicate that the animal dies be-
cause of insufficient energy requirements. The stored fat is mobilized
(lipemia) and burned; probably body tissue is also
burned down to a starvation minimum, after
which the animal dies. From the results of other
experiments we know that the food intake con-
tinues up until 2 or 3 days before death at a level
equal to that of the normal control.

The growth impulse in the tumors is obviously
much stronger than that in the normal body tis-
sues, since it stops growth in the animal's body and
consumes the stored energy. What is the basis of
the growth impulse? What is the growth factor? The
pituitary has been implicated, either directly
or indirectly through other organs, for example, the
adrenal. As an indication of adrenal involvement,
the "other sterol" fraction has been found in earlier
work (8) to be notably less in the adrenals of tu-
mor animals than in the controls. The same was
found for blood plasma (8). In the present work
the unsaponifiable fraction of the intestine is much
lower in the tumor-bearing animals than in the
controls. This fraction can be assumed to be re-
lated to the growth of the tumor, perhaps as a
growth-promoting substance or as raw material
for growth. The fraction contains desoxycorti-
costerone to the extent of about 50 μg/intestine
in the normal animal, and also the fat-soluble vita-
mins which would appear in the extract from the
alkaline saponification mixture. Further study of
this fraction is indicated and will be undertaken.

From the considerations noted above, the infer-
ence may be made that the starvation and final
death of the rats with tumors are due to insufficient
intestine, perhaps with exhaustion of the "other
unsaponifiable" fraction. The intestine probably
stops growing soon after transplantation (10 days),
while the tumor grows rapidly, with the result
that not enough intestine is present to supply the
needs of the animal. The stored fat is used and
finally the animal dies, although abundant food is
available. The part played by the "other unsaponi-
ifiable" fraction in these events remains to be de-
termined.

SUMMARY

In this study of the intestine of rats bearing
Walker carcinoma 256 as compared with that of
normal rats, the following differences were noted:
(a) the small amount of intestine relative to body
weight; (b) low values for neutral fat; (c) signifi-
cantly higher phospholipid content and normal
cholesterol; and (d) the low values of the "other
unsaponifiable" fraction (unsaponifiable other
than cholesterol).

These results indicate that the animal dies be-
1 Values obtained through the kindness of Dr. Ethel Ash-
worth of the Department of Medicine.
cause the amount of intestinal tissue is insufficient to support life and growth in the face of the competition of the tumor. The deficiency in the "unsaponifiable" fraction is probably a factor.

REFERENCES
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W. R. Bloor and Frances L. Haven