DNA synthesis. The continued availability of thymidine-H^3 to the chick embryo from a single application is in contrast to its fate in mammals, where it is rapidly metabolized, and therefore labels nuclei over only a short period of time(11). A preliminary report(12) of work similar to the present study illustrates this species difference, while confirming nuclear migration in the neural tube.

It should be emphasized that the fundamental concept involved here is not that of nuclear migration in itself, but rather a recognition of the structure of the early neural tube as a columnar epithelium(13,14). Nuclear migration is a necessary accompaniment to the rounding up of the cell in mitosis and its subsequent elongation. The cell maintains its firm terminal bar attachment at the lumen as long as it is an element of a columnar epithelium, hence, the nucleus is drawn toward the lumen as the cell rounds up in preparation for division. Following mitosis, the nucleus is carried peripheralward as the cell elongates to renew its attachment to the outer limiting membrane.

Conclusions. Radioautographs of early neural tube of chick embryos treated with thymidine-H^3 for varying intervals of time give evidence substantiating the concept of interkinetic migration of nuclei. Synthesis of DNA occurs only in nuclei of peripheral part of wall, and does not take place in those of juxta-luminal zone. The period of DNA synthesis continues for at least 4 hours, but does not extend much beyond this time.

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Serum Adenosine Deaminase Activity in Cancer.*† (25015)

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Straub and his associates(1) reported that adenosine deaminase, the enzyme that catalyzes the deamination of adenosine to inosine, was present in plasma and was elevated in 92% of the 527 cancer patients studied. A similar frequency was reported by Letnansky and Seelich(2). Such a high frequency of elevated serum or plasma enzyme activity indicated possible diagnostic utility. Our previous studies on other serum enzyme activities in patients with cancer(3,4,5) showed that elevations in these activities were related more directly to growth or activity of tumor, rather than to its presence. It was accordingly decided to determine, first, activity of the serum adenosine deaminase in groups of normal persons and patients with

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TABLE I. Eight Patients with Cancer Who Showed Elevated Serum Adenosine Deaminase Activity at First Determination.

Diagnosis	Serum deaminase activity (units)
Reticulum cell carcinoma	16.2
Ca breast	21.7
Reticulum cell carcinoma	44.0
Lymphosarcoma	25.2
Ca breast	17.4
Ca ovary	20.6
Ca breast	28.2
Reticulum cell carcinoma	38.6

cancer. Secondly, activities of this enzyme were determined sequentially and at frequent intervals during periods of one to 2 months in 4 patients with cancer and were correlated with clinical, biochemical or other evidence of growth or regression of tumor. Since similar features were evident in these 4 cases, detailed data are presented for only one case.

Materials and methods. The method employed was essentially that described by Straub and his associates(1). This is based on the release of ammonia effected in 1 hr at 37° by 1 ml of serum in a reaction mixture containing 0.9 ml of 0.014 M adenosine, 0.1 ml of 1.33 M phosphate buffer of pH 7.8 and 2 ml of serum. The released NH_3 was determined by nesslerization. Adenosine was obtained from Pabst Laboratories. One unit of activity was defined as equal to 1 μg of NH_3-N liberated under the stated conditions.

Results. Values in normal persons. The adenosine deaminase activity did not decrease in sera kept in the refrigerator or deep-freeze for at least one month. Mean value for this enzyme activity in 14 normal persons was 10.5 μg of ammonia N liberated/ml of serum in 1 hour (10.5 units). Standard deviation was 2.1 μg of ammonia N (2.1 units); and 2.5 standard deviations about the mean were used to designate the normal range, 5.3 to 15.8 μg of NH_3-N. These results are essentially in agreement with those obtained by Straub and his coworkers(1).

Serum deaminase activity in patients with cancer. The serum deaminase activity was elevated upon the first determination in 8 of 55 patients with various types of cancer (Table I). This frequency, 15%, was much less than that reported by Straub(1) or Letnansky(2). This low incidence is similar to those obtained for other serum enzymes in cases of proven cancer(6,7) and raises the possibility that, as for these other enzymes, serum deaminase elevations are related more specifically to activity or growth of tumor. The following case illustrates this feature.

The patient was a 46 year old woman who was diagnosed as having carcinoma of the breast in 1950. Mastectomy was carried out at this time. Three years later, skeletal metastases became evident, and castration by irradiation was performed. She received testosterone and prednisone. She was readmitted to the hospital on July 31, 1958 because of increasing pain in her left thorax. At this time she showed widespread osteolytic metastases, several nodules on the skull, a liver enlarged to 2 cm below the costal margin, elevated bilirubin concentrations, 1.2 and 1.9 mg per 100 cc, a bromsulfalein retention of 40% and an alkaline phosphatase level of 8.5 Bodansky units. Between Aug. 1 and Aug. 12, the daily urinary calcium excretions were above normal, ranging from 248 mg to 763 mg. The serum calcium was elevated to 12.4 mg per 100 cc on Aug. 1. On Aug. 6, administration of an actinomycin was begun at an intravenous dose of 1 mg per day, was stopped on Aug. 20 because of a low platelet count (42,000) and reinstituted on Sept. 9.

Serum deaminase determinations were begun on Aug. 12 (Table II). Increases of urinary calcium excretion and serum calcium levels on about Aug. 25 and elevations in bilirubin about Sept. 2, evidences of increasing growth of tumor in skeleton(8) and liver(3), were paralleled by increases in serum deaminase activities and in worsening of patient's clinical condition.

Discussion. Although earlier investigators determined the adenosine deaminase activity in plasma, Letnansky and Seelich(9) showed that there was no difference in activity between the plasma and serum of the same specimen. The low incidence of serum deaminase elevations obtained in our study would appear to be due to the fact that the group of patients in our study had less advanced neoplastic disease. Letnansky and Seelich(9) reported that other serious illnesses such as

TABLE II. Parallelism between Rise in Serum Deaminase Activity and Manifestations of Growth of Metastatic Carcinoma of Breast.

Date	Clinical status	Bilirubin, mg/100 ml	Serum Ca, mg/100 ml	Urinary Ca excretion, mg/24 hr	Serum deaminase activity, units
8-12	Widespread osteolytic metastases, skull nodules, slightly enlarged liver, some nausea, some pain	2.39		525	21.8
-13	Some improvement, regression of skull nodules		10.9	525	
-15			11.2		19.5
-18			12.1	241	22.2
-19	Abdominal girth greatly increased, edema	2.88		241	21.0
-20	Possible drug toxicity, otherwise condition about the same		11.2	259	20.4
		3.18	11.2	312	18.2
-25			11.5	476	19.5
-26		2.73		476	21.8
-29			13.0	539	
-31			14.1	557	
9- 2	Downhill course; increasing weakness, abdominal distention and disorientation	5.56	12.6	471	26.7
-10		21.20	13.4		28.5

tuberculosis and pneumonia yielded a high incidence of elevations in adenosine deaminase activities. This finding is similar to that obtained for other serum enzymes which are not specific but are also elevated in grave diseases involving tissue damage or destruction (10). The parallelism between increasing serum deaminase activity and evidence of increase in tumor growth in the patient described above supports this conclusion.

Summary. Serum deaminase activity was elevated in 15% of a group of 55 patients with proven cancer. Extent of elevation was shown to parallel tumor growth and clinical condition of patient. These findings are similar to those obtained for other serum enzymes.

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