Maternal Iodine Supplementation: 
Clinical Trials and Assessment of Outcomes

September 22-23, 2014

Executive Summary

The Office of Dietary Supplements (ODS), National Institutes of Health (NIH), began an iodine initiative in 2011 to provide new tools to advance investigator-initiated research relevant to iodine status and its relation to health outcomes. The ODS has been working with other government groups, including the U.S. National Institute of Standards and Technology (NIST) in an effort to improve existing analytical methods and develop new approaches to facilitate the evaluation of iodine status, with an emphasis on vulnerable population groups such as pregnant women. Participants at this workshop discussed issues of iodine status in pregnant women, the potential impact of sub-optimal status on pregnancy outcomes and child development, and suitable study designs for addressing iodine status concerns in regions with differing levels of risk.

This was the third in a series of three iodine-related workshops sponsored by the ODS. The first workshop, held April 22-23, 2014, focused on exposure, specifically the measurement of iodine intake from both foods and dietary supplements (the United States is one of the few developed countries that does not have mandatory iodine fortification). The second workshop, held July 22-23, focused on indices of status outside of urinary iodine concentration (the most widely used index of status), including those related to thyroid function. Workshop participants also discussed the development and use of standard reference methods and materials in addition to concepts fundamental to the quality of laboratory data.

The first day of this workshop included presentations grouped into two sessions: (1) Iodine Status Across the Range of Exposures, and (2) Study Design Considerations. The second day featured in-depth discussions led by Workshop Chair Dr. Abby Ershow (NHLBI, NIH) in the areas of ancillary studies, outcomes, and research resources. Major themes, research needs, and suggestions for future research that arose from the presentations and discussions appear below.

Ancillary Studies

• There are many pragmatic issues to be considered that will affect the selection of the best mechanism for conducting future work in this area. Options include a secondary analysis using existing data or samples, an ancillary study of a current study (that may or may not be focused on iodine), a before-after study, or a new multicenter trial.
• Videos and other recordings of child/infant assessments could be mined (possibly as part of an R21 project) to help determine what appropriate outcome measures might be as part of a larger effort.
• There is currently no good measure of an individual’s iodine status at a given moment in time—this is a pressing need. Not having an adequate measure of the impact of iodine supplementation in pregnancy is handicapping research in this area. Serum organic iodine may be an ideal biomarker for iodine status if a reliable method becomes available; however, the cost of these tests may be too prohibitive.
• A new multicenter clinical trial is likely needed to fully measure the impact of iodine supplementation. Such a trial will require significant time and significant funds. Before such a trial is undertaken, significant work is needed related to the validity and reliability of outcome
measures in the child as well as basic science on the neurobiology of thyroid hormones on the brain to enhance understanding of which neuropsychological tests are most appropriate.

Outcomes
- The developmental psychology field has a number of tools for assessing cognitive and motor development. To select the most appropriate tools, current knowledge of the affects of thyroid function on psychological development must be improved.
- A number of coordinated, small-scale studies could be conducted to adequately characterize iodine status in a systems-level approach to assessment that includes the identification of measures that appear to be sensitive.
- Most work suggests that there is very little correlation between Bayley scores and later IQ; there are information processing/attention-based measures used in infancy that correlate better with IQ and executive functioning (particularly frontal lobe types of tasks).
- Authoritative review articles that focus on the array of tests available for measuring cognitive development may be helpful for informing the design of future trials.
- A rich set of literature shows the improvements that occur in 8-12 year olds in response to correction of hypothyroidism. This appears to be a logical place to start in terms of planning future research activities for younger populations; there are likely infant analogs of the tests conducted in the 8-12 year olds that are already available and could be capitalized upon.
- That there are also measures of how infants habituate and how quickly they will react to a stimulus; these types of measures in infants correlate with later IQ scores and would be appropriate starting points to generate hypotheses about where early differences might show up.

Research Resources – Roundtable Discussion Highlights
- The current version of the NIH Toolbox was designed to be used in the population of 3-85 year-olds, there is nothing in the NIH Toolbox for children younger than 3 years at present. Adding items/tests/assessments to the NIH Toolbox for children under age 3 is a need.
- In addition to infants, populations of concern include pregnant women, those at risk of becoming pregnant, lactating women, adolescent girls, and older adults.
- Food, dietary supplements, and urinary iodine, all need to be factored in and correlated to arrive at an individual’s dietary status.
- Biomarkers for intake, nutritional status, and outcomes are needed. Safety is also a consideration—are there biomarkers of deficiency and excess that should be examined?
- Priorities include pregnancy outcomes, measures for outcomes of biochemical signs, and newer/more specific tests of development using a brain systems approach to examine the effects of iodine on brain development, motor development, and cognitive development. Linking these measures with existing tests is also a priority.
- Another need is for studies on early development and how different neural systems are affected by iodine.