Letters

International Cancer Congress: The View from Argentina

The National Academy of Medicine of Buenos Aires, a body of 35 Academicians elected because they are indisputably among the best in the country, constitutes the highest medical authority in Argentina.

The Academy is troubled by the false and malicious reports spread abroad by the press misrepresenting the social situation in our country. According to the rumors so insidiously started, it would be unadvisable to attend the International Cancer Congress, to be held in Buenos Aires in October 1978, because of the general climate of public insecurity, the breaking of human rights laws, the persecution of scientists, and so forth.

In the presence of this pernicious propaganda against our country, the Academy finds it is its duty to inform the scientific community of the following facts:

1) Neither the members of this Academy nor the scientific, technical, or auxiliary staff that constitute its institutes (more than 200 persons) have ever had their personal freedom or their professional activities injured by the authorities or by isolated individuals.

2) During the latter years, the scientific activities of this Academy and its institutions have received the government's total support without any compulsion or compromise.

3) The climate of public security has substantially improved, and the kidnapping of personalities or functionaries formerly performed by the terrorists has ceased. We can affirm now, without distorting the truth, that Buenos Aires, as all Argentine cities, is as safe as any large European or American city.

4) At present, the universities and research institutes are places of quiet and fruitful work, in contrast to the agitation, the activism, and the persecution of professors and scientists that were so frequent before March 1976.

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Liposomes: European Research

Having read "Liposomes: Research applications grow" by Jean L. Marx (Research News, 10 Mar., p. 1056), I am concerned that relevant research in Europe, where the liposome drug carrier concept (as well as a great many of the current ideas) originated (*1*), is reported only vaguely and parenthetically. Below I describe some of the work being done on this side of the Atlantic.

The use of liposomes in biological and medical research is the outcome of efforts during the last decade to harness drug action through the use of suitable drug carriers. These are expected to optimize, in their various ways, drug-target contact and the ensuing pharmacological effect (*2*). A possible role for liposomes as a drug carrier first became apparent in 1971 in experiments designed to control drug distribution and action (*3*). Our interest was in enzyme replacement therapy of lysosomal storage diseases, which are characterized by the absence or deficiency of specific lysosomal enzymes and the accumulation of substances in the lysosomes. We found that liposomes were capable of transporting enzymes into the lysosomes (and perhaps other compartments of cells) where, after disruption of their carrier, enzymes could then act upon stored materials. These initial experiments demonstrated that liposomes can introduce agents into cells and alter their metabolism; they thus opened the way for numerous potential applications in cell biology and therapy.

Previous therapeutic attempts with exogenous enzymes in the treatment of lysosomal storage diseases had failed for various reasons, including immunogenicity of the foreign enzyme, its premature inactivation, and its inability to reach, or act in, afflicted cells. Experiments on animals indicated that circumvention of some of these problems appeared likely, and we tested the approach (*4*) in a patient with adult Gaucher's disease. During 2 years of treatment with liposome-entrapped glucocerebroside:β-glucosidase isolated from human placenta, the general health of the patient stopped deteriorating, the liver decreased in size, and pressure in the abdomen diminished. However, using liposomes in the treatment of other lysosomal storage conditions (*5*) may be less hopeful. On the other hand, there is hardly anything else one can do with such diseases, and exploration of alternative relevant possibilities (*6*) offered by the system is worth pursuing.

One of the early proposed uses of liposomes was in cancer chemotherapy (*7*), where indiscriminate drug action prevents effective treatment. Studies of tissue distribution in humans and animals indicated that liposome-entrapped agents have considerable access to malignant tissues and that uptake of such agents by rapidly proliferating normal cells is diminished. Further, chemotherapy of mice with ascites tumors was promising in that cytotoxic drugs given by means of liposomes appeared more effective than free drugs in prolonging survival (*8*). Many laboratories are now engaged in studying how various liposomal preparations containing drugs interact with a number of tumor cell lines in vitro (*1*). At the same time, however, success in the management of cancer is ultimately dependent on the carrier finding its way to diseased areas. In this respect the roles of the liver and spleen, which normally intercept much of the injected dose; of blood components, which will alter the surface characteristics (and properties) of liposomes; and of the various anatomic barriers that exist between target cells and liposomes in the circulating blood are of paramount importance. Since "traveling" of liposomes to diseased areas precedes their interaction with relevant cells, resolution of such parameters warrants priority. Our recent work (*9*) shows that hepatic and splenic interference is diminished and the concentration of liposomal drugs in tumor areas is augmented when small liposomes (about 80 nanometers in diameter) are used. This is, of course, still a large size compared to that of most drug molecules, and free diffusion to tumors is bound to be restricted. But it is the size of the carrier along with other structural properties that prevents drugs from being wasted or from entering some of the more sensitive normal cells in the body. In addition, it may be possible to improve on the tendency of liposomes to concentrate in malignant tissues. We have shown (*10*) that enrichment of the liposomal surface with molecules (for example, antibodies to tumors) which exhibit a specific affinity for target cells, promotes selective association with the cells. Such association is an obligatory step for interiorization.

The avidity of the liver and the spleen for liposomes implies that the use of liposomes as carriers can be particularly helpful in the alleviation of diseases