RADIOLOGY CONTRAST IN THE PEDIATRIC POPULATION: CONTEMPORARY EVIDENCE AND STRATEGIES

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BACKGROUND

- Contrast agent selection and dosing presents unique challenges in children.

- The need to limit radiation exposure in pediatric imaging often goes hand in hand with shifts to alternate modality utilization, as contrast-enhanced CT has given way to ultrasound and MRI for many clinical indications.

Oncology Nurse Advisor. www.oncologynurseadvisor.com/ Accessed September 2023.

BACKGROUND

- Recent topics of interest include:
  - 2022 and 2023 shortages of iodine-based contrast media
  - Concerns over gadolinium retention in children
  - FDA and ACR recommendations related to concerns of hypothyroidism for children under 3 exposed to iodine-based contrast media

EDUCATIONAL GOALS

1. Discussion of contrast dosing, different agents, modality optimization and premedication regimens for children will be described.

2. Current consensus related to gadolinium will be reviewed including strategies to avoid unnecessary contrast utilization in pediatrics.

3. Ultrasound contrast agents and their applications will be reviewed with specific note to the emerging prospect of contrast-enhanced head ultrasound.

4. Recent statements from the American College of Radiology (ACR) will be referenced.

CONTRAST DOSING

- Limiting contrast volume administration may require precise timing of image acquisition
- Slower injection rates may prolong intravascular enhancement
- Smaller pediatric angiocatheters (24-gauge) and unique access sites in children may require injection rate reduction
  - Safe power injection max flow rate of ~1.5 mL/s and max pressure of 150 psi

CONTRAST AGENTS

- CT: Iodinated Contrast
- MRI: Gadolinium Contrast
- US: Bubble-based Media

Istock. https://www.istockphoto.com/ Accessed September 2023.

IODINATED CONTRAST

- High-iodine-concentration contrast has high osmotic pressure and viscosity
- This may facilitate a variety of adverse reactions related to compartmental fluid shifts
- Adverse reactions correlate with concentration, dose, and injection pressure

IODINATED CONTRAST

Osmolality: draws fluid into vessels

Children, are more susceptible to fluid shifts due to their small body size, particularly if cardiac conditions are present

Viscosity: increases pressure during contrast injection

Children predisposed to vessel rupture due to small vessel size

IODINATED CONTRAST: ADVERSE EFFECTS

- The selected iodinated contrast product should have the lowest iodine concentration possible while balancing study quality
- Nonionic contrasts are associated with fewer mild and moderate adverse events
- Less common severe reactions occur equally with ionic and nonionic contrast
- Premedication to prevent allergic-like reactions in children includes weight-based dosing of antihistamines and/or corticosteroids

FDA AND ACR STATEMENT ON IODINATED CONTRAST

2022 ACR

- Risk of clinically-relevant hypothyroidism related to iodinated contrast is low in the pediatric population under 3 months and minimal to absent in older children. Universal testing is not warranted and the decision to perform thyroid function tests should be on a patient-to-patient basis following review of risk factors.

2023 FDA

- Decisions regarding monitoring children from 0-3 years for possible hypothyroidism following iodinated contrast exposure should be based on each child's risk factors. (ie. prematurity, very low birth weight, and underlying medical conditions affecting thyroid function)

ACR STATEMENT ON IODINATED CONTRAST SHORTAGES

2022 ACR

- Utilize alternative studies
  - Non-contrast CT, MR, US, nuclear medicine, or PET/CT
- Consider alternative versions of contrast agents
- Source contrast from other vendors
- Contact your institution to determine if it is possible to repackage vials in smaller aliquots to reduce waste
- Minimize individual doses
- Reserve higher concentration agents for angiographic studies and multiphase studies
- Use alternatives to nonionic contrast for oral, rectal, and genitourinary administration.
  - Consider barium-based products for oral opacification in CT and PET/CT
- Collaborate with other departments that utilize iodinated contrast

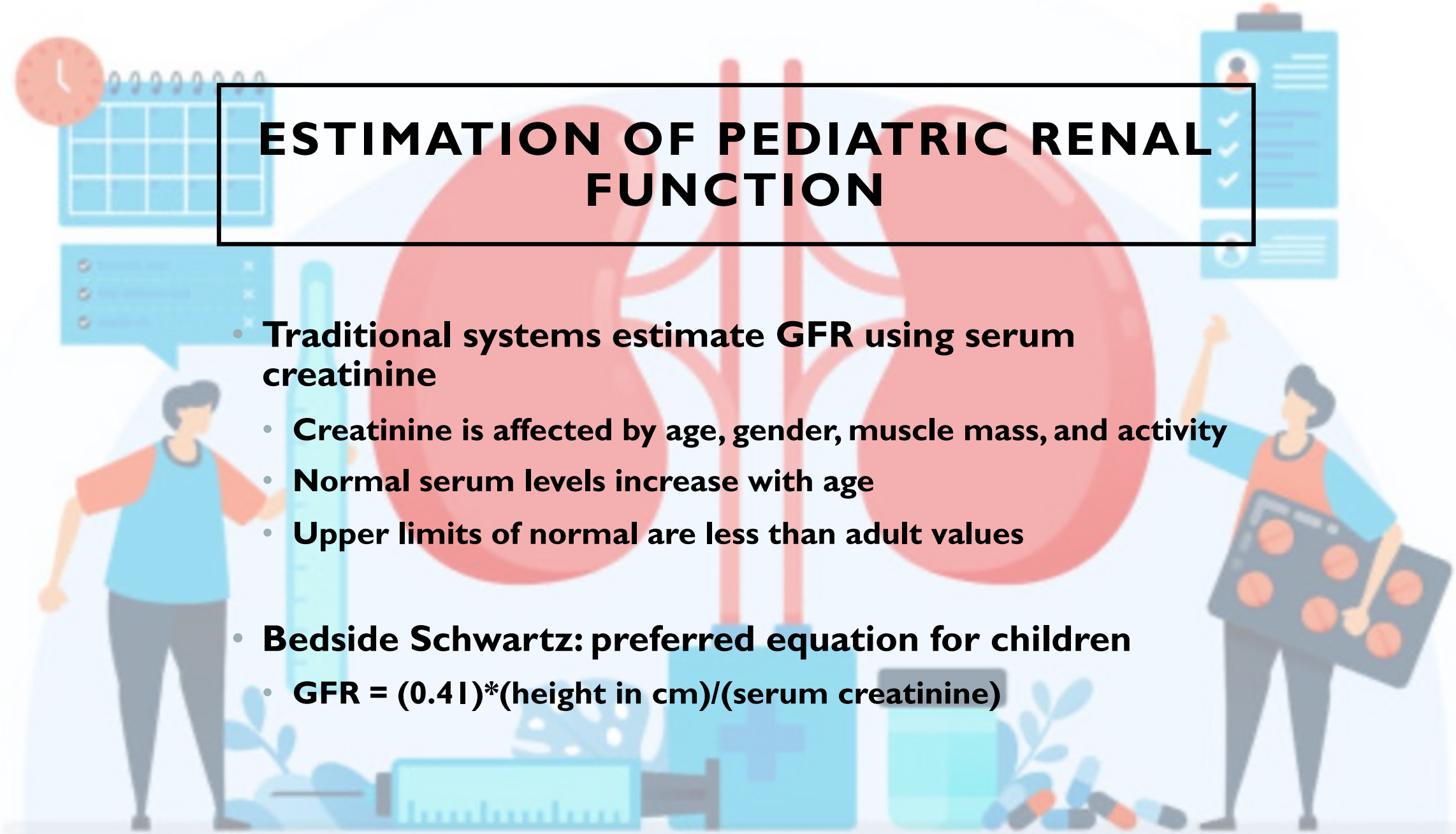
GADOLINIUM CONTRAST

- Rarely causes nephrogenic systemic fibrosis (NSF)
  - Should be used cautiously in patients with impaired renal function
  - Gadolinium-based contrast agents (GBCAs) in the group II classification are strongly preferred in patients at risk for NSF and pose little to no risk
  - Newer GBCA have been designated within group II

ESTIMATION OF PEDIATRIC RENAL FUNCTION

- **Traditional systems estimate GFR using serum creatinine**
  - **Creatinine is affected by age, gender, muscle mass, and activity**
  - **Normal serum levels increase with age**
  - **Upper limits of normal are less than adult values**

- **Bedside Schwartz: preferred equation for children**
  - **GFR = (0.41)*(height in cm)/(serum creatinine)**

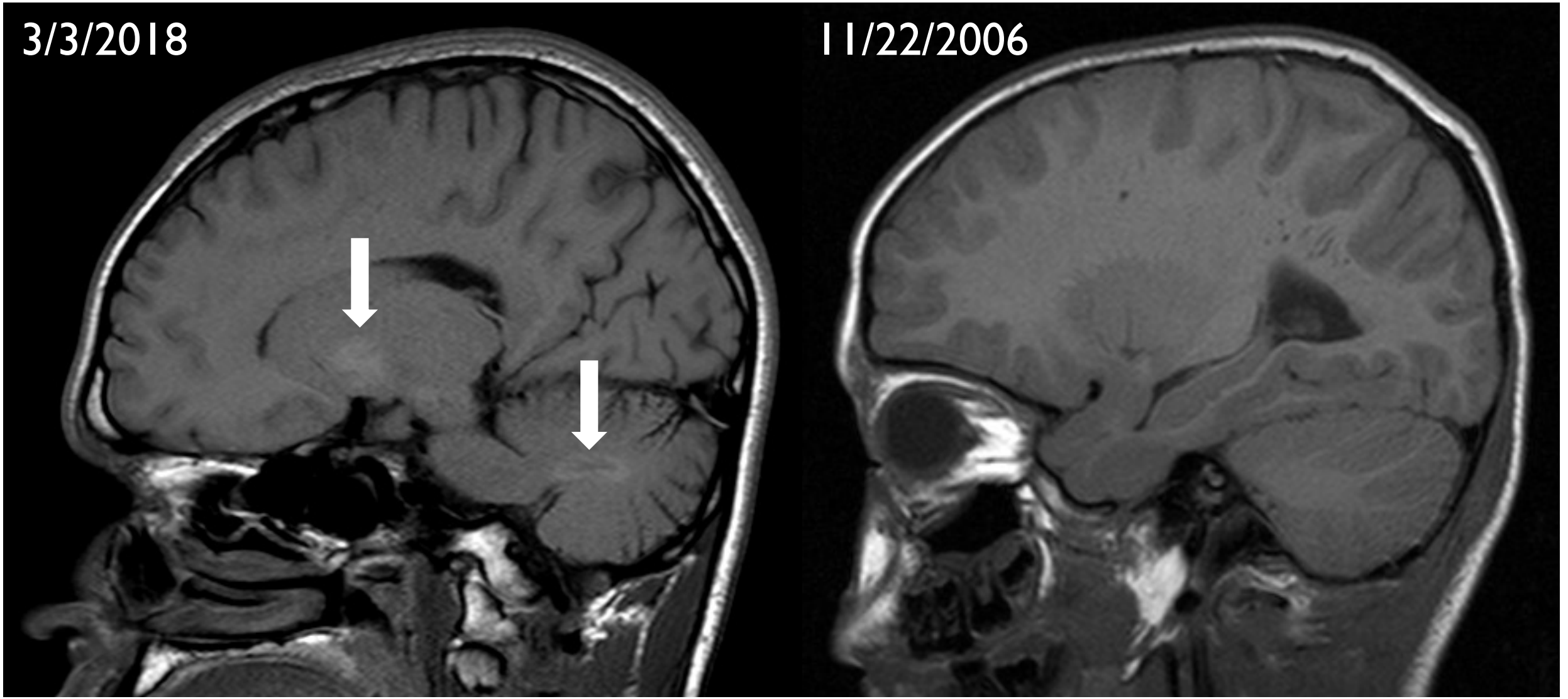


Creative Fabrica. https://www.creativefabrica.com/ Accessed September 2023.

GADOLINIUM CONTRAST: RETENTION

- Asymptomatic gadolinium deposition in the brain and bones with repeated MRI studies
  - More commonly with linear than macrocytic agents
  - No associated disease recognition, though exposure should be limited
  - New macrocyclic contrasts FDA approved for children under 2 years

T1 SHORTENING IN THE GLOBUS PALLIDUS AND DENTATE NUCLEI RELATED TO REPEATED GROUP I GBCA EXPOSURE



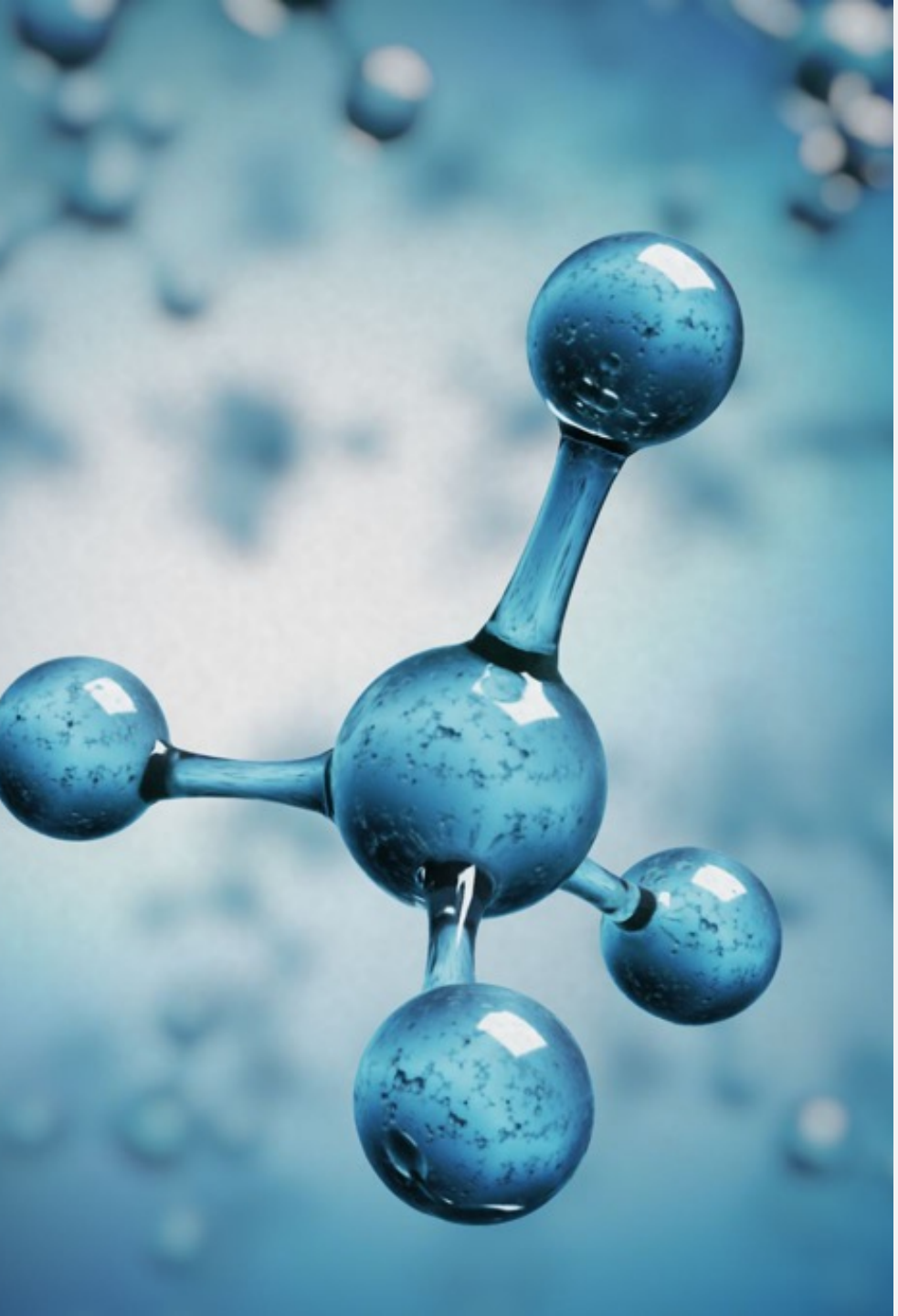
GADOLINIUM CONTRAST: CURRENT CONSENSUS

- Adult guidelines should be followed to identify at-risk patients for NSF, such as those with known medical renal disease or renal/urinary tract abnormalities

GADOLINIUM CONTRAST: ALTERNATIVES

- Active efforts are being made to identify new contrast agents that do not contain gadolinium
  - Superparamagnetic iron-oxide nanoparticles (SPIONs) such as Ferumoxytol
    - Not widespread in neuroimaging, though it is being used at some sites

- Other methods should be considered when clinically appropriate to reduce the risk of gadolinium contrast exposure



ULTRASOUND-BASED CONTRAST MEDIA

- US contrasts typically consist of an inert gas encapsulated in a shell (“microbubbles”)
- Particles typically remain in the blood pool because they are too small to enter the interstitial tissues
- Some remain for about 10 minutes and gradually excreted by the lungs
- These intravascular gas-liquid emulsions generate an intense signal on US, allowing for evaluation of organ microvasculature

ULTRASOUND-BASED CONTRAST MEDIA: OPTIMIZATION

- Interaction of US beam and bubbles causes more rapid destruction of contrast agent
  - Focus should be centered deeper on the image

- Prior to US contrast administration, regions of interest should be scanned in contrast-specific mode in to identify pre-existing hyperechoic areas

ULTRASOUND-BASED CONTRAST MEDIA: SAFETY

- Particles typically remain in the blood pool because they are too small to enter the interstitial tissues
- Society for Pediatric Radiology consensus statement backed safety of intravascular and intravesicular use of ultrasound contrast agents
  - Severe reaction rate of 0.01% across greater than 78,000 administrations of Definity and Lumason
- Potential contraindications
  - Risk for cardiopulmonary reaction may be elevated in children who have unstable cardiopulmonary disease
  - History of hypersensitivity to components of the contrast medium

APPLICATIONS OF ULTRASOUND-BASED CONTRAST

Useful for perfusion evaluation of organs like liver, kidneys, and bowel loops

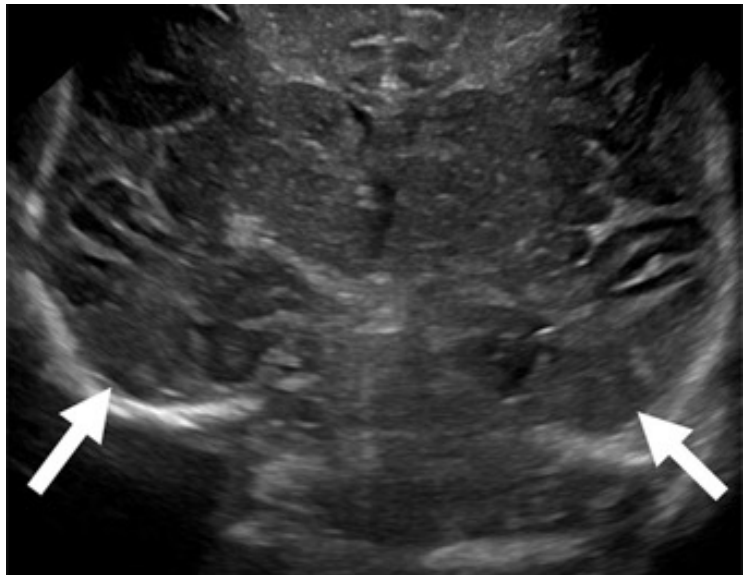
Focal liver lesions

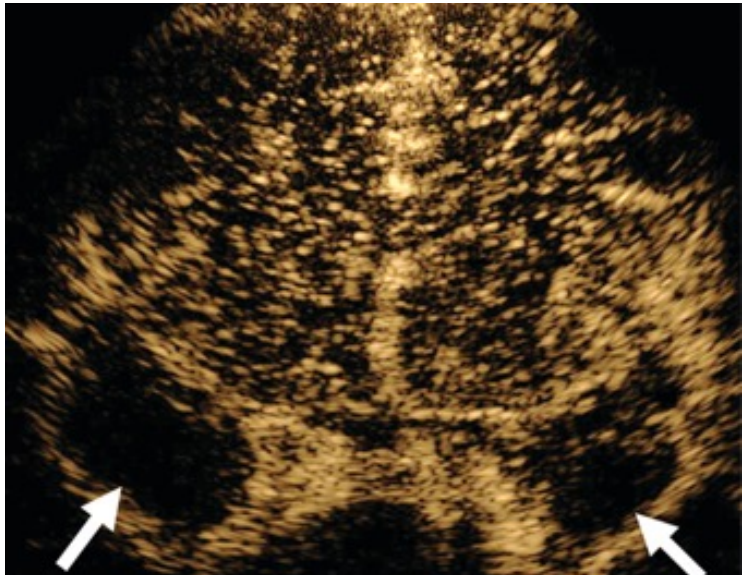
- Contrast-enhanced US has similar or even greater sensitivity and specificity than CT or MRI for diagnosis of focal liver lesions
- Often used to classify nodules previously characterized as indeterminate by other imaging modalities

Neuroimaging uses

- Emergence of contrast-enhanced head ultrasound in children under 6 months

CONTRAST-ENHANCED HEAD ULTRASOUND





Gray-scale and contrast enhances US of the brain of a 3-day-old female showing bilateral temporal lobe infarcts.

Squires JH, McCarville MB. Contrast-Enhanced Ultrasound in Children: Implementation and Key Diagnostic Applications. *AJR Am J Roentgenol*. 2021;217(5):1217-1231. doi:10.2214/AJR.21.25713

CONTRAST-ENHANCED HEAD ULTRASOUND: FUTURE IMPLICATIONS

- Bedside US as substitute for CT/MRI in critically ill neonates
  - Eliminates inconvenience and danger of transport
- Quantification of cerebral perfusion with time-intensity curve
  - Must be compared to "normal"
  - Main challenge in establishing universal quantitative method is acquisition of age-dependent data
- Monitoring post-ischemic reperfusion
  - Degree of ischemia and rate of reperfusion have an impact on clinical outcomes
  - Can increase understanding of this impact and guide therapeutic interventions

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