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Selected manuscripts from the issues of the Journal of Nuclear Medicine published 15 and 30 years ago.
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Vesicle Interactions with Polyamino Acids and Antibody: In Vitro and In Vivo Studies

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In Vivo Distribution of Vesicles Loaded with Radiopharmaceuticals: A Study of Different Routes of Administration

June K. Dunnick, I. Ross McDougall, Michael L. Goris, and Joseph P. Kriss

Artificial spherules or vesicles, formed from phosphatidylcholine and gangliosides and enclosing $^{99m}TcO4$, survive intact in the circulation of the mouse. These vesicles remain intact when polyamino acids are incorporated into and onto them.

Studies of the distribution of polyamino acid-vesicles and protein vesicles in vivo uncovered that the latter distribute differently compared with standard vesicles or with free protein alone. In contrast, aromatic polyamino acid-vesicles concentrate in the liver and spleen to a greater extent than standard vesicles.

The permeability and stability characteristics of vesicles may be preserved then, when they are modified by the addition of protein or polyamino acids. This modification of vesicles may be associated with an alteration of their fate in vivo.

The potential exists, therefore, to use vesicles as carriers of radiopharmaceuticals and other drugs and to direct the vesicles preferentially to tissue targets in vivo.

The in vivo distribution of vesicles containing radiopharmaceuticals in their cavities was studied using three routes of administration: intravenous, subcutaneous, and intraperitoneal. In vivo distribution in mice was determined by dissection of the animals and calculation of radioactivity in the organs. In rats, the in vivo distribution was assessed by scintigraphy using a scintillation camera-digital computer unit.

After i.v. injection of vesicles, the radioactivity is concentrated in, to some extent, the liver and spleen, but the pattern of distribution is different from that of the corresponding free radiopharmaceutical. The permeability of the vesicular membrane to contain radiopharmaceutical has been shown to vary according to the chemical composition of the vesicles.

We conclude that vesicles can be used to introduce materials in vivo and that the potential exists for their specific targeting by coupling other molecules to their surfaces. ■

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Half-Life

I. Ross McDougall

The article on vesicles, published 15 years ago in *The Journal of Nuclear Medicine*, was actually one of a pair of articles published back to back.

The laboratory work was done when I was a research fellow at Stanford University Medical Center. At that time (and now), one of the key problems was delivery of radiopharmaceuticals to target organs. In the course of discussion, the late Joe Kriss and I came across a series of articles in *Hospital Practice*, which dealt with the structure of cell membranes, including one about artificial membranes, liposomes, and vesicles. It occured to Joe and me that these might provide a mechanism whereby packages of radioactive tracers could be directed at target sites. Coincidentally, Michael Goris joined the faculty and was able to provide expertise in computing of in vivo distribution studies in animals. One hundred yards from the medical center, Harden McConnell, in the department of physical chemistry, was at the forefront of chemical studies using artificially prepared liposomes. The final building block was the good fortune of having June Dunnick, a PhD in chemistry, accompany her husband to his residency in diagnostic radiology. June was our "in-house" chemist; I was responsible for the biology and in vivo studies, Michael Goris for computer, statistical, and mathematical help, and Joe was our overall mentor. Our first publication, in the *Proceedings of the National Academy of Sciences*, demonstrated that vesicles loaded with radiopharmaceuticals could be injected into experimental animals and remain intact in circulation. The two articles published in *JNM* were corollaries to that article.

This was a very exciting period, but unfortunately I am not actively involved in vesicle research today. There are now companies devoted to the production of artificial lipid vesicles. Currently, George Segall, one of my colleagues, continues research with vesicles and I have a tinge of regret that time does not allow me to be more actively involved with his projects. ■