

FROM: SGHRI

9 August 1972

SUBJECT: Research Proposal

TO: SGS

I. TITLE: The spleen in malignancy

II. PURPOSE AND BACKGROUND: We propose to test two aspects of splenic function in patients with proven malignancy. First, do some cancer patients have enhanced reticuloendothelial phagocytic activity, and second, can such activity be reduced in cancer patients by the administration of a bacterial vaccine? Liver scans performed with technetium-^{99m} sulfur colloid normally show a preponderance of radioactivity in the liver as compared to the spleen. Indeed, 90% of the radioactive colloid is said to be extracted by the liver (1). Under certain conditions the intensity of scintillations from the spleen exceeds that from the liver. Cirrhosis has long been known to produce this situation (2). An assortment of other conditions has also been reported and includes anemia (3), sarcoidosis (4), congestive heart failure (5), and a number of myeloproliferative disorders (6). We have recently noted the occurrence of this phenomenon in patients with a variety of cancers, notably of the breast and lung as well as melanomas.

Increased splenic uptake of colloid has been explained in the past (6) on an increase in splenic bloodflow. That such a phenomenon may be operant in the case of diffuse parenchymal liver disease (either cirrhotic or infiltrative) seems reasonable from our knowledge of the histopathologic

nature of these diseases. Such a mechanism is not apparent in the case of iron deficiency anemia (3) or of our cases of malignancies in whom there is good circumstantial evidence that metastatic disease has not extensively invaded the liver.

We are, therefore, interested in the possibility that we are observing a phenomenon of increased phagocytic activity as suggested by Bases and Krakoff (7) who studied myeloproliferative disorders and found excessively rapid blood clearance of colloidal, heat-denatured I¹³¹-labeled human albumin.

III. BIBLIOGRAPHY:

1. Harper, P. V., Lathrop, K. A. and Richards, P.: Tc^{99m} as a radiocolloid (abs), J. Nucl. Med. 5:382, 1964.
2. Wagner H. N., Jr, and Mishkin, F.: Principles of nuclear medicine, p. 599, W. B. Saunders Co., Philadelphia, 1968.
3. Beckerman, C. and Gottschalk, A.: Diagnostic significance of the relative uptake of liver compared with spleen in ^{99m}Tc-sulfur colloid scintiphotography, J. Nucl. Med. 12:237, 1971.
4. McAfee, J. G., Anse, R. G. and Wagner, J. N. Jr: Diagnostic value of scintillation scanning of the liver. Arch. Intern. Med. 116:95, 1965.
5. Gould, L., Collier, C., Comprecht, R. F. et al: Scintiphotography in congestive heart failure. JAMA 219:1734, 1972.
6. Eddleston, A., Blendis, L., Osborn, S., and Williams, R.: Significance of increased 'splenic uptake' on liver scintiscanning. Gut 10:711, 1969.
7. Bases, R. E. and Krakoff, I. H.: Enhanced reticuloendothelial activity in myeloproliferative disorders. J. Reticuloendothel. Soc. 2:1, 1965.

IV. TECHNICAL APPROACH: Two experimental lines will be followed.

1. Phagocytic activity - In 10 patients with cancer who demonstrate the splenic uptake phenomenon, serial blood specimens will be withdrawn from an indwelling catheter over a period of 30-40 minutes. The clearance time of Tc-sulfur-colloid will be compared to that of 10 cancer patients who have normal colloid liver-spleen scans. Informed consent will be obtained.

2. Induced immunologic hyper-reactivity - We do not feel justified in exposing normal subjects to the radiation exposure of a colloid liver scan (as relatively small as it is) in order to ascertain whether increased splenic uptake occurs in "normal" persons. We would like to know, however, whether increased splenic phagocytosis can be induced. We will measure baseline typhoid agglutinin in 10 cancer patients who have normal liver-spleen scans. We will give each patient 0.1 ml of typhoid vaccine intradermally and repeat a spleen-liver scan and typhoid agglutinin titre in 7 days. Informed consent will be obtained in all patients. Typhoid agglutinin titers will be performed by the pathology laboratory, serology section.

Internal gamma doses from technetium sulfur colloid scans are enumerated:

liver	- 300 millirads
spleen	- 150 millirads
bone marrow	- 30 millirads

These doses are in the range of conventional x-ray exams. The clinical pathology laboratory has agreed to perform the serologies involved.

V. EQUIPMENT AND SUPPLIES: All equipment and supplies are on hand.

VI. INVESTIGATIVE SCHEDULE: Estimated time required will be 6 months.

VII. EXPERIMENTAL SUBJECTS: All subjects studied will be those with proven cancer. Informed consent will be obtained from all.

VIII. USE OF DRUGS: N/A

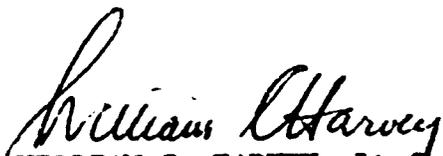
IX. PERSONNEL DATA:

Medical Facility Director: Paul W. Myers, Brigadier General, USAF, MC

Principle Investigator: William C. Harvey, Lt Colonel, USAF, MC

X. MANPOWER:

Lt Col AFSC 9836 100 hours duty time 100 hours off-duty time



WILLIAM C. HARVEY, Lt Colonel, USAF, MC
Chief, Nuclear Medicine Service