Intestinal Absorption of Cholesterol by the Nephrotic Rat

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Exogenous cholesterol, absorbed from the intestinal tract, is transported into the blood by the lymph of the thoracic duct. By means of thoracic duct cannulation and subsequent lymph collection following stomach feeding of 100 mg. of cholesterol dissolved in olive oil, it was found that the nephrotic rat has a diminished rate of cholesterol absorption. This could not be ascribed to a deficiency of lymph flow or of bile in the intestinal tract.

Although recognized for many years, the mechanism of hypercholesteremia in the nephrotic state remains to be determined. Studies of lipemia and other phases of nephrosis have been facilitated by the observation of Heymann and Lund that the chronic disease produced in rats by injection of rabbit anti-rat kidney serum rather closely simulates the nephrotic state as it is observed in humans. It was previously suggested that retention of excess cholesterol in the plasma might be causally related to the accumulation of excess bile acid consistently found in plasma of humans and rats with nephrosis. In the present investigation, we have utilized the experimental nephrotic rat to determine whether or not an alteration in the magnitude of absorbed dietary cholesterol plays a role in contributing to nephrotic hypercholesterolemia. A quantitative estimation of the amount of cholesterol absorbed from the intestinal tract was made possible by the previous demonstration from this laboratory that all absorbed cholesterol is transported via the thoracic duct lymph.

Materials and Methods

The nephrotic syndrome was produced in 7 week old male rats (Long-Evans) by intravenous injection of 0.5 cc. of rabbit anti-rat kidney serum on each of two successive days. The serum was prepared according to the method of Heymann and Lund. Ten days later the nephrotic state was well developed, as shown by the presence of lipemia, ascites, and generalized edema. At that time, and following an overnight fast, thoracic duct cannulation was performed as previously described in a group of nephrotic and normal control rats. Immediately postoperatively, each rat was stomach fed 100 milligrams of cholesterol dissolved in 3 cc. of olive oil. Thoracic duct lymph then was collected separately during two subsequent 24-hour intervals, the rats receiving only 0.5 per cent saline to drink during this period. Data was obtained from 7 nephrotic and 12 control animals during the first 24-hour interval, and from 6 nephrotic and 6 control rats during the second 24-hour period, the instances in which adequate continuous flow of lymph was observed and in which no evidence of obstruction of the thoracic duct by the cannula was found at autopsy.

Plasma total cholesterol was determined from tail blood obtained just prior to the cannulation, and the volume and concentration of cholesterol of each lymph specimen were determined according to techniques previously described.

Results

The data are presented in table 1. The average volume of lymph collected from the two groups was somewhat larger in the nephrotic rats in the first 24-hour collection period, but was somewhat less in this group of rats during the second 24-hour interval. The average concentration and total content of cholesterol in the lymph collected in the first 24-hour period were about one-half of the values obtained in the control group of animals, although there was essentially no difference in the concentration and total contents of cholesterol of the lymph collected from

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TABLE 1.—Cholesterol Content of Thoracic Duct Lymph of Nephrotic and Normal Rats*

<table>
<thead>
<tr>
<th>Type of Rat</th>
<th>No. of Rats</th>
<th>Av. Wt. (Gm.)</th>
<th>Av. Total Plasma Cholesterol (mg./100 cc.)</th>
<th>Lymph Volume and Cholesterol Content 0 to 24 Hours</th>
<th>24 to 48 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lymph Volume (ml.)</td>
<td>Concentration (mg./100 cc.)</td>
</tr>
<tr>
<td>Nephrotic</td>
<td>7</td>
<td>302</td>
<td>(212-190)</td>
<td>53</td>
<td>30</td>
</tr>
<tr>
<td>Control</td>
<td>12</td>
<td>299</td>
<td>(40-71)</td>
<td>58</td>
<td>(20-70)</td>
</tr>
</tbody>
</table>

* Following stomach feeding of 100 mg. of cholesterol in 3 ml. olive oil.
† Figures in parentheses refer to range of values.

the two groups during the second 24-hour collection period.

DISCUSSION

The hyperlipemia and hypercholesteremia of the nephrotic state are primarily endogenous in origin. The present study was performed to assess the contribution that dietary cholesterol might add to this endogenous hypercholesteremia. The data suggest that dietary cholesterol plays an insignificant, if any, role in nephrotic hypercholesteremia as observed in the nephrotic state in rats. Indeed, the data demonstrate a significantly diminished absorption of dietary cholesterol in the nephrotic rat. This could not be attributed to a decreased volume of lymph since an adequate flow of lymph occurred. In unpublished studies we have observed that the nephrotic rat excretes a volume of bile greater than that of the normal rat, and it contains an increased amount of bile acids. Therefore, the diminished cholesterol absorption of the nephrotic rat cannot be ascribed to a deficiency of bile or of bile acids. It is possible that edema of the intestinal wall, or other factors, underlie the diminished intestinal absorption of cholesterol in the nephrotic rat.

SUMMARY

Thoracic duct lymph was collected from a group of normal rats and a group of rats with experimental nephrosis, following administration of a test dose of cholesterol dissolved in olive oil. The data demonstrate a diminished absorption of cholesterol by the nephrotic rat which cannot be ascribed to a decreased volume flow of lymph or to a deficiency of bile or bile acids.

REFERENCES

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