Possible Links Between Radioactive Discharges and Cancer

TO THE EDITOR: The November 1990 issue of *The Journal of Nuclear Medicine* contained an article by Palash R. Ghosh reviewing recent studies that examined possible links between radioactive discharges and cancer (*1*). Among the studies mentioned was one conducted by Doctors Byers and Vena of the State University of New York at Buffalo, which examined cancer incidence in the vicinity of West Valley, New York. This study was not sponsored by the New York State Department of Health.

Pursuant to the New York State Low Level Radioactive Waste Management Act of 1986, the New York State Department of Health has been conducting a public information program on the health effects of radiation. As a part of this program, we have assembled available information on the health experience of populations residing near nuclear facilities in New York State and other states. The Byers and Vena study was one such piece of information. The study, which was not well-known, as it had not been published, was available on request from the authors. The Department of Health did not release the study but did prepare a brief fact sheet with the approval of Dr. Vena, which outlined the study and its results. This fact sheet was made available to the public along with information about other such studies. The names and addresses of the study's authors were also provided in the fact sheet for those who wished to obtain further information.

The article claims the New York State Department of Health said that the West Valley Coalition "had tried to rally the public against low-level waste sites" and "kept the study's results concealed." The Department has never made either statement.

REFERENCE

1. Ghosh PG. Cancer clusters: latest studies do not support link between cancer mortality and radiation discharges [Newsline]. *J Nucl Med* 1990;31:11A.

Rita Aldrich
State of New York
Department of Health
Albany, New York

Compensatory Splenic Growth

TO THE EDITOR: The interesting article by Budihna et al., "Long-Term Follow-up After Heterotopic Splenic Autotransplantation for Traumatic Splenic Rupture" (*J Nucl Med* 1991;32:204–207), and the associated editorial review, "Compensatory Splenic Growth: Role of Functional Indicators," by R. Spencer (*J Nucl Med* 1991;32:207–209) prompt these comments.

1. *Stimulus* for growth of splenic tissue. Jacob et al. (*1*) showed that the growth and function of spleen, spleen autografts and liver, as measured by their size and their ability to sequester altered red cells, was proportional to the "work" required. Spleen grafts in asplenic rats grew larger and functional more actively than did such grafts in normal and hemisplenectomized (hemisplx) rats. Increasing the "work load" by imposing a hemolytic process produced a hyperplastic response both in spleens and spleen grafts. The stimulus was thought to be local and particulate, since splenic tissue inside i.p. diffusion chambers (pore size 0.45 μ) in splx animals remained viable but did not grow.

2. *Maximum growth* of splenic tissue. Metcalf (*2*) found that when splx host mice were grafted with multiple histocompatible spleens per mouse, the eventual total mass of grafted splenic tissue reached a plateau which approximated that of the original normal spleen. In one group of patients with postsplx splenosis (*3*), the largest implant mass (133 g) was at the peak incidence of normal spleen mass (*4*). In a patient who underwent splx for Felty's syndrome, half of a transected accessory spleen was left in situ; two years later it too was removed after it had increased in mass to 1040 g (*5*). The ultimate mass of splenic tissue is thus determined by the work demand.

3. The *adequacy of immunological function* in asplenic patients with splenic grafts or implants. While such grafts preserve some spleen function, fatal infections have occurred in such patients (*6*). Splenosis patients with large implants are also still at risk. A patient had 92 g of ectopic splenic tissue following splx-for-trauma, yet died from infection (*7*). We have seen a patient who had undergone splx-for-trauma at age 4 yr (*8,9*). Operations at 8, 19, and 29 revealed progressive growth of implants. She had had many infections and at 35, nonimmunized, she had near-fatal pneumonia. At 39, imaging studies, including angiography, revealed widespread splenosis, with a good arterial supply from the right internal iliac artery to a large pelvic implant (>87 g), well visualized and measurable on ultrasound studies. Total mass of splenic tissue was in the range of that of a normal spleen (*4*).

Rabbit studies have shown that clearance of pneumococci was directly related to arterial blood flow/g of splenic tissue (*10*). Hemisplx reduced both only slightly, but splenic artery ligation alone (in which spleen mass remained normal) and splx with splenic tissue grafting reduced both markedly.

In a lucid review, Styrt (*6*) summarizes the immune function of the spleen as participating in the generation of a variety of mediators (of phagocytosis), perhaps mechanically filtering nonopsonized organisms, providing a setting in which cells of the immune system can interact for maximal anticapsular antibody production, and providing a critical population of phagocytes capable of ingesting microbes after a minimum of opsonization. Thus, an asplenic patient with ectopic splenic tissue could be immunologically deficient to a variable degree because of multiple factors: inadequate arterial perfusion (*10*); an insufficient mass of the normal components of splenic tissue; or structural defects within it (*7*).

It is time for more sophisticated correlative research on the spleen.

REFERENCES

1. Jacob HS, MacDonald RA, Jandl JH. Regulation of spleen growth and sequestering function. *J Clin Invest* 1963;42:1476–1490.
2. Metcalf D. Restricted growth capacity of multiple spleen grafts. *Transplant* 1964;2:387–392.
3. Corazza GR, Tarozzi C, Vaira D, et al. Return of splenic function after splenectomy: how much tissue is needed? *Br Med J* 1984;289:861–864.
4. Myers J, Segal RJ. Weight of the spleen. I. Range of normal in a nonhospital population. *Arch Path* 1974;98:33–35.
5. Fleming CR, Dickson ER, Harrison EG. Splenosis: autotransplantation of splenic tissue. *Am J Med* 1976;61:414–419.
6. Styrt B. Infection associated with asplenia: risks, mechanisms, and prevention. *Am J Med* 1990;88:5-33N–5-42N.
7. Rice AM, James JE. Ectopic splenic tissue failed to prevent fatal pneumococcal septicemia after splenectomy for trauma. *Lancet* 1980;1:565–566.

8. Auerbach RD, Kohorn EJ, Cornelius EA, Chambers JT. Splenosis: a complicating factor in total abdominal hysterectomy. *Obstet Gynecol* 1985;65:65S–68S.
9. Cornelius EA. Splenosis: physiology and imaging. *Invest Radiol* 1985;20:522.
10. Horton J, Ogden ME, Williams S, Coln D. The importance of splenic blood flow in clearing pneumococcal organisms. *Ann Surg* 1982;195:172–176.

E. Cornelius
Yale Medical School
New Haven, Connecticut

REPLY: The term used by Cornelius, "need," is a teleologic one and has to be translated into more specific terms such as: stimulus, effector pathway, and controlling factors.

1. At one extreme, a marked decrement in splenic size follows daily removal of a small amount of blood from rabbits over a period of several months (*1*). Even if this were to reduce the splenic "need" for sequestering aging red blood cells, does it also reduce the requirement for filtering bacteria and other particulates? The situation has to be more properly explored function by function.

2. Despite the multitude of cases of splenectomy that we have followed, in only one did an accessory or splenotic spleen reach a "normal" size. Is the equilibration size of the organ less than normal because of inadequate stimuli, a damaged effector pathway, or factors (hormonal or otherwise) limiting its growth?

3. The term "need" may also mask the effects of "foreign" stimuli, such as invading microorganisms. These are not "needed" but an analysis of which of their products stimulated splenic growth or function might yield clues as to the underlying molecular mechanisms.

A rational approach to analyzing splenic growth and function is to steer away from "need" and to concentrate on the stimuli, the effector pathway and any controlling factors.

REFERENCE

1. de Langen CD. Function of the spleen and blood. *Acta Med Scand* 1943;115:271–276.

Richard P. Spencer
University of Connecticut Health Center
Farmington, Connecticut

REPLY: We appreciate Dr. Spencer's editorial (*1*) accompanying our article (*2*) and we thank Dr. Cornelius for his comments. We are pleased that so much interest for this topic exists. However, this can also mean that many uncertainties about the function of accidental or intentional autotransplantation after post-traumatic splenic rupture persist.

Accidental splenosis is usually discovered because of some complication, either acute abdominal pain (*3*) or following postsplenectomy sepsis (*4*). Spontaneous or therapeutic splenic autotransplants that do not cause any problems are overlooked. A false impression is thus created that splenic autotransplants are ineffective and unable to exert part of the immunologic and clearance function. A constant fear of potential acute abdominal complications accompanies splenosis.

It was not the principal goal of our prospective work to answer the basic questions about the stimulus for autotransplants' growth nor to elucidate the complex mechanisms involved in immunologic mechanisms after removal of the primary organ. We followed the natural history of therapeutic transplants, their progressive growth and improved clearance function using splenic scintigraphy with heat damaged radiolabeled red blood cell. Most studies point out the two necessary factors to restore *part* of immunologic function after splenosis or autotransplantation, namely the appropriate vascular supply of the graft and adequate volume of the newly formed splenic tissue (*5,6*). It was also proven in animal experiments that the imposed workload has critical influence on transplant growth, but the ability to perform the required work depends on perfusion of the regenerates (*7*).

The size of individual transplants in our patients was measured from the surface area of grafts on the scintigrams. However, no attempt was made in our study to correlate the size of the transplants measured with the planar technique to their volume because of the unreliability of planar technique as compared to the tomographic measurements (*8*). The functional perfusion of autotransplants in our patients was good enough to maintain the clearance function as can be estimated from intensive uptake of the radiolabeled spherocytes. The increased intensity of tracer accumulation on the later scans was noted. Improved clearance function together with lack of serious infection or other complications allowed us to assume that partial restoration of immunologic function existed even with hypofunctioning heterotopic splenic tissue. On follow-up, the observed growth of autotransplant was not excessive. It was further pointed out that functioning heterotopic tissue per se does not guarantee the immunologic adequacy, but it is probably a valuable help in the host defense mechanisms as shown in human studies (*6,9*). Experiments with mice demonstrated better protection against aerosolized bacterial infection with at least partly preserved spleen when compared to splenectomized mice (*10*). It was shown that the "normal" weight of the spleen can range from 70 to 280 g in healthy white males and from 55 to 195 g in healthy white females (*11*). It remains unknown whether the size of the original spleen is related to the upper limit of the transplant growth. It cannot be predicted what will be the workload and its growth impact on a transplant. Additionally, correct histologic structure is probably one of the conditions for immunologic function restoration, which was not always the case in patients dying from sepsis. Autopsy studies were carried out in patients after overwhelming pneumococcal sepsis in the study of Millikan. No lymphocytes were found in the 20×20×3 mm splenic implants in an alcoholic patient with severe liver disease and severe reduction of immune competence (*12*). Poorly developed sinusoids were shown in other autotransplants after overwhelming postsplenectomy sepsis (OPSI). Splenotic nodules had a maximal weight of 3 g and the total weight of the splenic tissue in one of these patients reached 92 g (*4*). This report is in controversy with animal experiments in which the autotransplanted splenic particles undergo necrosis with consequent overgrowth of hystologically normal splenic tissue which is able to take over part of the normal splenic function (*13*).

We are not aware of the influence of the quantity of transplanted tissue on the regeneration, but it appears that the size of autotransplanted particles in patients with accidental splenosis is probably below the size of intentionally transplanted splenic particles in animal studies as well as in patients. Our patients did not have any complications after the transplantation and thus no histologic data were available. The relationship of histologic