UNIVERSITY OF CINCINNATI
COLLEGE OF MEDICINE

MAILING ADDRESS:
ISOTOPE LABORATORY
TI GENERAL HOSPITAL
INTL OHIO 45219

ACH1.000008.035t

November 30, 1970

Dr. Evelyn V. Hess
Chairman
Faculty Committee on Research
Division of Immunology
J-4

Dear Evelyn:

Thanks for your letter of November 19, 1970 and I must again apologize for our inability to meet with your committee on November 3.

I am, however, appreciative of the stringent requirements which all human research must fulfill. I have reviewed the protocol which was sent you and I do not consider it satisfactory! I blush that I permitted my name to be substituted for Ben Friedman's when it was sent up to you at your request. It is indeed out of date and I am currently rewriting it totally. This may take a couple of weeks because I am simultaneously preparing an article on our improved technique for marrow transplantation and will do the two concurrently. I am including the survival results of all patients with whom I have worked since my arrival here. The fact that two of the first three patients whom I treated died indicates only that I selected poor candidates for irradiation whose conditions were terminal at the time of the therapy. The doses given to each weren't sufficient to account for their deaths, for neither will cause life threatening hematologic depression.

The prospectus which you received mentions protocols A and B which I will try to dig out of Gene Saenger's old files. I'm uncertain as to what they are. Protocol C is yours, of course.

Tumor palliation is to be measured by constructing life tables to compare the per cent of those at risk surviving each year with available data on untreated patients. I do not feel that we have enough data to prepare such tables after only two years of work. However, Bernie Aron will concur that a striking number of our patients so treated have had a remarkably benign course. Whether this has been the result of patient selection or our therapy we do not know yet.

The palliation by bone marrow transplantation of hematopoietic depression induced by radiation is to be measured by peripheral blood counts as you noted.

Because storing bone marrow at low temperature decreases the survival of the cells somewhat, and because the techniques employed by my predecessor had given no clear evidence of a successful marrow transplant, I have elected not to store bone marrow at this time. Marrow is removed from the patient under general anesthesia, and when the patient is awake the radiotherapy is given; then about four hours after the marrow is removed it is reinfused intravenously. This gives us optimum cell survival and hence optimum clinical results. Marrow is given the same day as the irradiation rather than waiting until the blood counts have dropped. If one waits, then one can not differentiate natural marrow recovery from the effect of the graft.

The psychological problems of patients in Life Islands are well known to both of us. We are still planning to obtain a laminar flow unit at some time in the future but this is not available at this time.

There are no risks of clinically or pathologically significant pulmonary emboli with the techniques used. In fact, in Ben Friedman's protocol which you now have he notes on page 7 that the three patients to whom unfiltered marrow was given intravenously had been studied post mortem shortly after the infusion by Drs. Gall and Yamachuchi. According to his report, "no evidence of pulmonary emboli, pulmonary infarction or other disease as a result of marrow infusion was found by microscopic examination."* I have been obtaining electrocardiograms, lung scans and arterial gases on our marrow transplant patients before and after infusion of the marrow and there has never been a change.

In patients who have been previously irradiated there is some evidence for a serum factor which breaks the chromosomes of normal people but the experiments showing this are flawed. We have done extensive experimentation to confirm these findings and have not been able to do so.

I shall rewrite the voluntary consent form to have one for

* [illegible]

total body radiation and one for bone marrow transplantation.

Again, let me apoligize for allowing the old protocol to be sent you. I permitted my name to replace that of Ben Friedman on what was essentially the old protocol before I had had an opportunity to acquaint myself as fully with the field as I have now. The revised protocol, which should be done within two weeks, should reflect a bit better the quality of our work. I really didn't understand the thrust of your letter of November 19 until I had reread the old protocol! It leaves a lot to be desired.

Very sincerely,

Edward B. Silberstein, M.D.

EBS/ml