PEDIATRIC ENDOCRINE SOCIETY

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On March 30th, 2022 the FDA released a Drug Safety Communication recommending monitoring of thyroid function in infants and children under 3 years of age within 3 weeks of receiving an injection of iodinated contrast media (ICM) for medical imaging. An FDA warning about the risk of iodine-induced hypothyroidism will be included in the prescribing information of all ICM injections, which is available to patients, parents/caregivers, and medical providers. The FDA based its decision on a review of 11 publications that found decreased thyroid hormone levels occurring in 1 to 15 percent of patients in this age group between 8.5 and 138 days after ICM exposure. The groups at highest risk were identified as newborns, particularly those born premature, and children in their first 3 years with underlying conditions such as heart issues that may require cardiac procedures, including catheterization and repeated ICM-based computed tomography (CT). Although most cases of iodine-induced hypothyroidism were transient and did not require treatment, the FDA recommended that thyroid dysfunction be treated as clinically indicated "to avoid future cognitive and other developmental disabilities."

Following this FDA communication, pediatric subspecialists (including endocrinologists, cardiologists, neonatologists, hospitalists, and others) and radiologists have had to determine how to incorporate recommendations into clinical practice. In response, the Pediatric Endocrine Society Drug and Therapeutics Committee has invited a group of pediatric thyroidologists to review the existing literature and compose a position statement with specific recommendations for screening, monitoring, and treatment of ICM-induced hypothyroidism. The task force will seek input and review from other stakeholders in an effort to avoid multiple (potentially conflicting) sets of recommendations.

While the task force works to complete a more-detailed position statement, preliminary comments are offered. Our intent is to optimize the identification of patients at highest risk of ICM-induced hypothyroidism while avoiding unnecessary testing and treatment for the remainder of patients.

1. Appropriate monitoring of potential iodine-induced hypothyroidism should be individualized based on the age of the patient and diagnostic risk factors.
    a. Within the 0-to-3-year age group, the highest risk patients are preterm infants and acutely ill-term infants < 3 months of age.
    b. The risk of ICM-induced hypothyroidism is highest in ill, hospitalized infants and children, with the highest proportion of reported cases in infants with cardiac disease and/or reduced renal clearance (renal insufficiency). Within this cohort of patients, higher dose of ICM and repeated exposure to ICM may be associated with prolonged, and possibly permanent, hypothyroidism.
    c. Topical and in-line exposure to iodine during cardiac by-pass and dialysis are likely additive in regard to the risk of ICM-induced hypothyroidism.
    d. The risk of clinically significant ICM-induced hypothyroidism in term neonates, infants, and older children who receive a single dose of ICM for diagnostic radiological studies only (e.g., CT) remains unclear and requires further study.

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2. If performed, the single-best initial screening test is a thyroid stimulating hormone (TSH) level obtained via peripheral venipuncture 2 to 3 weeks after receiving ICM.
    a. Thyroid hormone production may be suppressed after receiving supraphysiologic levels of iodine through decreased expression of the sodium-iodine symporter and decreased activity of thyroid peroxidase, known by the eponym of the Wolff-Chaikoff effect. In most individuals, suppression is transient if the iodine exposure does not continue with thyroid hormone production typically returning to normal after 1-2 weeks. Thus, waiting 2 weeks to measure the TSH is intended to identify children who do not "escape" the Wolff-Chaikoff effect and have persistent ICM-induced hypothyroidism.
    b. The majority of patients with iodine-induced hypothyroidism will have TSH levels well above the normal range for age. While there are no data to provide a reliable TSH-cut off for when to initiate thyroid hormone replacement therapy, premature infants and acutely ill children typically have an inappropriately low or normal TSH level when assessed within the context of a low fT4.
    c. A screening TSH > 10 mU/L should be considered abnormal and warrants confirmatory testing that includes TSH and free T4.
    d. On confirmatory testing, levothyroxine should be initiated if TSH > 20 mU/L or if TSH is elevated and free T4 is low. A confirmatory TSH between 10-20 mU/L with normal free T4 warrants repeat assessment, with the decision to treat based on clinical judgement.
3. The risk of decrements in neurocognitive development are established for patients with untreated iodine deficiency and congenital hypothyroidism. However, there are no data to support the potential negative impact of a single episode of transient, ICM-induced hypothyroidism. As infants mature over the first three years, the risk to neurocognitive development from untreated hypothyroidism likely decreases.
4. Hospitals and clinical practices will need to create a system to identify and monitor patients at high risk of developing ICM-induced hypothyroidism. We recognize that this will likely require additional organization and resources and hope that details in our forthcoming position statement will help reduce variance between specialties and optimize the health and outcomes for our patients.
5. We encourage the FDA and industry to support prospective, multi-center studies to more accurately define risk groups as well as optimize protocols for thyroid screening and potential thyroid hormone therapy. This is particularly important secondary to published data reporting a high risk of developmental delay in preterm infants as well as term infants with chronic medical conditions, specifically congenital heart disease in the context of this statement.