Age-dependent Transplantability in Rats of Virus-induced Thymic Lymphoma Cultured in Vitro$^{1,2}$

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SUMMARY

Leukemic lymphoblasts originating from a thymic lymphoma induced by Gross passage A virus in a W/Fu rat were cultured in vitro over 18 months. Presence of virus in these cultures was established by bioassays in rats and mice. W/Fu, Sprague-Dawley (S-D), and Fisher (F) rats of different ages were given I. P. injections with cells harvested from these cultures. Lymphomas were produced in all of 87 W/Fu and 22 S-D rats as well as in 9 of 13 F rats injected at 1-15 days of age. The average period of latency was 15 days. None of 34 W/Fu, 10 S-D, or 1 F rats given injections of larger amounts of cells, at 21-154 days of age produced tumors, and resistance to transplantation was abolished only after whole-body x-irradiation of recipients. Lymphomas localized mainly in the parathymic lymph nodes, producing large mediastinal tumors that secondarily involved the thymus. The lumbar-aortic lymph nodes were also involved. Rats thymectomized at birth developed similar lymphomas. These experiments suggest that leukemic lymphoblasts grown in vitro for a long period of time, and carrying virus, are immunologically different from the normal lymphoid cells of the strain of origin. Transplantability in young animals is explained by immunologic immaturity and the major localization in parathymic lymph nodes, by an affinity of leukemic lymphoblasts to colonize and proliferate in this area.

It was shown that successful transplantation of leukemic lymphoblasts was dependent on the age of the recipient. The principal area of localization, causing death of the animal, was in the mediastinal lymph nodes about the thymus.

MATERIALS AND METHODS

Materials

A. Injected cells.—The culture LT$^1_1$ was the source for the leukemic lymphoblasts used in this study. This culture originated from a thymic lymphoma induced in a W/Fu rat by Gross passage A virus; at the time of this report, it is in its 18th month of continuous growth (11). This is a mixed culture in which both reticular cells and lymphoblasts, components of the lymphomatous thymus, grow in symbiosis. The leukemic lymphoblasts used for the injection of recipient rats were harvested at intervals between 14 and 388 days (Table 1). For comparison, cells obtained directly from a Gross passage A, virus-induced thymoma in a W/Fu rat were injected in sixteen rats.

B. Recipients.—Isologous W/Fu rats were used in most of the experiments (145 W/Fu rats out of 191). Fourteen Fisher (F) and 32 Sprague-Dawley (S-D) rats were used for comparison in similar experiments (Table

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17 W/Fu 1 374 $8 \times 10^3$ — 17/17 17 — Lumbar-aortic l.n.* 12
2 S-D 1 360 $5 \times 10^3$ — 2/2 2 — " " " 20
2 W/Fu 2 374 $8 \times 10^4$ — 2/2 2 — " " " 12
4 W/Fu 3 289 $8 \times 10^4$ — 4/4 4 — " " " 10
4 W/Fu 4 266 $4 \times 10^4$ — 4/4 4 — " " " 15
9 W/Fu 6 330 $3 \times 10^4$ — 9/9 9 — " " " 18
4 W/Fu 6 330 $3 \times 10^4$ Thymectomy 4/4 4 — " " " 12
2 W/Fu 7 377 $1 \times 10^4$ — 2/2 2 — " " " 13
3 W/Fu 7 377 $1 \times 10^4$ Thymectomy 3/3 3 — Lumbar-aortic l.n., kidney 13
2 S-D 7 377 $2 \times 10^4$ Thymectomy 2/2 2 — Lumbar-aortic l.n. 17
4 S-D 7 377 $2 \times 10^4$ Thymectomy 4/4 4 — Lumbar-aortic l.n., mesentery l.n., kidney, spinal cord 17
2 W/Fu 8 289 $6 \times 10^4$ — 2/2 2 — Lumbar-aortic l.n. 20
2 S-D 8 310 $3 \times 10^4$ Thymectomy 4/4 4 — Lumbar-aortic l.n., peripheral l.n., kidney 16
4 S-D 8 310 $3 \times 10^4$ Thymectomy 2/2 2 — Lumbar-aortic l.n. 16
2 W/Fu 9 345 $7 \times 10^4$ — 2/2 2 — " " " 17
3 W/Fu 9 345 $7 \times 10^4$ Thymectomy 3/3 3 — Lumbar-aortic l.n. 17
2 S-D 9 345 $2 \times 10^4$ Thymectomy 2/2 2 — " " " 13
6 S-D 9 345 $2 \times 10^4$ Thymectomy 6/6 6 — Lumbar-aortic l.n., mesenteric l.n., kidney 13
11 W/Fu 10 147 $3 \times 10^4$ — 11/11 11 — Lumbar-aortic l.n. 13
6 F 10 388 $4 \times 10^4$ — 4/4 4 — " " " 15
10 W/Fu 11 184 $2 \times 10^4$ — 10/10 10 — " " " 17
7 F 12 362 $8 \times 10^4$ — 2/5 5 — Lumbar-aortic l.n., kidney 18
2 W/Fu 13 373 $4 \times 10^4$ — 2/2 2 — " " " 20
6 W/Fu 14 181 $4 \times 10^4$ — 6/6 6 — Lumbar-aortic l.n. 14
6 W/Fu 15 181 $4 \times 10^4$ — 6/6 6 — " " " 18
1 W/Fu 20 318 $1 \times 10^4$ — 0/1 — — — — 34
2 S-D 20 367 $1 \times 10^4$ Thymectomy at birth 0/5 — — — — 115
5 S-D 20 367 $1 \times 10^4$ — 0/2 — — — — 115
6 W/Fu 30 107 $1 \times 10^4$ — 0/6 — — — — 125
2 W/Fu 35 107 $1 \times 10^4$ — 0/2 — — — — 26
9 W/Fu 56 364 $6 \times 10^4$ Total-body irradiation 500 r 9/9 5 4 Peritoneum, mesentery, kidney, ascites 19
4 W/Fu 60 292 $6 \times 10^4$ — 0/4 — — — — 68
6 W/Fu 62 43 $1 \times 10^4$ — 0/6 — — — — 195
1 W/Fu 75 184 $2 \times 10^4$ — 0/1 — — — — 65
1 W/Fu 84 318 $2 \times 10^4$ — 0/1 — — — — 65
3 S-D 90 364 $1 \times 10^7$ — 0/3 — — — — 65
1 F 97 386 $1 \times 10^4$ — 0/1 — — — — 75
4 W/Fu 103 58 $1 \times 10^4$ — 0/4 — — — — 165
2 W/Fu 120 292 $6 \times 10^7$ — 0/2 — — — — 86
3 W/Fu 150 292 $6 \times 10^7$ Mammo-sommatotropic tumor bearing 0/3 — — — — 86
4 W/Fu 154 14 $1 \times 10^4$ — 0/4 — — — — 195

* l.n. = lymph node.

1). The age of the recipients ranged from 24 hr. to 154 days. In a control experiment, 12 AZ mice, in 2 litters, were similarly injected at 2-4 days of age.

**METHODS**

A. Preparation of lymphoblast suspension from culture $LT_1$.—The leukemic thymic culture $LT_1$ was established and maintained as previously reported (11). Reticular cells grew attached to the glass and most lymphoblasts floated free in the medium. To obtain leukemic lymphoblasts, supernatants were removed, pooled, and centrifuged at 800 r.p.m. for 5 min. Cells were counted in a hemocytometer and resuspended in medium to adjust to
the appropriate number. The suspension of cells was injected immediately. Sterile procedures were observed.

B. Preparation of lymphoblast suspension from thymic lymphoma.—In a control experiment, a thymic lymphoma was removed. Fragments free of necrosis and capsule were minced with fine scissors and the cells were suspended in Puck's medium and counted.

C. Preparation of isotope-labeled lymphoblast suspension.—Matched subcultures simultaneously seeded with a similar number of cells in 5 ml of Puck's medium were labeled by introducing 12.5 μc of tritiated thymidine diluted in the same fluid. After 18 hr. of incubation at 37°C, with a constant flow of 5% CO₂ in air, a suspension of cells was prepared as were the cells from culture LT₁, in the first part of this experiment. Animals were given injections of the suspension, as will be described, and were sacrificed at 5, 19, and 24 hr. The thymus, spleen, axillary, parathymic, lumbar-aortic and mesenteric lymph nodes were removed, fixed in Carnoy's solution, and processed separately. Radioautographs were done of the sections of these tissues following the technic of Messier and Leblond (17).

D. Injection of recipients.—Rats received i.p. injections of the cell suspension: newborns 0.1 ml with 27-gauge needles; adults, 0.5—1.0 ml with 25-gauge needles. In a control experiment, mice received 0.05 ml similarly injected.

E. Thymectomy of recipients.—Twenty-nine newborn rats (ten W/Fu and nineteen S-D) were thymectomized during the 1st 48 hr. Only animals free of infection at the site of operation were used for this experiment. The effect of thymectomy was evaluated by white blood cell counts, which were constantly lower than in littermate controls, and by autopsy. Thymectomized rats and littermate controls were separated into 2 groups. The 1st group (24 thymectomized and 12 controls) received injections of LT₁ cells, by means of the procedure described, at 6—9 days of age, and the 2nd group (5 thymectomized and 2 controls), at 30 days of age.

F. Irradiation of recipients.—Total-body irradiation of 500 r was delivered to nine W/Fu rats at 56 days of age. The effectiveness of irradiation was evaluated by white blood cell counts, which dropped to one-eighth of the normal values.

G. Assays for presence of virus in LT₁ culture.—Homogenates of cultured cells, frozen-thawed, centrifuged, and resuspended in Puck's medium, were injected intraperitoneally into newborn AZ mice. Cell-free filtrates of similar homogenates were injected into newborn W/Fu rats. The presence of leukemia virus in LT₁ culture was demonstrated by the production of “late” thymomas (97—102 days) in 100% of AZ mice receiving injections. Thymomas with a latency period of 126 days were also produced in rats receiving injections of cell-free filtrate. Bioassays for viral replication in LT₁ culture will be published separately.

H. Evaluation of results.—The results of transplantation were evaluated after natural death of the recipient or after sacrifice of the remainder of the animals when the first littermates died of lymphoma. Gross appearance of the animals was recorded; blood smears and histologic sections of organs were examined.

RESULTS

A. Production of lymphoma in isologous rats by injection of leukemic lymphoblasts obtained from culture LT₁.—A total of 121 W/Fu rats, isologous to the rat from which the leukemic thymic culture LT₁ was derived, were given injections of these cells. All 87 receiving injections at 1—15 days of age developed lymphoma, with an average latency period of 15 days.

None of the 34 animals that were 20—154 days of age at the time of injection developed lymphomas (Table 1, Chart 1). Rats with lymphoma could easily be recognized at the last stage of the disease by labored respiration, emaciation, coarse hair, and bulging sternum. There was extreme pallor of mucous membranes and skin.

At gross examination, a constant and characteristic pattern was noted. Although cells were injected i.p. in all cases, the principal site of neoplastic disease was in the mediastinum. A huge tumoral mass involving parathymic lymph nodes and the thymus was present in all cases (Fig. 2). These masses—with an average diameter of 100 mm but, in some cases, as large as 200×150 mm—surrounded and compressed the trachea. The upper two-thirds of the lungs were compressed against the posterior wall of the thorax, and the heart deviated to the lower left angle. Milky fluid, 2—3 ml, filled the pleural cavities in most animals. When the tumor was examined at an earlier stage, the enlarged bilateral parathymic lymph nodes could be distinguished from the thymus (Fig. 1). This was no longer possible in more advanced cases when the tumor mass was very large (Fig. 2). In 71 of the group of 87 animals, the second major area involved was the lumbar-aortic lymph nodes, unilaterally or bilaterally (Figs. 1—3). Lymphoma in this region usually did not reach the size of the mediastinal tumor, having an average of 75 mm. In addition to these major sites, a few animals displayed lymphomatous mesenteric or retroperitoneal lymph nodes (Fig. 2). Neither peripheral lymph nodes nor the spleen were involved, and no visceral metastases were found. No recipient in this group of young animals displayed peritoneal tumor, ascites, or tumor at the site of injection.

Histologically, the mediastinal and lumbar-aortic tumors had the appearance of lymphoma similar to the Gross passage A, virus-induced thymoma of origin (Figs. 4, 5). The predominant histologic patterns in most areas were lymphosarcoma and, less frequently, reticulosarcoma. In smears of pleural fluid, as well as of peripheral blood, examined at the final stage, up to 96% leukemic lymphoblasts were identified.

The 34 rats given injections of the same suspension of cells, in larger amounts, at 20—154 days of age were sacrificed after 40—195 days. No tumor was observed grossly or histologically.

B. Production of lymphoma in homologous rats by injection of leukemic lymphoblasts obtained from culture LT₁.—All 22 S-D rats receiving injection at 1—9 days of age developed lymphomas with an average latency period of 15 days and a histologic appearance similar to that of the W/Fu group.

Ten S-D rats given injections at 30—90 days of age were free of tumor when sacrificed after 21—115 days. In the Fisher rats, 9 of 13 receiving injections at 10—12 days of age
developed similar lymphomas after 15–18 days. Four were free of tumor at autopsy after the same intervals, as was one receiving an injection at 97 days of age and sacrificed after 75 days.

C. Production of lymphoma in isologous rats by injection of leukemic lymphoblasts obtained from a thymic lymphoma.

—Of 15 W/Fu rats given injections at age 10–13 days of cells from a virus-induced thymic lymphoma, 12 had abdominal and mediastinal tumors after an average latency period of 25 days. One rat died with thymic lymphoma at 137 days after the injection. Of 5 rats given injections at 90 days of age, only 1 produced mediastinal and abdominal tumor with ascites, during lactation, after 36 days of latency.

The rats with lymphoma in this group, compared with the animals receiving injections of LT1 cells, displayed a different pattern of localization. The principal site was the abdominal cavity, where large masses of tumor were usually accompanied by peritoneal implants and ascites. Mediastinal tumor present was less developed than in the first 2 groups, with the exception of the one rat mentioned above that displayed a thymoma, probably of viral origin, after a long latency period (137 days).

D. Production of lymphoma in thymectomized rats by injection of leukemic lymphoblasts obtained from culture LT1.

—All rats given injections at 6–9 days of age, both thymectomized and control animals, displayed lymphomas after a latency period of 14 days. None of the rats thymectomized at birth and receiving injections at 30 days of age had lymphoma after 115 days.

The thymectomized rats were, in general, more susceptible to injected leukemic cells than the nonthymectomized rats. The tumors produced were larger and more invasive to adjacent organs and displayed frequent blood-borne metastases. Nine of 24 rats thymectomized and given injections at 6-9 days of age displayed kidney metastases, unilaterally or bilaterally. Metastases were also present in the lungs of two animals, in the diaphragm of one, and in the sternum of one. Two rats had paralysis of the posterior extremities. Leukemic lymphoblasts composed 96–98% of the nucleated cells of the peripheral blood. The principal tumor was mediastinal, occupying the upper half of the thorax and originating in the parathympic lymph nodes (Fig. 3).

In many thymectomized animals, the lymphoma involving parathympic lymph nodes gave the gross appearance of a thymoma. In 18 of the thymectomized rats receiving injections at 1–15 days of age, the lumbar-aortic lymph nodes were involved by large tumors. In 6 cases, the adjacent kidneys were invaded, with hydronephrosis and atrophy of the renal parenchyma in two. In some animals, peritoneal and mesenteric lymph nodes were also involved. The spleen was significantly smaller and paler in the thymectomized group of animals.

E. Production of lymphoma in x-irradiated rats by injection of leukemic lymphoblasts obtained from culture LT1.

The nine W/Fu, 56-day-old rats given injections of leukemic lymphoblasts 24 hr. after single total-body irradiation with 500 r were positive for lymphoma within 19 days. The pattern of tumor localization was similar in all, but different from that in rats given injections at less than 15 days of age. In this group, the major site was abdominal, and large tumors involved peritoneal lymph nodes and organs. Four of the rats had ascites. In the
mediate stern, thymus and para-thymic lymph nodes.

F. *Injection of leukemic lymphoblasts obtained from culture LT1 in rats bearing mammomomatropic tumors.* — Three W/Fu female rats (bearing mammomomatotropic tumors) that were given injections of leukemic lymphoblasts at 150 days of age were sacrificed after 86 days. These animals were large (average 450 gm), with macro-viscera and involuted thymus, as a result of hypersecretion of growth hormone produced by the tumors. No lymphomatous growth was found.

G. *Injection of leukemic lymphoblasts obtained from culture LT1 in isologous rats.* — Culture LT1 in AZ mice. — None of the 12 mice in 2 litters given I. P. leukemic lymphoblasts (1 × 10⁹) at 2–4 days of age developed "early" lymphomas (within 60 days). This ruled out the ability of these cells for heterotransplantation.

H. *Injection of isotope-labeled leukemic lymphoblasts obtained from culture LT1 in isologous rats.* — Culture-labeled leukemic lymphoblasts were injected into isologous rats of different ages to explore their comparative coloniza-tion in various lymphoid tissues.

Mediastinum, lymphoma involved thymus and para-radiated. A similar host resistance against isotransplantation in various lymphoid tissues.

No labeled cells were found after 5, 19, and 24 hr. in sections of the thymus, spleen, axillary, lumbar-aortic, and mesenteric lymph nodes. Scattered labeled lymphoblasts, up to four in one microscopic field, were observed in sections of parathympic lymph nodes.

**DISCUSSION**

In these experiments, transplantation of leukemic lymphoblasts originating in a virus-induced thymoma, grown in *vivo*, and carrying virus for a long period of time, was strictly dependent on the age of isologous recipients. A critical period at about 15 days of age was noted when total susceptibility to transplantation abruptly changed to complete resistance. Age-dependency proved to be a stronger factor than heterozygosity, in that animals of different strains were similarly receptive to transplantation up to 15 days of age and resistant thereafter.

Previous workers (3, 5–8, 16, 22) concluded that transplantation of leukemic lymphoblasts in adult isologous recipients was successful in 90–100% of cases. Early investigators (16), however, had already noted variations in the 'takes' of serially transplanted leukemias and lymphomas and explained them by 'changes in the line of transmitted material itself.'

During 29 years of transplantation and 16 years of *in vitro* cultivation of a mouse lymphoma, DeBruyn (4) isolated lines of cells which in time changed their capacity to produce tumors when inoculated into susceptible mice, although their morphology remained similar.

Klein and Klein (15) noted a variety of responses to transplants of a primary Moloney virus-induced lymphoma in untreated isologous recipients. Some animals died of generalized leukemia or had tumors at the site of injection; others had tumors which later regressed, and still others were totally resistant unless previously x-irradiated. A similar host resistance against isotransplantation of a Gross virus-induced lymphoma was demonstrated by Klein et al. (14). The C3H strain of mice used was maintained by single-line brother-sister mating for decades and was fully skin-compatible so that, according to the authors, isoantigenic differences due to residual heterozygosity were not sufficient explanation.

Similarly, in the present work, an isologous, skin-compatible strain of animals with years of pedigree-mating was used. After 15 days of age, however, these animals became totally resistant to grafts of isologous neoplastic cells. Thymectomy at birth or an involuted thymus (the mammomomatotropic tumor-bearing rats) were not sufficient to permit successful grafts after 15 days of age in isologous rats, and this resistance was overcome only by total-body x-irradiation. Rejection of grafted cells that not only originate in an isologous animal but also possess potentialities for neoplastic growth indicates that these cells are immunologically different.

The work of Sjögren et al. (24) and Habel (10) suggested that transformation of normal to tumor cells by polyoma virus probably alters the genome of the cell, directing the production of new antigens able to induce resistance to isologous transplantation. Similar evidence for the appearance of new "foreign" antigens in leukemia virus-infected cells is suggested by the recent work of Sachs (23), Klein et al. (14, 15), Axelrad (1) and Glynn et al. (9). Formation of 'foreign' cellular antigens in long-term, virus-supporting cultures of leukemic lymphoblasts may account for failure when transplantation of these cells is attempted in animals with a fully developed immunologic defense. In young animals, the incomplete competence to recognize new antigens may be overcome by a rapidly multiplying population of transplanted neoplastic cells.

A second fact worth considering is that the neoplastic cells injected intraperitoneally colonize and establish tumor growth mainly in the mediastinum, in the para-thymic lymph nodes. This disagrees with reports in the literature (3, 6, 7, 13, 16, 22) of the production of abdominal tumors accompanied by ascites when the I. P. route was used.

However, interesting peculiarities in lymphoma transplantation have been noted. Richter and MacDowell (22), using different spontaneous lymphomas for isotransplantation in the C58 strain of mice, derived lines of tumors which constantly localized in similar areas. Although the cells were injected intraperitoneally in all cases, they produced, according to the specific line, tumors of the spleen and lymph nodes, the liver, the kidney, and peritoneal tumors with ascites or 'chest tumors,' maintaining these characteristics in subsequent transmissions.

Affinity of injected leukemic lymphoblasts to colonize in particular organs was also reported by Furth et al. (7). This preference was strain-characteristic and impressive in the RG-1O mice, in which lymphoblasts injected I. V. localized exclusively in the ovaries and produced large bilateral leukemic tumors. In other strains there was a specific affinity for the kidneys; and in still others for the meninges, producing paralysis.

Similar strain-dependent affinity for specific areas in spontaneous lymphoma has been reported (21). In AKR mice, localization occurred mostly in the thymus; in SL mice, it occurred in the mesenteric lymph nodes. An earlier sexual maturation accompanied by relative thymic involution in the SL strain was offered as explanation.

The predominant site of localization of induced and...
transplanted lymphomas is probably determined, depending on the strain, by the age at which tissues and organs mature or senesce.

Thymic evolution depends on the age of the animal and is best expressed in the induction of lymphoma by viral or chemical agents. Gross passage A, virus-induced thymic lymphoma drops from over 90 to 43.5% when recipients receive injections after 17 days of age (2). In chemically induced lymphoma, the major site of the tumor, mostly in the thymus in the young and at the thymic lymphoma drops from over 90 to 43.5% when recipients receive injections after 17 days of age (2).

There are major differences between induced and transplanted lymphomas. The longer latency period and elective thymic localization are characteristics of the former. In the present transplantation experiments, similarities to the viral induction of lymphomas were noted. These are the resistance that occurs at about the same age and the preferential localization, in this case in the parathyroid lymph nodes.

The role of the young thymus in the induction of leukemia has been well documented (19, 20) and an undetermined, possibly noncellular, influence exerted by the thymus on lymphoid cells has been suggested (18). It is conceivable that factors stimulating multiplication of lymphoid cells are part of thymic influence as well as of the favorable environment it provides for them.

The parathyroid lymph nodes have a distinctive morphology (12), drain the thymus, and would be the first lymphoid structures to be exposed to its influence. Possibly they inversely follow the age-dependent evolution of the thymus, increasing in size as the former diminishes with age. The transplanted leukemic lymphoblasts circulating in these lymph nodes would then find a favorable site for colonization, proliferation, and production of local tumor, as well as for active replication of virus. The parathyroid lymph nodes are constantly involved in the formation of the thymic lymphoma, whether primarily, as in these transplantsations, or invaded secondarily as in viral induction of thymoma.

Both abrupt resistance to grafted leukemic lymphoblasts and resistance to viral induction of lymphoma at a similar age may possibly be explained by the effectiveness of the same virus to induce formation of new cellular antigens. The parathyroid lymph nodes, intimately related to the thymus and possibly developing under its influence, may influence the susceptibility of recipients to transplanted leukemic lymphoblasts.

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REFERENCES


2. AXELRAD, A. A., and Van der Gaag, H. C. Susceptibility to

Fig. 1.—W/Fu rat given injection of LT1 cells when 9 days old and sacrificed 10 days later. Involvement of parathymic lymph nodes greater on left side, with thymus free.

Fig. 2.—W/Fu rat given injection of LT1 cells when 6 days old. Died 18 days later. Huge mediastinal tumor involving both parathymic lymph nodes and thymus. Bilateral neoplastic growth in lumbar-aortic lymph nodes invaded kidneys and the mesentery is involved also.

Fig. 3.—S-D rat thymectomized at birth and given injection of LT1 cells when 8 days old. Died 16 days later. Large bilateral tumor in parathymic lymph nodes. Lumbar-aortic lymph nodes also involved.

Fig. 4.—W/Fu rat given injection of LT1 cells when 11 days old. Thymic cortex invaded by leukemic lymphoblasts (upper left). Normal lymphocytes still present in medulla (lower right). × 1000.

Fig. 5.—W/Fu rat given injection of LT1 cells when 7 days old. Histologic appearance of lymphoma in parathymic lymph node. × 1600.

Fig. 6.—W/Fu rat given injection of tritiated thymidine-labeled LT1 cells and sacrificed 24 hr. later. Labeled lymphoblasts in a parathymic lymph node. × 800.
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