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American Academy of Pediatrics
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Thyroid Monitoring After Intravascular Iodinated Contrast Media in Infants and Children Through 3 Years of Age

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In March 2022, the US Food and Drug Administration issued a drug safety communication (DSC) recommending monitoring of thyroid function in children up to 3 years of age who receive intravascular injection of iodinated contrast media (IV ICM) for medical imaging. In response, a group of pediatric and imaging experts convened to review the current scientific evidence on thyroid dysfunction after IV ICM and to provide recommendations on thyroid testing and management after IV ICM administration in infants and children. There are considerable gaps in knowledge related to the risk of thyroid dysfunction in young children exposed to IV ICM, and we strongly recommend that high-quality prospective studies be proposed and funded to clarify the incidence, risk modifiers, natural history, and outcomes of thyroid dysfunction after IV ICM exposure in this population.

INTRODUCTION

On March 30, 2022, the Food and Drug Administration (FDA) issued a drug safety communication (DSC) entitled, "FDA recommends thyroid monitoring in babies and young children who receive injections of iodine-containing contrast media for medical imaging: Children with underlying conditions and newborns at higher risk."[1] Recommendations were based on 11 publications related to thyroid function following iodine exposure in pediatric patients. The DSC stated that the FDA approved the addition of a warning in the prescribing information for all ICM for injection pertaining to the risk of disrupted thyroid function in children 3 years of age or younger. The DSC recommended thyroid testing within 3 weeks for all infants

abstract

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and children through age 3 years who receive intravascular (IV) ICM. The DSC also stated that treating iodine-induced hypothyroidism may be needed to "avoid future cognitive and other developmental disabilities." In an update released in April 2023, the FDA revised this guidance to recommend that decisions about thyroid monitoring following ICM administration in children 3 years and younger not be universal but based on individual risk factors such as prematurity, very low birth weight, and underlying medical conditions affecting thyroid function.[1]

The FDA's intent to increase patient safety is laudable, but the limitations in the data used to support the new recommendations raise several significant concerns. The 2022 DSC was informed by more studies than the initial DSC from 2015 that reported 10 cases of hypothyroidism in infants under 4 months of age that were temporally associated with exposure to ICM for medical imaging. However, data remain limited regarding the true risk of hypothyroidism after IV ICM and which patients are at greatest risk. The updated 2023 FDA recommendations are narrower but may still affect the care of tens of thousands of infants and children annually, entail potential risks of increased medical testing and treatment, be a source of patient/guardian anxiety, and incur increased costs to the medical system, despite the lack of clear data on the risks of exposure to ICM or evidence of benefit from thyroid hormone replacement therapy.

In an effort to provide a unified approach to IV ICM-induced hypothyroidism, the Pediatric Endocrine Society (PES), American Academy of Pediatrics (AAP), American College of Radiology (ACR), American Thyroid Association (ATA), Society for Cardiovascular Angiography and Interventions (SCAI), and Society for Pediatric Radiology (SPR) jointly convened a group of experts to review and critically evaluate the evidence on IV ICM-induced thyroid dysfunction in children, to propose recommendations for patient monitoring and treatment, and to advocate for additional prospective, controlled studies on this important topic.

BACKGROUND ON IODINATED CONTRAST MEDIA

Iodine-containing contrast agents have been used in medical imaging since 1920.[2] Clinical use of ICM expanded widely in the 1950s due to their ability to enhance the visibility of anatomic structures and abnormalities in medical imaging. ICM are used for ionizing radiation-based imaging modalities including computed tomography (CT), fluoroscopy, angiography, venography, and lymphangiography. Although the intravenous route of administration is most common, other routes of ICM administration include intra-arterial, intralymphatic, gastrointestinal, cystourethral, vaginal, intrathecal, and intra-articular. The FDA DSC specifically addresses ICM administered by intravascular (intravenous and intraarterial) injection.

ICM agents share a tri-iodinated benzene ring which increases the molecular size compared to a single iodide molecule, thus increasing attenuation in x-ray imaging as well as reducing the osmolality and risk of toxic effects from free iodide.[2,3] Ionic ICM agents generally are not used due to the potential for toxicity except in the gastrointestinal and genitourinary tracts. Nonionic ICM agents do not dissociate in solution and generally are preferred for intravascular imaging in pediatric patients due to their lower toxicity and lower osmolality. ICM are not highly protein-bound, thus their distribution is proportionate to the rate of perfusion of each organ. ICM agents are renally cleared via glomerular filtration without appreciable tubular reabsorption.[3,4] The elimination half-life of most iodinated contrast agents is 90–120 minutes in patients with normal renal function. A list of approved ICM agents for use in the US and their physical properties can be found in the American College of Radiology Manual on Contrast Media.[5]

NEONATAL THYROID PHYSIOLOGY

Immediately after birth, term infants experience a surge in thyroid-stimulating hormone (TSH) secretion that results in elevated levels of TSH for up to 24 hours followed by a decline over several days. The postnatal TSH surge drives increased production of thyroxine (T4) and triiodothyronine (T3) by the neonatal thyroid. Higher T4 and T3 levels persist through the first weeks of life. In healthy term infants, the serum TSH concentration approximates adult levels within 4 weeks while free T4 levels decline into the adult reference range after 3 months.[6–10]

In preterm infants, the postnatal TSH surge is smaller in magnitude and may be delayed, with peak TSH levels and the degree of postnatal rise in T4 correlating directly with gestational age.[11–14] Preterm infants often have prolonged low T4 levels without an accompanying rise in TSH ("hypothyroxinemia of prematurity") due to a combination of immaturity of the hypothalamic-pituitary-thyroid axis, acute illness, medications, and nutritional challenges.[15] In some cases, a delayed rise in TSH may occur weeks later with elevation in TSH occasionally reaching levels >25 mU/L.[12,15]

PATHOPHYSIOLOGY OF IODINE-INDUCED HYPOTHYROIDISM

Exposure to excess iodine can induce hypothyroidism, a phenomenon known as the Wolff-Chaikoff effect.[16] It is thought that iodine excess inhibits iodide organification, resulting in reduced thyroid hormone synthesis and release.[17] The effect is usually transient, with "escape" (adaptation) and resumption of thyroid hormone production usually occurring within 1–2 weeks. Because the ability to escape from the Wolff-Chaikoff effect typically develops between 36 and 40 weeks gestation, infants born prematurely are more susceptible than term infants to developing hypothyroidism after excess iodine exposure.[18]

The duration of iodine-induced hypothyroidism likely depends on age (corrected for prematurity), pre-exposure iodine status (pre-existing iodine insufficiency may prolong the effect), and cumulative amount and route of iodine exposure. In adults, iodine levels typically return to baseline within 4–6 weeks after administration of IV ICM, but in some individuals iodine levels may remain elevated for several months.[19,20] There are some data on clearance of iodine after ICM in children, including two of the studies cited by the FDA DSC. In a small group of premature infants who received ICM for intravenous catheter placement, urinary iodine peaked at the earliest measurement after catheter placement and decreased exponentially through 2 months of age.[21] Another study found that very low-birthweight (VLBW) infants with exposure to ICM or topical iodine had a rapid rise in urinary iodine concentration that returned to levels similar to controls by 2 weeks post-exposure.[22]

ICM-INDUCED HYPOTHYROIDISM: REVIEW OF THE LITERATURE

The recommendations of the FDA DSC were based on a review of 11 studies of thyroid function after IV ICM exposure in children. We conducted a Pubmed search on 6/25/22 and identified five additional relevant primary studies for review published in English. We initially identified 132 articles through a search for key words "iodinated contrast" and "hypothyroidism" limited to age <18 years. Systematic reviews were used to identify additional references meeting criteria for inclusion. We excluded case reports, editorials, review articles, articles that were not in English, reports on iodine exposure in pregnant women and studies that did not include IV ICM. We also excluded reports on use of iodine to prevent hypothyroidism or endemic goiter or to treat hyperthyroidism. The 16 studies included in this review are summarized in Supplementary Table 1 and report on a total of 3878 pediatric patients from birth through 18 years of age exposed to IV ICM. Five studies were prospective, one of which was a randomized controlled trial (RCT), while the other 11 studies were retrospective.

As indicated in the FDA DSC, most patients who had abnormal thyroid function testing after IV ICM developed transient subclinical hypothyroidism that was not treated with levothyroxine.[22–25] Some studies reported no abnormalities in thyroid hormone levels following ICM administration, including IV ICM for urography, placement of central venous catheters, and cardiac computed tomography.[26–29]

Seven studies reported patients receiving treatment for hypothyroidism following IV ICM, with the percentage of individuals treated ranging from <1% to 22%. Among patients exposed to IV ICM, several factors were associated with initiation of treatment for hypothyroidism. Premature (<37 weeks gestational age) and VLBW infants (<1500g) under three months of age appeared to be at highest risk. Multiple exposures to iodine (particularly in infants undergoing cardiac catheterization), kidney disease, and additional exposure to topical iodine also may increase the risk of hypothyroidism after IV ICM exposure.

Several studies investigated the risk of ICM-induced hypothyroidism in premature infants. A study of 17 VLBW infants identified transient TSH elevation >20 mU/L in two infants who received IV ICM and in one infant with both topical and intravascular iodine exposure, but none of these infants required treatment.[22] In another study, a single patient who received levothyroxine treatment was born at 28 weeks and received IV ICM at two days.[30] In these studies, it is not clear whether transient hypothyroidism was caused by IV ICM or could have been due to delayed rise in TSH associated with prematurity. In contrast, several controlled studies of IV ICM exposure in premature infants (including one RCT) reported no cases of hypothyroidism requiring treatment and no difference in risk of TSH elevation between IV ICM-exposed and control infants.[24,25,28,29,31] In addition, one propensity score-controlled study suggested that prematurity may not be associated with increased risk of ICM-induced hypothyroidism compared to term birth.[27] Multiple exposures to iodine appears to be associated with increased risk of hypothyroidism in preterm infants.[25,39] In summary, although hypothyroidism may occur in some preterm infants following IV ICM exposure, it remains unclear if IV ICM exposure is an independent risk factor for hypothyroidism in preterm infants, and if so, whether the risk of hypothyroidism after IV ICM exposure is greater in preterm infants than term infants.

Eight studies assessed the risk of hypothyroidism in neonates, infants and young children undergoing IV ICM studies for cardiac disease. Three studies including 89 individuals reported either transient TSH elevation or no TSH elevation following cardiac imaging.[23,24,26] Of the other five studies, the rate of hypothyroidism requiring treatment ranged from 0.1% to 11.5%.[31–35] Increased risk of hypothyroidism was associated with younger postnatal age (particularly under 1–3 months) at the time of iodine exposure[26,27,33,38] and with multiple exposures to IV ICM[33,36,38]. In one study, the odds of hypothyroidism were increased 3-fold in infants who underwent more than three cardiac procedures, after controlling for baseline risk, postnatal age, and prematurity.[33,35]

Younger age at the time of IV ICM exposure was associated with increased risk of hypothyroidism in several studies.[23,24,32,34] In a study of 843 patients newborn through 3 years of age, those who developed hypothyroidism had IV ICM exposure at a mean age of 38 days (range 2–133) vs 330 days (111–619) in those who did not develop hypothyroidism ($P = .006$).[34] Two other studies demonstrated

an association between younger age and transient TSH elevation following IV ICM exposure, including a mean age of 2.3 ± 2.6 months for infants with transient, mild TSH elevation (5.80 to 9.92 mIU/mL) vs a mean age of 7.8 ± 7.6 months for infants with normal TSH.[23,24] In one study, TSH values returned to normal within 12–35 days.[26]

Impaired kidney function appears to be associated with a higher risk of hypothyroidism after IV ICM. Thaker, et al identified a greater risk of hypothyroidism in neonates with serum creatinine in the highest quartile (>0.9 mg/dL), while L'Allemand, et al reported that 3 of 6 premature infants with kidney failure developed hypothyroidism.[35,36] Most other studies did not report kidney function or excluded patients with preexisting kidney disease. The risk of hypothyroidism after IV ICM may also be increased in children with trisomy 21,[26,27] and particularly in those undergoing cardiac procedures.[35] However, given the baseline increased prevalence of both hypothyroidism and congenital cardiac disease in children with trisomy 21, it is unclear whether IV ICM exposure is an independent risk factor for hypothyroidism in this population.

The available studies on hypothyroidism after IV ICM exposure in infants and young children have significant limitations. First, reference ranges for thyroid function testing varied among studies, and criteria for the diagnosis of hypothyroidism were also variable: several studies defined hypothyroidism based on low T4 concentrations, not on degree of TSH elevation. Iodine excess causes primary hypothyroidism, which is characterized by TSH elevation; in contrast, low T4 levels are common in acutely ill, preterm, and low birth weight infants and in the absence of TSH elevation may not indicate iodine-induced hypothyroidism. Furthermore, criteria for initiation of thyroid hormone replacement varied and in some studies were not clearly defined.

Second, most studies on this topic lack appropriate controls, which is particularly important because abnormal thyroid hormone levels are common in preterm and VLBW newborns.[37,38] Only four of eleven studies referenced by the FDA included control populations.[21,22,27,28] Of these, one study used an ionic ICM agent that is no longer in clinical use and two were confounded by concurrent use of topical iodine antiseptics. The fourth found no association of IV ICM with thyroid function in either term or VLBW infants. Three additional studies not reviewed by the FDA, including one using propensity-matched controls and one RCT, also found no significant association between exposure to ICM and development of hypothyroidism.[24,29] Thus, most studies on this topic did not include appropriate controls, and most that have done so have not shown an association between IV ICM and hypothyroidism.

Last, although hypothyroidism occurs in some infants exposed to IV ICM, most cases are transient and their clinical impact on neurodevelopment is unknown. Although there is reason for concern that transient elevations in TSH may increase the risk for additional negative impact on neurodevelopment in premature infants and infants with congenital heart disease, currently there are no outcome data demonstrating such a risk or establishing the benefit of levothyroxine replacement therapy in this setting.[39]

CONCERNS REGARDING THE FDA STATEMENT

Based on review of the available literature, the recommendations of the FDA DSC raise concerns due to limitations in the referenced articles, including; (1) inconsistent reporting of iodine dose, route(s) of exposure, and number of exposures, (2) variable definitions of hypothyroidism, (3) extended periods of time between iodine exposure and onset of hypothyroidism in some cases, indicating a possibility of an alternate etiology for thyroid disease, (4) lack of appropriate controls, and (5) inconsistent duration of follow-up. In addition, in contrast to untreated congenital hypothyroidism, there are no data indicating that ICM-induced hypothyroidism is associated with adverse neurodevelopmental outcomes in infants with previously normal thyroid function.[38,39]

There are potential risks and costs associated with the FDA recommendations. Parent/guardian anxiety about IV ICM-associated hypothyroidism could lead to deferment of radiological imaging, causing delays in diagnosis and/or necessary treatment. Although alternative imaging techniques are available, including contrast-enhanced magnetic resonance imaging (MRI) with gadolinium-based contrast material, children 3 years of age or younger who undergo MRI usually require sedation and/or general anesthesia and there is an FDA DSC warning on the use of gadolinium for this age range.[40] Second, these recommendations will result in increased need for laboratory testing and treatment with associated costs to parents/guardians including travel, missed work, and time to attend additional specialty appointments. There are also additional costs to the health care system, including increased use of staff resources for laboratory testing and consultations with specialists for interpretation and management.

RECOMMENDATIONS FOR INITIAL THYROID HORMONE FUNCTION TESTING AFTER IV ICM EXPOSURE

To balance the potential risks and benefits of screening for IV ICM-induced hypothyroidism, the panel proposes the following recommendations to identify infants and young children at greatest risk of hypothyroidism or adverse neurodevelopmental effects thereof. It is hoped that these initial recommendations will assist in developing screening programs and promote data collection that will allow for future improvements in screening and management. However, these recommendations do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

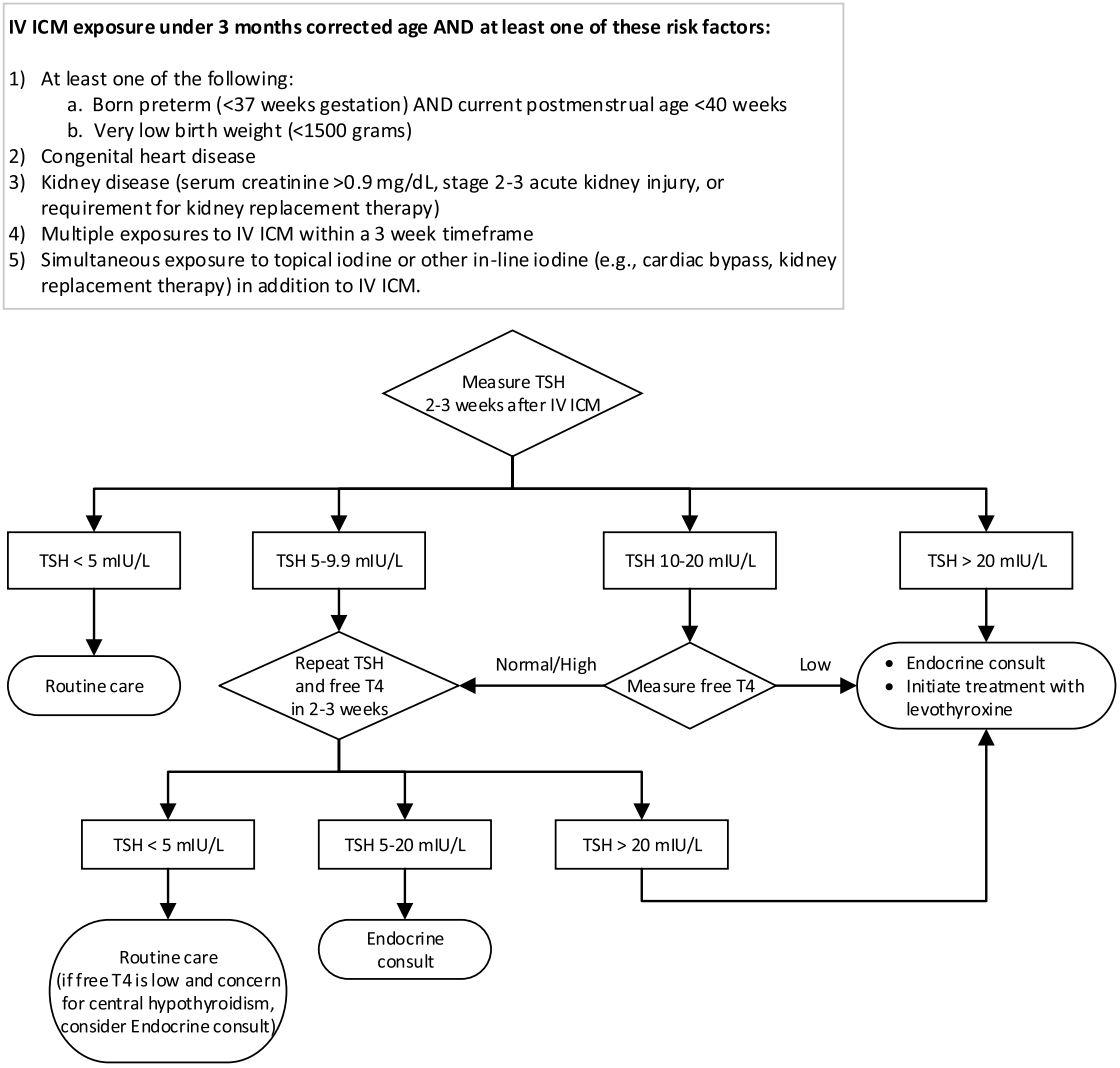

FIGURE 1.
Assessment and management algorithm for infants and children at risk of hypothyroidism following IV ICM exposure.

A. Universal thyroid testing of all children through age 3 years following IV ICM administration is not recommended.
B. For infants under 3 months corrected age exposed to IV ICM, providers should consider measuring a serum TSH level 2 to 3 weeks after exposure if any of the following are present (Figure 1):
   1) At least one of the following:
      a. Born preterm (<37 weeks gestation) AND current postmenstrual age <40 weeks
      b. Very low birth weight (<1500 g)
   2) Congenital heart disease
   3) Kidney disease (serum creatinine >0.9 mg/dL, stage 2–3 acute kidney injury, or requirement for kidney replacement therapy)
   4) Multiple exposures to IV ICM within a 3 week timeframe
   5) Simultaneous exposure to topical or other in-line iodine (eg, cardiac bypass, kidney replacement therapy) in addition to IV ICM.

   The presence of 2 or more risk factors further increases the likelihood of thyroid dysfunction.
C. For initial monitoring after exposure to IV ICM, measurement of T4 (free or total) or T3 (free or total) is not recommended.
D. For infants and children 3 months corrected age or older who receive a single dose of IV ICM for diagnostic radiological studies only (eg, CT), we do not recommend routinely monitoring thyroid function because the risk of clinically significant hypothyroidism is low.

However, serum TSH testing should be considered 2–3 weeks after exposure in any child 3 years of age and under with multiple iodine exposures within 3 weeks.

E. Special populations:
   1) Other risk factors for hypothyroidism in infancy include trisomy 21 and medications known to affect thyroid function, such as amiodarone. In these situations, measuring a baseline TSH level prior to IV ICM exposure may be considered to identify pre-existing thyroid dysfunction.
   2) If IV ICM is indicated in the perinatal period prior to collection of an initial or repeat newborn screening (NBS) sample, we suggest collection of the NBS sample prior to IV ICM administration.

As with all clinical recommendations, monitoring for potential iodine-induced hypothyroidism should be guided by clinical assessment of overall risk in the individual patient, including for patients who do not have the specific risk factors listed above.

MANAGEMENT OF THYROID TESTING AND IODINE-INDUCED HYPOTHYROIDISM

Current guidelines from the European Society of Pediatric Endocrinology and the American Academy of Pediatrics state that a TSH>5 mIU/L after 4 weeks is abnormal in a healthy, term infant.[39,41] In premature infants, normative data are limited for TSH and thyroid hormone levels beyond the first week of life, and serial assessment of thyroid function is recommended to confirm that TSH decreases and T4 increases to an age-appropriate range.[12,41,42]

Given the lack of outcome-based evidence to establish a threshold for initiating levothyroxine therapy for ICM-induced hypothyroidism, recommendations for management are based on consensus guidelines and evidence for the treatment of infants with congenital hypothyroidism, with modifications related to the differences in the underlying etiology and expected natural history of ICM-induced hypothyroidism (Figure 1).[39,41,43,44]

Based on the results of initial serum TSH obtained 2–3 weeks after IV ICM administration:

1. If TSH<5 mIU/L, proceed with routine care.
2. If TSH is 5–9.9 mIU/L, repeat serum TSH with free T4 in 2–3 weeks.
3. If TSH is 10–20 mIU/L, meaure serum free T4:
   a. If free T4 is low, levothyroxine should be initiated in consultation with a pediatric endocrinologist.
   b. If free T4 is in the reference range, TSH and free T4 should be repeated in 2 weeks.
4. If serum TSH is >20 mIU/L, levothyroxine should be initiated in consultation with a pediatric endocrinologist.
5. If repeat testing is performed in steps 2 or 3, then upon repeat testing:
   a. If TSH is <5 mIU/L:
      i. If free T4 is normal, proceed with routine care.
      ii. If free T4 is low and there is concern for central hypothyroidism, consult with a pediatric endocrinologist.
   b. If TSH is 5–20 mIU/L, consult with a pediatric endocrinologist.
   c. If TSH is >20 mIU/L, levothyroxine should be initiated in consultation with a pediatric endocrinologist.

A pediatric endocrinologist should be consulted if needed for interpretation of abnormal thyroid function tests and to make recommendations regarding initiation and follow-up of levothyroxine replacement therapy. When initiating levothyroxine for IV ICM-induced hypothyroidism in newborns and infants <3 months of age, we recommend an initial levothyroxine dosage of 8–10 μg/kg/d. For children 3–12 months a dose of 6–8 μg/kg/d is appropriate. Serum TSH and free T4 should be monitored 4–6 weeks after initiation or any dosage change. The dosage should be titrated to achieve TSH in the reference range, and optimally free T4 in the upper half of the reference range.[39,41] Once stable on therapy, thyroid function testing should be followed and levothyroxine administered in accordance with published guidelines and established clinical practice.[39,41] Liothyronine is not recommended for the treatment of iodine-induced hypothyroidism.[45]

The duration of levothyroxine therapy should take into consideration that IV ICM-induced hypothyroidism is expected to be transient and that infants with critical illness or congenital heart disease may be at increased risk of cardiac failure and hypermetabolism with overtreatment.[44] To avoid risks of iatrogenic hyperthyroidism and unnecessary treatment and testing, a trial discontinuation of levothyroxine may be considered 2 months after initiation in a child in whom there is no ongoing iodine exposure, no other suspected etiology of hypothyroidism and no other significant risk factors for hypothyroidism. A decision to trial off therapy should be made in consultation with the pediatric endocrinologist. If a trial off therapy is attempted, levothyroxine may be discontinued without tapering the dose, and TSH and free T4 should be measured 4 weeks after discontinuation of treatment. Guidance for managing thyroid function results during a trial off therapy are provided in published consensus guidelines for congenital hypothyroidism.[39,41]

DEPLOYING RECOMMENDATIONS INTO CLINICAL PRACTICE

Systems to identify and screen high-risk infants and young children receiving IV ICM will need to be developed across multiple disciplines and settings. Challenges in implementation include determining which providers will be responsible for identifying at-risk patients for thyroid screening, ordering testing, interpreting test results, and ensuring appropriate management and follow-up. This will likely differ among

the various clinical settings in which IV ICM is used, such as inpatient, emergency department, and ambulatory testing/imaging, and management approaches will need to be designed according to the needs of each institution.

In the inpatient and emergency department settings, interventional cardiologists utilizing IV ICM and clinicians requesting studies requiring IV ICM will likely have greatest familiarity with relevant clinical information and thus be best suited to assessing the need for, ordering, and reviewing results of thyroid function testing in patients at risk of hypothyroidism. Procedural guidelines or policies should be implemented based on institutional practices and preferences regarding which providers will responsible for assessing the need for, ordering, and reviewing results of thyroid function testing in patients at risk of hypothyroidism. If the patient has been discharged, the provider assuming care of the patient and the parents/guardians should be informed of the need for thyroid function testing, including timing of blood collection.

Given the delay of 2–3 weeks between IV ICM administration and thyroid testing, patients may transition between care settings, eg, inpatient to outpatient, emergency department to primary care, before thyroid testing is needed. For patients who meet testing criteria, it is essential that administration of IV ICM and the potential need for thyroid function testing be communicated during transition of care. Patients referred for ambulatory testing utilizing IV ICM present a particular challenge as radiologists may not receive all of the clinical information needed to determine if a patient requires thyroid testing, and the ordering provider may be unaware of the exposure to IV ICM or of the recommendation for associated thyroid function testing. Radiology and interventional cardiology practices may find it useful to include in their reports a recommendation to the referring provider to consider thyroid testing on patients at risk of hypothyroidism following IV ICM administration. This may not always be practical and given differences in local practices, workflows, and electronic health records in use, any solutions will need be to be tailored to the particular technology and needs of each practice (referring to this document for guidance).

As with all health care, participation of ancillary support, including nursing staff, will help ensure that patients are not lost to follow-up. With the increasing use of the electronic health records, warnings, notifications for testing, and communication about results may be automated in an effort to optimize screening and care.

ADVOCATING FOR FUTURE STUDIES

Understanding the relationship between IV ICM exposure and hypothyroidism is critical to caring for our highest-risk infants and young children. Given the lack of existing high-quality evidence and the continued gaps in knowledge about the risk of thyroid dysfunction in neonates, infants, and young children exposed to IV ICM, we strongly disagree with the FDA's statement that further research on this topic, sponsored and financially supported by the manufacturers, is no longer needed. Therefore, we encourage our industry partners to pursue, and the FDA to support, prospective, appropriately controlled studies to define more accurately which patients are at clinical risk of adverse outcomes, to optimize thyroid screening and treatment in these children.

CONCLUSION

Based on current evidence, the children at greatest risk for hypothyroidism appear to be infants born preterm or VLBW and infants with congenital heart disease who require early and/or repeated cardiac imaging and interventions utilizing IV ICM. Other potential risk factors, such as repeated (non-cardiac) exposure to IV ICM, concomitant exposure to non-IV iodine-containing agents or medications, kidney disease, trisomy 21, and overall severity of illness should be investigated further. Studies are needed to clarify the incidence, timing, severity, and resolution of hypothyroidism after IV ICM exposure. Finally, even with carefully designed studies, it may be difficult to assess the potential impact of transient IV ICM-induced hypothyroidism on neurodevelopment as there is an increased incidence of development delay in premature infants as well as patients with congenital heart disease. Expert recommendations will help to identify patients at greatest risk while minimizing the burden of low-yield thyroid function testing on patients, parents/guardians, and health care systems, and provide guidance for future studies to optimize the diagnosis and management of IV ICM-induced hypothyroidism.

ABBREVIATIONS

BW: birth weight
CHD: congenital heart disease
CPT: current procedural terminology
CT: computed tomography
DSC: Drug Safety Communication
FDA: Food and Drug Administration
ICM: iodinated contrast media
IQR: interquartile range
IV: intravenous
LBW: low birth weight
MRI: magnetic resonance imaging
NBS: newborn screen
PICC: peripherally inserted central catheter
PVP-I: povidone iodine
RCT: randomized controlled trial
SD: standard deviation
T3: triiodothyronine
T4: thyroxine
TSH: thyroid stimulating hormone
VLBW: very low birth weight

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