A new in vitro method is presented, based on the ‘uptake’ of 1-131 T-3 by red blood cells from whole blood. The simple test accurately differentiates hyper-, hypo-, and euthyroidism, is unaffected by iodine exposure, avoids administration of radioactivity to patients, and indicates several epiphenomena of wide biologic and clinical interest. [The SC® indicates that this paper has been cited over 320 times since 1961.]

Milton W. Hamolsky
Department of Medicine
Brown University
Rhode Island Hospital
Providence, RI 02902

October 30, 1980

Our studies were based on a) the fact that thyroxin (T-4) and triiodothyronine (T-3) molecules are both hydrophilic and lipophilic, and b) the notion that their hormonal action might therefore involve alignment at, and alteration of, the aqueous plasma-lipid membrane interface.

"We found: 1-131 T-4 or 1-131 T-3 passed in vitro from buffers to olive or mineral oil, lipid extracts of tissue or cell components, to the rat diaphragm, foreskin, or red blood cell nicely ‘diagnosed’ the thyroid status of the plasma donor — ‘uptakes’ were greater from hyper- than from euthyroid plasmas. The standard clinical test involved addition of 1-131 T-3 to a 3 ml. aliquot of whole blood, incubation at 37° for two hours, determination of percent incorporation of T-3 by the washed red cell mass, corrected for hematocrit. 'Crisscross' studies (euthyroid cells in hyperthyroid plasmas, etc.) revealed that 'uptakes' were determined by the thyroid status of the plasma donor. This served as the basis for widespread use of resins, coated charcoal, clay, etc., in place of the red cell as the competitive binder of 1-131 T-3 from plasma or serum.

"We offered then the in vitro T-3 uptake test which was simple, rapid, reproducible, avoiding administration of radioactivity to the patient, with a differential diagnostic accuracy equal or superior to then available methods, accurate in following therapy of hyper- or hypothyroidism. The test was modified—for pediatrics—to use only 0.5 ml. whole blood. Results were not affected by prior exposure to iodine containing compounds or X-ray dyes which vitiated the then current PBI or 1-131 thyroid uptake tests.

"In continuing series (3,900 tests!), we found uptakes were decreased by estrogen and pregnancy (failure of lowered uptake in pregnancy presaged miscarriage) and in families with excess TBC, increased in nephrosis, acidoses, anticoagulant therapy, Dillantin — phenomena which led to studies in many laboratories around the world. For, in addition to the above advantages, citation of our article may be attributed to its introduction at a time of explosive ferment of biological and clinical studies of the thyroid gland.

"In 1977, I was selected by the Mallinckrodt Company as a 'Founder of Nuclear Medicine' for the development of 'the first T-3 in vitro diagnostic test.'"