Neoplasia introduces into the body a new race of cells derived from tissues common to ontogeny but differing biologically, structurally, and chemically from their ancestors. The new members of the community of organs and tissues intrude themselves on the nicely balanced economy of the organism. Adjustments are necessary. The stresses imposed by the new growth often transcend the power of homeostatic mechanisms to maintain the host's integrity.

Many disease processes, neoplastic or otherwise, kill by producing anatomic lesions that are incompatible with life. Unrelieved obstruction of a hollow viscus or essential pathway, ulceration with overwhelming sepsis or exsanguinating hemorrhage are lethal regardless of their etiology. A few neoplasms secrete biologically active substances either identical with or similar to naturally occurring hormones. The intense pharmacologic responses elicited ultimately threaten the existence of the host. Some neoplastic and related diseases kill without producing either of these effects. A primary anatomic lesion has often been eradicated by effective therapy, but discontinuous dissemination of tumor cells through the body is found at necropsy. The structural defects produced by the metastases are seldom of sufficient magnitude to threaten life solely for anatomic reasons. Extensive involvement of the liver, for instance, is rarely associated with a syndrome characteristic of hepatic insufficiency. If the same lesions were composed of scar tissue rather than neoplastic cells, the affected individuals might not only be alive but in reasonably good health. The mere presence of an adequate concentration of growing neoplastic cells within the body may cause death. Such cells are cancerous, and their deleterious effects must be described in terms of pathologic physiology.

 Pronounced avidity of cancerous tissue for amino acids reflects its remarkable capacity for protein synthesis. Isotopically labeled glycine (23, 40, 51, 64), tyrosine (48, 62), or methionine (10, 31) administered orally or parenterally is taken up by various neoplasms in concentrations approximating those found in the normal structures known to be intimately concerned with protein metabolism. Some investigators have demonstrated that the labeled compounds have been incorporated into tumor protein. The concentration of an isotope in the tumor declines less rapidly with time than it does in normal tissues (23, 51). Reduction in specific activity does not necessarily indicate establishment of an equilibrium of isotope between the cancer and other tissues. A progressively growing neoplasm, unlike the normal structures of the adult organism, increases its mass constantly through continuous manufacture of protoplasm. Anabolism exceeds catabolism. The amount of tagged protein formed by the tumor will depend in some measure on the concentration of labeled amino acid present in its substrate. The specific activity of the plasma reaches a maximum level, then falls progressively with time. Contribution of nonisotopic amino acids from body

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stores or dietary sources probably dilutes the specific amino acids being studied. If the rate of protein synthesis is reasonably constant in the neoplasm, its concentration of isotope necessarily decreases, yet the total amount may increase steadily as long as tagged precursors remain in the blood. Data on the relation of time to the total labeled amino acid in neoplastic tissue, both protein and nonprotein, may yield valuable information. How much exchange exists between the neoplasm and its host? Is the nitrogen metabolism of the cancer essentially a one-way passage? Is the necrotic material in a tumor simply dead and inert, or do split products gain access to the blood stream? Tumors in which the vascular bed is essentially circumferential and those penetrated by a rich network of blood vessels might give different results. The answers to these questions seem to lie within the realm of isotope research, probably cannot be acquired by simpler technics, and are important in formulating a better concept of the tumor-host relationship. An excellent discussion of the use of isotope technics in the study of the protein metabolism of tumors and normal tissues has been published recently by Zamecnik (63).

What is the ultimate source of building blocks used by the growing cancer? The immediate source must be the blood plasma, the composition of which the body attempts to maintain within fairly narrow limits. The principal constituent of neoplastic tissue other than water seems to be protein. Therefore, a study of nitrogen metabolism may be expected to reflect the source of tumor protein. Cramer and Pringle (15) attacked this problem in 1910 by studying the nitrogen balance of rats during the first 2 weeks of growth of the Jensen sarcoma. "In our experiments," they wrote, "the cells of the new growth derived their nitrogenous matter necessary for the building up of new tissue by a sparing action on the protein metabolism. The tumor cells do not proliferate at the expense of the tissues of the host nor is there any evidence that they have a higher affinity for nutritive material than the growing cells of the host." The authors recognized that this physiologic state was replaced later in the course of development of the Jensen sarcoma by pathologic effects which they did not describe. The "sparing action on protein metabolism" that Cramer and Pringle postulated refers principally to a greater increment in mass per unit of nitrogen stored, reflecting the considerably lower concentration of nitrogen and higher water content of the neoplasm they studied (16). Their meager data on nitrogen retention only suggest that the cancerous rats actually stored more nitrogen than the normal rats that ate the same amount of food.

Several observers reported that various transplanted rodent tumors grew at the expense of host tissue, as shown by progressive increase in tumor mass, while carcass weight (animal minus tumor) declined (6, 32, 33, 38, 39). The specific constituents of the carcass tissues that were lost during tumor growth were not defined. Some malignant tumors possess an extremely high priority for building blocks. F. R. White (61) proved conclusively that a transplantable mouse mammary adenocarcinoma could obtain enough nitrogen for its growth from the normal tissues of its host when the diet contained almost no nitrogenous substances. The Walker rat carcinoma 256 grew, although at a diminished rate, even though a strongly negative nitrogen balance was induced by injection of cortisone acetate (29).

It was shown subsequently that large specimens of the Walker carcinoma contained more nitrogen than was stored by their hosts during the course of tumor growth when they ate freely a semi-synthetic diet adequate for growth, pregnancy, and lactation in normal rats (37). Comparable data, listed in Table 1, were obtained from a study of the Murphy-Sturm transplantable rat lymphoma. The contribution of ingested nitrogen to the metabolic pool may be adequate to provide protein building blocks for this neoplasm when it comprises up to 10 per cent of the total body weight (rat plus tumor), but larger lymphomas contain more nitrogen than could have been derived from dietary sources. A similar situation with respect to the Walker carcinoma may be inferred from data reported recently (35).

Sherman et al. (52) found that most of the organs and tissues that lost nitrogen during the course of simple caloric starvation also relinquished nitrogen during progressive growth of Walker carcinoma 256. The liver and spleen actually acquired nitrogen, at least temporarily. No consistent significant differences between urinary and fecal excretion of nitrogen by rats bearing Walker carcinoma 256 and pair-fed noncancerous rats of the same age, sex, and initial weight have been observed in this laboratory during the greater part of tumor growth if the cancerous rats ate freely a semi-synthetic diet adequate for growth, pregnancy, and lactation in normal rats. One suspects that the nitrogen lost from body tissues in the cancerous subjects was translocated to the neoplasm. The nitrogen lost from tissues represented only potential building blocks for the cancerous cells, since the methods used measured over-all or net change rather than step-wise alterations.

Norberg and Greenberg (40) injected carboxyl-
Ingested glycine-C\textsuperscript{14} intravenously into C3H mice bearing transplanted Gardner lymphosarcoma. The specific activity of the proteins of plasma and various tissues was determined at intervals up to 48 hours and compared with that of the same moieties in noncancerous mice of the same strain. The sarcomatous animals incorporated more isotope into their proteins than did the normal mice at corresponding periods of observation. The uptake was lower in the protein of the wasting muscles of the tumor-bearers than in the muscle protein of normal mice. These differences suggested increased protein turnover among cancerous mice by those parts of the body concerned with protein synthesis and transport, with muscle serving as a main source of protein precursors to supplement dietary intake.

Undoubtedly, some more indolent cancers may obtain adequate supplies of building blocks from ingestion of phosphorus and potassium in the proportion in which the three elements exist in the principal tissue or tissues being built or being destroyed. Active osseous metabolism requires that the phosphorus balance be corrected for the phosphorus bound to calcium in bone. Most of the protoplasm of the body is in skeletal muscle. For all practical purposes, the ratio among nitrogen, phosphorus, and potassium found in muscle may be used to indicate changes in protoplasmic mass of the average individual. Albright and other investigators have shown the essential correctness of this thesis, since these elements are excreted or stored in such proportions by relatively normal subjects and those with certain non-neoplastic diseases (4, 20, 49, 58). It should be emphasized that calculations must be made only on a balance basis, the algebraic difference between ingestion and excretion of a particular substance. Any

### TABLE 1

<table>
<thead>
<tr>
<th>Rat</th>
<th>Tumor weight (per cent)</th>
<th>Change in carcass N (gm.)</th>
<th>Net N balance nitrogen* (gm.)</th>
<th>Tumor nitrogen + plus tumor N balance (gm.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.6</td>
<td>+0.069</td>
<td>+0.444</td>
<td>+0.404</td>
</tr>
<tr>
<td>2</td>
<td>8.3</td>
<td>+0.310</td>
<td>+1.062</td>
<td>+0.306</td>
</tr>
<tr>
<td>3</td>
<td>10.6</td>
<td>−0.589</td>
<td>+0.450</td>
<td>+0.446</td>
</tr>
<tr>
<td>4</td>
<td>22.7</td>
<td>−1.076</td>
<td>+0.494</td>
<td>−1.595</td>
</tr>
<tr>
<td>5</td>
<td>24.5</td>
<td>−1.470</td>
<td>+0.037</td>
<td>−1.415</td>
</tr>
</tbody>
</table>

* Tumor nitrogen bears a negative sign, since it is not available to the uses of the body under conditions of progressive tumor growth. The net nitrogen balance plus tumor nitrogen (column 6) is the algebraic sum of columns 4 and 5.

No information is available on the sources of nitrogen for spontaneous neoplasms in experimental animals, but metabolic studies on a few patients with lymphomatous diseases have been made which provide some insight into the clinical situation. The experiments were based on the principle that an individual fed a constant diet will achieve a dynamic equilibrium among its various compartments. Protoplasm contains nitrogen, phosphorus, and potassium in ratios characteristic of its particular type. Storage or wastage of protein will be associated with retention or excretion of phosphorus and potassium in the proportion in which the three elements exist in the principal tissue or tissues being built or being destroyed. Active osseous metabolism requires that the phosphorus balance be corrected for the phosphorus bound to calcium in bone. Most of the protoplasm of the body is in skeletal muscle. For all practical purposes, the ratio among nitrogen, phosphorus, and potassium found in muscle may be used to indicate changes in protoplasmic mass of the average individual. Albright and other investigators have shown the essential correctness of this thesis, since these elements are excreted or stored in such proportions by relatively normal subjects and those with certain non-neoplastic diseases (4, 20, 49, 58). It should be emphasized that calculations must be made only on a balance basis, the algebraic difference between ingestion and excretion of a particular substance. Any
panied by an increased storage of the other two elements in the direction of the proportions in which they were found in the neoplasm rather than in muscle.

Fenninger and Waterhouse (21) studied one patient with acute leukemia who ate a constant diet and retained nitrogen for 67 days. The proportions of nitrogen to phosphorus and potassium stored were neither those characteristic of muscle nor of the patient’s leukemic cells. They derived an equation to determine the partition of nitrogen between the host and the neoplasm. Application of the formula indicated that all of the ingested nitrogen retained and additional nitrogen derived from the normal tissues were used for tumor formation. The calculated rate of tumor growth correlated well with clinical and autopsy findings. Similar studies in a patient with lymphosarcoma indicated that excess nitrogen excreted prior to therapy was derived mainly from host tissues, though the tumor grew progressively. Induction of a clinical remission with ACTH caused excretion of nitrogen, phosphorus, and potassium in the ratio in which they were found in the subject’s neoplasm.

Some clinical cancers or related lesions, then, may derive building blocks from body stores. This again is a net result and does not reflect the actual dynamics of intermediary metabolism. The methods used in these studies seem basically sound but probably can be used only when relatively large quantities of rapidly growing neoplasms are present. The common observation of weight loss in cancer patients whose neoplasms are obviously growing may be further evidence for translocation of protein from normal to neoplastic tissue. The demonstration of negative nitrogen balance in such individuals would permit of no other rational conclusion.

If the growing cancer can derive nitrogenous building blocks from normal tissues, it should be able to draw on more labile body proteins. Parfentjev and Duran-Reynals (43) observed a decrease in Proteus agglutinin of chicken sera throughout the development of Rous sarcoma. Eighty per cent of the sera from people with nonneoplastic diseases agglutinated with Proteus antigen, but only 28 per cent of the sera from cancer patients whose lesions were untreated reacted similarly (42). Diminished antibody titers and associated impairment of immunologic response in patients with leukemia (22) and Hodgkin’s disease (19, 57) have been reported. Wharton et al. (60) found that rapidly growing neoplasms of mice yielded lower titers of antisera when immunized with various antigens than did similarly treated normal mice. The difference in response was not found after regression of tumors nor in mice that bore slowly growing neoplasms. They also found evidence for an abnormally high destruction of antibody protein in cancerous mice, since passive transfer of immune serum from normal to cancerous mice failed to increase the antibody titer of the tumor-bearing subjects to the same extent as it did in noncancerous animals. Lastrapes1 studied rabbits that had been immunized against horse serum prior to intratesticular transplantation of the Brown-Pearce carcinomas. Progressive growth of the cancer with or without subsequent regression was accompanied by pronounced reduction in antibody titer. Noncancerous rabbits maintained their precipitins against horse serum at a high level. No difference in the total circulating gamma globulins was detected among the three groups.

Perhaps the cancerous host diverts both antigenic and antibody proteins to serve bodily functions and the demands of tumor growth. A hierarchy exists among the various uses for protein in the animal’s economy. Apparently, the priority ratings may be altered in response to poorly defined stresses. The work of Cannon and his colleagues is pertinent (12). Elimination of an essential amino acid from the diet or reduction in food intake to the extent of protein depletion diminished the antibody response to antigenic stimuli. Failure of alimentation frequently accompanies the growth of cancer in man and experimental animals. This factor must be considered in evaluating immunologic responses.

Hypoalbuminemia often accompanies clinical cancer (18, 27, 34, 44, 45, 50). It may be found among those patients in good nutritional state whose neoplasms are small. The degree of hypoalbuminemia increases as cancerous growth progresses. The concentration of plasma albumin falls more rapidly than does the concentration of total plasma proteins due to an absolute increase in globulins, particularly alpha globulins and fibrinogen (34). A decrease in serum albumin is frequently considered presumptive evidence of depletion of body protein. In those patients with pronounced anorexia and wasting of body tissue, it seems probable that protein depletion has occurred and doubtless has contributed to the production of low plasma albumin. Diminished food intake need not be the only mechanism by which hypoalbuminemia is produced in cancerous patients. On theoretical grounds, at least, the translocation of nitrogen from general body stores to form neoplastic tissue might bring about a reduction in plasma

1 Personal communication.
albumin. On the other hand, the finding of hypoalbuminemia in relatively early cases of cancerous growth suggests that some other mechanism must be operating.

Cuthbertson and Tompsett (17) described a fall in plasma albumin and marked rise in plasma globulins following trauma to dogs. Maximum alterations in the concentrations of plasma proteins preceded the catabolic phase of reaction to injury. Peters (46) observed a rapid decline in serum albumin during the 48 hours immediately following surgical operations. Nitrogen excretion was not large during this period, nor could blood loss, shock, or hemodilution account for the change. While an insult sufficiently severe to initiate the “stress reaction” mediated through the adrenal glands characterized the work of Cuthbertson and Tompsett and of Peters, no such acute episode can be demonstrated in the history of the average cancer patient who has not been subjected to definitive surgery. It is possible, however, that the same or similar mechanism may operate in the absence of an acute stress. Evidence for altered hepatic function in the genesis of hypoalbuminemia is provided by workers who studied certain standard liver function tests in patients with cancer, principally those of gastrointestinal origin (1, 5, 47, 54). They found that a considerable proportion of the tests used gave results that would not be expected in an average, healthy adult. The specificity of various tests of hepatic function is open to considerable question, but it can hardly be denied that the cancerous subjects they studied had some metabolic alteration in which liver dysfunction played a part. Dysfunction is used in the sense of any deviation from the accepted norm rather than connoting a parenchymal disturbance so severe as to seriously limit the capacity of the organ to metabolize the substances studied. The key position that hepatic tissue holds in the body’s metabolism would require it to react to various stimuli that threaten the existence of the host. It is not surprising that cancer should be one such stimulus. The mechanism by which hypoalbuminemia is attained in the patient with comparatively early cancer is by no means clear and requires intensive investigation. It is unfortunate that the information currently available on the state of plasma proteins among cancerous subjects is limited to observations of concentration of these substances in the circulating plasma. A good study of the total circulating proteins might add much to our knowledge.

Whereas the dispensable fraction of nitrogen in normal components of the body is available to meet changing demands, that within cancerous cells is lost unless progressive growth of the tumor can be arrested. Large Walker carcinomas which had killed their hosts seldom contained as much nitrogen as was lost from the bodies of rats that died of simple caloric starvation (37). Depletion of normal protein stores doubtless contributes importantly to the deleterious effects that neoplasms produce in their hosts.

Synthesis of proplasm requires expenditure of energy. Cachexia is a common consequence of cancer both in man and experimental animals, but the mechanism by which this state is attained is difficult to evaluate. Cramer (14) found that the respiratory quotients of rats bearing Jensen sarcoma did not differ from those of normal rats until weight loss occurred in the cancerous host. Thereafter, more carbon dioxide was eliminated per unit of oxygen inspired. Combustion of fat reduces the nonprotein respiratory quotient. Progressive growth of either Walker carcinoma 256 or the Murphy-Sturm lymphoma in rats is accompanied by steadily decreasing food intake. Anorexia does not commence with the inception of tumor growth but apparently starts after the neoplasm has reached a critical size. Rats in which the Walker tumor grew progressively lost significantly more lipid than did pair-fed noncancerous rats of the same age, sex, and initial weight (36). The caloric value of the amount of fat lost equaled the total calories lost from the body during tumor growth as determined by bomb calorimetry (35). It seems clear from carcass analysis of rats bearing the Walker tumor that progressive lipid loss does not begin until the onset of anorexia.

Haven, Bloor, and Randall (34) stated that the proportion of carcass lipids in rats bearing Walker carcinoma 256 varied inversely with the size of the tumor and that the blood lipids were often markedly increased, owing principally to an increase in fatty acids. They showed (25) subsequently that the lipemia reached a peak during the course of cancerous growth, after which interval blood lipids declined to normal values before the death of the subject. Begg and Dickinson (8) noted lipemia in the sera of rats bearing Walker carcinoma 256 which was not present in noncancerous rats fed the same diet. Adams (2) found that CBA mice bearing Gardner lymphosarcoma developed fatty livers if they were fasted for 48 hours. This phenomenon was not observed either during the very early or very late phases of tumor growth. Perhaps lipemia reflects an increased mobilization of lipids to meet increasing energy demands. The rats in which there is a progressive growth of the Walker carcinoma 256 use saturated fatty acids preferentially and seem to hoard the unsaturated forms (25).
The lipid content of the Murphy-Sturm lymphoma, the Walker carcinoma (37), and the Gardner lymphoma (3) also decreases as the neoplasms grow larger. The reason for this is not known. It might conceivably be related to availability of lipid to the tumor, since rats which ingested a diet containing 72 per cent of total calories as fat (Crisco) maintained a constant lipid concentration in their cancers of approximately 2 per cent.

Carbohydrate and fat provide the principal sources of energy for most mammals. The caloric expenditure of these substances by rats bearing the Walker carcinoma was estimated by a combination of chemical analysis of body lipid and bomb calorimetry (36). A constant relationship was suggested between energy expenditure and tumor growth, but the former was independent of growth rate. Further experimentation with more precise techniques is required to establish this point.

Weight loss of itself implies excessive expenditure of energy only in relation to dietary intake. Diminished alimentation is accompanied by decrease in basal metabolic rate in average healthy subjects (9, 30). Does the cancerous individual react in the same way to the stress of reduction in food intake? This question cannot be answered categorically. Pertinent data regarding the clinical situation indicate great variation in the basal energy expenditure of the subjects studied. It may be significant, however, that the literature records few instances of significantly lowered basal metabolic rates among patients with extensive cancerous lesions, whereas definitely increased rates are listed frequently (11, 26, 38, 56). Some of the earlier workers believed that an increased energy expenditure in cancerous patients was of grave prognostic import.

The absence of weight loss among many patients whose cancers are amenable to definitive treatment indicates that malignant neoplasms do not increase the caloric requirements of their hosts at all stages in the evolution of the malignant state. Waterhouse, Fenninger, and Keutmann (59) studied eight patients with widely disseminated but different anatomic types of neoplastic or related diseases. They ate diets that should have provided adequate caloric and protein intakes for maintenance of weight in average healthy subjects of similar age and habitus. All except one febrile patient retained nitrogen. Four of the subjects spent more energy as calculated by Newburgh's method than the diets provided. The excessive caloric expenditure was not always reflected by loss of weight, since some patients with advanced cancer tended to store large quantities of water. These observations require confirmation, preferably by some other method for measuring caloric output.

Circumstantial evidence exists, then, for an increased energy expenditure by some cancerous hosts under poorly defined conditions. It may be useful to speculate on possible reasons for this phenomenon. In the final analysis, the basic mechanisms must involve either a failure of the organism to realize the potential caloric value of its food-stuffs or the initiation of some processes within the body that require expenditure of additional energy or both. The former idea seems rather improbable.

High rates of aerobic and anaerobic glycolysis characterize carbohydrate metabolism of most cancer tissues in vitro. There is good evidence that tumors glycolyze rapidly in the body as well. Efferent blood from the tumors studied in vitro by the Coris (13) contained less glucose and more lactic acid than did the afferent blood. Voegtlin et al. (55) demonstrated a decrease in the pH of the neoplastic tissue following parenteral administration of glucose to its host. From the first law of thermodynamics it follows that the total energy derived from aerobic or anaerobic degradation of glucose to carbon dioxide and water must be the same. This does not mean, however, that all the energy liberated can be used for metabolic processes. Current concepts suggest that high energy phosphate bonds are a major source of metabolic energy. Despite the high lactate content of efferent blood from cancers, no systemic acidosis can be demonstrated. Evidently, the lactate is metabolized by normal tissues, probably chiefly by the liver. If the lactate be oxidized to pyruvate, and the latter burned completely through the tricarboxylic acid cycle, then the full potential value of the parent carbohydrate can be realized. On the other hand, the lactate may be synthesized to glycogen before complete utilization. Such a route would require the investment of high energy bonds to establish lower energy bonds. The extensive use of such an indirect pathway would waste energy. Apparently, the cancerous organism is able to metabolize both carbohydrates and fats completely as far as their end products are concerned. No evidence of ketonuria or of an increase in titratable acidity of the urine was found during uncomplicated neoplastic growth.

Protein metabolism in the cancerous host may conceivably require more energy than in pair-fed normal rats. The nitrogenous constituents of normal tissues that are released into the blood stream can probably not be utilized directly by all the other cells in the body. They first must be built into materials that the cells can metabolize. Native proteins probably must be converted to plasma.
proteins, to polypeptides or amino acids if they are to be available for the synthesis of protoplasm. Amino acids may be deaminated in order that their residues may furnish needed energy. The specific dynamic action of protein seems to be due principally to cleavage and deamination or to other forms of molecular arrangement of nitrogenous substances. A heightened degradation, then, would be expected to increase specific dynamic action. Strieck and Mulholland (58) found that the ingestion of egg white by three cancer patients whom they studied did not increase the basal metabolic rate. This failure to observe specific dynamic action after protein ingestion deserves further study. It is possible that the cancerous individual at certain stages of tumor growth may be metabolizing proteins and amino acids at a maximum rate even under resting conditions; this fact, in part, may account for excess expenditure of energy.

The metabolic energy of foodstuffs available to the cancerous host will depend upon the relative efficiency of intermediary metabolism. Obviously, the growing neoplasm utilizes energy. This might be of little or no consequence if a large supply of combustibles were provided through a compensatory increase in appetite. This has not been observed. Anorexia restricts the availability of food for the organism, and the meager amount ingested must serve the needs of both host and cancer. Apparently, a considerable proportion of the energy available to the cancerous organism is utilized by the tumor. Thus, normal structures may be further deprived of energy sources.

Perhaps the foregoing discussion applies only to those cancerous subjects in which food intake is seriously impaired. Begg and Dickinson (8) fed Ingle's high fat diet in which the egg albumin was replaced by an equal amount of lactalbumin to circumvent the possibility that a relatively high intake of avidin might impede tumor growth. The animals received the diet from the time of weaning, and after they reached 100 gm. in weight the daily intake approximated 31 calories. Walker carcinomas commenced to grow when the rats weighed 290 gm. Most of the animals developed anorexia, but two rats maintained their appetites for 5 weeks when the tumors constituted 20 per cent of body weight. The carcasses (rat minus tumor) of the cancerous rats weighed 78 and 282 gm., respectively, while a normal rat of the same age and sex which had grown at the same rate while eating identical quantities of the same diet weighed 325 gm. The failure to achieve as good weight increment in the cancerous carcasses as in the noncancerous rats is doubtless due to the appreciably lower caloric intake provided. The important point to determine is the ultimate pathologic effects of cancerous growth in subjects whose protein and energy requirements are maintained through adequate alimentation. Begg and Dickinson (8) have already shown that anemia, adrenal enlargement, and depression of hepatic catalase activity occurred among their cancerous rats in the absence of weight loss from the carcass. It remains to be shown that the carcasses of the tumor-bearers had the same general composition as did the noncancerous control rats. Perhaps forced feeding merely prolongs the early period of tumor growth so that the onset of the starvation phenomenon is delayed. Other aberrations in the host's physiologic reactions may be equally lethal, for occasional rats ingesting our standard diet in unrestricted amounts maintain a good intake of protein and the principal calorigenic foodstuffs. These animals invariably contain considerable quantities of total body lipid at death and do not exhibit an "ante mortem rise" in urinary nitrogen excretion. Our knowledge of nitrogen and energy metabolism in cancerous hosts is far from complete.

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Some Aspects of Nitrogen and Energy Metabolism in Cancerous Subjects: A Review

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