CROSS-REACTION OF SCHWARZ/MANN DIGOXIN ANTIBODY WITH A NORMAL CONTROL SERUM

We would like to report on the underestimation of digoxin serum levels that can result from the use of the ^{125}I-Digoxin radioimmunoassay kit (Schwarz/Mann) in combination with Moni-trol I (Lot # LTD 120B) manufactured by Dade (Division of the American Hospital Corporation). Moni-trol I is often used as the digoxin-free serum required in the preparation of the standard curve and control tubes, i.e., tubes containing no antibody and/or no "cold" digoxin standard.

We have found that the S/M digoxin antibody (Lot # YN 6208) cross-reacts with something in this particular lot of Monti-trol I, perhaps another serum steroid. This results in a displacement of ^{125}I-digoxin from the antibody and will produce a digoxin serum level in the therapeutic range. Other digoxin-free serum samples assayed at the same time did not show this displacement.

If Moni-trol I is used in the preparation of the standard curve, this will result in an *underestimation* of digoxin serum levels. Both the 100% tubes (antibody + ^{125}I-digoxin, no cold digoxin) and the standard curve tubes contain spuriously lower binding of ^{125}I-digoxin to antibody due to antibody cross-reaction with some substance in the Moni-trol I serum. Thus, patient serum sample compared with lower percent binding of standards leads to an underestimation of the digoxin serum level.

Moni-trol I was checked in two other assay systems (^{3}H-digoxin kit from New England Nuclear and ^{125}I-digoxin system using antibody developed at WHMC), and no displacement of tracer was noted in either procedure. Therefore, it is concluded that it is the S/M antibody cross-reacting with some substance in the Moni-trol I that is producing the false digoxin level.

Moni-trol I (Lot # LTD 120B) was assayed in triplicate in three different S/M digoxin assays by two different technicians and a "digoxin" serum value of 0.51 ± 0.04 (s.e.m.) was obtained. This interference was detected due to digoxin-free serum samples producing large negative digoxin levels, i.e., percent of antibody bound to digoxin in the serum sample was much greater than 100%.

This points out the need for assaying and checking for cross-reactivity of normal control serums before their use in radioimmunoassay procedures even though it is thought to be hormone- or drug-free and/or the antibody is thought not to cross-react with other serum steroids.

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RADIONUCLIDE CISTERNOGRAPHY—PREDICTION OF CLINICAL RESULTS OF NEUROSURGICAL SHUNTING IN PATIENTS WITH COMMUNICATING NORMAL PRESSURE HYDROCEPHALUS—FACT OR FANTASY

The concept of a correctable form of communicating hydrocephalus associated with normal cerebrospinal fluid pressure and certain neurological findings has been considered as a clinical entity since the work of Foltz and Ward, 1956 (*1*) and Raymond Adams and his associates in 1965 (*2*). Since that time there has been more than an abiding interest in this syndrome among clinicians after evidence was presented that improvement in the clinical status of these patients could be achieved by neurosurgical shunting. In the past several years radionuclide cisternography has been offered as one of the modalities that could be used in helping to evaluate this condition and assist in the selection of those patients most likely to benefit from shunting.

The classical criteria for considering a radionuclide cisternogram compatible with communicating hydrocephalus has been penetration of the radiopharmaceutical into the ventricular system with delayed or absent migration of the tracer around the cerebral hemispheres (*3*). Delayed absorption of the radiopharmaceutical from the ventricles or from the cerebral subarachnoid spaces has been reported as being characteristic in the more "positive" cases. Much controversy has existed concerning the significance of "early penetration" of the tracer into the ventricles and its subsequent rapid disappearance. Similarly, a "slow rate" of migration of the tracer around the cerebral hemispheres has been considered to be compatible with cortical atrophy but there appears to be a difference in the rate of migration with various tracers, possibly depending upon their molecular characteristics, leading to the difficulty in determining what the "normal rate" is.

Correlative studies between the findings on cisternography and the results of shunting have not

given clear-cut answers to the predictability of beneficial results following various neurosurgical shunting procedures, probably because no series has been large enough to provide definitive data on the subject. Recently, two articles (*4,5*) have suggested that there is poor correlation between a "positive" cisternogram and the results likely to be achieved by shunting. These articles have further suggested that patients with "normal" cisternograms may nonetheless show improvement in neurological status following surgery. Thus, we are faced with at least three questions. First, is a "positive" radionuclide cisternogram an adequate indicator of communicating hydrocephalus? Second, can the success of shunt in any given patient be predicted by the particular cisternographic abnormality observed? Third, are there other entities not definable by radionuclide cisternography that may be amenable to shunting? In other words, are we denying surgery to patients based on a "normal" cisternogram? Conversely, are we unintentionally participating in the decision to offer surgery to too large a segment of our aging population based on too little knowledge on our part concerning the sensitivity and specificity of cisternography as well as the overall risk and cost of this diagnostic test.

The understanding of rates of tracer migration and early ventricular entry are, likewise, areas for study. For reasons already mentioned, it would seem appropriate for nuclear medicine to embark upon a multi-institutional study concerning the usefulness of radionuclide cisternography in the evaluation of this disease spectrum. Until such time as a more definitive study is undertaken, there will continue to be a serious question concerning the value of cisternography in helping to select patients most likely to benefit from various neurosurgical interventions. It is time to resolve this question and we would like to know who would be interested in participating in such a project.

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RADIONUCLIDIC CONTAMINATION OF ELUATES FROM FISSION-PRODUCT MOLYBDENUM-TECHNETIUM GENERATORS

The USAEC and the agreement states have promulgated regulations that limit the presence of specific radionuclidic contaminants in eluates from ^{99}Mo generators whether they are produced from irradiated molybdenum or separated from fission products. Additionally, they have imposed a gross limit on other gamma-emitting impurities in the eluates. Thus, it is required that the licensee, or user, perform at least a "pseudoradionuclidic" impurity check before the administration of any eluate to patients so that these limits will not be exceeded.

The current state of the art in the manufacture of molybdenum-technetium generators is such that a serious breakthrough of the parent ^{99}Mo in the eluate is not likely. Indeed, only two such instances have been observed in our laboratories over the past 3½ years. We still consider it necessary, however, to perform a radionuclidic purity check each time a generator is eluted for at least two reasons:

1. To guard against massive breakthrough of the parent which may be caused by any break in the integrity of the alumina column or filter frit;
2. To identify any other radioactive impurities that may be present in the eluate.

We note with interest that others have confirmed the presence of ^{132}I in fission-product generator eluates (*1*). We note also with interest the concern of Bardfeld and Rudin (*2*) in radionuclidic contamination of instant ^{99m}Tc. We would encourage them to augment their investigation with firm radionuclidic identification.

In eluates from irradiated molybdenum generators, we have found ^{92}Nb to be more common than ^{99}Mo. In eluates from fission-product molybdenum generators we have found only trace amounts of ^{99}Mo but we have found some measurable amount of ^{132}I in every eluate. On occasion we have detected in