influence of a high-pressure system which had moved in from the northwest. The activity level decreased from 2.9 to 0.32 pc/m^3 after the weather front moved through.

Almost all the nuclear reactors currently in operation are located in the middle latitudes of the Northern Hemisphere. Dispersion of the effluent from these reactors is fairly rapid latitudinally and also vertically up to the mean mixing height. It takes about 30 days (*5*) for the effluent to travel around the earth, but in a matter of hours it reaches its mean mixing height, which varies from about 200 to 4000 m, depending on location, weather conditions, and season (*7*). Vertical dispersion above the mean mixing height and beyond the temperate latitudes proceeds more slowly, requiring 1 to 2 years for dispersion throughout the earth's atmosphere.

The half-life of 5.29 days for ^{133}Xe is such that dispersion on a regional and hemispheric scale can be followed. Isotopes with significantly longer half-lives, such as ^{85}Kr (10.76 years), accumulate throughout the atmosphere, making regional dispersion measurements difficult. Further measurements of ambient ^{133}Xe could be correlated with more detailed information on the amount of ^{133}Xe being discharged from the various sources and on the climatologic and geographic parameters. Such an approach would provide a more comprehensive model for estimating regional and hemispheric dispersion of all airborne pollutants, both radioactive and nonradioactive.

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Lymphocyte-Induced Angiogenesis in Tumor-Bearing Mice

Abstract. *The presence of a growing tumor can lead to a significant curtailment of a graft-versus-host reaction as measured by the ability of allogeneic spleen cells to induce a host vascular response. This interference with the normal pattern of immunological reactions may be a reason for the survival of tumors in an immunologically alien environment.*

In describing the effect of intradermal transfer of immunocompetent lymphocytes on the host vascular system (*1*), we have called the host response—which is manifested by increased vascular tortuosity, visualization of more vessels, and histological changes reflecting endothelial cell differentiation—lymphocyte-induced angiogenesis (LIA).

At the same time, we remarked on the similarity between the vascular response induced by foreign lymphocytes and that induced by grafted tumor tissues (*1*). Subsequently we reported in more detail on that similarity (*2*). We now report on the effects of the presence of a growing tumor on the capacity of the host animal's vascular system to respond to the inoculation of foreign immunocompetent lymphocytes.

The methods used for induction and quantitative evaluation of the vascular response have been described (*1*). In brief, cell suspensions were prepared from spleens of normal mice of various strains, the concentration was adjusted so that an inoculum of 0.1 ml would contain 2×10^6 cells, and trypan blue was added to facilitate later visualization of the site of injection. Cells were injected intradermally into recipient tumor-bearing or control normal animals irradiated a few hours previously with x-rays (800 roentgens). After 2 to 3 days, the animals were killed with ether, the injection sites were exposed by dissection, and the number of scar-associated vascular branches was determined. We used the C57BL/6 C755 mammary carcinoma cells grown either in C57BL/6 or BDF$_1$ (C57BL/6 × DBA/2) hosts, while donor spleen cells were obtained from Ha/ICR (H2-q), CBA (H2-k), BALB/c (H2-d), and C57BL/6 (H2-b) strains of mice.

The results are shown in Fig. 1. As was expected, no vascular responses were seen in syngeneic combinations. In confirmation of our earlier work, 2×10^6 allogeneic spleen cells inoculated into irradiated normal recipients gave a typical vascular response (43 mice; the mean number of vessels was 22.3). In contrast, an equivalent number of allogeneic cells inoculated into mice bearing a large C755 mammary carcinoma elicited only a weak response (43 animals; the mean number of vessels was 8.6). Hosts with moderate tumors gave intermediate vessel counts (seven mice; the mean number of vessels was 11.0). Similar results have been obtained in preliminary experiments with line 129/J mice bearing OTT6050 teratoma.

We have no ready explanation for our

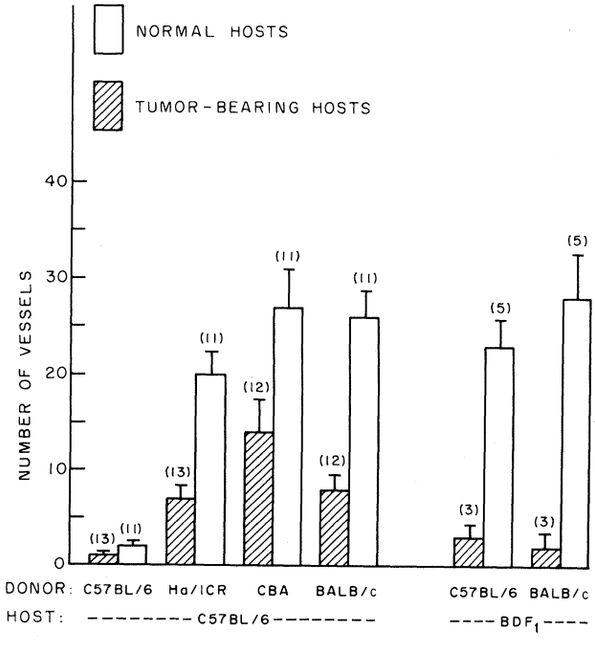

Fig. 1. Mean and standard error of extra blood vessels observed in lethally irradiated normal and tumor-bearing hosts in response to the intradermal inoculation of 2×10^6 allogeneic or semiallogeneic spleen cells; the number of host animals is shown in parentheses.

observation of reduced vascular responsiveness of tumor-bearing mice. While we are aware that the presence of tumors may result in lowered immune function (*3*), our previous work has shown that LIA is essentially the result of a local graft-versus-host reaction and that the host's own immune system is not directly involved (*1*). Moreover, we have observed that immunosuppression of the host with cyclophosphamide does not interfere with the animal's responsiveness to LIA (*4*). In contrast, we have found that normal lymphocytes injected intravenously into irradiated C755 tumor-bearing animals are restricted in their ability to function in the humoral immune response to sheep red blood cells (*4*). The data from experiments with cancer patients are conflicting: Hattler and Amos (*5*) suggested that cancer patients had an impaired ability to react to allogeneic cells in the normal lymphocyte transfer reaction; Aisenberg (*6*) indicated that patients with Hodgkin's disease had an abnormally protracted response to such allogeneic cells (*7*); and Levin *et al.* (*8*) found that the response to allogeneic lymphocytes transferred into patients with lymphomas or other cancers did not differ significantly from the reaction of healthy persons in frequency, character, or intensity.

An alternative explanation of our results would be that tumor-bearing animals have a reduced number of circulating stimulator cells (*9*). We know such cells are required for activation of the donor lymphocytes in our system. A less likely possibility is that the tumor, having provided a continual source of angiogenesis-inducing factors (*10*), has already led to maximal activation of some target cell (such as the mast cell) population or of the host endothelial system itself, and that for this reason the host animal is incapable of responding to yet an additional stimulus for vascular differentiation and endothelial cell proliferation.

Whatever the basis for our observations, we should emphasize the importance of recognizing that tumor-bearing animals have a reduced responsiveness to immunocompetent lymphocytes, as measured by a deficient vascular reaction. That growing tumors can thwart this process must be considered a serious handicap in our efforts to harness the immune system for the control of malignancy.

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Ingestion of *Streptococcus mutans* Induces Secretory Immunoglobulin A and Caries Immunity

Abstract. *Ingestion of killed cells of a highly cariogenic strain of* Streptococcus mutans *induced specific antibodies in both saliva and milk but not in serum of gnotobiotic rats. These antibodies were associated with the immunoglobulin A class. When infected with* Streptococcus mutans, *orally immunized animals developed significantly fewer carious lesions than nonimmunized infected controls.*

The bacterium *Streptococcus mutans* has been implicated as a principal etiologic agent of dental caries, an infectious disease that afflicts more than 95 percent of the world's population (*1*). The possibility of controlling this disease by active immunization is currently under intensive investigation (*2*).

Dental caries develops in an oral milieu of secretions that contain locally produced immunoglobulin A (IgA) as the predominant antibody (*3*). Earlier unsuccessful attempts to protect experimental animals against caries by immunization can perhaps be partially explained by the limited induction of antibodies in saliva after systemic administration of antigen (*4*). Injection of *S. mutans* into either the oral mucosa, the salivary glands, or the parotid duct has stimulated salivary IgA antibodies (*5, 6*) and, in some instances, has protected against *S. mutans*–induced caries (*6*). However, these routes of immunization are not likely to be suitable for use in humans (*2*). Recent studies have indicated that specific antibodies in the IgA class can be induced in secretions of rabbit and human mammary glands by oral administration of antigen (*7*). We report here that ingestion of killed cells of *S. mutans* induces production of antibodies in the IgA class to *S. mutans* in saliva and milk, and provides significant protection against dental caries in gnotobiotic rats.

Young gnotobiotic rats (Charles River Laboratories) that were fed a purified caries-promoting diet were used in this study (*8*). Drinking water containing formalin-killed *S. mutans* strain 6715, mutant C211 (final concentration, 10^8 cells per milliliter) was provided freely to one group of weanling rats (group A) until the day they were killed; their littermates (groups B and C) were maintained in separate isolators and were provided sterile drinking water. At 45 days of age, rats in groups A and B were challenged with 50 μl of an 18-hour culture of *S. mutans* 6715, C211 containing 5.4×10^6 to 5.7×10^6 colony-forming units. Previous studies in this laboratory have shown this mutant to be highly virulent (*9*). Colonization of *S. mutans* was confirmed the day after challenge by culturing oral swab samples on Mitis-Salivarius agar (Difco Laboratories). Rats in group C served as nonimmunized, uninfected controls.

All rats were removed from the isolators at 90 days of age. Individual saliva samples were collected after pilocarpine stimulation (*6*). Animals were killed by cardiac exsanguination, and serum was collected. *Streptococcus mutans* 6715, C211 was reisolated from dental plaque of each infected animal (groups A and B), and no other bacteria were detected. Both mandibles from each animal were cleaned, stained, and then scored for caries by the Keyes procedure (*10*).

Table 1 gives the levels of immunoglobulins and mean agglutinin titers to *S. mutans* in the serum and saliva of 90-day-old gnotobiotic rats (*11*). Significant differences were not evident in the levels of either serum immunoglobulins or salivary immunoglobulin G (IgG) for the three groups of animals. No immunoglobulin M (IgM) was detected in saliva. Rats receiving *S. mutans* in their drinking water (group A) had significantly higher levels ($P \leq .01$) of IgA in their saliva than animals in either group B or group C. Low agglutinin activity was observed in