

Recent Advances and Concepts in Nuclear Hematology

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The use of ^{32}P by Lawrence for the treatment of polycythemia vera and leukemia and the use of ^{59}Fe by Hevesy for the study of anemia were the beginnings almost fifty years ago of both Nuclear Hematology and modern Nuclear Medicine using man-made radionuclides. In the forties red cell volume was determined with ^{32}P , plasma volume with ^{131}I , to be replaced in the fifties and sixties by ^{51}Cr and ^{125}I , respectively. At that time ^{51}Cr was also used to measure red cell and platelet survival and sequestration. ^{59}Fe was used as a cohort label to quantitate and localize red cell production and destruction and used to investigate iron absorption and metabolism. The use of DF^{32}P for the measurement of leukocyte and platelet kinetics as well as red cell survival was also introduced in the fifties. The use of ^{51}Cr for measurement of platelet survival and splenic sequestration was superceded in the seventies by imageable ^{111}In , which was also used to label white blood cells. Currently, in the eighties, new advances in nuclear hematology are unfolding through the use of $^{99\text{m}}\text{Tc}$ and the development of new coupling reagents, receptor-mediated labeling, and labeled monoclonal antibodies.

The use of $^{99\text{m}}\text{Tc}$ labeled pretinned red cells for blood pool imaging is superior to $^{99\text{m}}\text{Tc}$ -HSA. In addition to widespread use for imaging cardiac chambers, $^{99\text{m}}\text{Tc}$ -RBC is also used for the sensitive and specific localization of gastrointestinal bleeding. The $^{99\text{m}}\text{Tc}$ label is sufficiently stable in vivo for the accurate determination of red cell volume and the in vivo crossmatching of bank blood with possible simultaneous use of ^{111}In -RBC or ^{51}Cr -RBC. Heat treated $^{99\text{m}}\text{Tc}$ -RBC provides excellent selective imaging of the spleen. While ^{51}Cr -RBC are still used to assess the extent of splenic sequestration in hemolytic anemias, in vivo ^{59}Fe cohort labeling of RBC is superior, providing more rapid and accurate measurement of possible splenic extramedullary erythropoiesis as well as red cell sequestration and destruction. Imaging of erythropoietic sites is most conveniently performed with ^{111}In , even though reticuloendothelial cells as well as immature red cells are labeled. The use of radioiron for selective labeling of erythrocyte precursors is preferable; however, either a specialized high energy scanner for ^{59}Fe or a positron camera for ^{52}Fe is required. Noninvasive quantitation of total body mobilizable iron is best performed by measurement of a 6 hour urine collection after intravenous injection of ^{59}Fe -DTPA.

The use of ^{111}In for labeling platelets permits both measurement of survival and imaging of aggregation sites. While oxine (18-hydroxyquinolone) is the most commonly used lipophilic ^{111}In ligand used for both platelet and leukocyte labeling, other chelates, particularly tropolone, may provide some advantages. ^{111}In -platelets are useful in determining platelet kinetics and survival, imaging sites of sequestration—particularly evaluation for splenectomy, and imaging thrombi.

Monoclonal antiplatelet antibodies labeled with ^{111}In or ^{123}I show promise for imaging thrombi and vascular lesions. ^{111}In -leukocytes are now widely used in a sensitive and specific procedure for acute abscess localization. Oxine is the most popular lipophilic chelating agent for labeling mixed leukocytes for scintillation camera imaging of focal inflammation. Recent experience with tropolone, another indiscriminate lipophilic cell-labeling agent, demonstrates its superiority because of its ability to label cells in small volumes of plasma. Procedure time is reduced, injury from wash-out is eliminated, and subsequent *in vivo* lung sequestration is avoided, thereby permitting more rapid localization and imaging of granulocytes. A number of continuing efforts to develop a $^{99\text{m}}\text{Tc}$ cell-labeling agent comparable to the ^{111}In lipophilic chelates have yet to succeed. Significant recent advances include isolation and labeling of specific leukocyte cell types such as granulocytes, lymphocytes, and their specific subsets, in order to study their migration and kinetics *in vivo*. New techniques of cell harvesting are utilized and more selective ligands for specific cell surface receptors are being developed so as to avoid laborious separation techniques and decrease radiation injury. Current labeling of lymphocytes with lipophilic chelating agents internalizes the radionuclide so that radiation injury of the sensitive lymphocyte is a major problem in the study of its migration. Use of a gamma-emitting agent which binds irreversibly to the cell membrane would reduce radiation of the nucleus. Selective labeling of lymphocyte subsets is required to discover differences in their migration and function in health and disease. Radiolabeled monoclonal antibodies against cell-surface antigens appear particularly promising for selective leukocyte labeling.

The past fifty years in nuclear hematology have encompassed remarkable advances in radionuclide production, instrumentation, radiochemistry, molecular biology, cell receptor, and immunologic techniques. During this entire period, the central guiding and productive motivation of the development of nuclear hematology has been and continues to be the demonstration of human function in health and disease. These demonstrations are permanent advances. A recent prospective controlled prolonged comparative study of ^{32}P , chemotherapy and venesection demonstrated that ^{32}P therapy of polycythemia vera still remains the treatment of choice.