The amounts of cholesterol in β-lipoprotein were similarly reduced and $\frac{\alpha}{\alpha+\beta}$ ratios were increased. There was no consistent effect on lipid phosphorus concentrations. Cobalt in the diet did not seem to influence activity of the thyroid. When given either in the diet or intravenously, cobalt did not change the structure of the pancreatic α-cells. (2) Subcutaneous injection of cobaltous chloride generally increased the incidence and severity of aortic lesions and concentration of cholesterol in blood. These findings are similar to those of Caren and Carbo in the rabbit(8). (3) The influence of cobalt in the diet on lipid pattern and aortic lesions was opposite to that of parenterally administered cobalt. It did not produce other effects indicative of previously reported specific systemic actions. Siperstein, Nichols, and Chaikoff(1) concluded that blood-cholesterol-lowering effect of ferric chloride given in the diet was due to precipitation of bile acids, resulting in decreased cholesterol absorption. It is concluded here that the effect of cobalt in the diet of cholesterol-fed chickens similarly is due to a local action in the intestinal tract.

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Abnormal Fat Absorption in Tumor-Bearing Rats.* (24081)

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A number of workers have shown that loss of body weight accompanying tumor growth is associated with depletion of total body lipids(1,2). This loss in body weight, however, is not due to anorexia alone, since force-feeding will not overcome depletion of carcass lipid previously described(3). Despite this lipid loss, a progressive, marked hyperlipemia is often associated with tumor bearing in rats when tumor weight exceeds 10% of total body weight(4). Studies of intestinal absorption in cancerous animals have never been described, although absorption may play a very signifi-

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cant role in the above phenomena. Consequently, gastrointestinal absorption of fat in normal, tumor-bearing and pair-fed control rats by use of triglyceride labeled with I^{131} was investigated.

Materials and methods. Three groups of Sprague-Dawley male rats were maintained on isocaloric, synthetic diet complete with salts and vitamins.† The tumor-bearing groups ate *ad libitum* while controls were pair-fed. Water intake was not restricted. Tumors were transplanted by the usual trochar technic into subcutaneous tissue of right inguinal region of rats weighing 130-150 g, using a piece of Walker Carcinoma 256.‡ Tumors were allowed to grow to 15-18% of total body weight, at which time the rats of all 3 groups were placed in restraining cages after thoracic duct cannulation by the technic of Bollman *et al.* (5). All experimental animals had free access to 1% sodium chloride but were not fed throughout post-operative period. Twenty-four hours after surgery, 0.5 ml of I^{131} labeled triolein (Abbott's Laboratories) dissolved in olive oil (total activity 20 μc/ml) was introduced into stomach by gavage, followed by 5 ml of water. Lymph was collected for 6 hours following feeding of radioactive diet. The collected lymph was diluted with 10% potassium iodide and an aliquot of this was mixed with some plasma. The lymph lipids were coprecipitated with plasma proteins upon subsequent addition of 40% trichloracetic acid. The precipitate was washed with 10% KI, and any inorganic I^{131} present was removed (6). Radioactivity of lipid precipitates described above was determined in deep-well scintillation counter (Technical Measurement Co.). The results were expressed in radioactivity in any given sample as percent of total dose administered (%TD).

Results. The percent of total dose found in lymph of normal, pair-fed control and tumor-bearing rats is shown in Table I. These data indicate that tumor-bearing animals absorb considerably less fat *via* the thoracic duct lymph, than do normal and pair-fed control rats. (Ptumor, control $<<.001$; Ptumor, normal $<<.001$; Pnormal, control $= 1$). Furthermore, it was observed that cannulation eliminated hyperlipemia in both normal and tumor-bearing animals. Therefore, it was concluded that the hyperlipemia of the tumor-bearing rat may be primarily attributed to absorbed, exogenous fat. In view of this, Begg's contention(3) appears valid, that it is unlikely that hyperlipemia of tumor-bearing animals is due to mobilization of endogenous fat. The apparent paradox of excessive hyperlipemia coupled with markedly decreased fat absorption might be resolved by assuming that rate of fat clearance from blood is profoundly reduced in the tumor bearing animal. Reference to this has been made by others(7). The fat absorbed by lymph, then, accumulates in blood and creates the observed hyperlipemia.

TABLE I. Lymphatic Absorption of Dietary Fat Expressed in % of Total Dose (% TD).

Type	Animals No.	Animals Mean body wt, g	% TD in lymph Mean	% TD in lymph S.D.
Normals	8	195	15.3	5.1
Controls	5	204	15.4	5.1
Tumor (15-18%)	4	235	5.3	0.5

Loss of carcass lipids may be primarily attributed to marked decrease in fat absorption, and this, coupled with the high energy requirement imposed upon the host by the tumor(8), would account for the cachectic condition of the tumor-bearing animal.

Summary. Absorption of triglyceride labeled with I^{131} in the rat bearing Walker Carcinoma 256 has been studied. The amount of fat recovered from thoracic duct lymph of the tumor rat is significantly less than that recovered from lymph of normal and pair-fed control rats.

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† National Biochemical Corp. Vit. B Complex Diet supplemented with Vit. Diet Fortification Mixture and Salt P-H mixture.

‡ Courtesy of Dr. J. White, Nat. Cancer Inst., Bethesda, Md.

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Effect of N-Desacetyl Thio Colchicine (TC) and N-Desacetyl-Methyl-Colchicine (MC) on Rat Fetus and Litter *in utero*. (24082)

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TC, when first synthesized by Velluz and Miller(7), had antimitotic activity in non-toxic doses. The single LD-50 for rats, according to Branceni, *et al.*(1) is 175 mg/kg for intraperitoneal doses and 37 mg/kg for intramuscular doses. This is approximately 25 to 100 times less than LD-50 for Colchicine. Rats tolerated daily i.p. doses of 3 mg/kg indefinitely, and 8.5 mg/kg for 21 consecutive days. In preliminary experiments, Jaquier and Feyel-Cabanes (personal communication) found that 10 daily doses of 2.5 mg/kg starting on 2nd, 4th, 8th and 12th day of gestation, had no effect on rat fetuses from 2nd to 12th day, nor when given on 5 consecutive days after 16th day of gestation. TC, however, arrested embryonic development when given beyond 12th day of gestation. Its action appeared directly on the fetus and not on the mothers.

Methods. Experiments were conducted with Long-Evans strain rats bred and reared in our own colony. Only animals which had one satisfactory previous litter were used. Animals were kept on White Breeding diet of Long-Evans, were approximately 6 months old and weighed 250 g each. The compound was given l.p. to groups of rats in different stages of pregnancy. Onset of gestation was determined by massive sperm findings in the vagina. Pregnant animals were kept in single stainless steel cages to avoid urinary or fecal contacts. Mother rats were sacrificed under ether anesthesia on 21st day of gestation. Uteri were removed and contents recorded, weighed and fixed. The fetuses were sectioned or cleared to study skeletal developments. Maternal internal organs were inspected macroscopically, fixed in formalin and studied in H and E paraffin sections.

Results are listed in Tables I and II. TC had no effect on subsequent ovarian cycles or litters when given twice, prior to insemination, to 6 rats (Table II). Doses of 5 mg/kg, given the morning after insemination (day 0) and on day 1 of gestation, were also without effect on litters of 12 rats. Two doses of 7 mg/kg, given on 4th and 5th day of gestation, led to resorption of 23% of fetuses, and complete litter failure in 20% of the experimental group (3 out of 15 rats). Three fetuses were also found dead and 3 others stunted. On 7th and 8th day of gestation, at time of fetal implantation, doses of 5 mg/kg destroyed 34% of all fetuses but only 20% of all litters, whereas 7 mg/kg doses destroyed 65% of all fetuses, and 36% of all litters. On 10th day of gestation a single dose of 1 mg/kg had no effect; 2.5 mg/kg of TC led to resorption of 30% of all fetuses. Only one stunted surviving fetus was found after single 7 mg/kg dose. On 11th day of gestation, a single dose of 5 mg/kg destroyed in one series all litters completely, but in a second series, destroyed only 89% of all litters. However, 2 doses of 5 mg/kg given on 11th and 12th days of gestation destroyed all litters. The 5 mg/kg dose, given on 15th and 16th days of gestation destroyed

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