

Use of Gadolinium Contrast in Children Under 2 years of age: Brain and Spine (Central Nervous System)

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Children's National

Washington DC



About Children's National

- Has served the nation's children for 140 years
- Care for > 360,000 patients each year
 - come from throughout the region, nation and world
- Perform ~10,000 MRI examinations per year



Overview

- Short history of MRI
- MR contrast agents
 - Safety in children
- Sedation/anesthesia: special for children
- Use of contrast agents in children < 2 years of age

MR Imaging

1982

Clinical NMR Imaging of the Brain: 140 Cases

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R. E. Steiner¹
I. R. Young²
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J. Marshall³
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Cranial nuclear magnetic resonance (NMR) scans were performed on 13 healthy volunteers and 140 patients with a broad spectrum of neurologic disease and compared with x-ray computed tomography (CT) scans. The NMR scans included a variety of sequences reflecting proton density, blood flow, T_1 , and T_2 as well as transverse, sagittal, and coronal images. White matter, gray matter, and cerebrospinal fluid were clearly distinguished in the normal brain with inversion-recovery (IR) sequences, and normal progressive myelination was demonstrated in infants and children.

Acute hemorrhages displayed short T_1 values, but other pathologic processes such as infarction, infection, demyelination, edema, and malignancy were associated with long T_1 values. Cysts had very long T_1 values (about that of cerebrospinal fluid). Spin-echo (SE) sequences showed increased values of T_2 in a variety of conditions and

Bydder AJR 1982

MR Contrast

- 1984: initial human clinical experience
 - 20 patients reported (Carr, AJR 1984)

Gadolinium-DTPA as a Contrast Agent in MRI: Initial Clinical Experience in 20 Patients

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Magnetic resonance imaging (MRI) was performed in 20 patients before and after intravenous administration of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) in a dose of 0.1 mmol/kg. Twelve of the patients had clinical and histologic diagnoses of cerebral tumor, six had hepatic tumors, one had hepatic cysts, and one had transitional cell carcinoma of the bladder. Contrast enhancement was seen with all tumors, but not with the hepatic cysts. The degree of enhancement was greater than that seen with computed tomography (CT) in 13 cases, equal to it in six, and less in one. Contrast enhancement was detectable as long as 18 hr after injection of Gd-DTPA in one case of cerebral tumor. The margin between cerebral tumor and peritumoral edema

MR Contrast - children

- **1989**: first large comprehensive study of pediatric patients
 - 65 consecutive children
 - age one day to 18 years

Gd-DTPA–Enhanced Cranial MR Imaging in Children: Initial Clinical Experience and Recommendations for Its Use

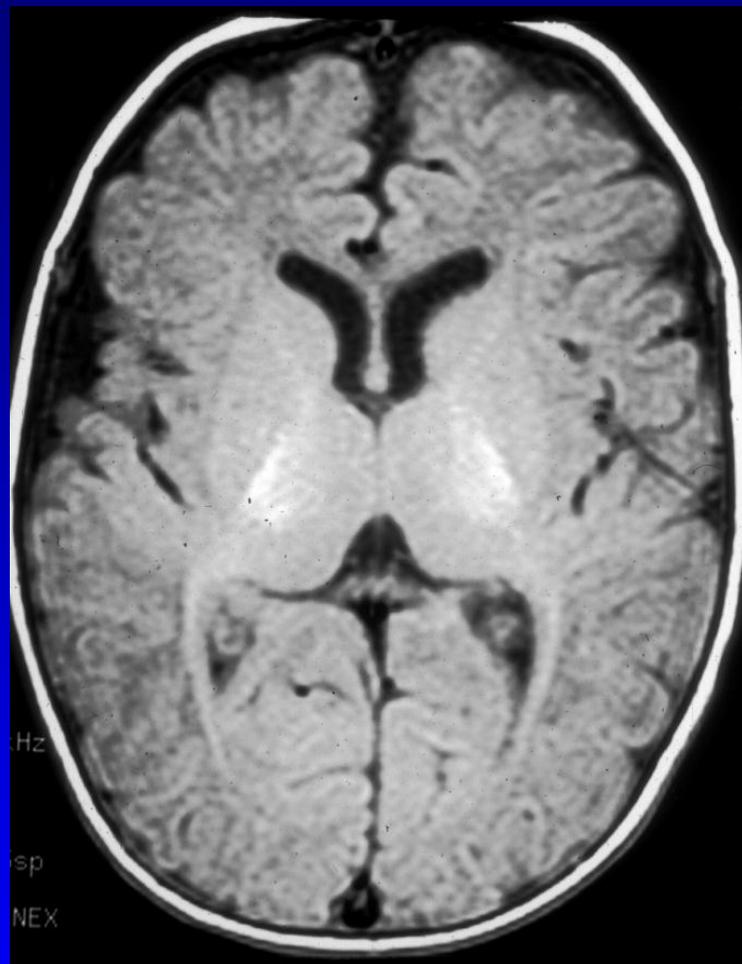


Allen D. Elster¹
Geoffrey D. Rieser

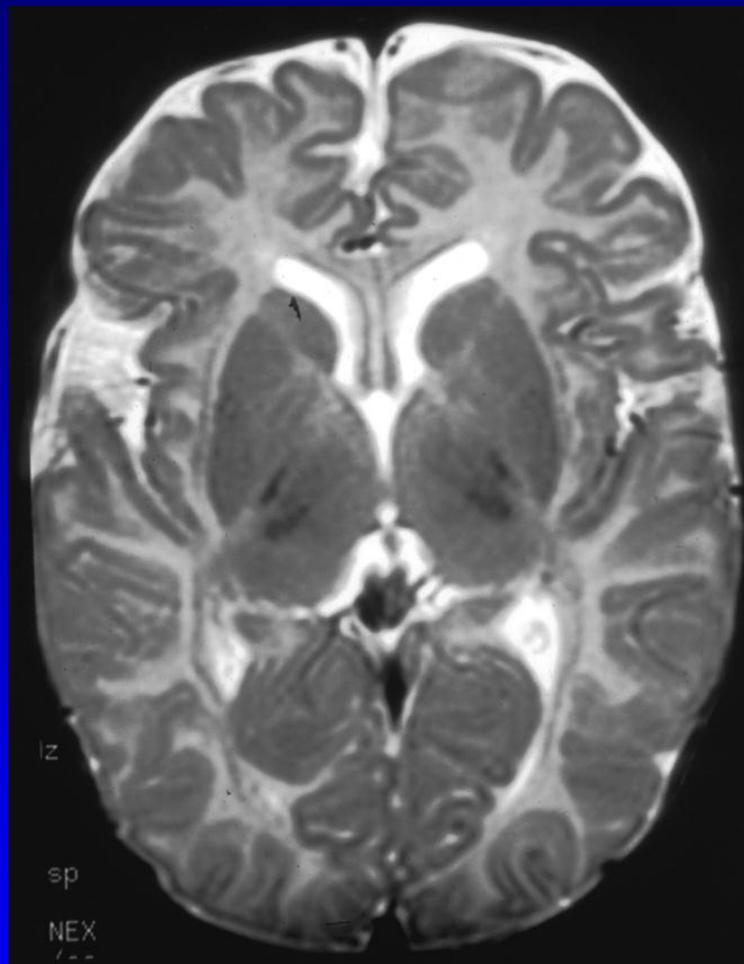
Gd-DTPA was administered prospectively to 65 consecutive children (ages 1 day to 18 years, mean 9.6 years) to document its utility and safety for routine cranial MR imaging. Precontrast T1- and T2-weighted scans and postcontrast T1-weighted scans were obtained. No complications or significant adverse reactions were encountered.

Appearance of MRI image

- Governed by relaxation times:
 - T1 and T2
 - rate with which hydrogen protons return to their magnetic ground state following excitation
 - rate at which they “relax”



T1



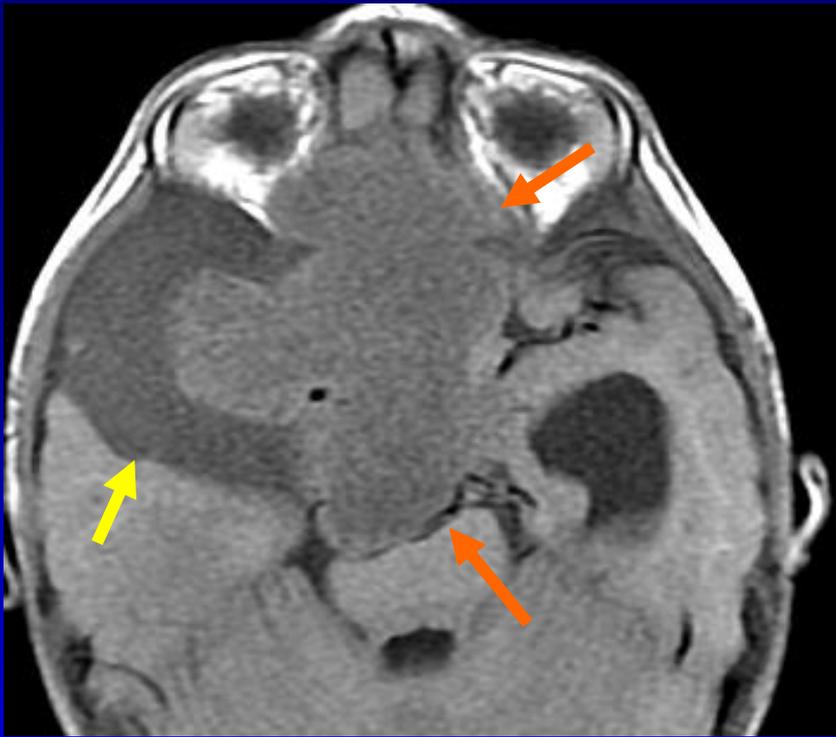
T2

Paramagnetic contrast agents

- Accelerate T1 relaxation
- Contain one or more unpaired electrons
 - gives them a permanent magnetic moment
 - promotes relaxation of hydrogen protons

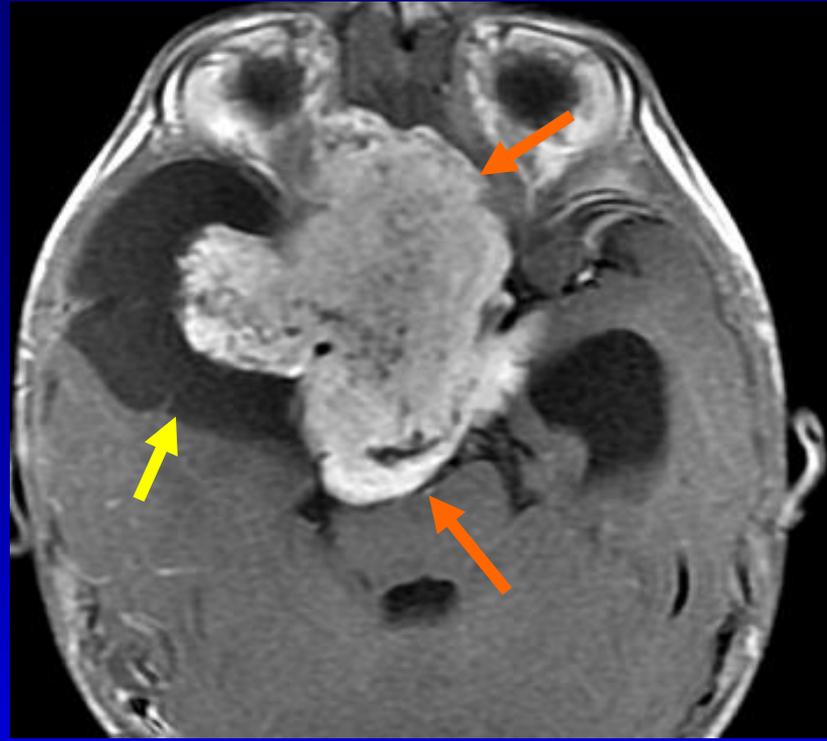
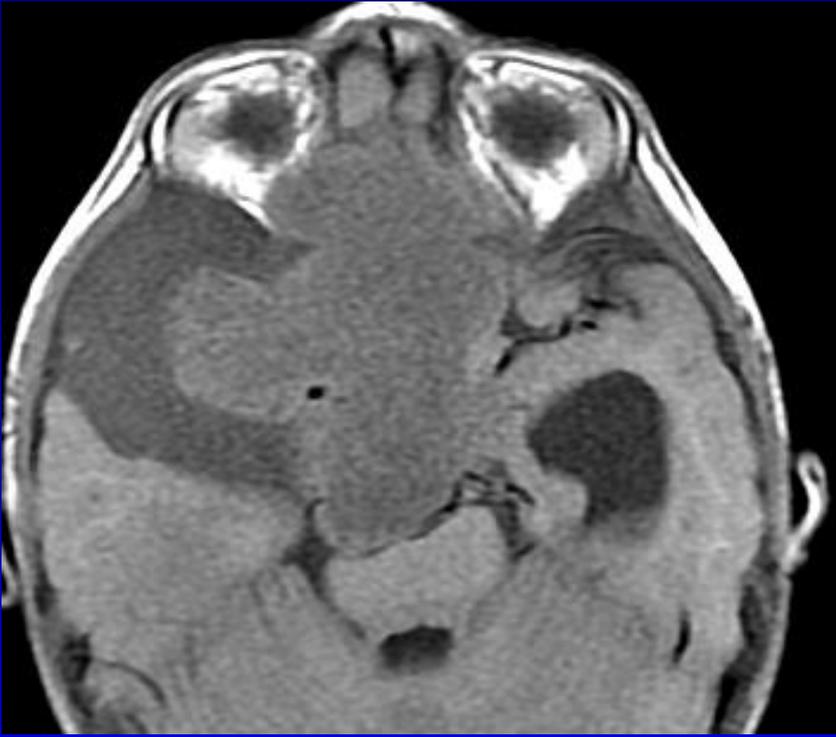
Paramagnetic contrast agents

- Accelerate T1 relaxation
- Contain one or more unpaired electrons
 - gives them a permanent magnetic moment
 - promotes relaxation of hydrogen protons
- Produce tissue enhancement on MR images
 - tissue with contrast turns bright on T1 images
 - improves diagnostic accuracy and sensitivity

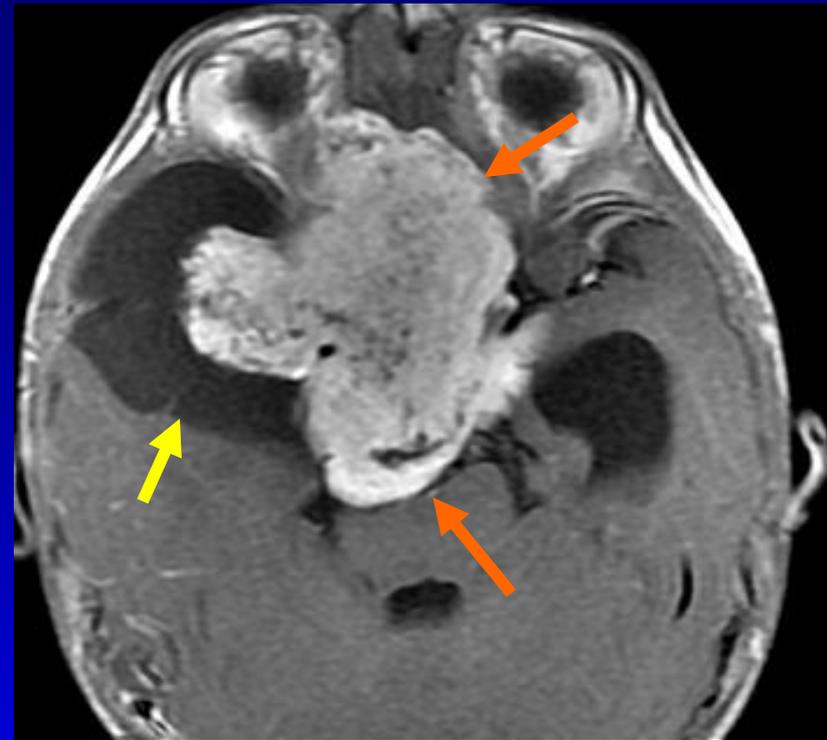
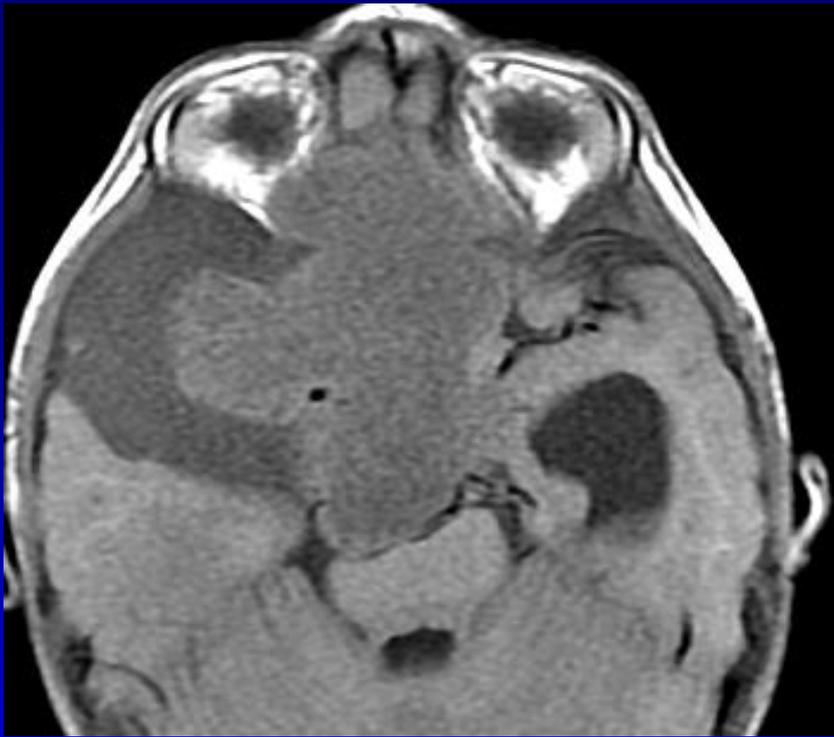


T1 pre contrast

1 year old
Astrocytoma



T1 post contrast



In the brain and spinal cord:
enhancement indicates breakdown or absence of the
blood brain barrier

MRI contrast agents: early adoption

- Without administration of intravenous contrast, MRI could not replace
 - CT with contrast
 - myelographyin the evaluation the blood brain barrier, and specifically of patients with tumors and infections of the brain and spinal cord

Gadolinium

- Rare earth element
- 7 unpaired electrons

Periodic Table of Elements

A Resource for Elementary, Middle School, and High School Students

| Group | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|--------|--------------------------|--------------------------|--------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|----------------------------|---------------------------|----------------------------|---------------------------|----------------------------|----------------------------|
| Period | | | | | | | | | | | | | | | | | | |
| 1 | 1 <u>H</u> 1.008 | | | | | | | | | | | | | | | | | 2 <u>He</u> 4.003 |
| 2 | 3 <u>Li</u> 6.94 | 4 <u>Be</u> 9.012 | | | | | | | | | | 5 <u>B</u> 10.81 | 6 <u>C</u> 12.01 | 7 <u>N</u> 14.01 | 8 <u>O</u> 16.00 | 9 <u>F</u> 19.00 | 10 <u>Ne</u> 20.18 | |
| 3 | 11 <u>Na</u> 22.99 | 12 <u>Mg</u> 24.31 | | | | | | | | | | 13 <u>Al</u> 26.98 | 14 <u>Si</u> 28.09 | 15 <u>P</u> 30.97 | 16 <u>S</u> 32.06 | 17 <u>Cl</u> 35.45 | 18 <u>Ar</u> 39.95 | |
| 4 | 19 <u>K</u> 39.10 | 20 <u>Ca</u> 40.08 | 21 <u>Sc</u> 44.96 | 22 <u>Ti</u> 47.88 | 23 <u>V</u> 50.94 | 24 <u>Cr</u> 52.00 | 25 <u>Mn</u> 54.94 | 26 <u>Fe</u> 55.85 | 27 <u>Co</u> 58.93 | 28 <u>Ni</u> 58.69 | 29 <u>Cu</u> 63.55 | 30 <u>Zn</u> 65.39 | 31 <u>Ga</u> 69.72 | 32 <u>Ge</u> 72.64 | 33 <u>As</u> 74.92 | 34 <u>Se</u> 78.96 | 35 <u>Br</u> 79.90 | 36 <u>Kr</u> 83.79 |
| 5 | 37 <u>Rb</u> 85.47 | 38 <u>Sr</u> 87.62 | 39 <u>Y</u> 88.92 | 40 <u>Zr</u> 91.22 | 41 <u>Nb</u> 92.91 | 42 <u>Mo</u> 95.96 | 43 <u>Tc</u> (98) | 44 <u>Ru</u> 101.1 | 45 <u>Rh</u> 102.9 | 46 <u>Pd</u> 106.4 | 47 <u>Ag</u> 107.9 | 48 <u>Cd</u> 112.4 | 49 <u>In</u> 114.8 | 50 <u>Sn</u> 118.7 | 51 <u>Sb</u> 121.8 | 52 <u>Te</u> 127.6 | 53 <u>I</u> 126.9 | 54 <u>Xe</u> 131.3 |
| 6 | 55 <u>Cs</u> 132.9 | 56 <u>Ba</u> 137.3 | * | 72 <u>Hf</u> 178.5 | 73 <u>Ta</u> 180.9 | 74 <u>W</u> 183.9 | 75 <u>Re</u> 186.2 | 76 <u>Os</u> 190.2 | 77 <u>Ir</u> 192.2 | 78 <u>Pt</u> 195.1 | 79 <u>Au</u> 197.0 | 80 <u>Hg</u> 200.5 | 81 <u>Tl</u> 204.38 | 82 <u>Pb</u> 207.2 | 83 <u>Bi</u> 209.0 | 84 <u>Po</u> (209) | 85 <u>At</u> (210) | 86 <u>Rn</u> (222) |
| 7 | 87 <u>Fr</u> (223) | 88 <u>Ra</u> (226) | ** | 104 <u>Rf</u> (265) | 105 <u>Db</u> (268) | 106 <u>Sg</u> (271) | 107 <u>Bh</u> (270) | 108 <u>Hs</u> (277) | 109 <u>Mt</u> (276) | 110 <u>Ds</u> (281) | 111 <u>Rg</u> (280) | 112 <u>Cn</u> (285) | 113 <u>Uut</u> (284) | 114 <u>Fl</u> (289) | 115 <u>Uup</u> (288) | 116 <u>Lv</u> (293) | 117 <u>Uus</u> (294) | 118 <u>Uuo</u> (294) |

| | | | | | | | | | | | | | | | |
|--------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Lanthanide Series* | 57 <u>La</u> 138.9 | 58 <u>Ce</u> 140.1 | 59 <u>Pr</u> 140.9 | 60 <u>Nd</u> 144.2 | 61 <u>Pm</u> (145) | 62 <u>Sm</u> 150.4 | 63 <u>Eu</u> 152.0 | 64 <u>Gd</u> 157.2 | 65 <u>Tb</u> 158.9 | 66 <u>Dy</u> 162.5 | 67 <u>Ho</u> 164.9 | 68 <u>Er</u> 167.3 | 69 <u>Tm</u> 168.9 | 70 <u>Yb</u> 173.0 | 71 <u>Lu</u> 175.0 |
| Actinide Series** | 89 <u>Ac</u> (227) | 90 <u>Th</u> 232 | 91 <u>Pa</u> 231 | 92 <u>U</u> 238 | 93 <u>Np</u> (237) | 94 <u>Pu</u> (244) | 95 <u>Am</u> (243) | 96 <u>Cm</u> (247) | 97 <u>Bk</u> (247) | 98 <u>Cf</u> (251) | 99 <u>Es</u> (252) | 100 <u>Fm</u> (257) | 101 <u>Md</u> (258) | 102 <u>No</u> (259) | 103 <u>Lr</u> (262) |

Gadolinium based contrast agents (GBCA) in children

- Magnevist – gadopentetate dimeglumine
- Omniscan - gadodiamide
- ProHance - gadoteridol
- MultiHance - gadobenate dimeglumine
- Gadavist – gadobutrol
- **Dotarem – gadoterate meglumine**

Elimination of GBCA

- Mostly eliminated through the kidneys
 - Glomerular Filtration Rate (GFR)
- Mean elimination half-life (normal children, adults): ~1.5 hours

Neonates, young infants

- Renal function underdeveloped
- GFR reduced
 - Newborn: 20 – 40% of adult GFR
- Calculated half life of GBCA
 - 6 - 8 week infant: 1.6 hours
 - 4 week: 2.1 hours
 - Newborn: 6.5 hours

(Elster Radiology 1990)

GBCA dosage: neonates

- Serum half life prolonged
- Neonate extracellular fluid volume is approximately twice as large as in adults
 - Blood GBCA concentration only 1/2 that of an adult for same dose
- 0.1 mmol / kg = adult dose

GBCA for children < 2 years

- Not FDA approved
- Physicians administer GBCA use best judgment
- Risk of adverse reaction
vs.
benefit of investigation for patient management

Safety

- GBCA considered safe in majority of patients
- Precautions undertaken to avoid adverse drug reactions
 - Immediate
 - Delayed

Immediate Reactions

- Most common side effects
 - Nausea/vomiting
 - Discomfort at injection site
 - Rash
 - Headache, lightheadedness
 - Bronchospasm
- 0.2 % to 5.8% of children
- Immediate severe reactions
 - allergic-type hypersensitivity / anaphylaxis
 - 1/40,000 incidence (children and adults)
(Prince, AJR 2011)

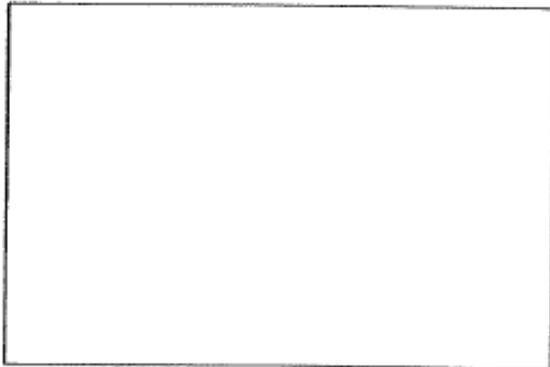


CNMC

Department of Diagnostic Imaging & Radiology

Contrast Administration Screening Form

Form Completed by _____



Date _____

Source of Information _____

Type of Exam _____

Diagnosis _____

| | | | |
|--------------------------------------|---|-------------------------------|--|
| Does patient have history of: | | | |
| Allergies | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | List | |
| Asthma | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | Asthma medications: | |
| Eczema | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Kidney Problems | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Sickle Cell Anemia | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Heart Failure | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Diabetes | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Glucophage/Metformin Use | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | Last Menstrual Period: | |
| Pregnant? | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Long Term Central Lines | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| IV contrast in last 24 hours | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | | |
| Reaction to contrast | <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> unknown | Describe: | |

Delayed Reaction: Nephrogenic Systemic Sclerosis (NSF)

- Systemic condition characterized by a fibrosing dermatopathy
 - Can lead to severe contractures and disability
- Fibrosis also involves lungs, joints, liver, muscles
 - May be fatal
- Reported since 2000
- Clinical use of GBCA's can trigger NSF

Nephrogenic Systemic Sclerosis

- At risk: patients with chronic renal disease or end-stage renal failure
 - GFR < 30 mL/min (normal ~ 130): contraindicated
 - GFR 30 – 60 mL/min: careful consideration
- Link between NSF and the underdeveloped renal function in infants has yet to be reported

Screening for renal function

- Done on all pediatric in-patients
- Selectively in out-patients
 - risk factors
 - presence of active renal disease
 - impaired renal function
 - risk for impaired renal function
- BUN, creatinine
- GFR measurement or estimation

Sedation

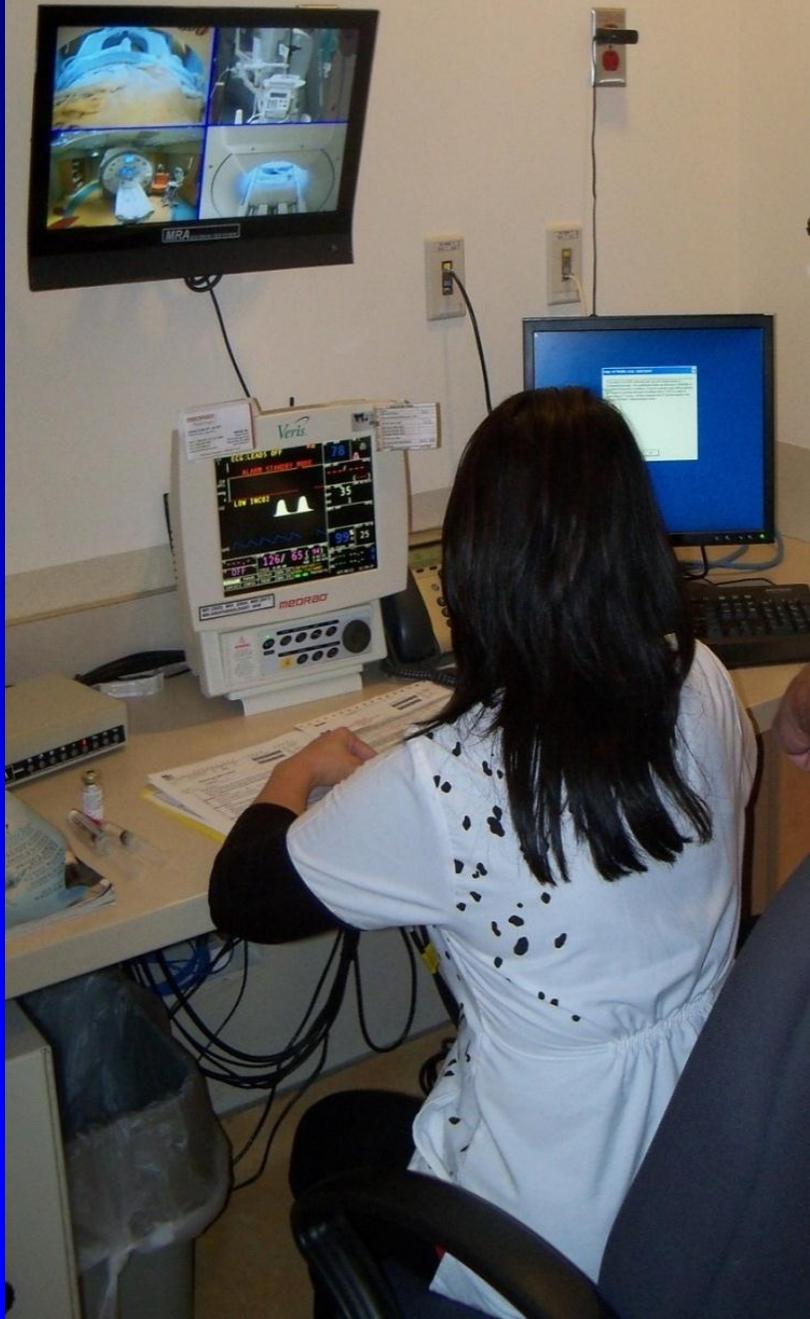
- Children under the age of 6-8 years are generally sedated



Anesthesiologist
induces sedation
(anesthesia)



Transport
sedated
patient with
MRI monitors
to MRI
scanner



Nurse (special training) monitors child from outside of magnet



Anesthesiologist
immediately
available
outside MRI
scanner

MRI sedation increases complexity



MRI compatible equipment

Infusion pumps

Monitors

Anesthesia machines

Carts, poles

Hypothermia

Deep sedation

Despite complexity of sedation

Indiscriminate use of contrast agents in MR imaging of patients younger than 2 years of age is not warranted

Gadopentetate dimeglumine-enhanced MR of the brain: clinical utility and safety in patients younger than two years of age. Eldevik AJNR 1994

Neuro MRI exams December 2012 Children's National

- 550 exams - all ages (1 day – 18 years)
- Contrast given: 20% (107 cases)
 - 98 exams < 2 years of age
 - Contrast given: 16% (16 cases)

Indications: Pediatric CNS

- Tumors
 - Brain
 - Head and neck, spinal cord, spinal canal
- Infection / inflammatory diseases
- Characterization of lesions seen on precontrast scan

Indications: Pediatric CNS

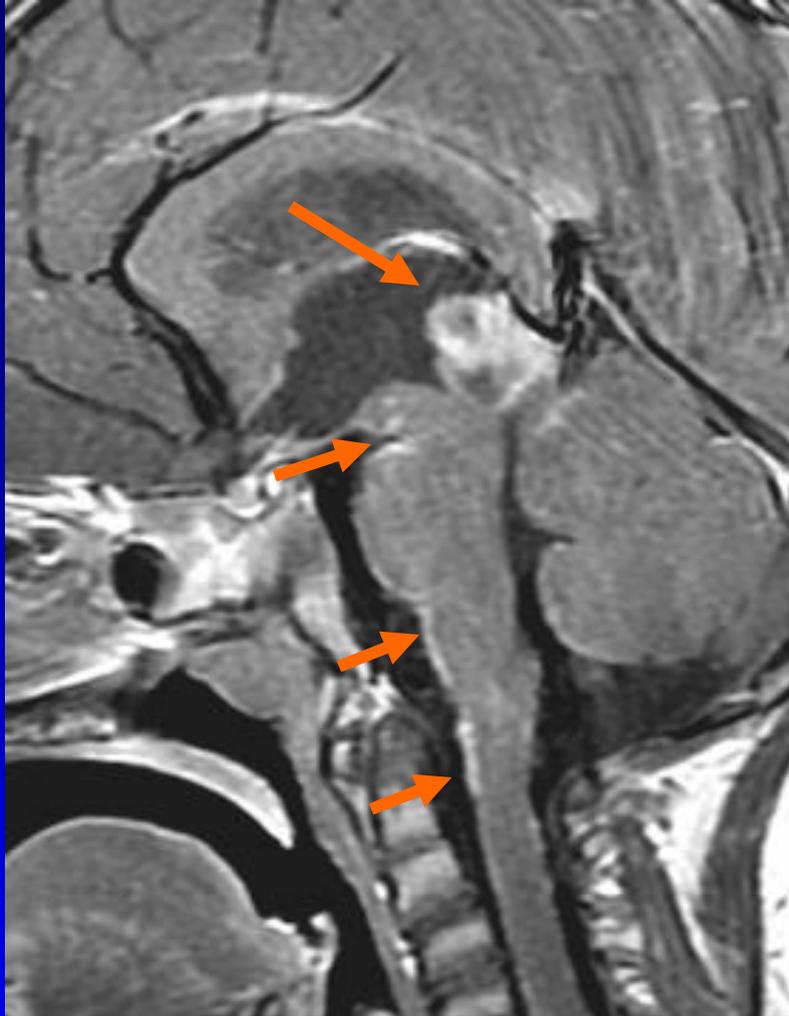
- Tumors
 - Brain
 - Head and neck, spinal cord, spinal canal
- Infection / inflammatory diseases
- Characterization of lesions seen on precontrast scan

- Evaluation of hydrocephalus, abnormal fluid collections
- Evaluation of nerves (cranial, spinal)
- Evaluation of meninges
- Neurocutaneous disorders

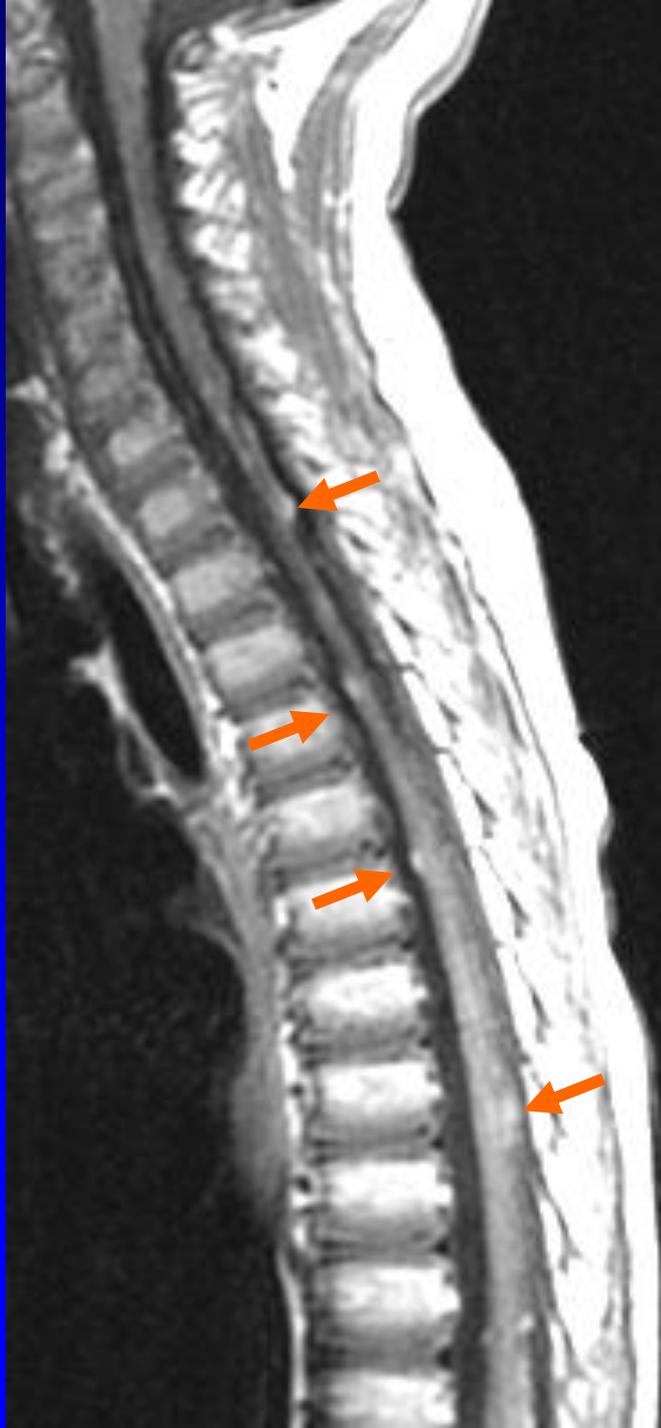
- Vascular evaluation (MRA, MRV)

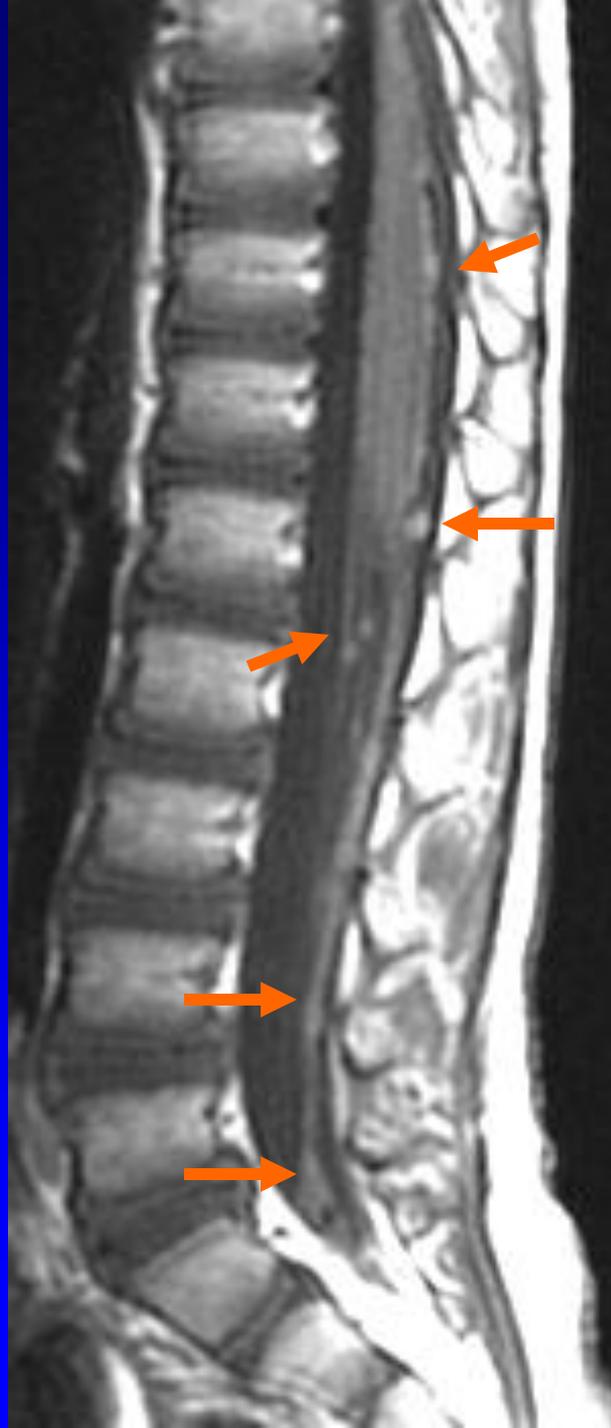






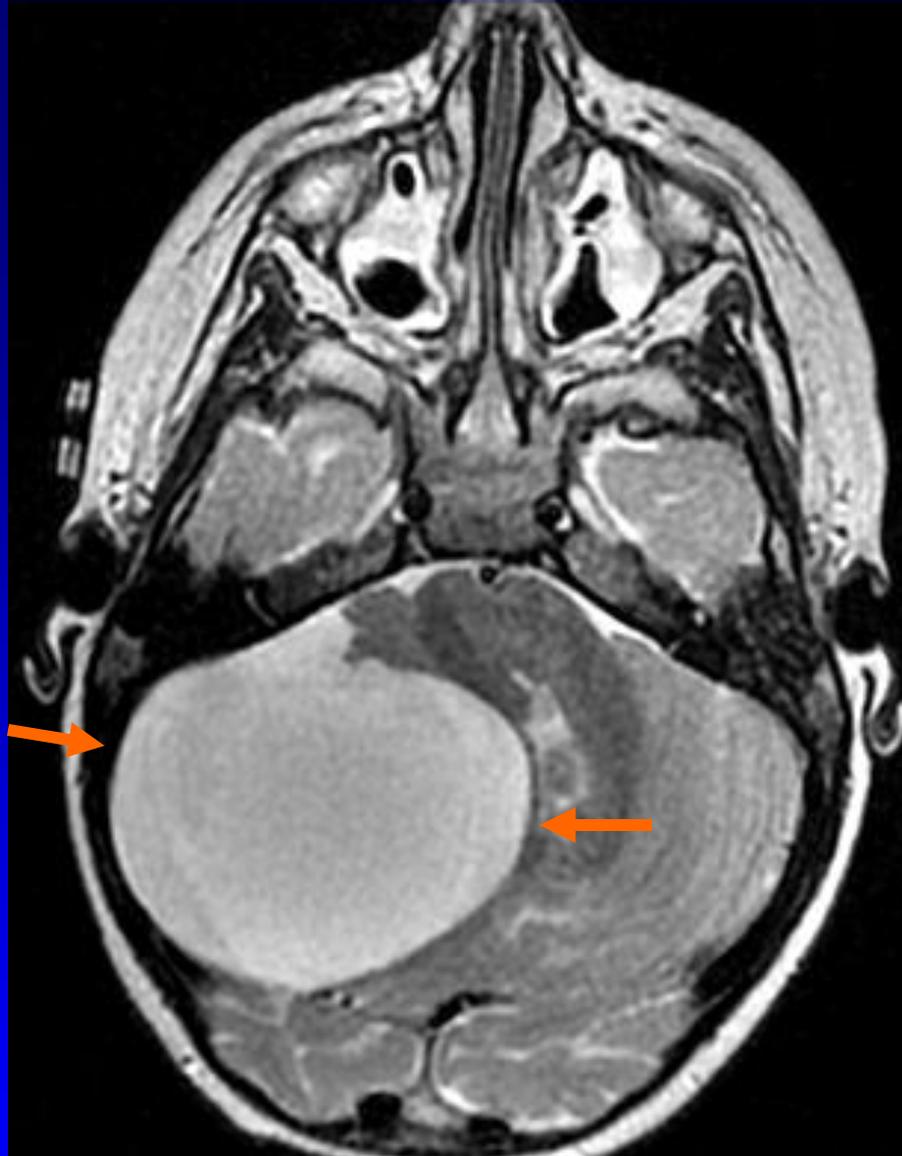
Leptomeningeal dissemination





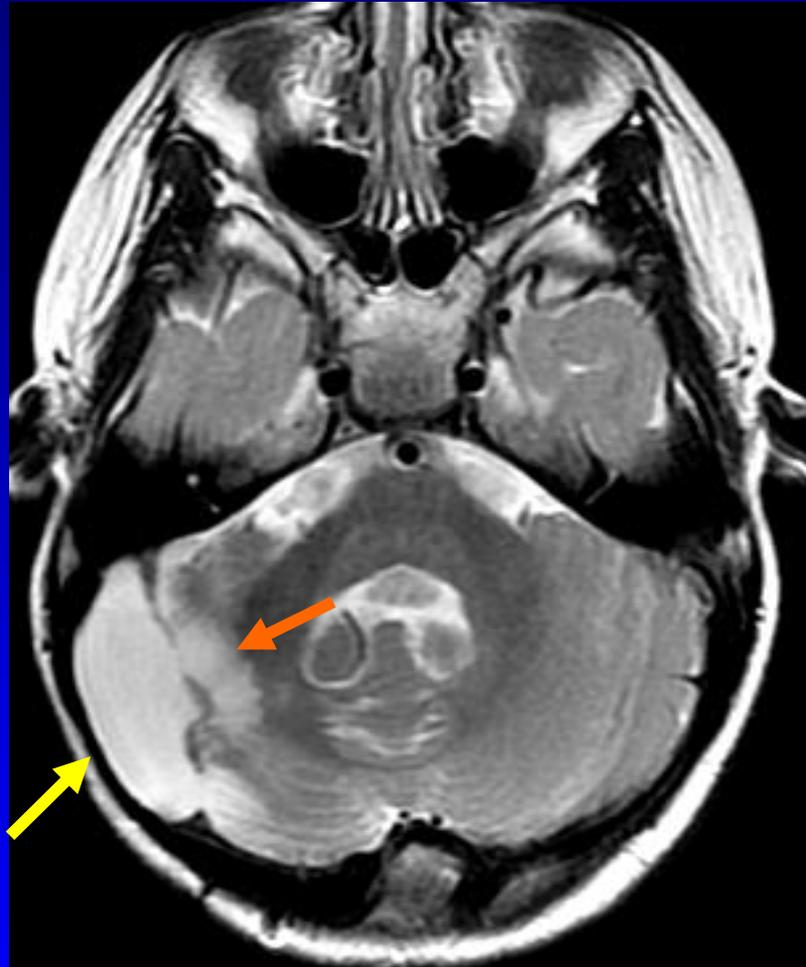
Brain tumors: contrast

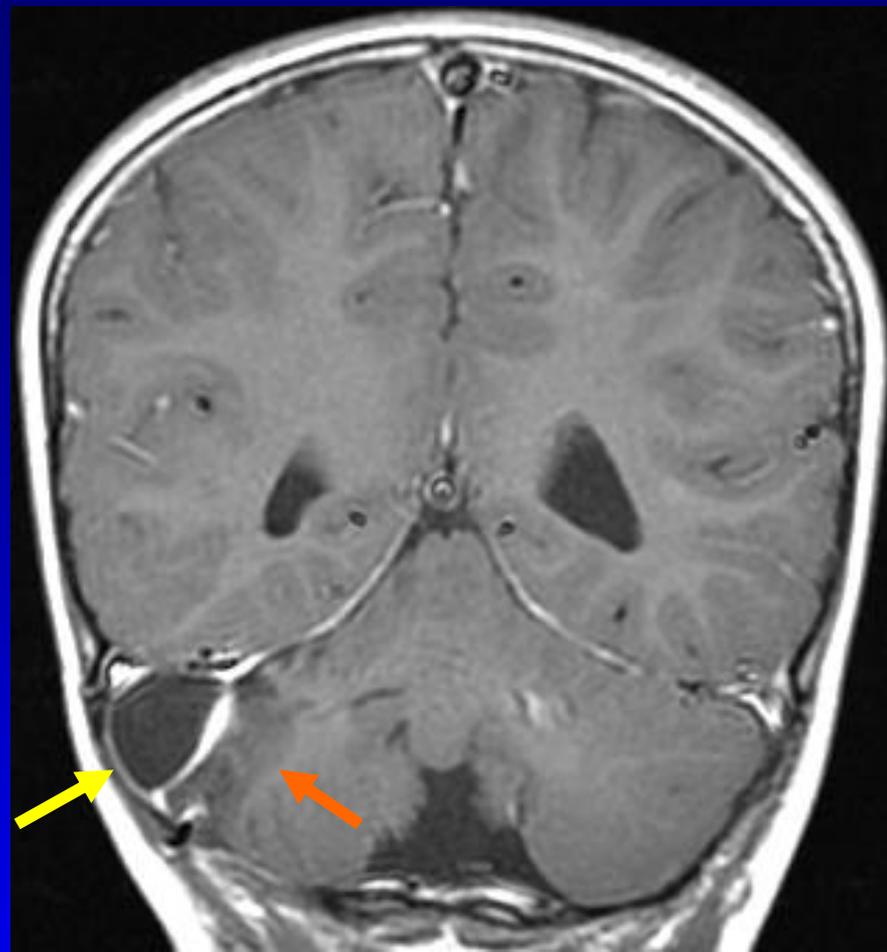
- Characterization
- Extent
- Tumor vs cyst
- Tumor vs edema
- Leptomeningeal dissemination
 - Presence strongly affects prognosis
 - Changes treatment (intensity)



1 year old, posterior fossa mass

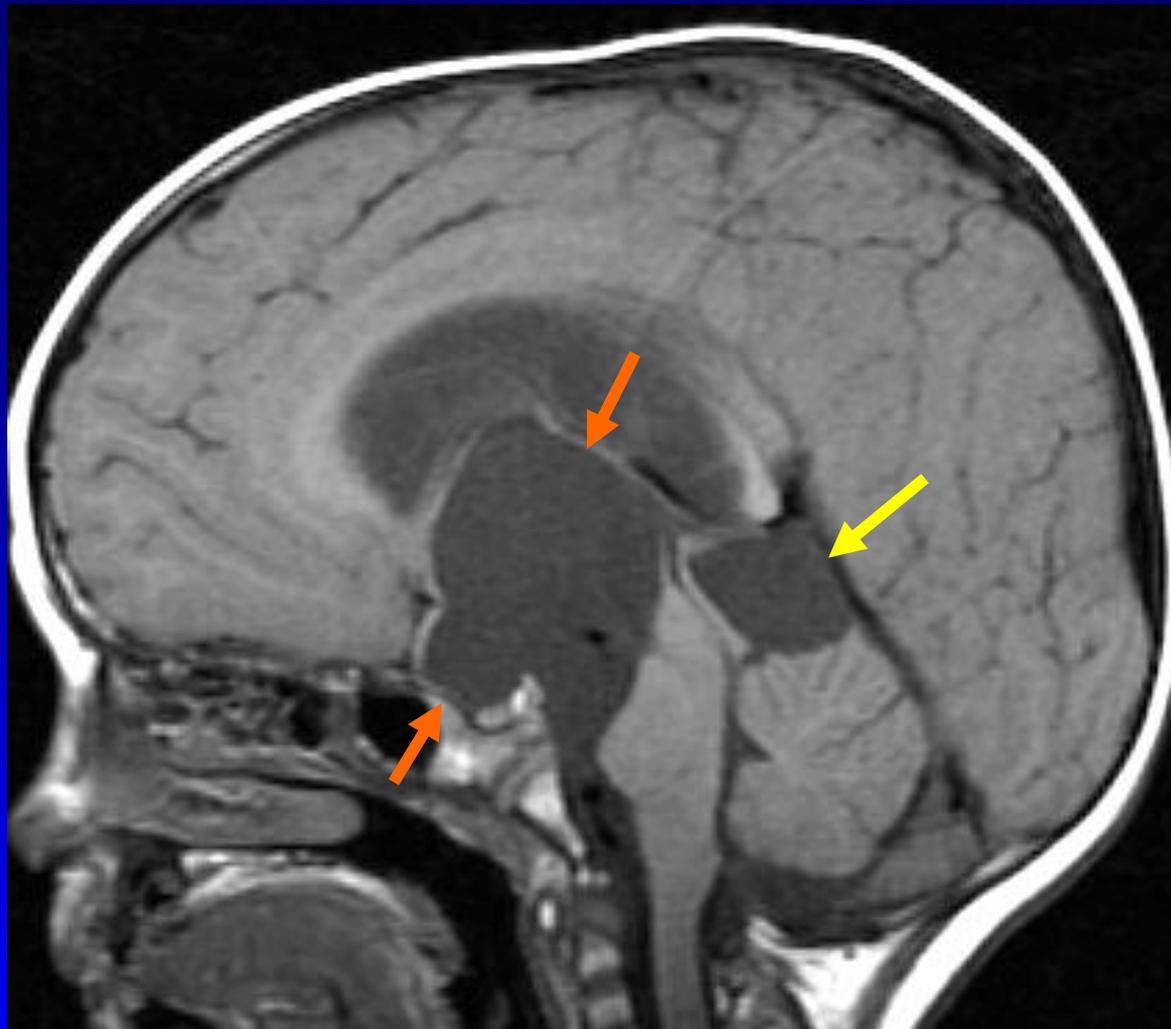




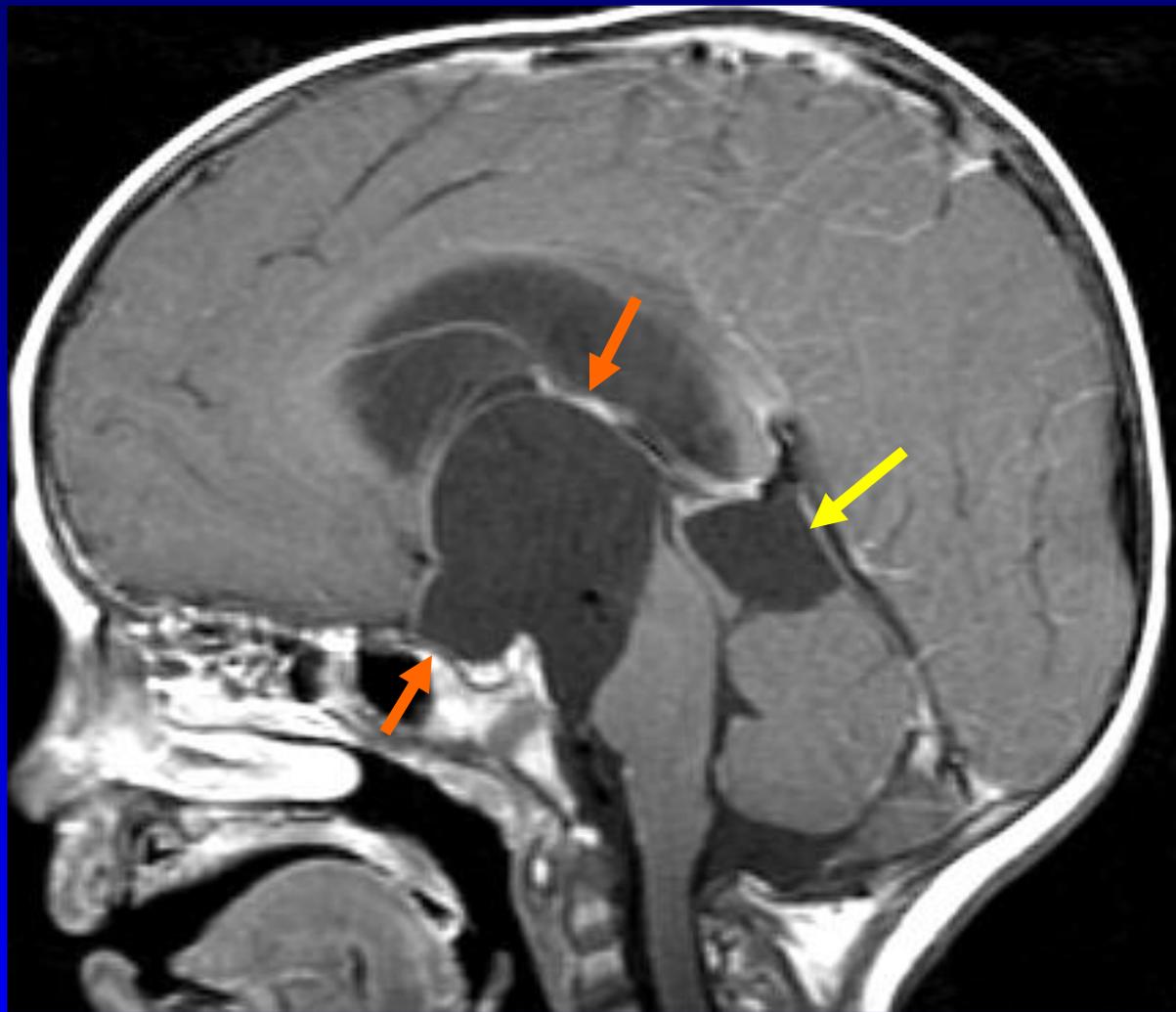


Surgery - Irradiation – Chemotherapy

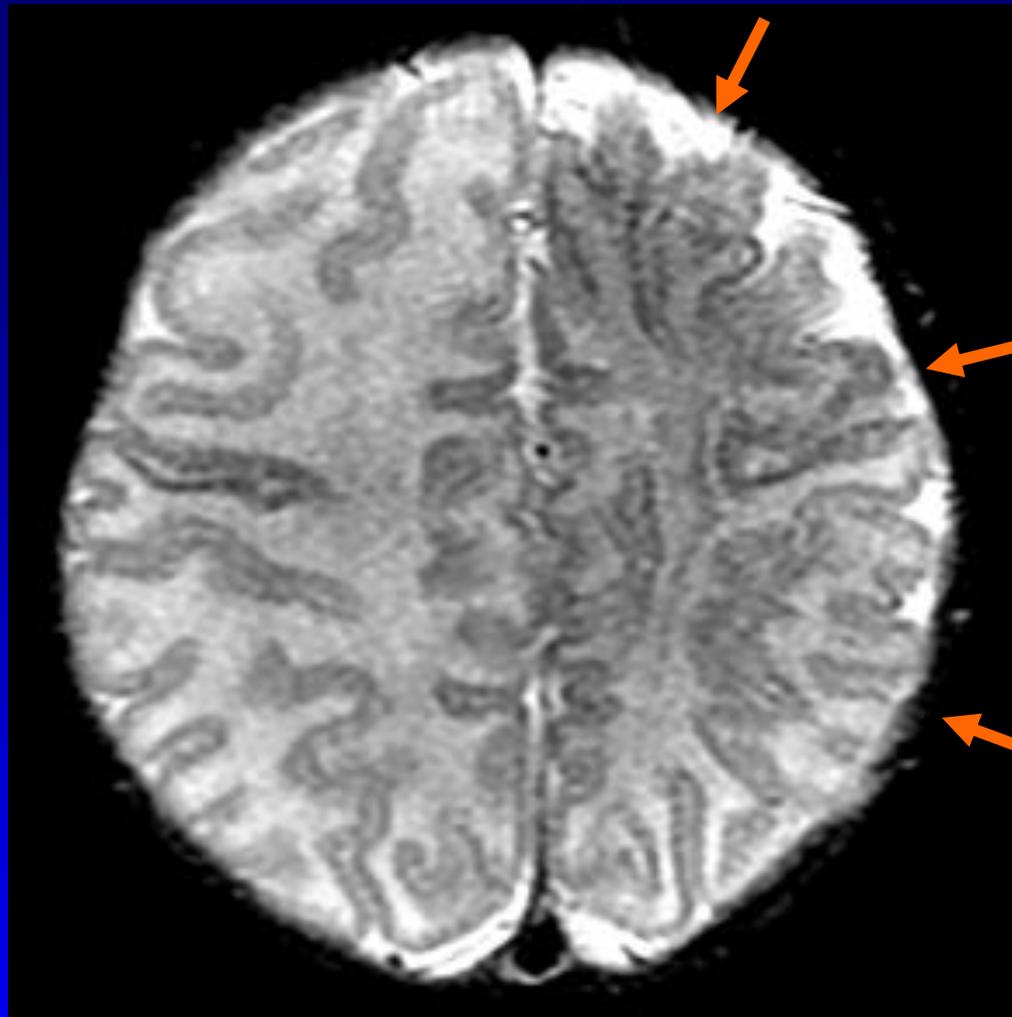
- Treatment related changes in brain/spinal cord
 - Edema
 - Ischemia
 - Scar
 - Demyelination
 - Necrosis
- Contrast crucial to differentiate treatment related changes from residual or recurrent tumor



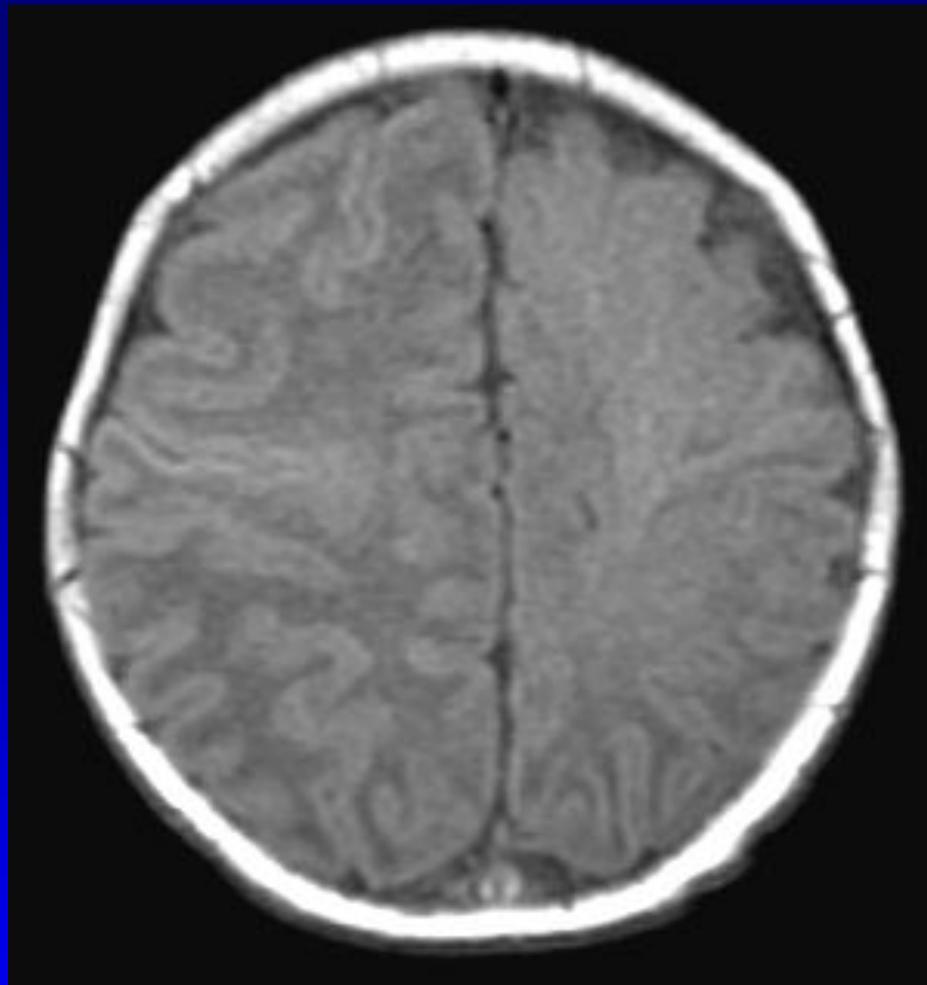
1 year old cystic masses

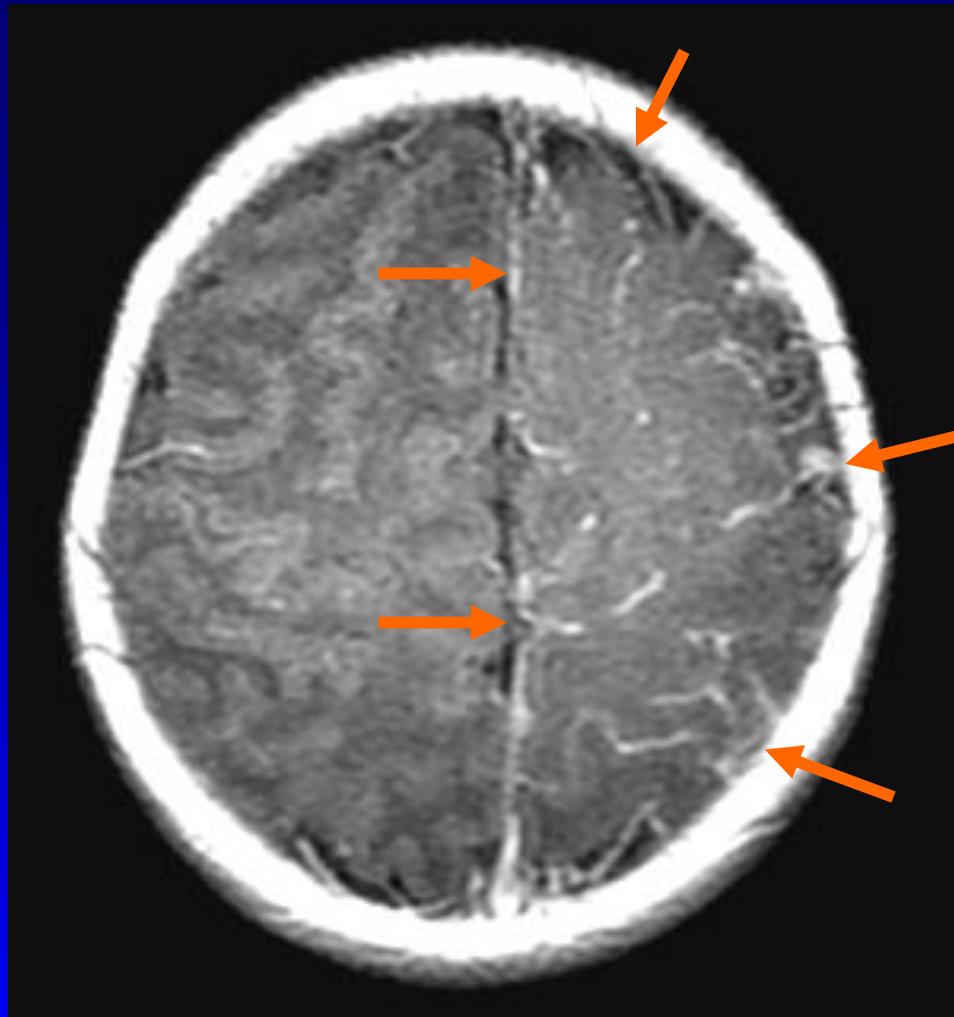


Arachnoid cysts

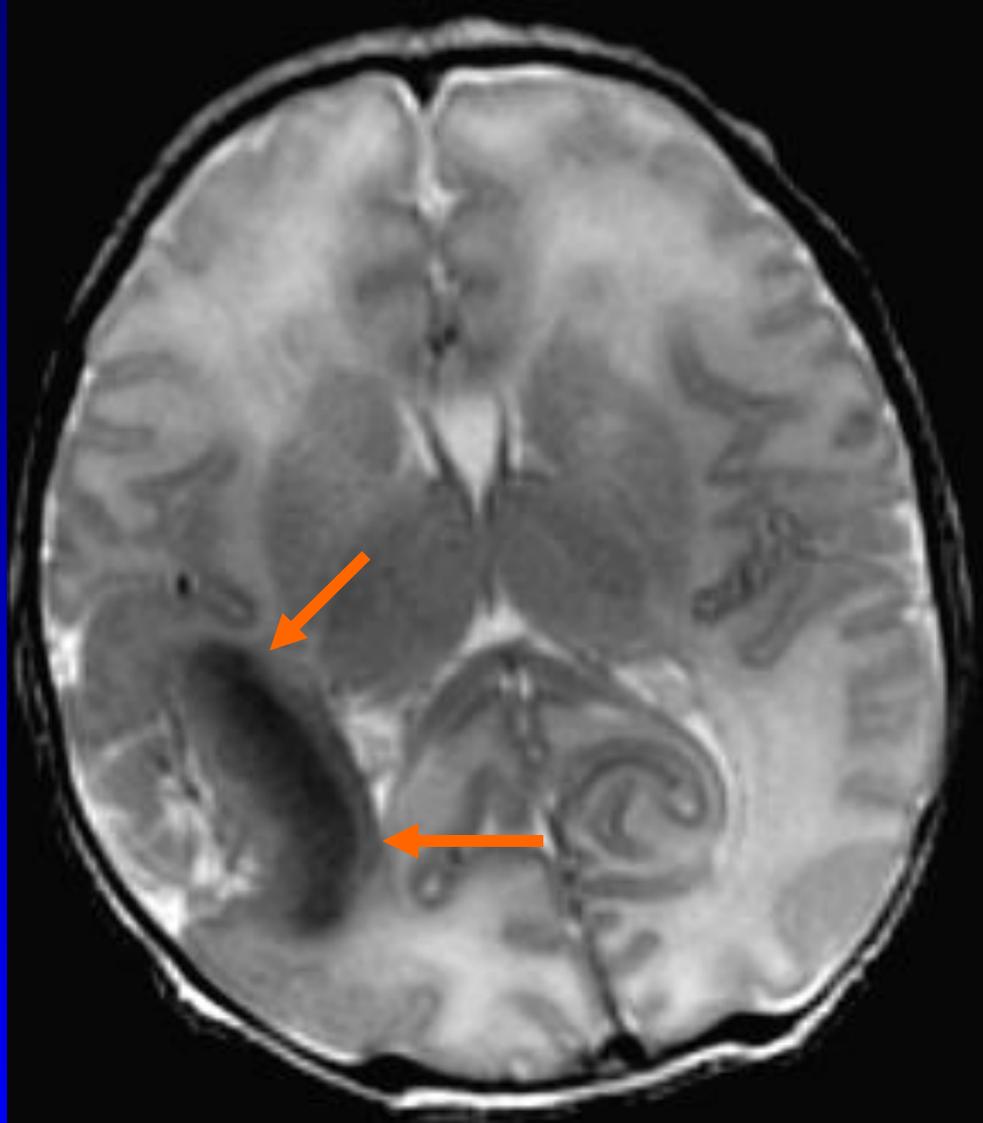


16 day old, seizures

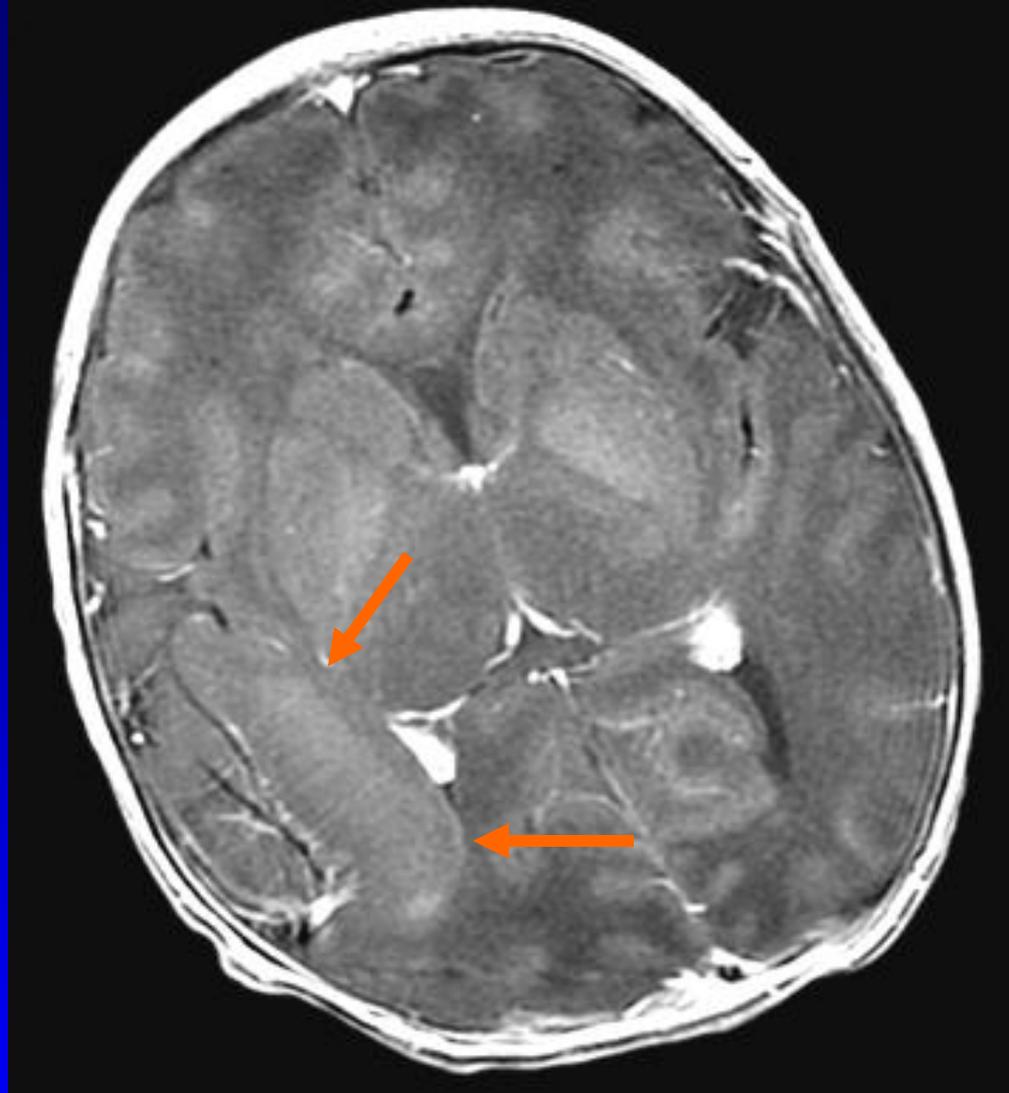




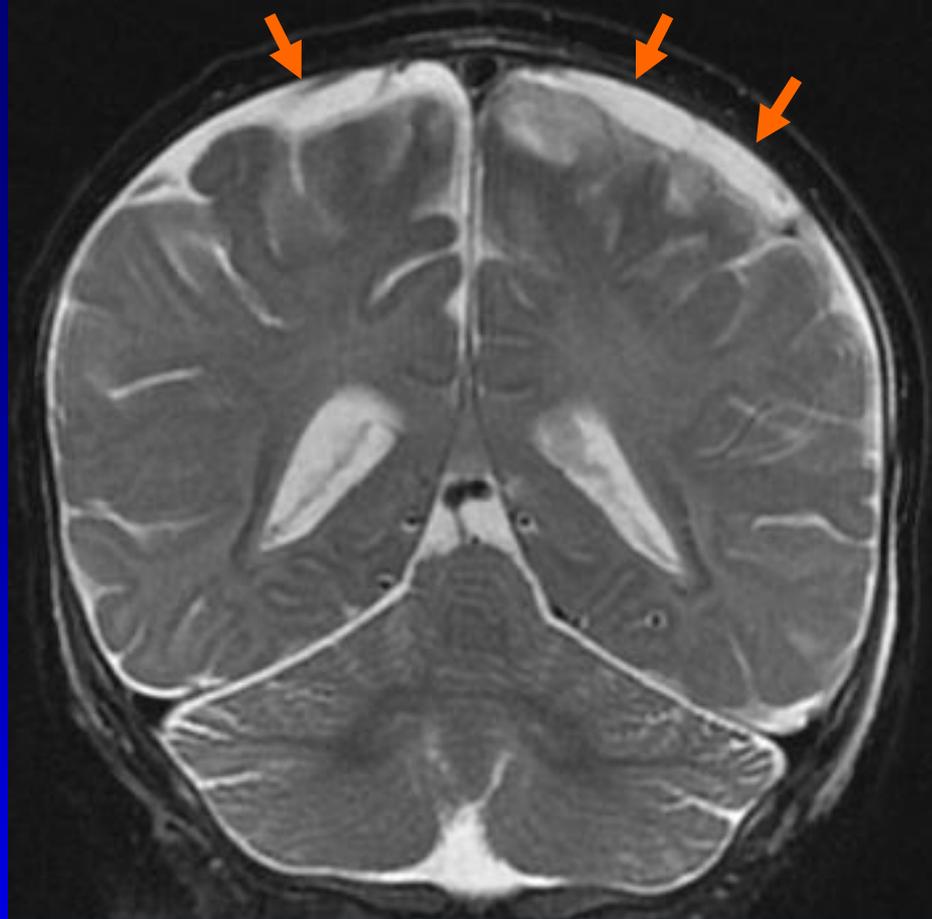
Sturge Weber
(neurocutaneous disorder)



Neonate, focal seizures



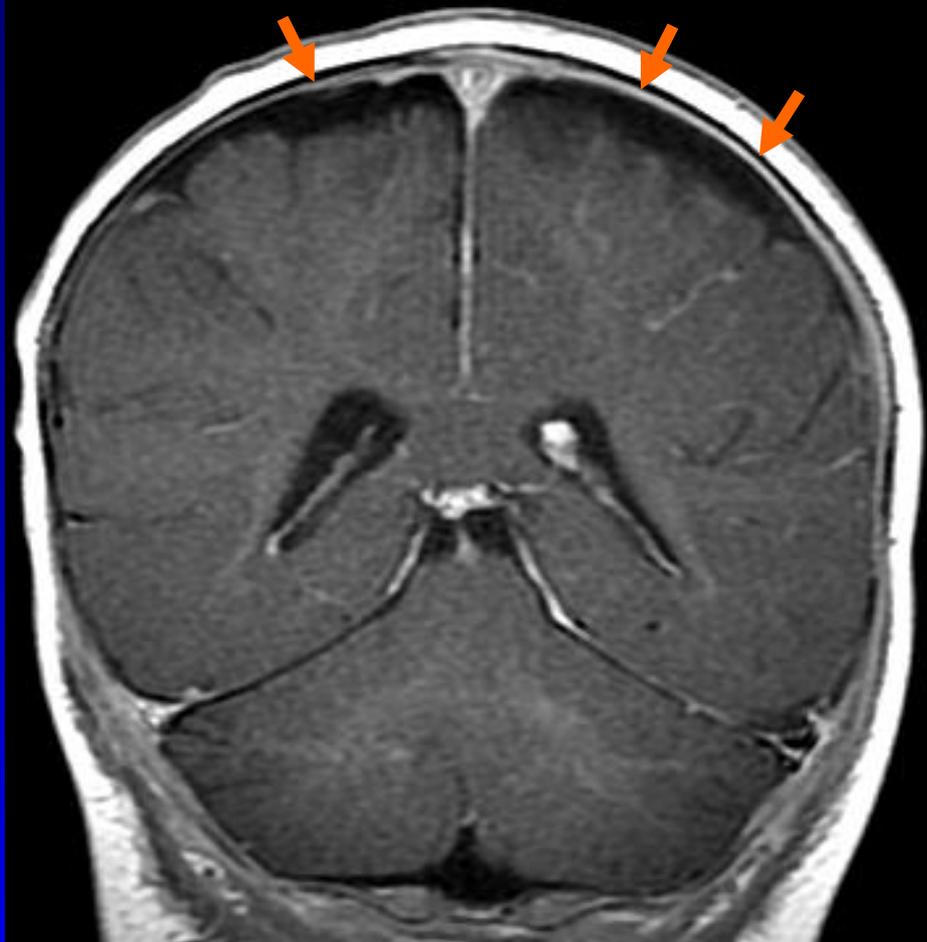
Focal cortical dysplasia

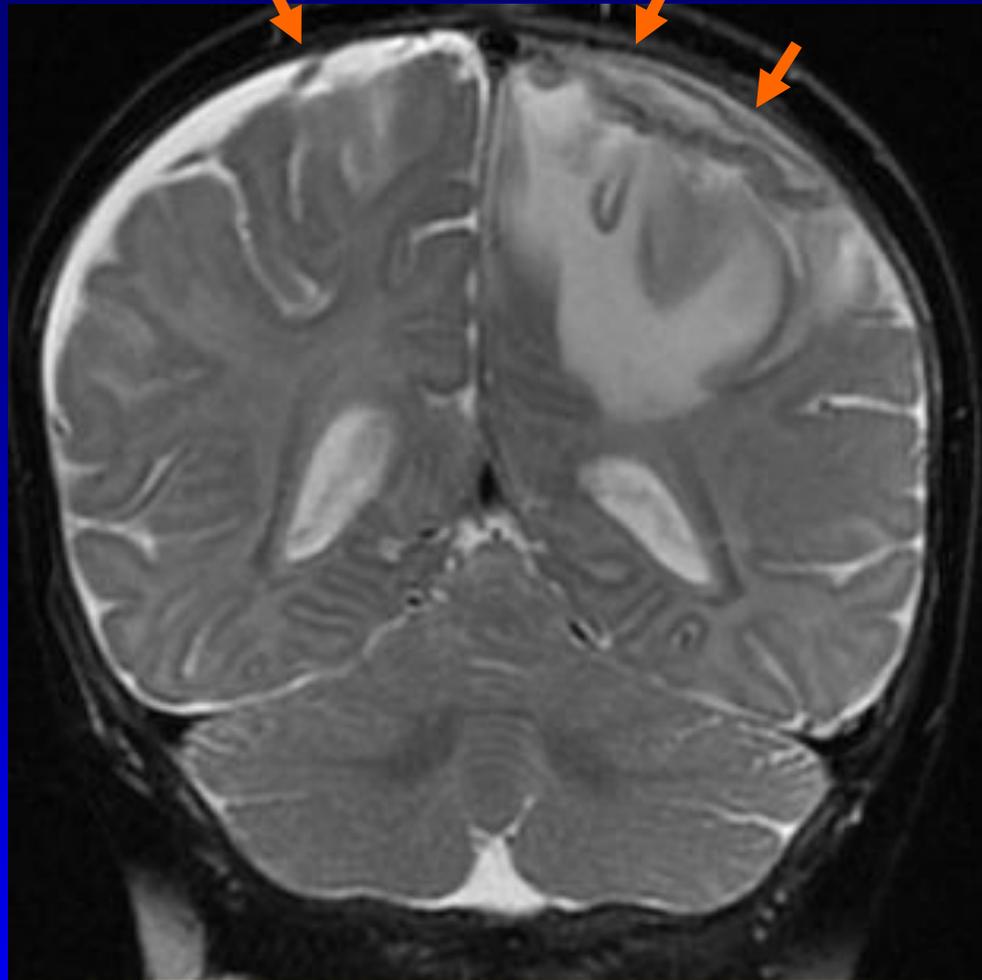


4 month old

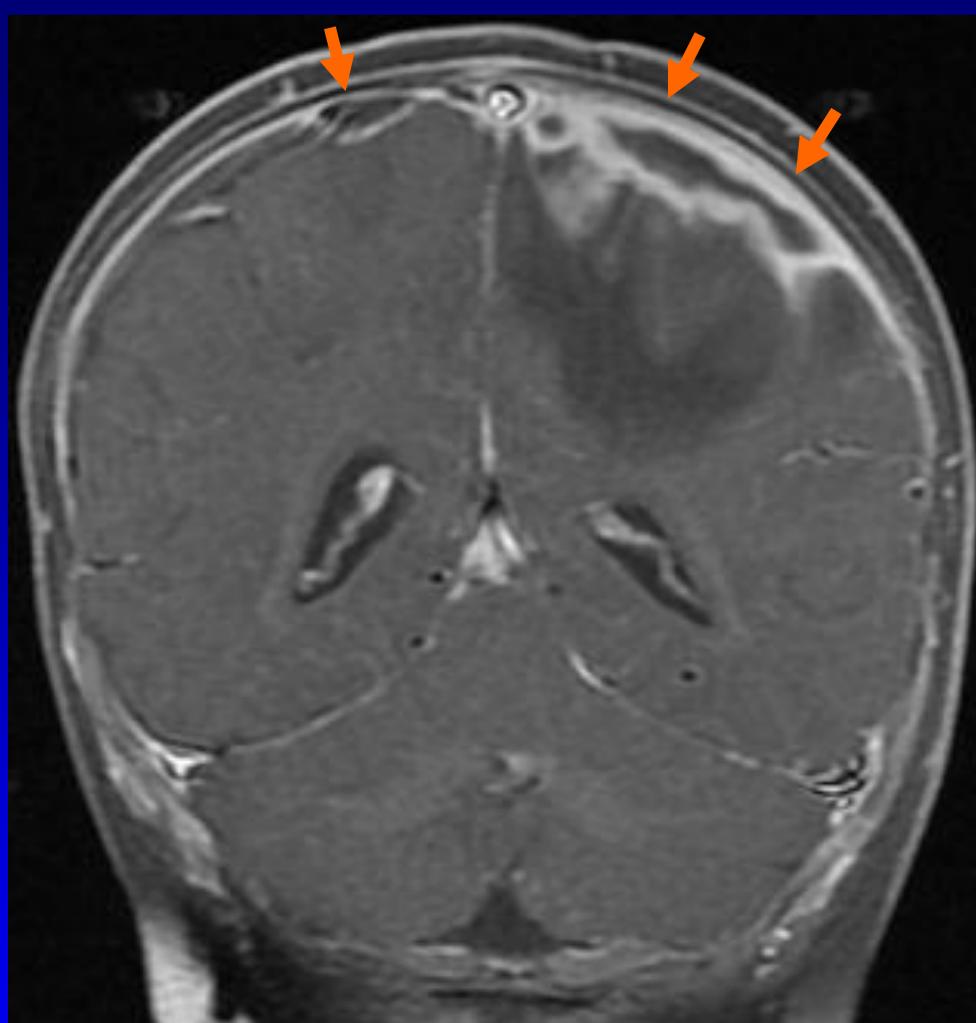
Group B strep meningoenkephalitis

Subdural fluid, ? Effusion ? Empyema

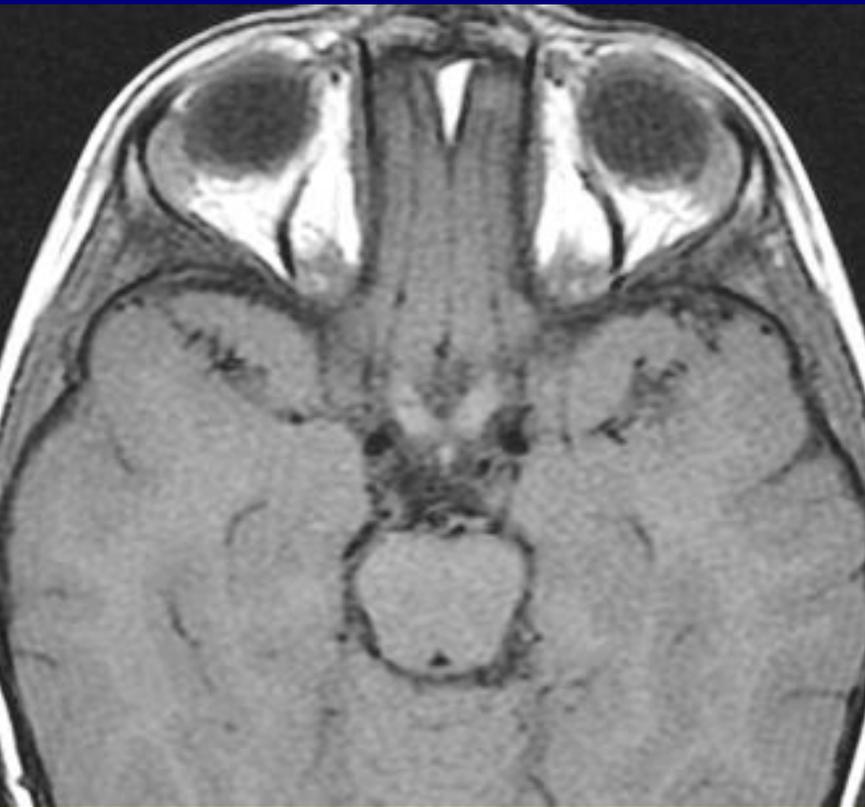




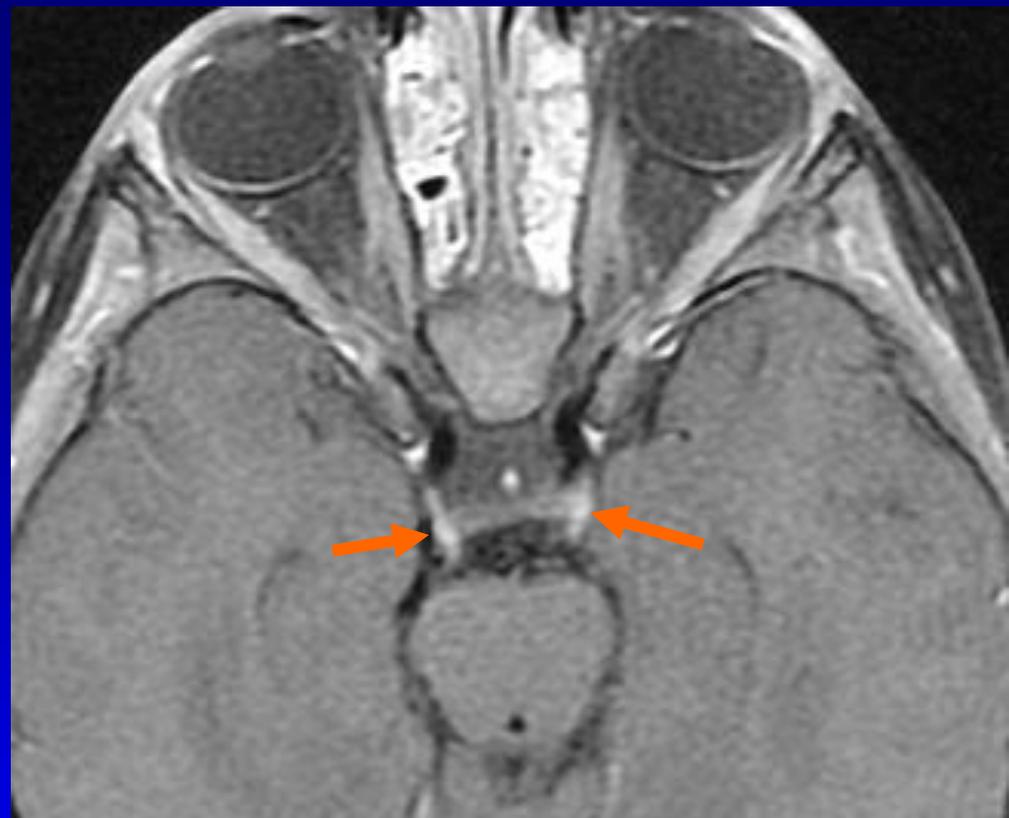
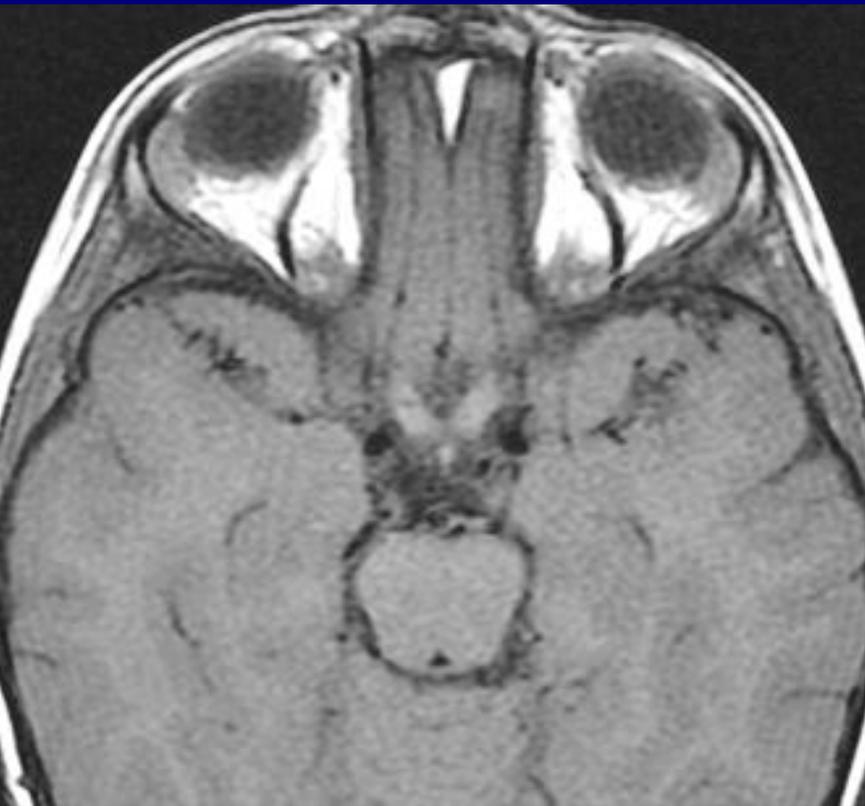
2 weeks later

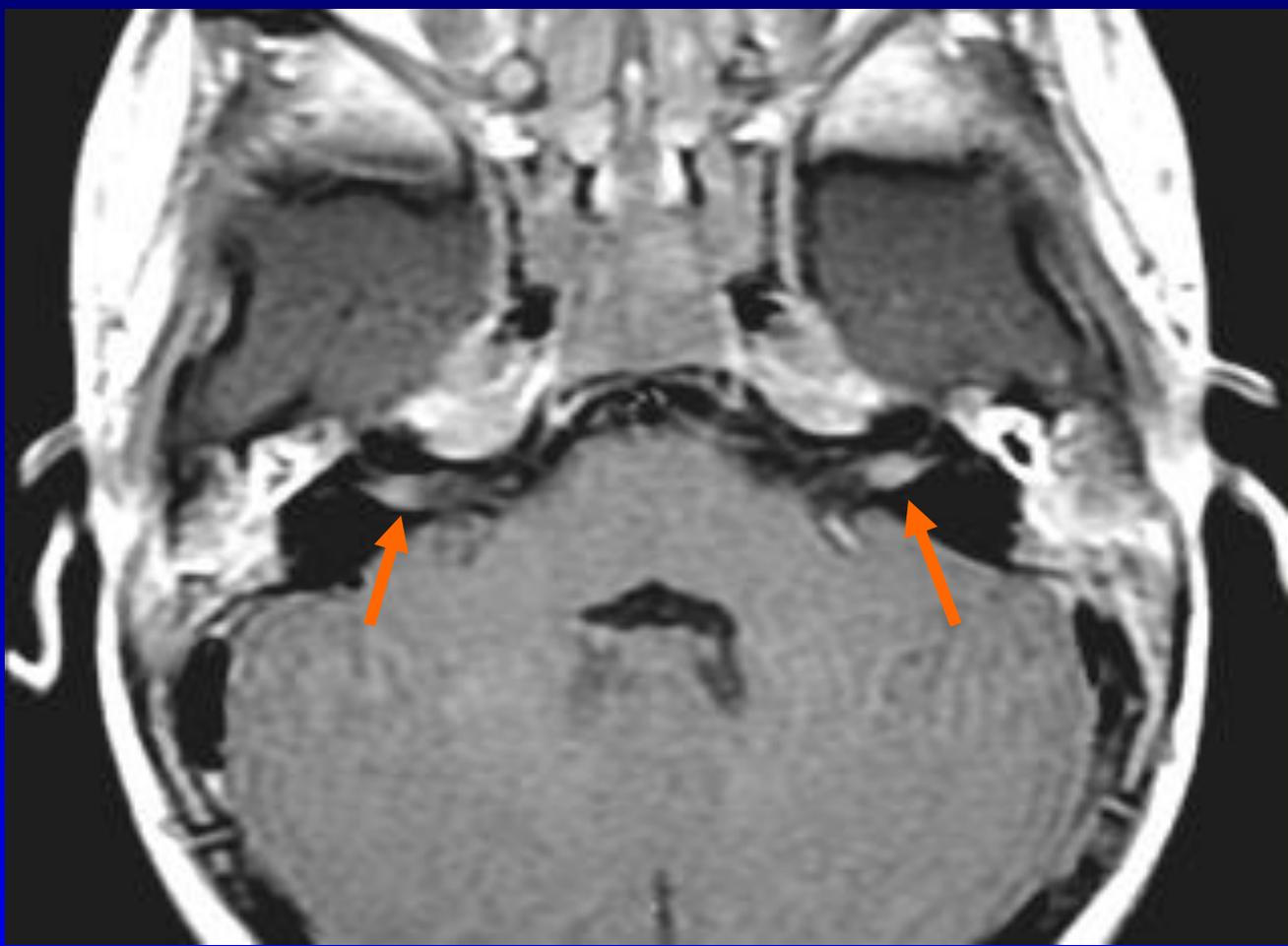


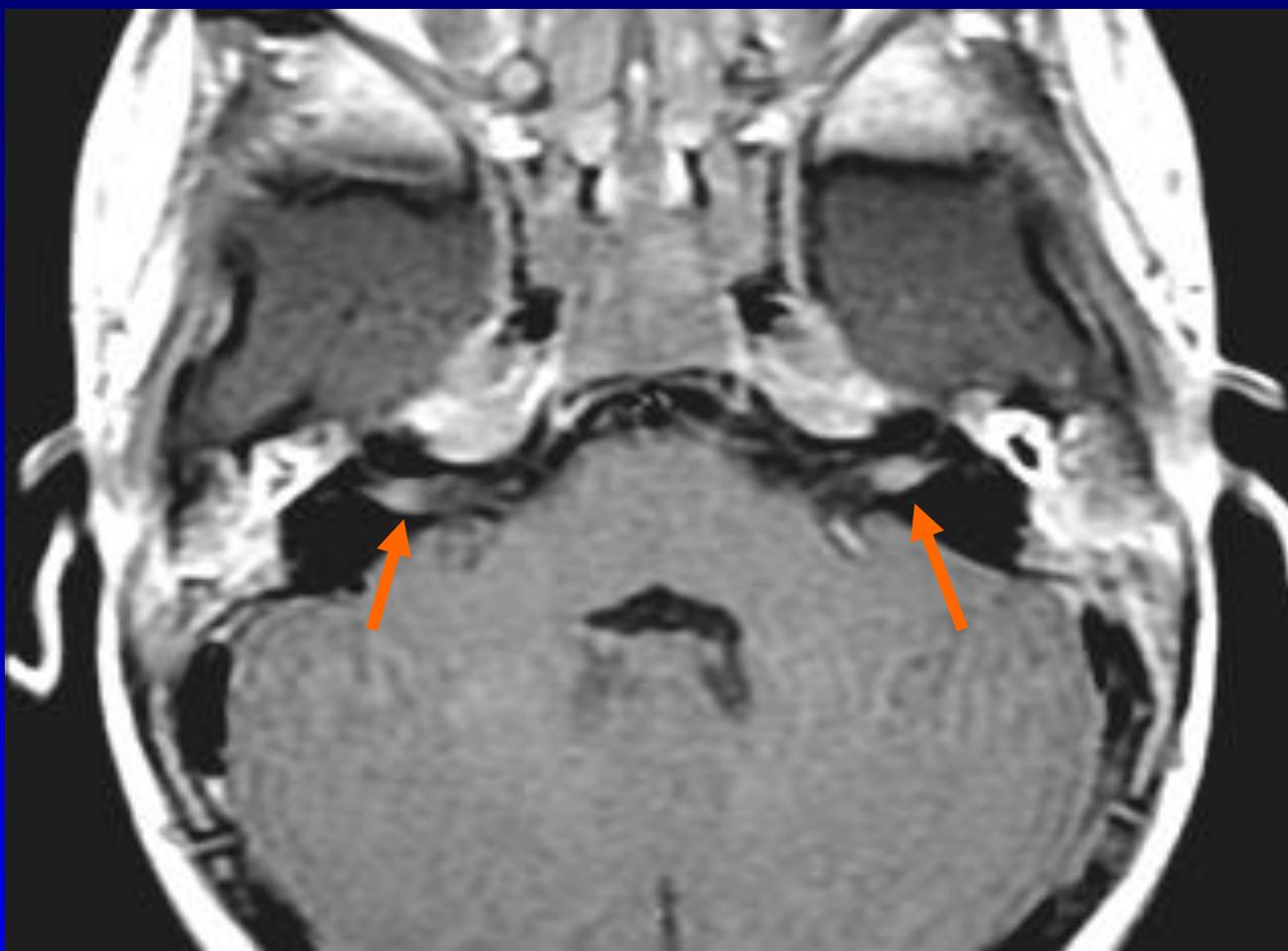
Empyema



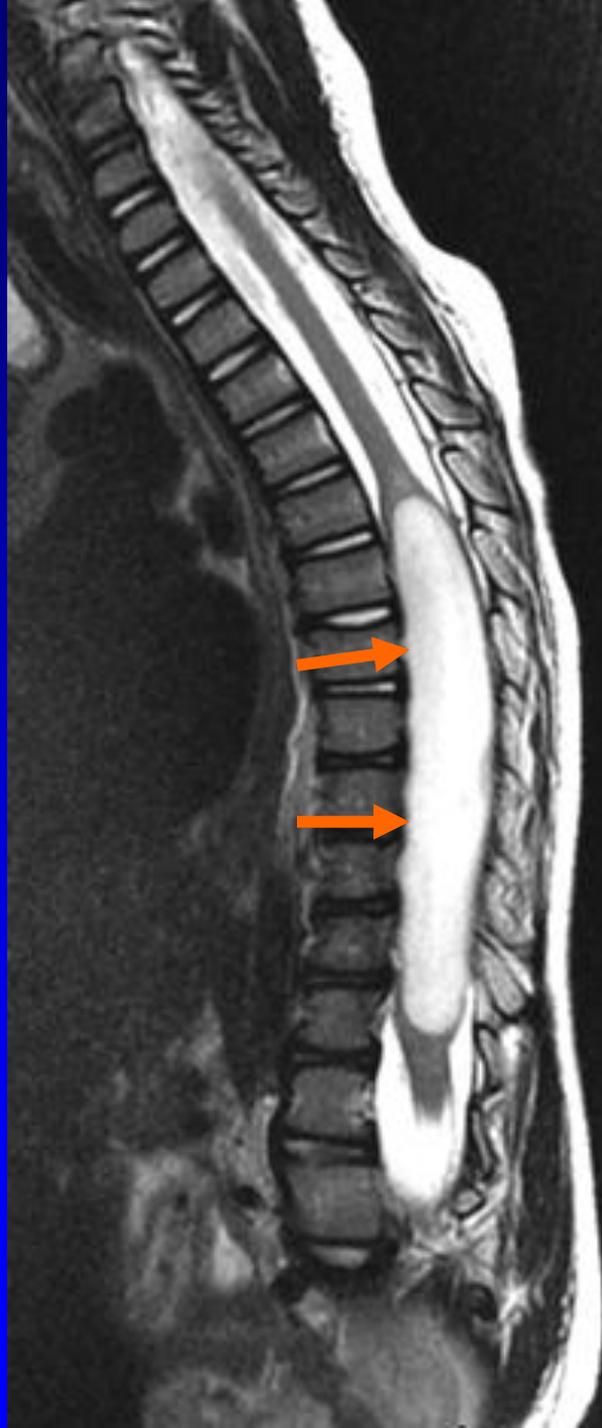
1 year old
Delayed development
Esotropia







Metachromatic leukodystrophy



1 year old
Spinal cord mass

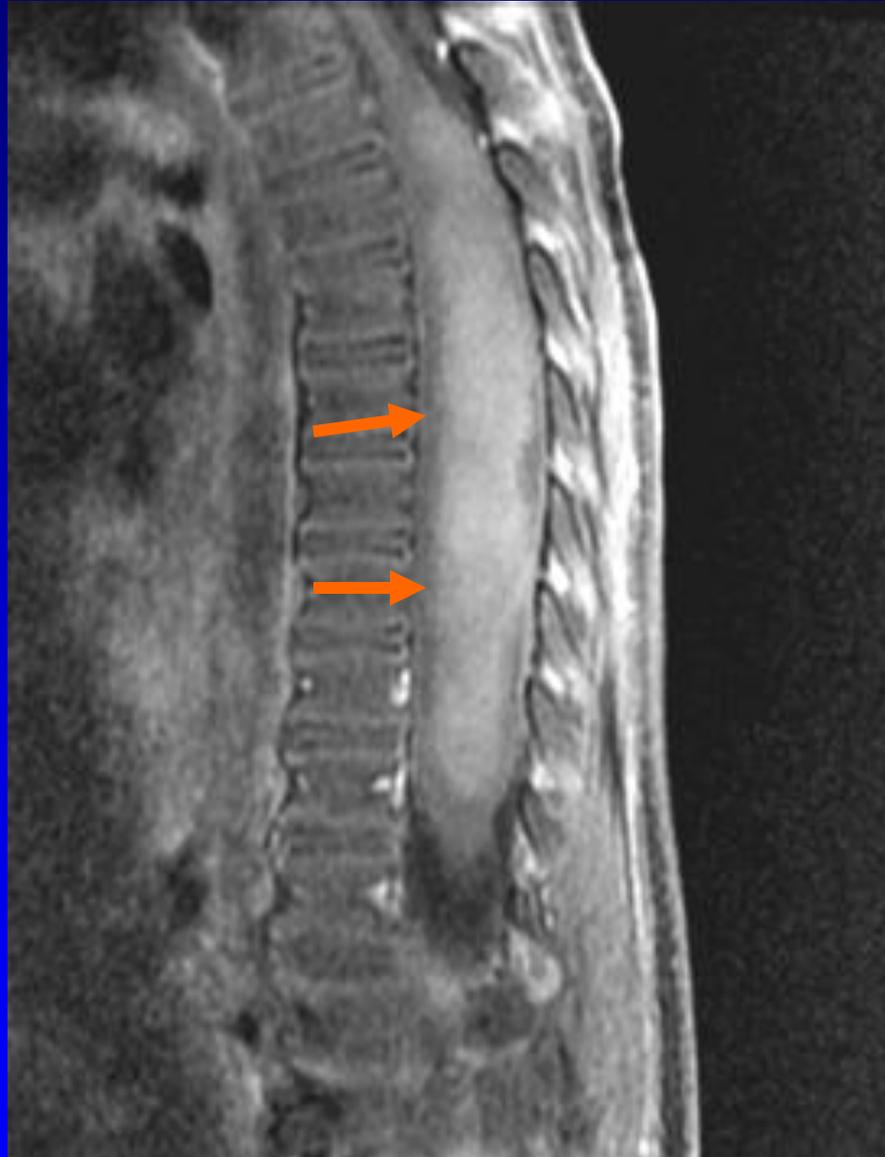
?Cyst
? Tumor

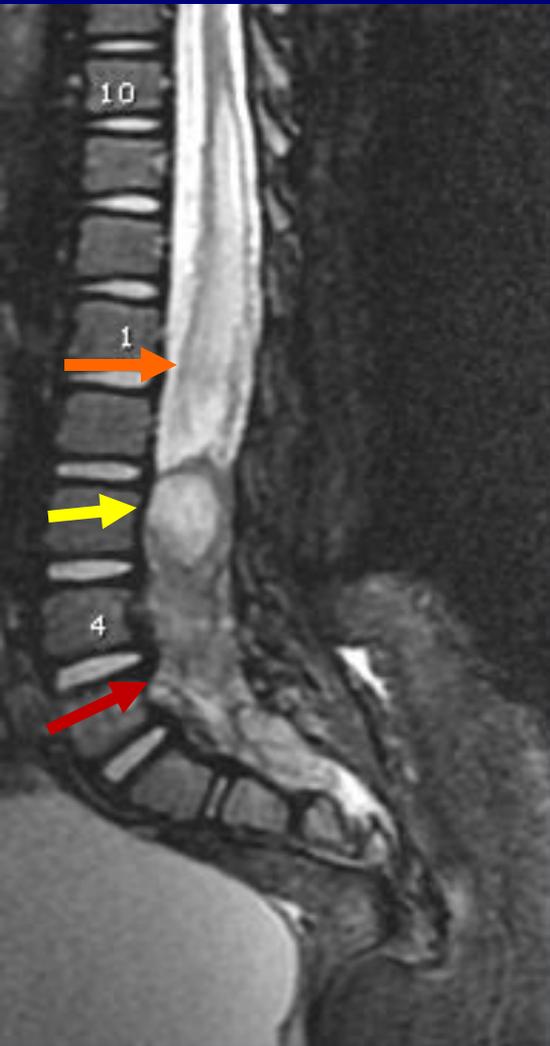


T1 no contrast

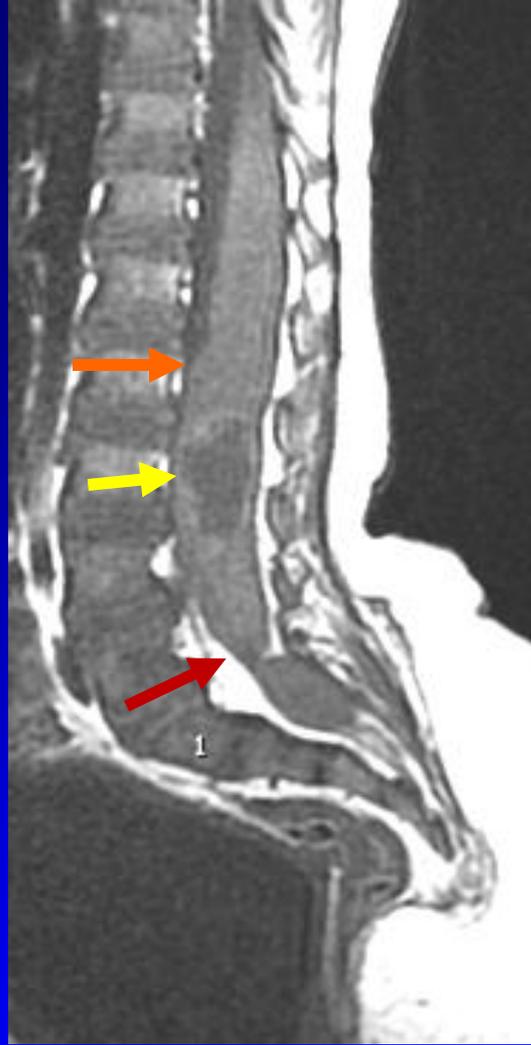
?Cyst

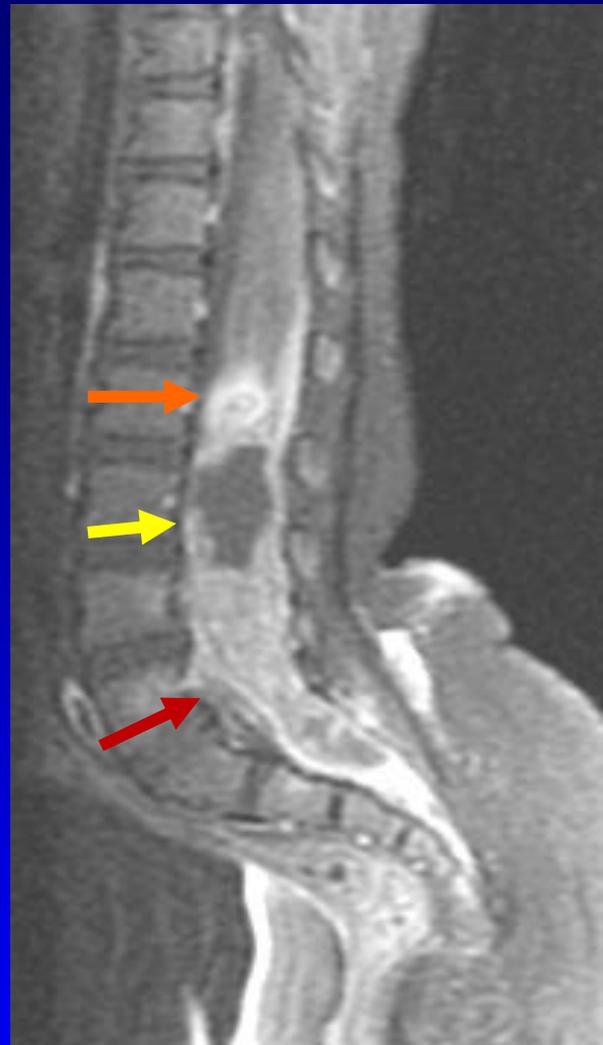
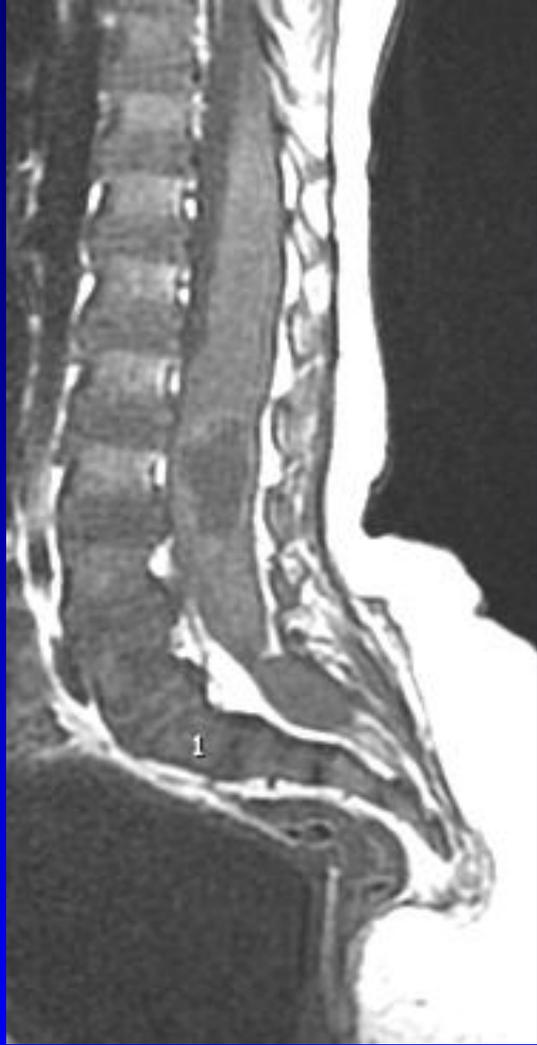
? Tumor





1 year old
Infected dermal sinus





Conclusion: GBCA's < 2 years

- Benefits
 - lesion
 - detection
 - characterization
 - extent
 - direct therapy
 - assess efficacy of therapy
 - saves lives
- Safe
- Prudence in use
 - risk of adverse reaction vs benefit
 - appropriate precautions as indicated