

## LETTERS TO THE EDITOR

### Detrimental Effect of Indium-111 on Human Lymphocytes?

In a recent issue of the *Journal*, ten Berge et al. concluded that indium-111 "has detrimental effect on human lymphocytes" (1). This article must certainly be viewed with apprehension, since several centers are using indium-111 labeling techniques. As we are also involved in the study of indium-111 cytotoxicity, we would like to question ten Berge's data and their conclusions.

According to ten Berge, lymphocyte proliferation was inhibited by doses of indium-111 greater than 2  $\mu\text{Ci}$  for  $10^7$  cells. We have found that even larger doses do not affect lymphocyte phenotypic expression as evaluated by monoclonal antibodies (2) and that the cells are capable of recirculating and migrating into peripheral organs (3). As far as chromosomal aberrations induced by indium-111 are concerned, the data published by ten Berge included only two subjects. In one of them, the reported cellular spontaneous aberrations (i.e., cells not incubated with indium-111) were 14%, whereas the accepted normal level of spontaneous aberrations is no more than 3%. In our opinion this subject should have not been included. Furthermore, using 3  $\mu\text{Ci} \times 10^7$  cells, ten Berge observed over 50% chromosomal aberrations. As 3  $\mu\text{Ci} \times 10^7$  cells correspond only to 85 rad for 48 hr exposure, or 128 rad for 72 hr exposure—the culture times used by ten Berge—even without allowing for the radioactive decay (4), this finding is in contrast with data previously produced by one of the coauthors (5), indicating that lymphocyte irradiation with 100 rad induced acentric and dicentric aberrations below 20%.

Last but not least, since it has been shown that "there is not one human radiosensitivity to chromosomal aberrations production but, even amongst normal donors, there exist great differences" (5), we doubt whether on the basis of one single subject, ten Berge et al. can claim that "indium-111 has detrimental effect on human lymphocytes."

Further studies on a much larger number of subjects are necessary before drawing any conclusion on indium-111 cytotoxicity.

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#### REFERENCES

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3. POZZILLI P, POZZILLI C, PANTANO P, et al: Tracking of indium-111 oxine labelled lymphocytes in autoimmune thyroid disease. *Clin Endocrinol* 19:111-116, 1983
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### Reply

In reply to the letter of Pozzilli et al., I would like to make the following comments regarding the data on chromosome aberrations.

1. Irrespective of the frequencies of spontaneous aberrations, lymphocytes from both the subjects responded with a dose-dependent increase in chromosomal aberrations on incubation with In-111, which indicates that In-111 induces chromosomal aberrations.

2. The comparison of the induced frequencies of aberrations by In-111 and x-rays is not totally valid, as the treatment regimes are different. X-irradiation is done during  $G_0$ , a relatively radio-resistant cell stage, whereas In-111 was present during all the stages of cell cycle, some of which are extremely radiosensitive. In addition, there are the concepts of RBE and LET in the radiobiological effects of different radiations, and Pozzilli et al. do not seem to be aware of this.

3. The interindividual variability for radiosensitivity is within a factor of two, and there is no really great difference. Irrespective of the inherent sensitivity, there is always a good dose response, which is the case with the two subjects used in our study.

I suggest that the physicians should use the concepts of "benefit-risk assessment" for the patients before using In-111-labeled lymphocytes.

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### Re: First-Pass Measurements of Regional Blood Flow with External Detectors

In a recently published article, Drs. Mullani and Gould presented a first-pass model to measure blood flow (1). Using peak-counts method, they applied the model to the measurement of myocardial blood flow using rubidium-82 as the tracer. An excellent linear correlation between the blood flow measured by their method and by the labeled-microsphere method was seen, indicating the general validity of the peak-counts method. The slope of the relationship deviated from the ideal slope of unity, however, indicating a systematic error in the method. I would like to suggest a source for this error.

The first-pass model requires that the sampling time be shorter than the shortest transit time of the tracer through the capillary bed in the region of interest. This shortest transit time can be measured by rapid sequential venous sampling after bolus arterial