ASTRO REFRESHER
Pediatric Malignancies
2013
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Conflicts

- No Conflicts
Overview

- Review for Management of Pediatric Malignancies
  - Overview for each site
  - Work up, treatment & RT guidelines
  - Appropriate RT modalities

*what you need to know to manage and treat a patient*
Pediatric Malignancies

- CNS Tumors
  - Medulloblastoma/SPNET
  - Ependymoma
  - ATRT
  - Low Grade Glioma
  - High Grade Glioma
  - DIPG
  - Craniopharyngioma
  - Germ Cell Tumors

- Non-CNS
  - Hodgkin’s Disease
  - Wilm’s Tumor
  - Neuroblastoma
  - Rhabdomyosarcoma
  - Ewing’s Sarcoma
  - Osteosarcoma
  - Sarcoma (other)
  - Retinoblastoma
  - Leukemia
  - Langherhan’s
Clinical Case

- 5 y/o boy presents with HA

- For oral boards
  - Always safe to start with H & P with detailed exam of organs affected by specific malignancy
    - HA, n/v, cranial nerve deficits (double vision, facial droop, etc.), torticollis, back pain, neuropathy, neuro exam
  - Almost all children with a brain tumor will have a finding on neuro exam in addition to HA
  - CT or MRI brain should be ordered
Describe Images; Top 4 in differential
Differential Posterior Fossa Mass

- Pilocytic Astrocytoma
- Medulloblastoma
- Ependymoma
- ATRT (Atypical Teratoid Rhabdoid Tumor)
Frozen Path Medullo

- Most of the tumor is easily removed. There is a thin carpet on the brainstem measuring 5 mm by 1 mm. Removal carries risk of brainstem injuring.

- How do you want to proceed? What amount of disease has been shown to increase the risk of recurrence?

- What additional work up is required?
Medulloblastoma

- Goal for medulloblastoma is to achieve less than 1.5 cm² residual tumor

- Additional work up includes
  - post-operative MRI (within 48 hours of surgery)
  - MRI spine (10-14 days post-surgery)
  - CSF (10-14 days post-surgery)

*Ok to get MRI spine at diagnosis before surgery, but NOT CSF (why?)*
Standard versus High Risk

- **Standard Risk**
  - Not metastatic
  - $\leq 1.5 \text{ cm}^2$ residual
  - $\geq 3 \text{ yrs. old}$

- **High Risk**
  - Any of these factors
Is there a subgroup of “standard risk” patients that are no longer eligible for COG standard risk protocol?
Standard risk Medulloblastoma: prognostic impact of anaplasia in localized disease

CCG-A9961
N = 379 pts.

Anaplasia in 15% of pts.
(diffuse or focal)

Excessive Anaplasia:
EFS = 73% at 5 yr.

No Anaplasia:
EFS = 83% at 5 yr.

Fig 4. Event-free survival by anaplasia.

Packer et al, JCO 2006

Note: Large Cell/Anaplasia no longer allowed on SR COG Study
Staging of Medulloblastoma- Chang (pre-MRI and even pre-CT era)

- T1 – tumor < 3 cm in diameter
- T2 – tumor ≥ 3 cm in diameter
- T3a extension into aqueduct of foramen
- T3b invasion of brain stem (generally defined by intraoperative demonstration)
- T4 midbrain, 3rd ventricle or upper cord involved
- M0 no metastasis
- M1 microscopic CSF involvement
- M2 gross seeding of 3rd ventricle
- M3 gross seeding of cord
- M4 extra-CNS metastases (esp. bone marrow, bone)
Standard Risk Medulloblatoma

- CSI within 31 days of surgery to a dose of 23.4 Gy f/b posterior fossa (or involved field*) boost

- Is this patient eligible for protocol?
ACNS0331

- Randomizes children <8 to 18 CSI versus 23.4 CSI
- Second randomization for all patients involved field versus whole posterior fossa
- Weekly Vincristine during radiation
- Cisplatin based chemotherapy after RT
Children’s Oncology Group
Average Risk Medulloblastoma
ACNS0331 Schema

Age 3-7 years

- CSRT 18Gy (PF 23.4Gy)
  - R
  - CSRT 23.4Gy
    - PF boost 54Gy
    - IF boost 54Gy

Age 8-21 years

- CSRT 23.4Gy
  - R
  - PF boost 54Gy
  - IF boost 54Gy

Weekly vincristine during XRT
Chemotherapy

- Weekly Vincristine f/b 8 cycles of Vincristine, Cisplatin, CCNU

Or Alternating AAB,AAB,AAB

A – Cisplatin (75 mg/m²) IV over 6 hours on Day 1
Lomustine (CCNU) (75 mg/m²) orally on Day 1
Vincristine (1.5 mg/m², maximum dose 2.0 mg) IV Days 1, 8, and 15

B – Cyclophosphamide (1000 mg/m²) IV over 1 hour on Days 1 and 2
Vincristine (1.5 mg/m², maximum dose 2.0 mg) IV push on Days 1 and 8
MESNA (360 mg/m²/dose) IV push 15 minutes prior to Cyclophosphamide and repeated at 3 and 6 hours.
Posterior Fossa Syndrome

- Swallowing dysfunction
- Ataxia
- Mutism
- Emotional Labiality

(SAME)

Does this change your management?
Treatment Planning

- Simulation and Planning
- CSI
- Involved Field and Posterior Fossa
CSI

- Pt. placed prone with prone mask on.

- Spine: Plan first
  - Inferior: bottom of thecal sac + margin (determined from MRI, about S2)
  - Superior: C5-6 (or as low as possible while still clearing shoulders on WB, so that when you feather up you won’t go through brain or mouth (photons)-for protons helps with dose distribution but exit is not an issue)
  - Lateral: about 1 cm lateral to vertebral body and to catch sacral nerve roots inferiorly field may be wider
CSI

- Then WBRT set up
  - 2 angles
    - 1) Rotate the collimator to match the divergence of the spine field. \{arctan (L/2)/SSD\}
    - 2) Kick the couch TOWARD beam to avoid divergence of the WBRT field into the spine field. \{arctan (L/2)/SAD\}

- Also, angle WB gantry to avoid contralateral retina/lens, i.e.: RAO/LAO (for protons this is different RPO/LPO)
CSI

- If spine field is too long, do extended distance. If field is still too long, split spine field into two, but leave a gap at cord and feather jxn weekly. Gap calculation usually around 3mm.

- Feather all matches weekly (every 9 Gy)
*Collimate brain field to match divergence from spine field
*For photons, use RAO and LAO to avoid divergence of brain field into contralateral retina
* Match spine fields anterior to cord to avoid a hot spot (results in cold spot but “safer” to avoid toxicity)

Figure 1: Craniospinal Irradiation Technique—The patient is placed in a prone position. The lateral brain fields are angled to match the divergence of the beam from the upper posterior spine field. The angle $\theta$ depends on the length of the upper spinal field. When two posterior spine fields are used, a skin gap(s) is utilized to account for the divergence of the two fields and to prevent overdosing of the spinal cord at the junction site.

Therapist will put marker on patients back each day
Small hot spot if no couch kick

Kick couch
(feet towards gantry of brain field being treated)
Matching the divergence
Spinal cord match line

inferior  mid  superior

Matching depth
Spinal cord match line

Matching depth
RAO/LAO (photons)
Cribiform Plate
CSI Protons

3D Protons 3D Photons
PF and IF

• Posterior Fossa - C1 (inferior) to tentorium (superior) to bones of occiput and temporal bones (lateral). THIS IS A CTV.
  • PTV 3 to 5 mm margin; should extend to posterior clinoid and C1/C2
  • 95% of volume should receive prescription dose and no portion should receive less than 50 Gy

• Involved Field- gross tumor + resection cavity + 1.5 cm margin (excluding bone and tentorium)
Medulloblastoma; Posterior Fossa

Protons

IMRT

Gy
57
54
45
42
39
36
30

IJROBP; 58; 3; 2004
Critical Structures

- For oral boards, be able to find these critical structures on CT/MRI
  - Cochlea
  - Pituitary gland
  - Hypothalamus
  - Brainstem
  - Spinal cord
Side Effects

- Nausea, vomiting, fatigue, skin irritation
- Diminished bone growth
- Infertility
- Gastrointestinal distress
- Second cancers

- Neurocognitive deficits
- Hearing loss
- Pituitary axis dysfunction
- Hypothyroidism
- Cardiac dysfunction
- Restrictive pulmonary disease
What is the treatment for High Risk Medulloblatoma or SPNET?
High Risk

- 36 Gy f/b boost to 54 Gy (IF or whole PF)
- For spinal mets 45 Gy
- Supratentorial PNET is treated just like High Risk Medulloblastoma and these patients are eligible for High Risk COG Trial

**Babies (< 3) although HR are tx with chemo first f/b RT (usually IF RT)**
Children’s Oncology Group
Other Than Average Risk (High) Medulloblastoma
ACNS0332 Schema

Age 3-21 years

- 1st randomization: +/-daily carboplatin 35 mg/m2/day for 30 doses over 6 ½ weeks and all get weekly vincristine 1.5 mg/m2 for a total of 6 doses.
- CT with cisplatin, vincristine, and cyclophosphamide in 28 day cycles for a total of 6 cycles. (Cumulative cisplatin dose possible 450 mg/m2)
- 2nd randomization to +/- Isotretinoin (80 mg/m2 twice daily on Day 1 and Days 16-28 in 28 day intervals during chemotherapy and days 15-28 after chemotherapy for a total of 12 cycles.)
Outcomes

- Standard Risk Medulloblastoma
  - 5 year EFS 83% no anaplasia 73% anaplasia

- High Risk Medulloblastoma
  - 5 year EFS 67%

- Supratentorial PNET
  - 5 year EFS 68%

- Baby Medulloblastoma
  - 5 year EFS approximately 50%

Packer, JCO 2006
Chintagumpala, Neuro-Oncology 2009;1:33-40
ATRT

- Recognized as a distinct entity since discovery of INI-1 tumor suppressor gene (loss of INI-1 indicates ATRT)
- Usually occur in very young children
- Poor prognosis but curable when disease is localized
- Localized disease is treated with high dose chemotherapy followed by IFRT to 50.4 Gy
- CSI for localized or metastatic disease and if child is over 3
Ependymoma
Ependymoma

- Median age 5-6 years
- $\frac{2}{3}$ are infratentorial; $\frac{1}{3}$ supratentorial
- Prognostic Factors
  - GTR!!!
    - Maximal surgical resection is very important for this disease
  - Histology
- Work up is the same as medulloblastoma
Ependymoma

- RT involved field to 54 – 59.4 Gy **

- If metastatic disease on spine MRI or CSF 36 Gy CSI for children > 3 years

- Chemotherapy on protocol but not proven to provide benefit for localized disease

- Outcomes- Close to 80% for GTR; 30-40% for STR

* Our standard is 54-55.8 Gy because of brainstem tolerance; COG protocols use 59.4 and other institutions use 59.4 Gy
Involved Field to 54 Gy

Protons

IMRT
Involved Field

Protons

IMRT
Best Available Published Data

- 153 patients with localized disease treated with 3D conformal photon therapy
- 7 yr. LC 87%; EFS 69% and OS 81%
- 7 yr. EFS grade II/III: 79% and 61%
- 7 yr. EFS GTR v STR: 77% v. 34%
- 7 yr. OS GTR v STR: 88% vs. 52%

Merchant et al, Lancet Oncology 10:258, 2009
Best Available Published Data

- Very high rate of GTR (81.7%)

- Complications
  - 3 pts. with brainstem necrosis, steroids/HBO, 1 died, other impaired (9 and 12 months from RT) (2.5%, S+RT)
  - 4 cases cervical subluxation (all had laminectomies)
  - 7 yr. CI of 2\textsuperscript{nd} malignancy: 4.1 % (n=4, 3 gliomas, 1 thyroid)
  - 1 Moya-moya (12 months after RT, age 1 at RT)

Merchant et al, Lancet Oncology 10:258, 2009
Proton Data

- 70 patients with localized disease treated with involved field proton therapy
- 3-year local control (LC), progression free (PFS), and overall survival (OS) was 83%, 76% and 95%, respectively
- STR was significantly associated with worse PFS (54% versus 88%; p=0.001) and OS (90% vs. 97% for GTR; p=0.001).

MacDonald, et al
PFS by histology and GTR

**A**  
Progression-free Survival (years)
- Differentiated
- Anaplastic

**B**  
Progression-free Survival (years)
- GTR
- STR/NTR

$p=0.509$  
$p=0.001$
Patterns of Failure

• We are seeing less local failures

• Proportionally more distal failures but no increase in absolute # of distal failures
Ependymoma COG ACNS 0121

- 3 main groups for this study
  - Supratentorial non-anaplastic
    - Observation arm (no RT)
  - GTR
    - Received RT only to recommended dose of 59.4 Gy
  - STR
    - Received 7 weeks of chemotherapy f/b second look surgery if feasible

Anticipating publication in near future; this will represent largest Ependymoma study (280 patients)
Low Grade Gliomas

- Most common pediatric brain tumor

- Many (cerebellum, cerebral hemispheres) can be completely resected with 90% DFS without any additional therapy

- LGG of the optic chiasm, hypothalamus, thalamus, tectum, and brainstem often cannot be completely resected and radiation or chemotherapy recommended
Histology

Juvenile Pilocytic Astrocytoma

Diffuse Fibrillary Astrocytoma
Optic/Hypothalamic
LGG of Tectum
Tx Recommendations

- Biopsy for some sites if safe (usually no biopsy for optic glioma or tectal glioma), surgery or shunt/3rd ventriculostomy to relieve symptoms or hydrocephalus

- Radiation Therapy 45-54 Gy; usually 50.4 -54 Gy

- Chemotherapy to delay radiation therapy (reasonable under the age of 10; preferred under the age of 5 and for kids with NF1; should always be discussed in multidisciplinary setting)
Chemotherapy

- Delay SE’s of RT
  - Endocrine
  - Vasculopathy
    - moya-moya
  - Cognitive impairment
  - Second malignancy
  - Children with NF

- Rarely prevent need for RT so use in patients where a delay is of benefit

- Carboplatin & Vincristine most common 1st line regimen
Radiation

- Effective and definitive
- Most patients will ultimately require RT
- New techniques; less toxicity
- Permanent vision loss & endocrine deficits if chemo is ineffective and tumor grows
- If older, chemotherapy is less likely to be effective
- For optic/hypothalamic, if endocrine deficits at presentation less to lose
ACNS 0221 LGG study

- Eligibility: pts. 3-21 years with progressive LGG, pts. <10 must have had 1 or more chemotherapy trial.
- Primary objectives: to measure the PFS and OS of patients treated with conformal radiotherapy to 54 Gy.
- RT guidelines:
  - GTV: all visible tumor on MRI (T1Gad and T2/Flair)
  - CTV: 5 mm margin
  - PTV: 3-5 mm
Third Ventriculostomy

- Procedure to relieve hydrocephalus
- Creates flow from 3rd ventricle to pre-pontine space
- Other option – shunt
Protons 50.4
IMRT 50.4
What changes can you see on imaging 6-12 months later?
Tectal Glioma: Radiation treatment effect

Pre Radiation Images:

Post Radiation Images:
6 y/o boy presents with 1 week of ataxia, slurred speech, and double vision (6\textsuperscript{th} nerve palsy apparent on exam: asymptomatic prior to this)
Diffuse Infiltrating Brain Stem Glioma

- No need for biopsy
  - Regardless of path DIBSG prognosis is poor
    - Only biopsy if looks atypical or does not look like DIBSG- i.e. dorsally exophytic

- 54 Gy RT to tumor + small margin
  - Tumors promptly response in 70% + --ssx improve
    - Response is not durable and most will recur in 6-12 months
    - Median OS 1 year
    - Many protocols investigating useful chemotherapeutic agents but no clear benefit
High Grade Gliomas Treatment

- Standard of care includes maximal safe resection and RT
- Chemotherapy usually included but unclear benefit
- 3 yr. EFS for AA and GBM is 13% and 7% (Cohen, Neuro-Onc 13:317, 2011)
  - Apparently worse than CCG 945, 5 yr. EFS 33% and 5 yr. OS 36% (Finlay, 1995)
  - Thought to be due to more stringent path diagnosis, 14% in CCG 945 not truly HGG (LGG most common, ependymoma second)
XRT/TMZ followed by TMZ + CCNU

2 yr. EFS: ACNS0423 = 24%
ACNS0126 = 18%

2 yr. OS: ACNS0423 = 35%
ACNS0126 = 29%

Jakacki, COG study progress report 2010
TMZ/CCNU compared to VCR/CCNU

- TMZ + CCNU appears equivalent to VCR/CCNU/Prednisone
- TMZ not as significant a player as in the adult population
High Grade Glioma RT

- 54 to 59.4 Gy depending on location
- T2 flair with margin to 45 Gy
- T1 post contrast to total 54-59.4 Gy
Adolescent Male with HA, impaired upward gaze
Germ Cell Tumors

- 3-5% of all primary CNS childhood tumors
- 120-200 cases/year in USA
- <1% of primary adult CNS tumors
GCT symptoms

- Suprasellar
  - Diabetes Incipidus
  - GH abn
  - Other hormonal abnormality
  - Visual deficit

- Pineal
  - Hydrocephalus
  - Parinaud’s Syndrome
  - Do not react to light
    - Pseudo-Argyll Robertson pupil
Work up

- MRI of the brain and spine with attention to the suprasellar and pineal regions

- Serum and CSF HCG & AFP

- Biopsy unless markers +
  - still a bit controversial

- Procedures to relieve hydrocephalus if needed
Clinical categories of CNS germ cell tumors

- Germinoma (60 +%)
  - HCG < 50 mIU/ml in serum and CSF (this is soon to change to < 100)
  - No elevation of AFP

- Non-germinoma germ cell tumors (NGGCT) (40-%)
  - Embryonal carcinoma (βHCG + AFP)
  - Endodermal sinus tumor (yolk sac) (AFP)
  - Choriocarcinoma (βHCG)
  - Immature teratoma

- Mature teratoma (1%)
Age at diagnosis

- Peak incidence in the 2nd and 3rd decades
- Very rare in early childhood
Sex predilection by site

- Pineal: male predominance (>5/1)
- Suprasellar: equal male/female ratio
Variable incidence by region and/or ethnicity

- Western populations: 3%
  - Rickert C, Childs Nerv Sys 17:503, 2001

- Japan and Far East: 10%
  - Nomura K, J Neurooncol 54:211, 2001
Site predilection

- Midline sites (95%)
  - Pineal (45%)
  - Suprasellar (40%)
  - Multifocal – pineal and suprasellar (10%)
- Non-midline sites (5%)
Sagittal T1 post gadolinium contrast image showing 3rd ventriculostomy defect. What additional info can you gain from this procedure?
Multifocal 5-10%

- Multifocal Disease- seen on MRI
- OR one lesion symptomatic and the other site asymptomatic
- ALSO look for decrease in size of pineal or infundibulum following chemo
Treatment expectations

- Germinomas are malignant tumors that are very responsive to cytotoxic therapies.
  - Radiotherapy (RT)
  - Chemotherapy (CHT)
- Germinomas are highly curable
- NGGCT are not as responsive and have a poorer prognosis
Radiation Therapy

• Historically, radiation therapy was a diagnostic tool in the treatment of germinomas

• Pineal region mass → 20 Gy to a local field
  • →Repeat head CT: if marked response, a diagnosis of germinoma was assumed

• ***We don’t do this anymore***
For pure GCT

- What are treatment options for localized disease

- What are treatment options for disease that has spread to the spine?
RT for pure GCT

- Highly curable tumor with radiotherapy alone
- 10 year survival with RT $\geq 85-95$
  - 30-36 Gy to the CSI/WBRT/ventricles
  - 45-50 Gy to the primary tumor

- MOST STANDARD ANSWER FOR RT ALONE FOR LOCALIZED DISEASE
  - Whole vent to 24 Gy f/b boost to 45 Gy

- MOST STANDARD FOR DISSEMINATED RT ALONE
  - CSI to 24 Gy f/b boost to 45 Gy
RT + Chemo for pure GCT

- MOST STANDARD for localized
  - 2-4 cycles of carbo/etoposide or plantinum based chemo f/b 21 Gy WVRT f/b boost to 30 Gy (if CR to chemo)
  - *** do not use IFRT after chemotherapy b/c of reports of high rates of ventricular relapse

- MOST STANDARD for disseminated
  - Same chemo f/b 21 Gy CSI f/b boost to 30 Gy
Ventricular relapses after chemotherapy and IFRT

Site of relapses following combined treatment

- Ventricular system: 8/10
  - V only: 5/8
  - V + Post Fossa: 1/8
  - V + T. bed: 2/8
  - positive CSF: 1/8
- Subfrontal (optic nerve encasement): 1/10
- Spinal leptomeningeal: 1/10

Primary site
- Pineal
- Suprasellar
- Bifocal

Alapetite, C. et al. NEURO ONCOL 2010 0:noq093v1-93; doi:10.1093/neuonc/noq093
Lateral, 3rd, 4th ventricle, +/- pre-pontine cistern; go over this volume with your radiologist!! Atlas available on QARC website

Always draw your involved field volume at the same time and be sure it is included in WV volume!!
Outcome after radiotherapy alone

- 10-year overall survival in most series exceeds >85-90%.

- **Late effects** in children are the primary concern in long term survivors.
  - Neurocognitive
  - Endocrine
  - Second malignant neoplasms
NGGCT

- Always chemo + RT (RT alone OS 20-45%)
- For now, Cisplatin based chemotherapy and CSI (36 Gy f/b involved field boost to 54 Gy)
  - MOST COMMON REGIMEN
    - 6 CYCLES ALTERNATING CARB/ETOP AND IFOS/ETOP
- Last ACNS protocol indicates approx 85% OS with this regimen (failure to achieve CR poor PF)
- Next ACNS will use same chemo with similar RT doses but change in RT volume to WVRT f/b boost
Current COG Trial For Localized GCT & NGGCT

ACNS1123
Phase 2 Trial of Response-Based Radiation Therapy for Patients with Localized Central Nervous System Germ Cell Tumors
ACNS1123

- Combines NGGCT and pure GCT (2 strata)

Primary objectives:

1. To determine, as measured by 3 year PFS if volume/dose of RT can be reduced for NGGCT and if chemotherapy f/b low dose WVRT plus IF RT is effective for pure GCT.

2. To prospectively evaluate the cognitive, social, and behavioral functioning of children and young adults who are treated with reduced RT dose/volume.
Eligibility

- **Stratum 1 (NGGCT)**
  - Patients with identified levels:
    - Serum and/or CSF ß-HCG >100 mIU/mL, or,
    - Any elevation of serum and CSF AFP > 10 ng/mL, or greater than the institutional normal, irrespective of biopsy results.
  - Patients with any of the following elements on biopsy/resection, irrespective of serum and/or CSF ß-HCG and AFP levels:
    - endodermal sinus tumor (yolk sac), embryonal carcinoma, choriocarcinoma, malignant/immature teratoma, mixed GCT with malignant GCT elements.
Eligibility

• Stratum 2 (Germinoma)
  • Patients with institutional normal AFP and ß-HCG 5 - ≤ 50 mIU/mL in serum and/or CSF are eligible.
  • Patients with bifocal involvement or pineal lesion with DI and ß-HCG ≤ 100 mIU/mL and institutional normal AFP in serum/CSF are eligible.
  • Patients with histologically confirmed germinoma or germinoma mixed with mature teratoma and ß-HCG ≤ 100 mIU/mL and institutional normal AFP in serum/CSF are eligible.
ACNS1123- NGGCT

- Radiation Volume/Dose Question
- Chemotherapy identical to ACNS0122
- Can dose and volume of irradiation can be safely reduced to 30.6 Gy WVRT f/b IFRT to 54 Gy for patients achieving “complete response”?

36 Gy CSI f/b IF boost to 54 Gy
30.6 Gy WVRT f/b IF boost to 54 Gy
ACNS1123- pure GCT

- Chemotherapy
  - 4 cycles of Carboplatin/Etoposide
- Radiation
  - WVRT to 18 Gy
  - IFRT to bring primary disease to total 30 Gy
RT Guidelines

- 3D planning required
- 3D photons, IMRT, protons allowed
- 2 CTV’s
  - Whole Ventricles
  - Involved Field
- IF CTV must be contoured upfront and added to whole ventricle volume to ensure full coverage
WVRT for all patients

- While few patients were treated with WVRT on prior studies, all patients enrolled on ACN1123 will receive WVRT.
- Difficult volume to contour with variability among clinicians.
- Review of volumes from ACNS0232 demonstrated need for clear guidelines.
- ACNS1123 will allow for smaller margins and more conformal techniques.
Whole ventricle atlas

- To improve consistency
- Provide a visual guide
- Decrease protocol violations

- Available on QARC website
Describe images (arrows): What do you think this is? What sx might this child have?
Craniopharyngioma

- Common presenting ssx
  - Visual
  - DI
  - Other endocrine
  - Increased ICP

- How do you want to proceed?
Surgery

- Surgical morbidity can be high in this region and it is rare that complete resection can allow for complete avoidance of RT.

- Surgical morbidity may include:
  - DI
  - Hypothalamic obesity
  - Memory loss/personality change
  - Vision loss
  - Vasculopathy

- What do you recommend post-partial resection?
Radiation

- 54 Gy (range 50.4-54 Gy) to tumor bed + 5 mm margin

- What do you need to consider during RT?
  - Cystic component can change; may need to image during RT and adjust volumes

- What is long term disease control?
  - 90%
Craniopharyngioma

IMRT
What disease is likely?

What other ssx are likely? How do you want to proceed?
Work up includes EUA, MRI orbits and brain (r/o trilateral retinoblastoma; If extra ocular involvement or high risk features bone scan, bone marrow biopsy, and CSF
No pathology unless eye is removed
International Classification System for Retinoblastoma

**Group A:** Small tumors confined to retina not involving optic disc or fovea, < 3mm, at least 2DD from fovea and 1DD from optic nerve, no vitreous seeding or retinal detachment

**Group B:** All remaining discrete tumors confined to the retina, no sub retinal or vitreous seeding, no retinal detachment > 5 mm from tumor base, no sub retinal fluid beyond 3 mm from tumor

**Group C:** Local sub retinal seeding or fine vitreous seeding <2DD from tumor, no retinal detachment > 5 mm from tumor base
International Classification System for Retinoblastoma

**Group D:** Diffuse disease with significant vitreous or sub retinal seeding or “snowballs” or tumor masses, sub retinal fluid involving up to total retinal detachment.

**Group E:** Tumor touching lens, tumor anterior to anterior vitreous face involving ciliary body or anterior segment, diffuse infiltrating, neovascular glaucoma, opaque media from hemorrhage, tumor necrosis with aspetic orbital cellulitis, phthisis bulbi.

*For radiation we are usually treating Group C,D, E*
Staging: Reese-Ellsworth Grouping

Prognostic classification to predict vision preservation after EBRT

**Group I:** Solitary or multiple tumors, < 4 disk diameters (DD), at or behind equator

**Group II:** Solitary tumors 4-10 DD, at or behind equator; or multiple tumors behind equator

**Group III:** Any lesion anterior to equator, Solitary tumors >10 DD behind the equator

**Group IV:** Multiple tumors, some >10 DD

Any lesion extending anteriorly to the ora serrata

**Group V:** Massive tumors involving more than half of the retina, Vitreous seeding (Group Vb)
Genetics - distribution

10% family history +

10% bilateral, Heritable

90% no family history

20-30% bilateral

20-30% Bilateral, heritable

70-80% unilateral

10% unilateral, heritable

60-70% Unilateral, Non-heritable

bilateral

unilateral

heritable

Non-heritable
Genetics

- Two-hit hypothesis
  - Hereditary form: germline mutation exists in one allele
  - Single somatic mutation to second allele results in cancer
  - Random mutations to RB1 are relatively common in retinal cells
  - Sporadic form: no germline mutation
  - Requires somatic mutations to both copies of RB1 in the same retinal cell

Alfred Knudson: 1971 sentinel paper. Original question: How does one explain such a tumor that can be either heritable or non-heritable?
Patterns of spread

- Arises in the retina and proliferates rapidly
  - Endophytic or exophytic growth
  - May “seed” the vitreous and fill the globe
  - Spreads along optic nerve toward brain
  - May extend outside the globe, into the orbit
  - Extra orbital spread in the CNS or bone marrow

- Trilateral RB: involvement of the pineal gland
  - Rare (6%) hereditary form with poor prognosis
Treatment options

- Enucleation
- Exenteration
- Local therapies:
  - Cryotherapy
  - Photocoagulation
  - Laser hyperthermia
  - Radioactive plaque therapy
- External beam radiation therapy
- Chemotherapy
Enucleation

- Appropriate when little or no useful vision in the eye
- Resect long segment of optic nerve
- Avoid penetration of the globe; risk of tumor spill
- Orbit growth is impaired
- Good cosmesis with prosthesis
- Used for 90% of unilateral tumors in U.S.
Exenteration

- Removal of:
  - Globe
  - Extra ocular muscles
  - Lids
  - Nerves
  - Orbital fat

- Indications: extensive tumor breaching the globe (F/U with EBRT and chemo)
- Recurrence of tumor in the socket after enucleation
Chemotherapy

- Goal is to delay or avoid EBRT
- Focal therapies (cryotherapy, laser therapy, photocoagulation) are still required
- Vincristine, carboplatin, etoposide x 6
  - CHOP regimen
- Carboplatin alone
  - MSKCC regimen
EBRT

- EBRT indications
  - Preservation of useful vision
  - Tumor within the macula
  - Tumor too extensive for focal therapy
  - Bilateral advanced intraocular disease
  - Salvage after failure of local therapy
  - Treatment of extra ocular or metastatic disease

** MOST COMMON SCENARIOS to use EBRT?**
EBRT-Indications

1) VITREOUS SEEDING
2) LARGER TUMOR IN MACULA– CONSOLIDATION POST CHEMO
3) POST ENUCLEATION HR FEATURES (MOST COMMON POSITIVE OPTIC NERVE MARGIN)

DOSE IS ALWAYS 45 Gy; Volume is 1) Posterior globe/nearly whole globe 2) tumor with generous margin 3) orbit with optic nerve up to chiasm
Retinoblastoma

Photons, 1984

Protons
Treatment Results

- 5 year survival is >90% in U.S.
- Preservation of eye with EBRT
  - 95% Stage I
  - 50% Stage IV-V
- Visual acuity is excellent in most patients (20/40)
  - Worse if macula involved

Blach et al IJROBP 35:45 1995
Complications

- Cataract formation
- Dry eye
  - Uncommon if conjunctiva and lacrimal glands spared
- Retinopathy
  - Low risk with doses < 45 Gy
- Bone growth abnormalities
  - Occur with EBRT or nucleation
Second cancers

- Increased risk with germline RB mutation
  - Increased risk regardless of RT
  - Higher risk in RT field
  - Higher mortality for in-field sarcomas
  - Sarcomas most common (bone and soft tissue)
  - Higher mortality from 2\textsuperscript{nd} tumors than RB in U.S.
Second cancers

- NY & MA: 1604 patients from 1914-1984

- Hereditary RB:
  - RR = 30
  - Cumulative incidence 51% at 50 years
  - Radiation dose response for sarcomas (rate drops to 27% for patients not receiving radiation therapy).

- Nonhereditary RB:
  - Cumulative incidence 5% at 50 years

Wong et al JAMA 278: 1284, 1997
2 y/o with abdominal pain, fever, hematuria

What is your differential diagnosis?

Wilm’s Tumor and Neuroblastoma
Wilm’s Tumor

- Most common abdominal malignancy of childhood
- Children usually present with painless abdominal mass
- Work up includes US abdomen to start, CT abdomen, Chest CT
- Surgery upfront (US standard)
- For Rhabdoid histology add bone scan and MRI brain
- For Clear Cell, add bone scan
Wilm’s Tumor

• Staging
  • Stage I: tumor limited to capsule and completely resected
  • Stage II: Tumor beyond kidney and completely resected
    • Beyond kidney includes
      • Penetrates Renal capsule
      • Lymphatics or veins of Renal sinus
      • Tumor in Renal vein
    • Stage I and II- resection with negative margins; no LN
Wilm’s Tumor

- Staging
  - Stage III:
    - **SLURPP**
      - S: Spillage (localized and diffuse)
      - L: Lymph Nodes
      - U: Unresectable
      - R: Residual
      - P: Peritoneal implants
      - P: Prior biopsy

** changes since NWTS-5- localized spillage and biopsy now stage III (before Stage II)

***SLURPP is important to remember for indications for RT for FH Wilm’s
Wilm’s Tumor

- Staging
  - Stage IV: Hematogenous Mets or spread beyond abdomen
  - Stage V: bilateral disease
Histology

- Favorable Histology
- Focal Anaplasia
- Diffuse Anaplasia
- Clear Cell Sarcoma of the Kidney
- Rhabdoid tumor of the Kidney
Epidemiology

- Associated with clinical syndromes
  - **WAGR** (Wilms’ Tumor, aniridia, genitourinary malformations, mental retardation) WT1 – 11p13
  - **Denys-Drash syndrome** (pseudohermaphroditism, mesangial sclerosis, renal failure, Wilms’ Tumor)– also WT1
  - **Beckwith-Wiedmann syndrome** (gigantism, omphalocele, macroglossia, genitourinary abnormalities, ear creases, hypoglycemia, hemihypertrophy, Wilms’ Tumor) “WT2” – 11p15

WT1 - tumor suppressor
RT

- No RT for FH Stage I or II
- RT for ALL focal and diffuse anaplasia, CCSK, Rhabdoid
- Flank to 10.8 Stage III FH, Stage I-III focal anaplasia, Stage I-II diffuse anaplasia, Stage I-III CCSK; Flank to 19.8 Gy for Stage III DA
  - 10.8 boost to any residual
- WART to 10.5 Gy for +cytology, tumor spill, peritoneal seeding, prior biopsy (indications that put whole abdomen at risk*)
RT

- WLI 10.5 Gy (< 12 mo.) and 12 Gy > 12 mo.
- Whole brain 21.6 Gy
- Liver focal- 19.8 Gy
- Bone mets 25.2 Gy < 16 years; 30.6 Gy > 16 years
- LN RT resected 10.8 Gy; not resected 19.8 Gy
Chemo for Wilm’s

- VAA- Vincristine, Actinomycin D, Adriamycin (occasionally only VA for FH early stage)

- CAVE for Clear Cell – Cytoxan, Adriamycin, Vincristine, Etoposide

- CEC for Rhabdoid – Carboplatin, Etoposide, Cytoxan
Neuroblastoma

- Variable prognosis
- 4th most common malignancy
- Most common malignancy in children < 18 months
- Tumor of neural crest tissue/sympathetic nervous system chain
Clinical Presentation

- Abdominal mass with organ compression (children less well than Wilm’s typically)
- Metastases common and systemic symptoms common (pain, fever, refusal to walk)
- Neck mass (Horner’s Syndrome)
- Spinal cord compression
- Respiratory compromise : Pepper Syndrome (caused by liver mets)
- Rare
  - Intractable diarrhea (VIP)
  - Opsoclonus-myoclonus-truncal ataxia (paraneoplastic)
  - Blueberry muffin sign
  - Skull mets (orbital ecchymosis)
Work up?
- CT and/or MRI of primary site
- Bone marrow biopsy
- MIBG scan
- Chest/Abdomen/Pelvis CT for metastatic disease
- Urine catecholamine's (VMA and HVA)
Staging INSS

- 1- localized and completely resected N0
- 2A- localized and incompletely resected N0
- 2B-localized (complete or incomplete resection) + ipsi LN
- 3- unresectable unilateral and crossing midline +/- LN; unilateral tumor with contra + LN
Staging INSS

- 4- distant mets
- 4S- localized primary tumor (1, 2, 2A) in patient < 1 year old with skin, liver, bone marrow involvement
Prognostic Factors

- Age (>1, >18 months)
- MYCN amplification
- LOH 1p or 11q
- Shimada histology (UF)
- Hyperdiploid better than diploid
ANBL0532

- High Risk Neuroblastoma
  - Phase III examining role of intensified consolidation chemotherapy, use of new drugs during induction, and local RT
  - Randomizes to 1 or 2 transplants
High Risk

- Patients with newly diagnosed neuroblastoma with INSS Stage 4 are eligible with the following:
  - a. MYCN amplification, regardless of age or additional biologic features.
  - > 18 months (>547 days) regardless of biologic features.
  - Age 12 – 18 months (365-547 days) with any of the following three unfavorable biologic features (MYCN amplification, unfavorable pathology and/or DNA index = 1) or any biologic feature that is indeterminate/unsatisfactory/unknown.
Patients with newly diagnosed neuroblastoma with INSS Stage 3 are eligible with the following:
- **MYCN**, regardless of age or additional biologic features
- Age > 18 months (> 547 days) with unfavorable pathology, regardless of **MYCN** status
Patients with newly diagnosed **INSS Stage 2a/2b**
- with **MYCN** amplification, regardless of age or additional biologic features
- **4S with N-Myc amplification**
RT-Neuroblastoma

- Primary site post induction chemo volume (PRIOR to surgery)
  - 21.6 Gy

- Residual Disease
  - Additional 14.4 Gy (to total 36 Gy) (after surgery and induction chemo)

- Metastatic Disease (if persistent after cycle 6 of induction)
  - 21.6 Gy

@ 1.8 Gy per fraction
Neuroblastoma

- Organs at Risk
  - Liver
    - No > 50% of liver > 900 cGy
    - No > 25% of liver > 1800 cGy
Neuroblastoma

- Organs at Risk
  - Kidney
    - If well lateralized, ipsilateral kidney may receive 1440 cGy; 50% may receive 1980 cGy; for contralateral 50% may receive 800 cGy; no more than 20% should receive 1200 cGy
    - If not well lateralized, both kidneys may receive a mean dose of 1440 cGy and no > 50% receive 1980 cGy
What is tx of 4S with respiratory compromise?

- Can try chemo first
- For RT, 1.5 Gy x 3 to liver
Rhabdomyosarcoma
RMS: Work up

- Hx and PE
- CT and MRI of primary site
- Biopsy
- Chest/Abdomen CT
RMS: Work up

- BMBx
- Bone scan
- (PET is very helpful! Need to get prior to CT to be helpful though)
- If parameningeal, then CSF cytology and brain MRI
RMS Primary site is prognostic

- **Favorable sites:**
  - Head/neck (non parameningeal)
  - Orbit
  - GU (non bladder/prostate)
  - Biliary tract

- **Unfavorable sites:**
  - Parameningeal
  - Bladder/prostate
  - Extremities
  - Other: Trunk/retroperitoneum
## RMS: Clinical Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Extent of disease/surgical result</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td><strong>A</strong> Localized tumor, confined to site of origin, completely resected</td>
</tr>
<tr>
<td></td>
<td><strong>B</strong> Localized tumor, infiltrating beyond site of origin, completely resected</td>
</tr>
<tr>
<td>II Micro</td>
<td><strong>A</strong> Localized tumor, gross total resection, but with microscopic residual disease</td>
</tr>
<tr>
<td>Micro +</td>
<td><strong>B</strong> Locally extensive tumor (spread to regional lymph nodes), completely resected</td>
</tr>
<tr>
<td></td>
<td><strong>C</strong> Locally extensive tumor (spread to regional lymph nodes), gross total resection, but microscopic residual disease</td>
</tr>
<tr>
<td>III Gross</td>
<td><strong>A</strong> Localized or locally extensive tumor, gross residual disease after biopsy only</td>
</tr>
<tr>
<td>Gross dz</td>
<td><strong>B</strong> Localized or locally extensive tumor, gross residual disease after major resection (50% debulking)</td>
</tr>
<tr>
<td>IV mets</td>
<td>Any size primary tumor, with or without regional lymph node involvement, with distant metastases, irrespective of surgical approach to primary tumor</td>
</tr>
</tbody>
</table>
## Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sites</th>
<th>Invasiveness</th>
<th>Size</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Fav site</td>
<td>Orbit, Head and neck*, GU (non-bladder/prostate), Biliary tract</td>
<td>T1 or T2</td>
<td>a or b</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>2 Unfav site, N0, small</td>
<td>Bladder/prostate, Extremity, Cranial parameningeal, Other</td>
<td>T1 or T2</td>
<td>a</td>
<td>N0 or Nx</td>
<td>M0</td>
</tr>
<tr>
<td>3 Unfav site, Big or node +</td>
<td>Bladder/prostate, Extremity, Cranial parameningeal, Other</td>
<td>T1 or T2</td>
<td>a</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td>4 mets</td>
<td>All</td>
<td>T1 or T2</td>
<td>a or b</td>
<td>N0 or N1</td>
<td>M1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T Stage</th>
<th>N Stage</th>
<th>M stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1: Confined to anatomic site of origin</td>
<td>N₀: Not clinically involved</td>
<td>M₀: No distant metastases</td>
</tr>
<tr>
<td>T2: Extension</td>
<td>N₁: Clinically involved</td>
<td>M₁: Distant metastases present</td>
</tr>
<tr>
<td>a: 5 cm in diameter</td>
<td>Nₓ: Clinical status unknown</td>
<td></td>
</tr>
<tr>
<td>b: &gt;5 cm in diameter</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Risk Stratification

- **Low risk**: localized, embryonal, any resected site (group I/II) AND favorable sites group III

- **Intermediate risk**: any localized alveolar (group I-III) or embryonal unfavorable site (group III)

- **High risk**: metastasis

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Histology</th>
<th>Stage</th>
<th>Clinical Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Embryonal (with variants)</td>
<td>1</td>
<td>I, II, III</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Embryonal (with variants)</td>
<td>2, 3</td>
<td>I, II</td>
</tr>
<tr>
<td></td>
<td>Embryonal (with variants)</td>
<td>2, 3</td>
<td>III</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Alveolar</td>
<td>1, 2, 3</td>
<td>I, II, III</td>
</tr>
<tr>
<td>High</td>
<td>Embryonal or Alveolar</td>
<td>4</td>
<td>IV</td>
</tr>
</tbody>
</table>
RMS: RT Timing per open COG protocols

- Low risk: week 13
- Intermediate risk: week 4
- High risk: week 20 (primary and some mets) unless emergent or ICE with PM RMS, which is week 1) more mets can be treated at week 47)

*Timing may change on the next COG RMS Protocols*
RMS: RT Dose Guidelines

- 0 Gy: Group I embryonal
- 36 Gy: Resected node negative disease (alveolar) and after delayed primary resection of embryonal, or for group Ila (pos margins); except low risk pts. (see below)
- 41.4 Gy: Resected node positive disease, (also Low risk pts. with micro margins +; yes, counter-intuitive)
- 45 Gy: dose for gross disease in orbit (may change for next COG trial to 50.4 Gy)
- 50.4 Gy: dose for gross disease (non orbit)
Sarcomas of Bone

Codman’s Triangle, Onion skin

What are the 2 most common types of Bone tumors in children? What are classic Radiographic appearances?
Sarcomas

- **Osteosarcoma**
  - Most common – 600 cases in US per year/3% malignancies
  - Metaphyseal
  - Lytic destruction and new bone formation ("sunburst"); Codman’s triangle may be seen

- **Ewing’s**
  - 2nd most common- 250 cases per year in US
  - Diaphyseal
  - Onion skin and Codman’s triangle
Osteosarcoma Staging

Technetium bone scan

Chest CT
Osteosarcoma

- Epidemiology
  - Peak incidence in 2\textsuperscript{nd} decade
  - 20% have mets at dx
    - 80% of mets are lung
    - 20% involve bone
Osteosarc: sites of disease

- Most common sites:
  - Distal femur (48%)
  - Proximal tibia
  - Proximal humerus
  - Pelvis

Bielack, JCO 2002
Prognostic Factors

- Stage (localized vs. metastatic)
  - Localized extremity lesions:
    5 yr. EFS = 65 - 70%
  - Metastatic disease: 5 yr. EFS = 15 – 40%
    - Bone mets, bilat lung mets, ≥4 lung nodules:
      5 yr. EFS = 15-20%
Treatment

• Surgery alone (amputation) until mid-70’s
  • Only 15-20% survival
  • > 80% of pts. died of recurrent, metastatic disease

• Addition of chemotherapy in 1970’s – 1980’s
  • Active agents
    • Methotrexate
    • Doxorubicin
    • Cisplatinum
    • Ifosfamide

• Must attempt to resect all identifiable sites
Role for XRT?

- RT reserved for close/positive margins or inoperable sites
  - Skull base
  - Spine (?)
  - Pelvis (investigational)
- Very limited published data re: local control with RT only
- Dose > 60 Gy if feasible
Ewing’s
Ewing’s

- Male predominance
- May arise from soft tissue
Work-up

- CT/MRI of primary
- CXR, CT of chest
- Bone Scan
- Bone Marrow Biopsy
- Labs (ESR/LDH)
- Biopsy
- PET at many institutions
Prognostic Factors

- Metastasis
- Location, distal better than proximal, failures 5% for distal, 25% for proximal, 35% for central
- Size, < or equal to 8 cm better than > 8 cm (failure rate of 10% v. 30%)
- Elevated LDH
- Age > 17 years (or <10, 10-17, >18)
Response to chemo-St Jude’s Study

- Correlation of imaging response - reduction of soft tissue mass with chemo - with outcome

- Response to chemo:
  - 5-y EFS 64% for CR
  - 5-y EFS 13% for PR/NR

- Tumor size:
  - < 8 cm, 90% LC
  - > 8 cm, 44% LC
Standard Chemo: VDC + IE

Grier et al, NEJM 2003

Old Std chemo: VCR/Doxo/CTX/Actino
Exper chemo: above alt with Ifos/Etop
Intensity of Chemo (q 2 wks vs. q 3 wks)

Intensive Regimen: VCR/Doxo/CTX alt with Ifos/Etop Courses q 2 wks (previously q21 days)

COG study AEWS0031
R Womer, PI:
Intensive EFS = 75%
Standard EFS = 65%
POG 8346

- XRT alone: 65% LC
- No difference between whole bone and tailored field
- Local control correlated with quality of XRT port:
  - 80% for appropriate port
  - 48% for minor deviation
  - 16% for major deviation
Ewing’s

- **Primary tumor**
  - 45 Gy to pre-chemo tumor + 2 cm margin f/b CD to post-chemo soft tissue but whole bone extent of involvement+2 cm margin to 55.8 Gy; try to spare strip of skin and joints if possible

- **Bone mets 45 Gy**

- **Lung mets 15 Gy**
What is your differential dx?
Langerhans's

- LCH is accumulation or proliferation of clonal population of cells with phenotype of LCH cells
- May affect skin, bone, lymph nodes, lungs, GI tract, CNS by causing DI
Syndromes

- **Letter-Siwe Disease**
  - < 2 years
  - Splenomegaly, hepatomegaly, LAD, anemia, hemorrhagic diathesis
  - Poor prognosis

- **Hand-Schuler-Christian**
  - > 2 years
  - Exophthalmos, lesions of skull/bone
  - DI
  - Good prognosis
Treatment

- If asymptomatic, may be observed
- Surgery (spontaneous regression following biopsy may be seen)
- Steroids
- Chemotherapy (controversial, topical for skin)
- Radiation – usually for symptomatic vertebral body lesions, skull lesions, rare use for DI.
- Dose 5-10 Gy in 3-5 fractions
Pediatric Hodgkin’s

- Patients usually present with fever, night sweats, shortness of breath
- Excisional lymph node biopsy for diagnosis
- Avoid steroid administration prior to biopsy
- Work up CT, PET/CT, labs including LDH, ESR, LFTs
- B ssx or advanced disease- consider bone marrow biopsy
Staging

- Stage I: Involvement of single lymph node region (I) or localized involvement of a single extra lymphatic organ or site (IE).

- Stage II: Involvement of 2 or more lymph node regions on the same side of the diaphragm (II) or localized contiguous involvement of a single extra lymphatic organ or site and its regional lymph node(s) with involvement of 1 or more lymph node regions on the same side of the diaphragm (IIE).

- Stage III: Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by localized contiguous involvement of an extra lymphatic organ or site (IIIE), by involvement of the spleen (IIIS), or both (IIIE+S).

- Stage IV: Disseminated (multifocal) involvement of 1 or more extra lymphatic organs or tissues, with or without associated lymph node involvement, or isolated extra lymphatic organ involvement with distant (non-regional) nodal involvement.
Treatment

- Multi-agent chemotherapy followed by involved field or involved nodal radiation
- ABVD f/b 21 Gy IFRT most standard
- Treatment evolving to be response based and trials exploring omission of radiation
Leukemia

- Cranial RT to 12-18 Gy (most give 12 Gy) at 1.8 Gy per fraction or 1.5 Gy per fraction
  - T cell disease and high WBC (>50K)
  - CNS 3 (>5 WBC/ul in CSF and blasts) – usually 18 Gy
  - Age > 10

- RT is considered as part of treatment for CNS recurrence (CSI 18 Gy; CrI 18-24 Gy) and testicular relapse/persistent testicular disease (20 Gy)
Almost finished!

TAKE SURVEY NOW!
What is your recommendation for a 2 y/o M with anaplastic ependymoma of the 4th ventricle s/p GTR, negative CSF and spine MRI

- A) CSI to 36 Gy f/b IF boost to 54 Gy
- B) IFRT to 54 Gy
- C) chemotherapy for 6 months to delay radiation until the child reaches the age of 3 years
- D) Chemotherapy alone and RT only for tumor recurrence
- E) Observation
B) IFRT to 54 Gy
Which of the below characteristics is NOT included in the traditional stratification for medulloblastoma into standard or high-risk disease, but has been found to confer a less favorable prognosis?

- A) age less than 3
- B) + CSF
- C) anaplastic histology
- D) Desmoplastic histology
- E) > 1.5 cm²
C) Anaplastic histology
Which of the following regimens would NOT be acceptable for management of a localized pure germinoma of the pineal gland for a 17 y/o Male?

- A) 24 Gy to the whole ventricles f/b a boost to the pineal gland to total 45 Gy
- B) Carboplatinum/Etoposide for 2-4 cycles f/b 21 Gy to the whole ventricles f/b IFRT to the pineal gland
- C) Carboplatinum/Etoposide for 2-4 cycles f/b IFRT to 30 Gy
- D) Carboplatinum/Etoposide for 4 cycles f/b 18 Gy to the whole ventricles f/b boost to 30 Gy on COG study
• C) Carboplatinum/Etoposide for 2-4 cycles f/b IFRT to 30 Gy
Thank you!