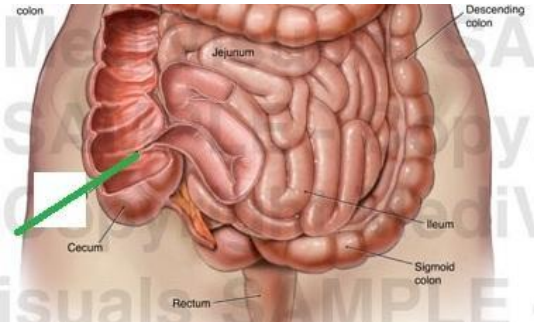
Assessment and Diagnosis of Abdominal Masses (& Pain) in Childhood

Miklós Garami

Case Presentation #1

* A child complaining of severe **abdominal pain** associated with **vomiting** is brought to the operating room (OR) for an appendectomy.
* Instead of an inflamed appendix, however, the surgeons find a **mass**. Biopsy reveals that this mass originated from cells within **Peyer patches**, close to the iliocecal junction.
* **What is the associated genetic mutations?**



Case Presentation #2

* A 2-years-old child is brought to the pediatrician with the complaint of constipation. Further questioning reveals a 3-month history of fatigue and loss of appetite. Physical examination is significant for an abdominal mass, and eventual biopsy shows small, round, blue cells.
* **What tumor markers would be elevated in the urine?**

General Practitioner (GP)

2-year-old boy complains of **abdominal pain** and **loss of appetite.**

Physical exam is significant for a **large palpable abdominal mass.**

Table of Contents

Abdominal Masses

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
- Summary: Exam content outline …

Trends

- **Abdominal masses are most common in children under the age of 5 years**
- Most abdominal masses in neonates are retroperitoneal, of kidney origin and are not malignant
- The older the child the more likely the mass represents a malignant process

Differential Diagnoses

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
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Possible Diagnoses of Abdominal Masses in Infancy and Childhood

Region	Organ	Diagnosis
Epigastrium	Stomach	Distended stomach from pyloric stenosis, duplication
	Pancreas	Pseudocyst
Flank	Kidney	Hydronephrosis, Wilms tumor, dysplastic kidney, ureteral duplication
	Adrenal	Neuroblastoma, ganglioneuroblastoma, ganglioneuroma
	Retroperitoneal	Neuroblastoma, ganglioneuroblastoma, ganglioneuroma, teratoma
Lower abdomen	Ovary	Dermoid, teratoma, ovarian tumors, torsion of ovary
	Kidney	Pelvic kidney
	Urachus	Urachal cyst
	Omentum, mesentery	Omental, mesenteric, peritoneal cysts
Pelvic	Bladder, prostate	Obstructed bladder, rhabdomyoscarcoma
	Uterus, vagina	Hydrometrocolpos, hydrocolpos, rhabdomyosarcoma
Right upper quadrant	Biliary tract	Cholecystitis, choledochal cyst
	Liver	Hematomegaly resulting from congestion, hepatitis, or tumor; mesenchymal hamartoma; hemangioendothelioma; hepatoblastoma; hepatocellular carcinoma; hepatic abscess; hydatid cyst
	Intestine	Intussusception, duplication
Left upper quadrant	Spleen	Splenomegaly resulting from congestion, infectious mononucleosis, leukemic infiltration or lymphoma; splenic abscess; cyst
Right lower quadrant	Appendix	Appendiceal abscess
	Ileum	Meconium ileus, inflammatory mass (complicated Crohn disease), intestinal duplication
	Lymphatic	Lymphoma, lymphangioma
Left lower quadrant	Colon	Fecal impaction
	Lymphatic	Lymphoma, lymphangioma

Atlas of Pediatric Physical Diagnosis, Fourth Edition

Neonatal Abdominal Masses

Renal 55%
- Hydronephrosis 35%
- Cystic disease 10%
  - Multicystic dysplastic
  - Polycystic dysplastic
- Solid Tumors 10%
  - Mesonephric nephroma
  - nephroblastomatosis

Pelvic / Genital 15%
- Teratoma
- Ovarian Cysts
- Hydrometrocolpos
- Obstructed bladder

non-Renal Retroperitoneal 10%
- Adrenal
  - Hemorrhage
  - Neuroblastoma

Gastrointestinal 15%
- Duplication
- Mesenteric omental cyst
- Pseudocyst from complicated obstr.
- Meconium ileus

Hepatobiliary 5%
- Hepatic tumors
  - Hemangioendothelioma
  - Cystic mesenchymal hamartoma
  - Hepatoblastoma
  - Neuroblastoma
- Choledochal cyst

Kirk et al., 1981 Radiol. Clin. North Am., 19:527-545

Abdominal Masses in Older Children

Renal 55%
- Wilms (& other) 25%
- Hydronephrosis 20%
- Cystic disease 5%

Non Renal

Retroperitoneal 23%
- Neuroblastoma 21%
- Teratoma 1%
- Other 1%

Gastrointestinal 12%
- Appendiceal Abscess
- Lymphoma

Hepatobiliary 6%
- Tumors
  - Hepatoblastoma
  - HCC

Genital 4%
- Ovarian Cysts and Teratoma

Kirk et al., 1981 Radiol. Clin. North Am., 19:527-545

Examination of the Pediatric Abdomen

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
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Examination of the Pediatric Abdomen

- **History**

  time the **abd. mass** has been present,

  rapidity of growth, sy.

- **Undress patient**: evaluate for genetic

  or inherited predisposition as well as the belly

- **Palpate from the pelvis toward the thorax**

  Describe location Size

  Consistency Ascites

  Venous congestion of surface

Golden and Feusner, 2002, Pediatr Clin N Am, 49:1369-1392

Abdominal Pain

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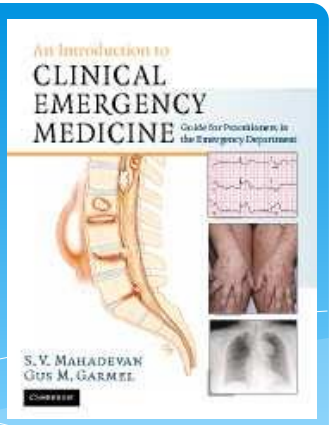
Abdominal Pain

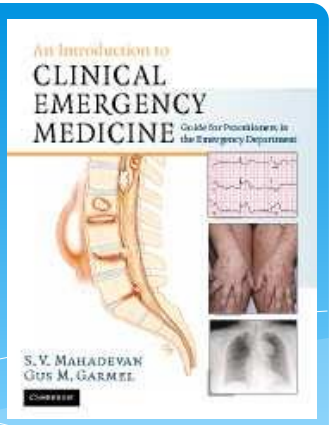


Scope of the problem

Anatomic Essentials

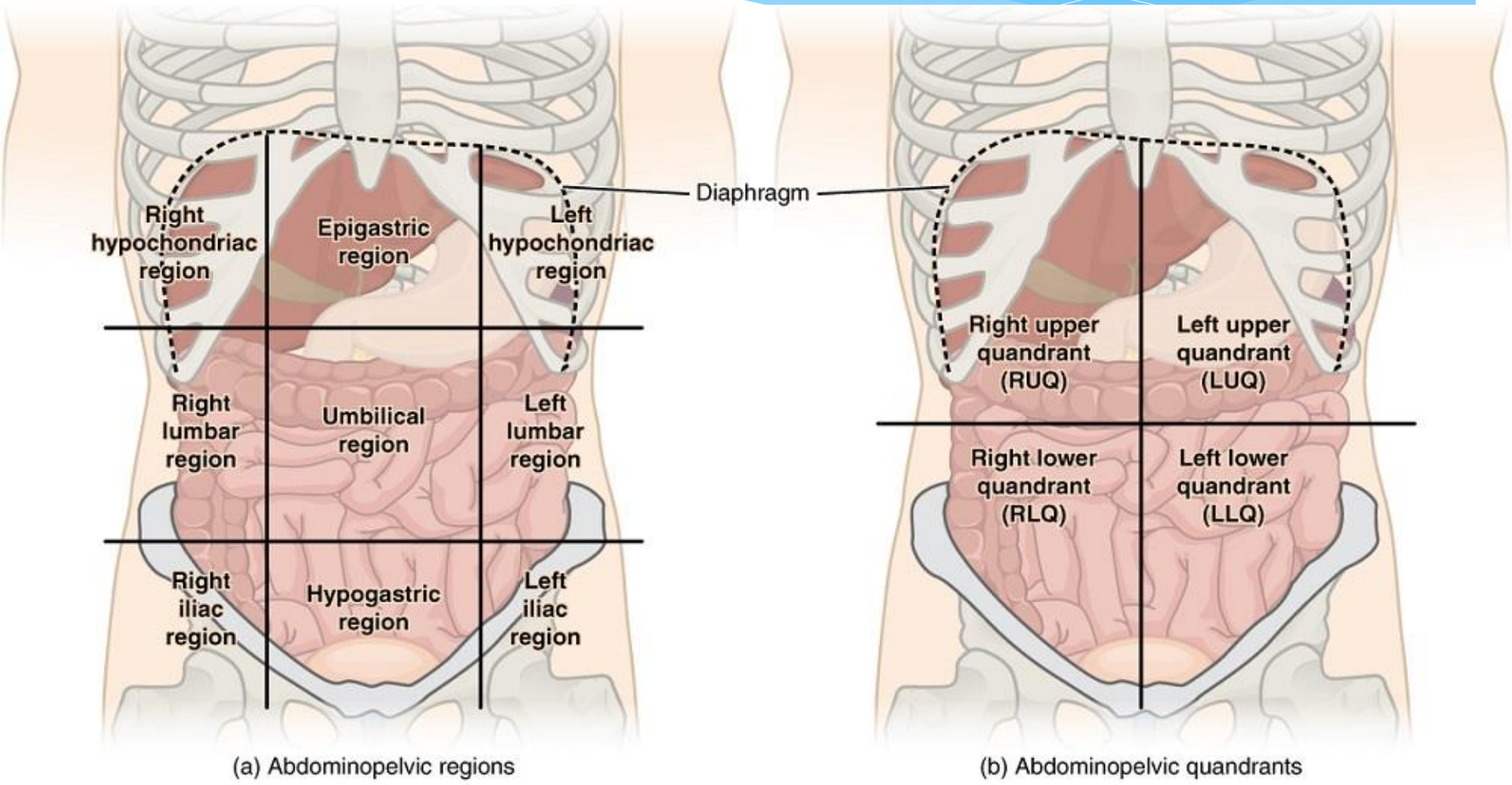
- Visceral Pain
- Parietal Pain
- Referred Pain

History

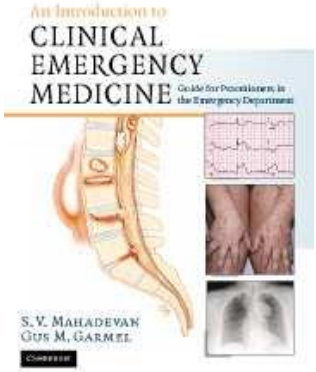


- ***Where is your pain?*** *Has it always been there?*
- *Does the pain radiate anywhere?*
- *How did the pain begin (sudden vs. gradual onset)?* ***How long have you had the pain?***
- *What were you doing when the pain began?*
- *What does the pain feel like?*
- *On a scale of 0–10, how severe is the pain?*
- *Does anything make the pain better or worse?*
- *Have you had the pain before?*

Abdominal Quadrant Regions

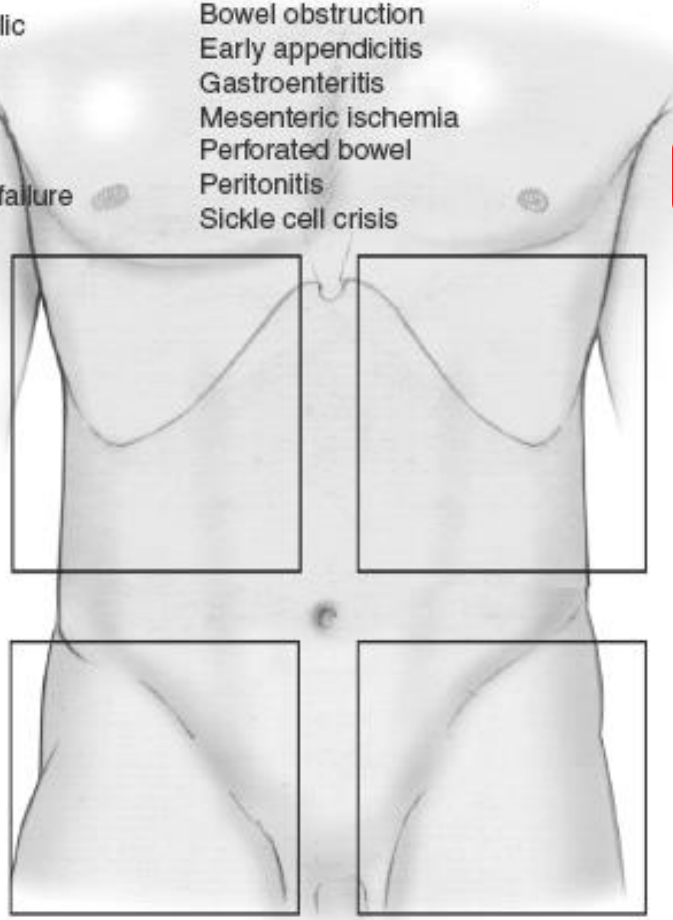


Diffuse pain
Acute pancreatitis
Aortic dissection or ruptured abdominal aortic aneurysm
Bowel obstruction
Early appendicitis
Gastroenteritis
Mesenteric ischemia
Perforated bowel
Peritonitis
Sickle cell crisis



Right upper quadrant
Acute cholecystitis and biliary colic
Acute hepatitis
Acute pancreatitis
Appendicitis
Hepatic abscess
Hepatomegaly/congestive heart failure
Herpes zoster
Myocardial ischemia
Perforated duodenal ulcer
Right lower lobe pneumonia

Left upper quadrant
Acute pancreatitis
Gastric ulcer
Gastritis
Left lower lobe pneumonia
Myocardial ischemia
Splenic enlargement, rupture, infarction or aneurysm

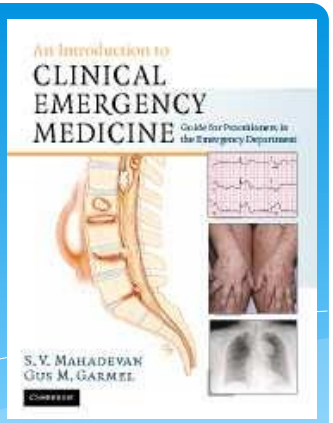


Right lower quadrant
Abdominal wall hematoma
Appendicitis
Cecal diverticulitis
Endometriosis
Incarcerated or strangulated inguinal hernia
Meckel's diverticulitis
Mesenteric adenitis
Mittelschmerz
Pelvic inflammatory disease
Psoas abscess
Regional enteritis
Ruptured abdominal aortic aneurysm
Ruptured ectopic pregnancy
Seminal vesiculitis
Terminal ileitis (Crohn's disease)
Torsed ovarian cyst
Ureteral calculi

Left lower quadrant
Endometriosis
Incarcerated or strangulated inguinal hernia
Mittelschmerz
Pelvic inflammatory disease
Psoas abscess
Regional enteritis
Ruptured abdominal aortic aneurysm
Ruptured ectopic pregnancy
Seminal vesiculitis
Sigmoid diverticulitis
Torsed ovarian cyst
Ureteral calculi

Figure 9.1
Differential diagnosis of acute abdominal pain by location. Adapted from Wagner DK. *Curr Topic* 1978;1(3).

History (continued)



Associated symptoms

- Gastrointestinal
- Genitourinary
- Gynecologic
- Cardiopulmonary

Past medical

Table 9.1 Important extra-abdominal causes of abdominal pain

Systemic causes	Pneumonia
Diabetic ketoacidosis	Pulmonary embolism
Alcoholic ketoacidosis	Herniated thoracic disk
Uremia	
Sickle cell disease	**Genitourinary**
Porphyria	Testicular torsion
Systemic lupus erythematosus	Renal colic
Vasculitis	**Infectious**
Glaucoma	Strep pharyngitis (more often in children)
Hyperthyroidism	Rocky Mountain spotted fever
Toxic	Mononucleosis
Methanol poisoning	
Heavy metal toxicity	**Abdominal wall**
Scorpion bite	Muscle spasm
Black widow spider bite	Muscle hematoma
	Herpes zoster
Thoracic	
Myocardial infarction	
Unstable angina	

Adapted from Purcell TB. Nonsurgical and extraperitoneal causes of abdominal pain. *Emerg Med Clin North Am* 1989;7:721–740.

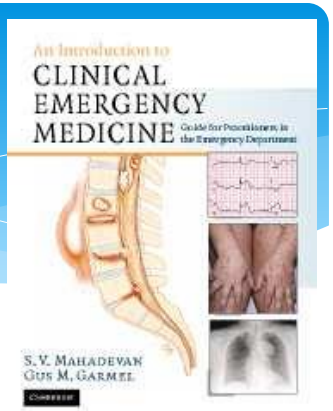
Physical Examination - Directed

General appearance

Vital Signs

Abdomen

- Inspection
- Auscultation
- Percussion
- Palpation



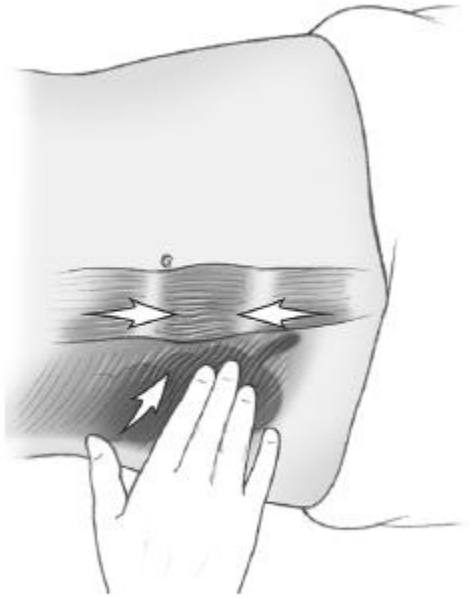
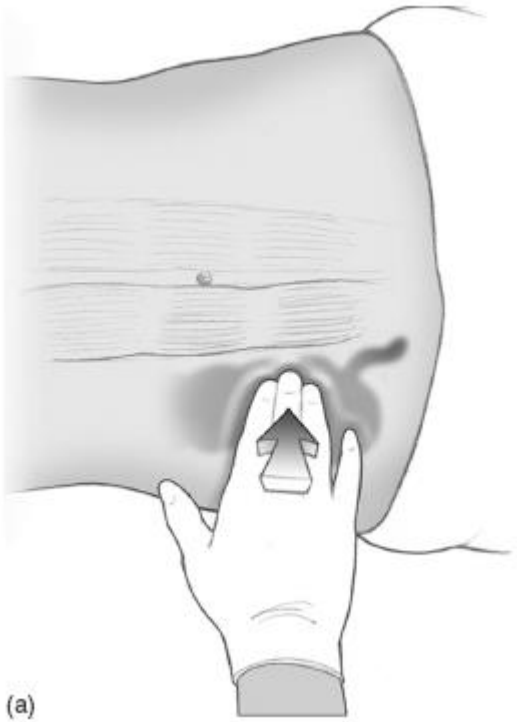
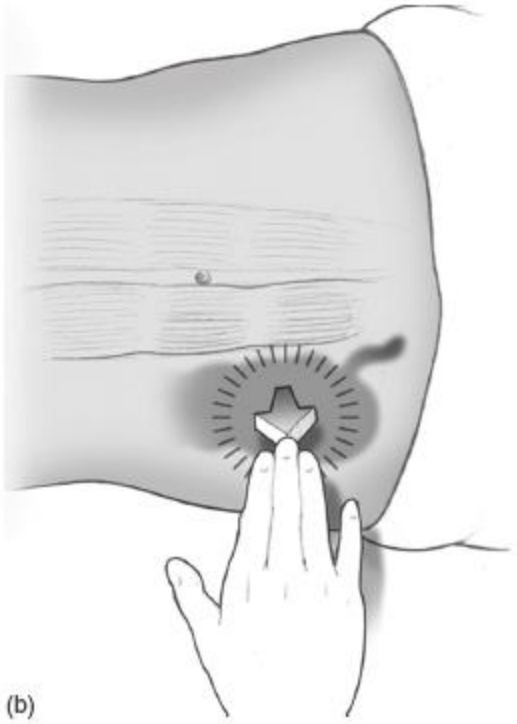


Figure 9.2
Guarding.

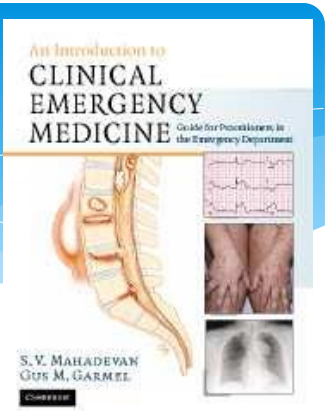


(a)



(b)

Figure 9.3
Rebound (a) hand down (b) hand up.



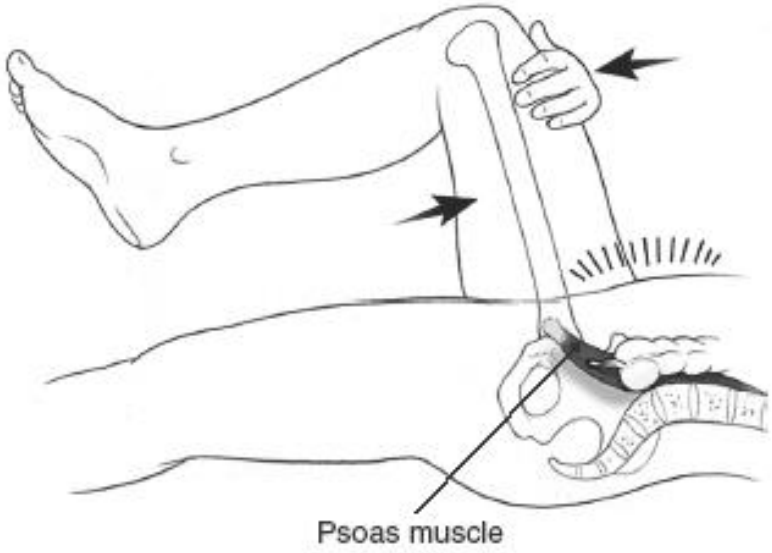


Figure 9.4
Psoas sign.

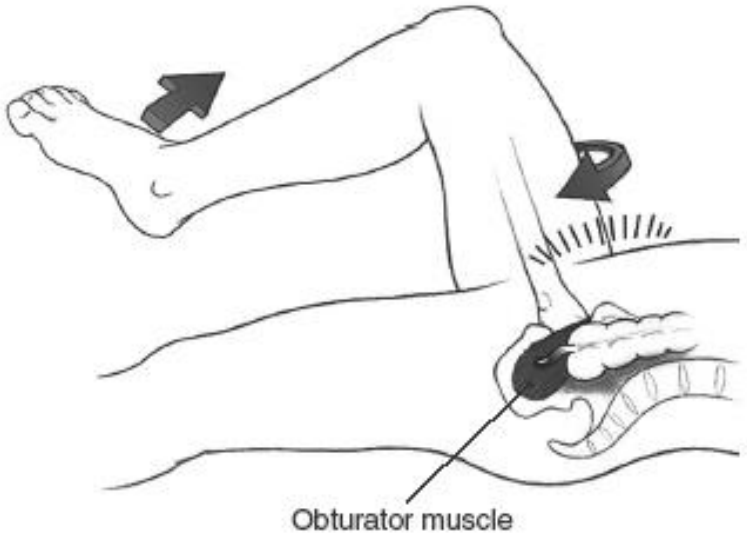
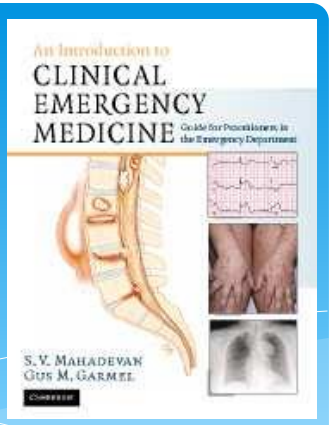


Figure 9.5
Obturator sign.

Physical Examination - Directed

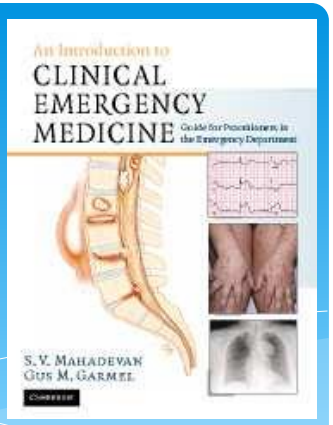
- Pelvic
- Genital
- Back
- Rectal
- Head-to-toe

Differential Diagnosis



- **Appendicitis**
- Biliary colic, cholecystitis, cholangitis
- Bowel obstruction
- Diverticulitis
- Ectopic pregnancy
- Gastroenteritis
- Intussuception
- Mesenteric Ischemia
- Ovarian torsion
- Pancreatitis
- Pelvic Inflammatory Disease (PID)
- Perforated peptic ulcer
- Ruptured or leaking abdominal aortic aneurysm (AAA)
- Testicular torsion
- Ureteral colic
- Volvulus

Diagnostic Testing



Laboratory Studies

- CBC
- Urinalysis
- Pregnancy
- Amylase/Lipase
- Other

Electrocardiogram

Diagnostic Testing - continued

Radiologic Studies

- Plain Films
- Ultrasound
- MRI / CT

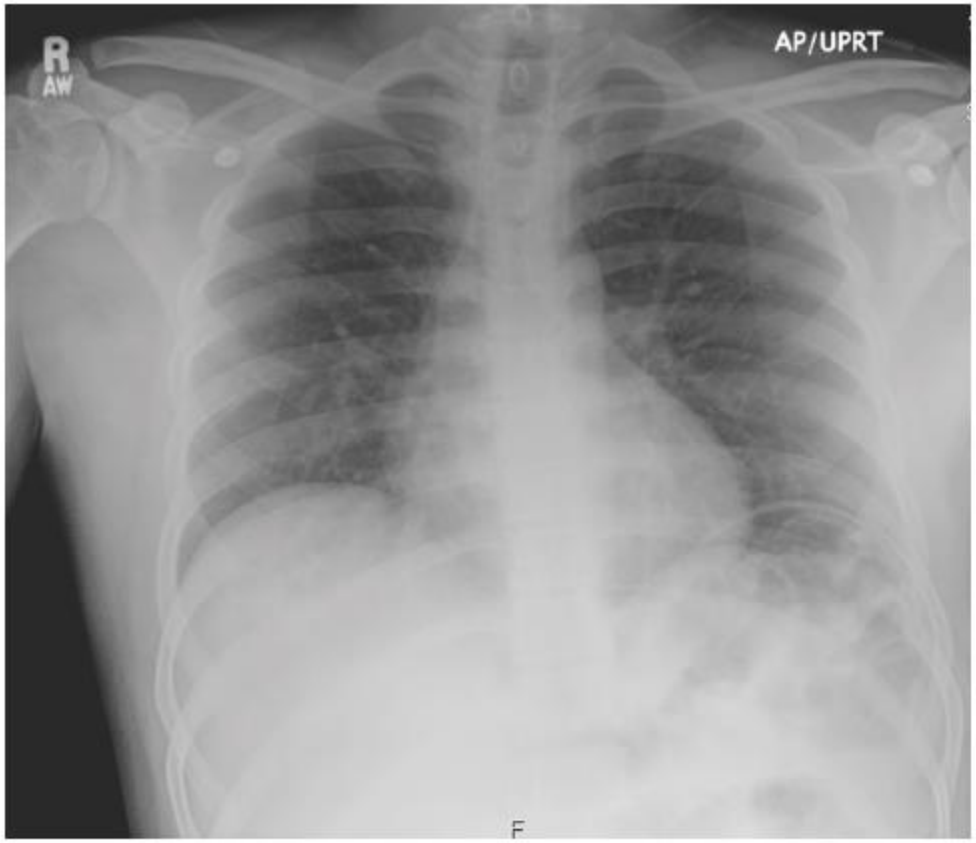


Figure 9.6
Pneumoperitoneum. AP erect chest X-ray reveals free air beneath the left hemidiaphragm consistent with pneumoperitoneum.

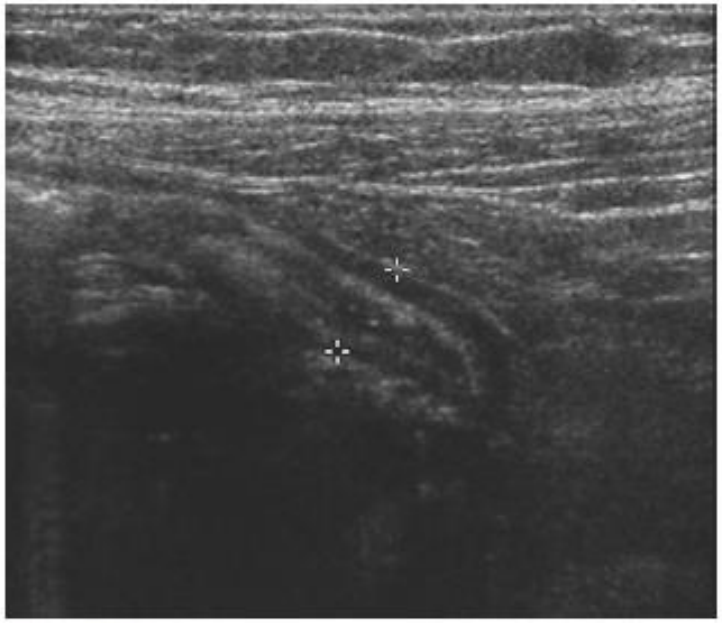


Figure 9.7
Appendicitis on ultrasound. Gray scale longitudinal ultrasound demonstrates enlarged non-compressible appendix (cursors) >7 mm, consistent with acute appendicitis. *Courtesy*: GM Garmel, MD.

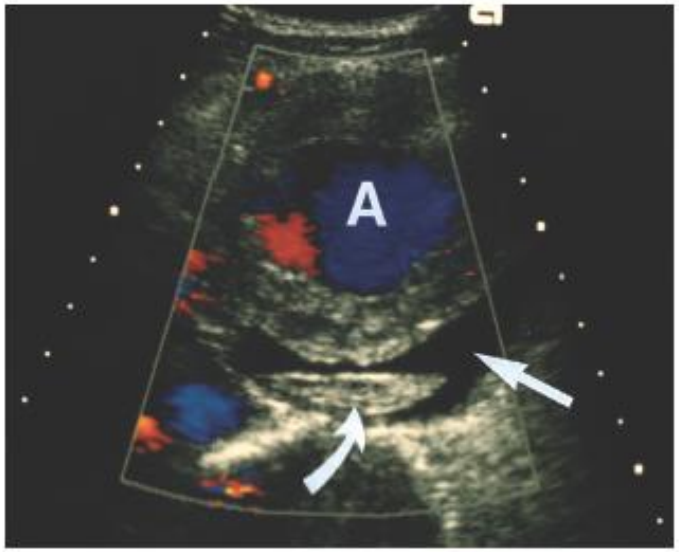


Figure 9.8
Ruptured abdominal aortic aneurysm (AAA) on transverse color Doppler sonogram. Note color flow within aneurysm (A) and retroperitoneal clot and hemorrhage posterior to AAA (arrows). *Courtesy*: R. Brooke Jeffrey, MD.

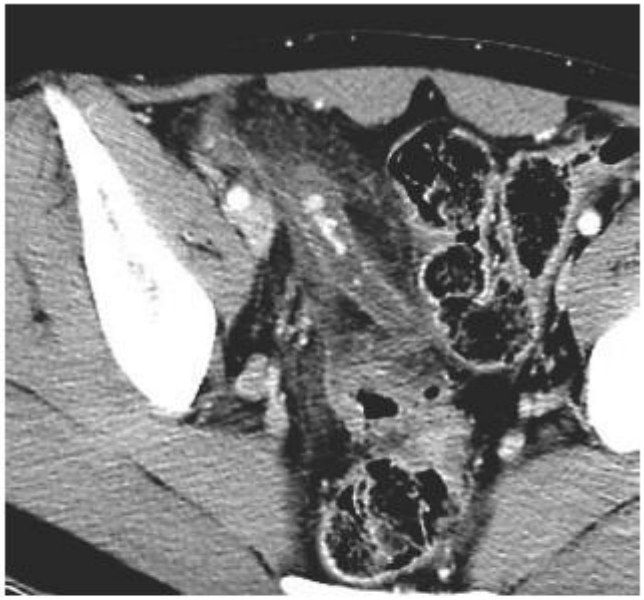


Figure 9.9
Acute appendicitis on contrast enhanced CT. Note enlarged appendix with multiple appendicoliths. Periappendiceal fat stranding is apparent. *Courtesy*: R. Brooke Jeffrey, MD.

Causes of Abdominal Pain by Age of Onset

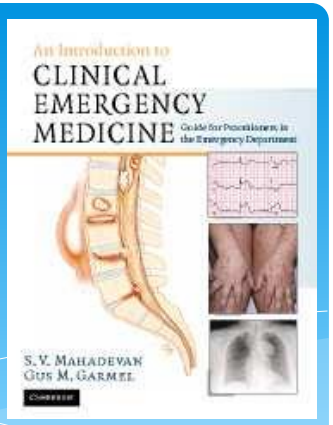


Table 9.3 Causes of abdominal pain by age of onset

Birth to 1 year	2–5 years	6–11 years	12–18 years
Constipation	Appendicitis	Appendicitis	Appendicitis
Gastroenteritis	Constipation	Constipation	Constipation
Hirschsprung's disease	Gastroenteritis	Functional pain	Dysmenorrhea
Incarcerated hernia	Henoch–Schönlein purpura	Gastroenteritis	Ectopic pregnancy
Infantile colic	Intussuception	Henoch–Schönlein purpura	Gastroenteritis
Intussuception	Pharyngitis	Mesenteric lymphadenitis	Mittelschmerz
UTI	Sickle cell crisis	Pharyngitis	Ovarian torsion
Volvulus	Trauma	Pneumonia	PID
	UTI	Sickle cell crisis	Testicular torsion
	Volvulus	Trauma	Threatened abortion
		UTI	

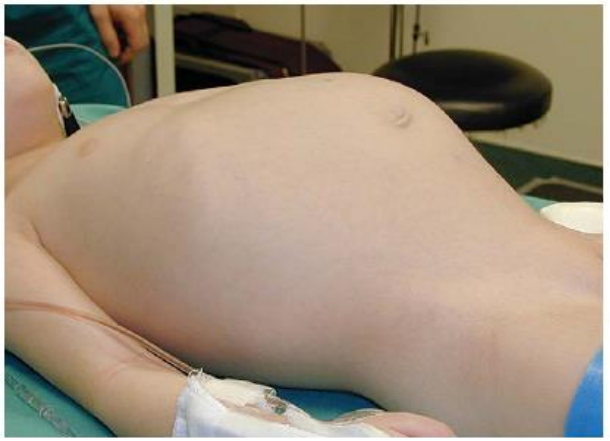
PID: pelvic inflammatory disease; UTI: urinary tract infection.
Adapted from Leung AKC, Sigalet DL. Acute abdominal pain in children. *Am Fam Physician* 2000;67(11).

General Aproach to Solid Tumors

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
- Summary: Exam content outline …

General Approach to Solid Tumors

- What is it?
- Where is it?
- Where can it go?



- **Answer to any one** of these questions will help answer the other two

Work up – Two Components

Medical history
Physical examination

Staging

- X-ray of primary site
- MRI chest, abdomen, & pelvis
- CXR (baseline)
- bone scan
- Specialty tests
  - Gallium, MIBG, PET
  - Bone marrow
  - ESR

Evaluate for complications of the tumor

- CBC with diff
- TPN panel
  - LDH, uric acid – tumor lysis, rapid cell growth
  - Lytes, creatinine – renal function
  - Transaminases – hepatic involvement
- Specialty tests
  - Tumor markers
    - HCG, AFP
    - HVA/VMA ….

Histological Diagnosis

- Incisional biopsy
- Excisional biopsy
- Special cases…
  - Calicified suprarenal mass + bone scan – might consider getting dx from bone marrow
- FNA vs excisional biopsy
  - Bias towards excisional → sufficient sample to be representative and to send for special research studies (histology, chromosomes, special studies, research studies)

Neuroblastoma

- Abdominal masses
- Differential diagnoses
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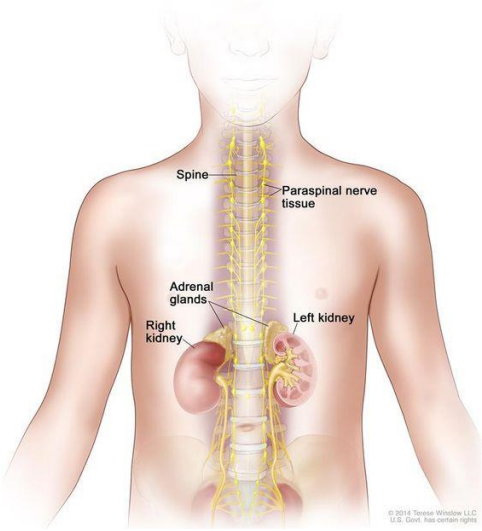
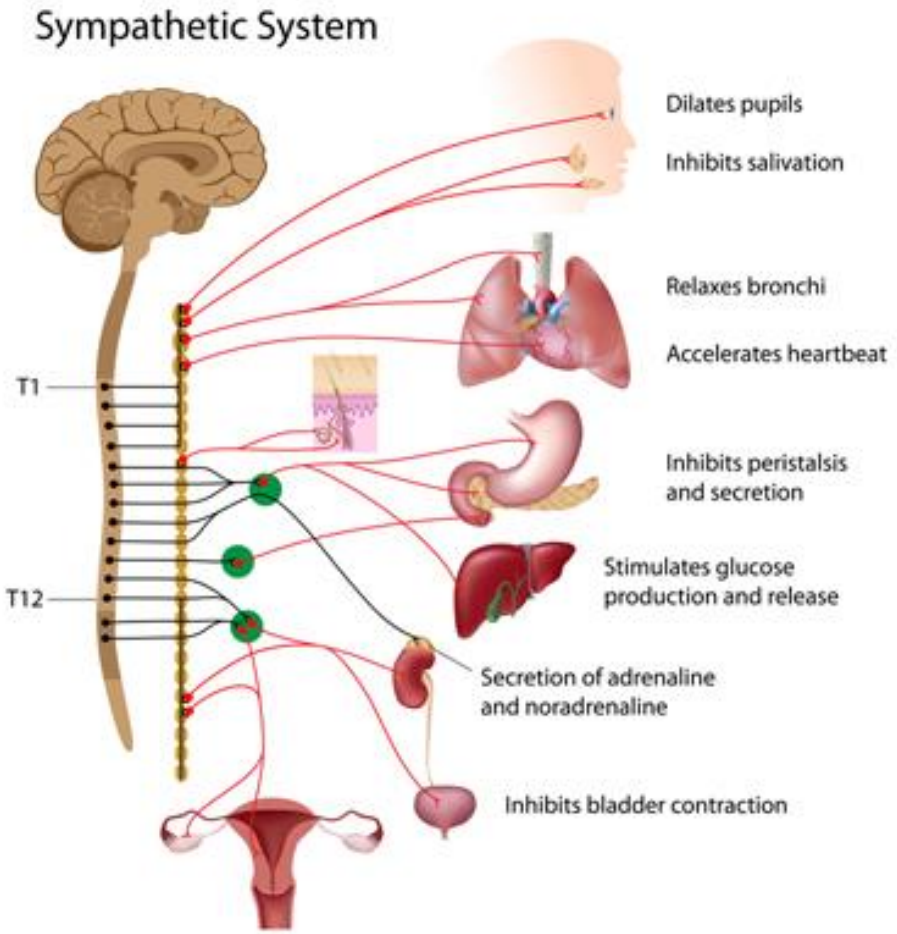
Neuroblastoma

- **Malignancy in neural crest cells in sympathetic ganglia, adrenal medulla, chest, abdomen;** small round blue tumor cells
- Nonmalignant form is ganglioneuroma
- Clinical effects r/t tumor size and location
- Genetic links/factors involved:

  N-myc oncogene, chromosome deletion



Sympathetic System



NBL / Periorbital Ecchymosis

NB Incidence/ Etiology

- **4th peds cancer (7-10%)**
  Most common cancer in infants – accounts for 50% of cancer in NBs. M:F ratio: 1.2:1

- **Average age is 18 months;** 80% < 5; small #,

- **May be a "Silent" tumor**
  presenting with widespread disease at dx 50 (younger) – 70 (older) % of time

Clinical Presentation

- **Pain, abd mass, other masses, malaise; skin**
- Can occur anywhere in sympathetic NS
- >50% are retroperitoneal; head/neck, pelvis, posterior mediastinum; +/- spinal cord compression
- Metastatic to lymph nodes, bone, BM, liver
- Fever and malaise;

  catecholamine secretion: HTN, sweats, irritability; diarrhea;

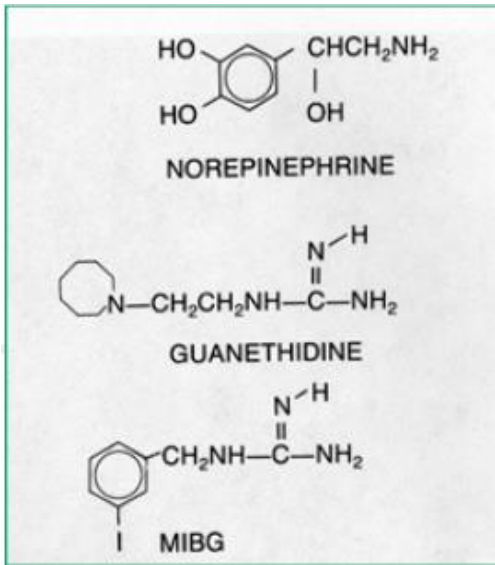
  opsoclonus-myoclonus; cerebellar ataxia

Diagnostic Workup

- Hx: catecholamine related sx (htn, flushing, sweating, irritability); wt loss, pain, limp
- PE: preorbital ecchymosis, cutaneous nodules; **abd mass**; weakness/paralysis
- CT/MRI to locate tumor; bone scan;
- MIBG (MIBG is picked up only by active tumor and not bone growth/re-growth as occurs with a routine bone scan)
- Labs (urinary catecholamines);
- Bilateral BMA & bx; chromosome studies

MIBG Scan

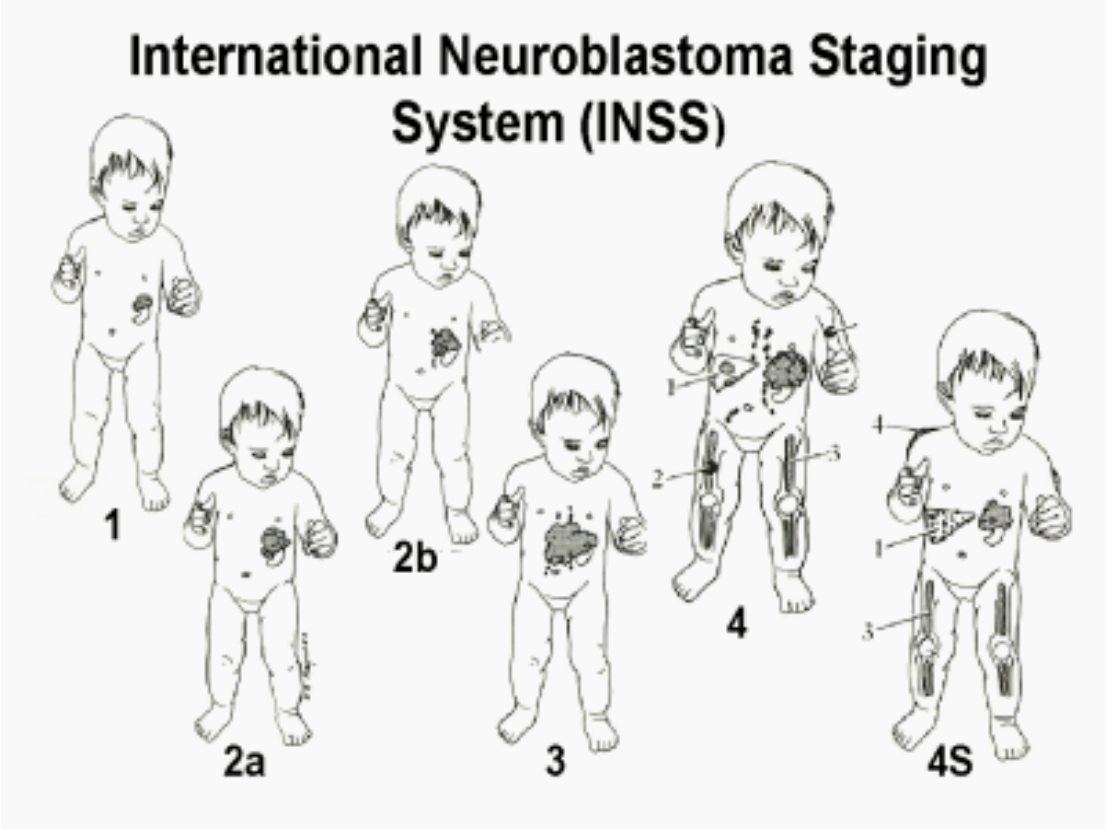
- Radioactive iodine-123(or 131)-**meta-iodobenzylguanidine**
- Noradrenaline analog
- Localizes in adrenergic tissues, catecholamine-producing tumors & their metastases
- Liquid radioactive material is injected into a vein
- Gamma camera (scanner) finds or confirms the presence of neuroendocrine tumours



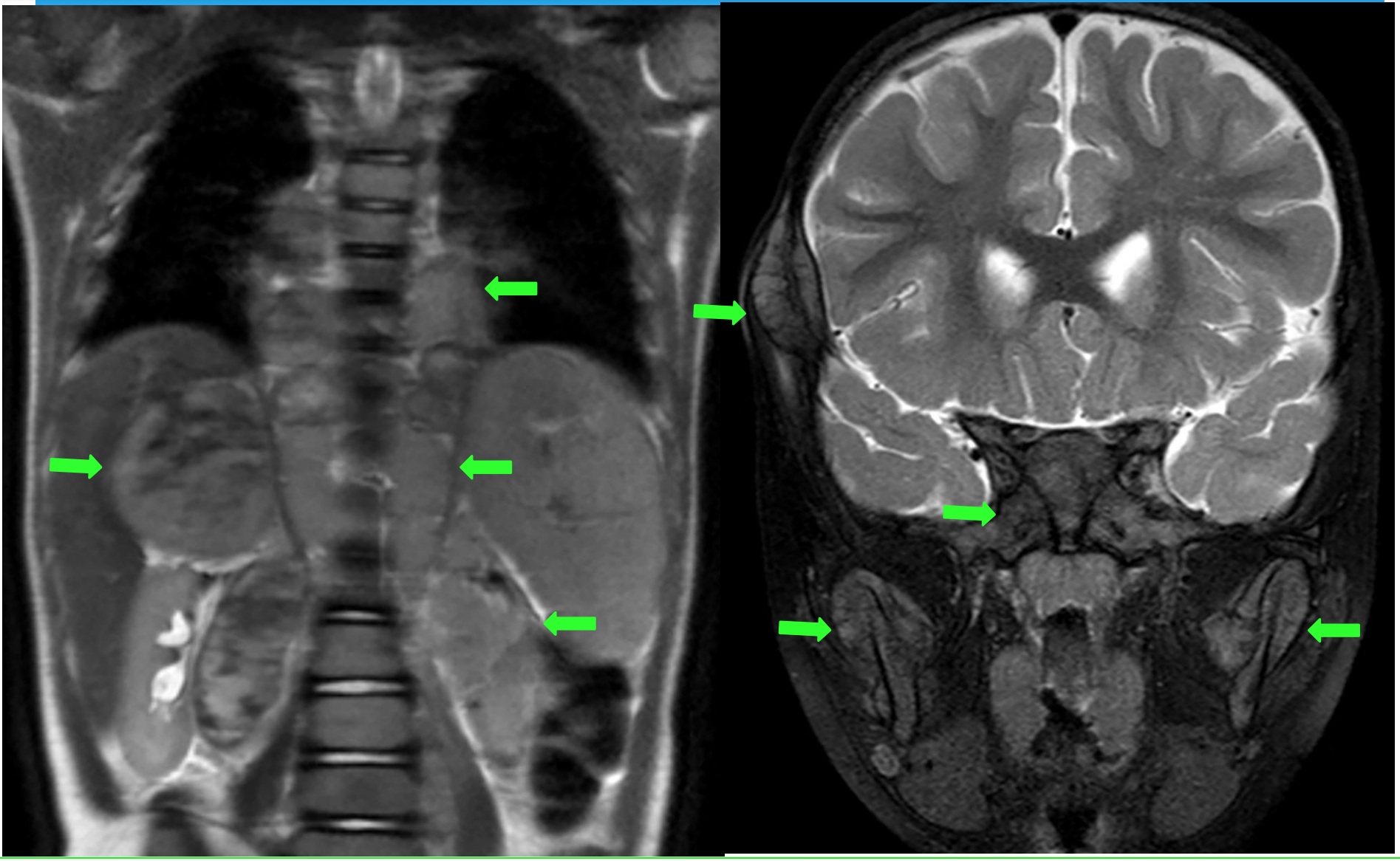
Neuroblastoma Staging

1	Localized tumor; complete excision
2A	Unilateral, incomplete gross resection; negative microscopic nodes
2B	Unilateral, positive ipsilateral nodes; negative contralateral
3	Across midline, or contralateral nodes
4	Dissemination: bone marrow, liver, skin, bones
4S	<1y: local stage 1-2 with mets to BM, liver, skin

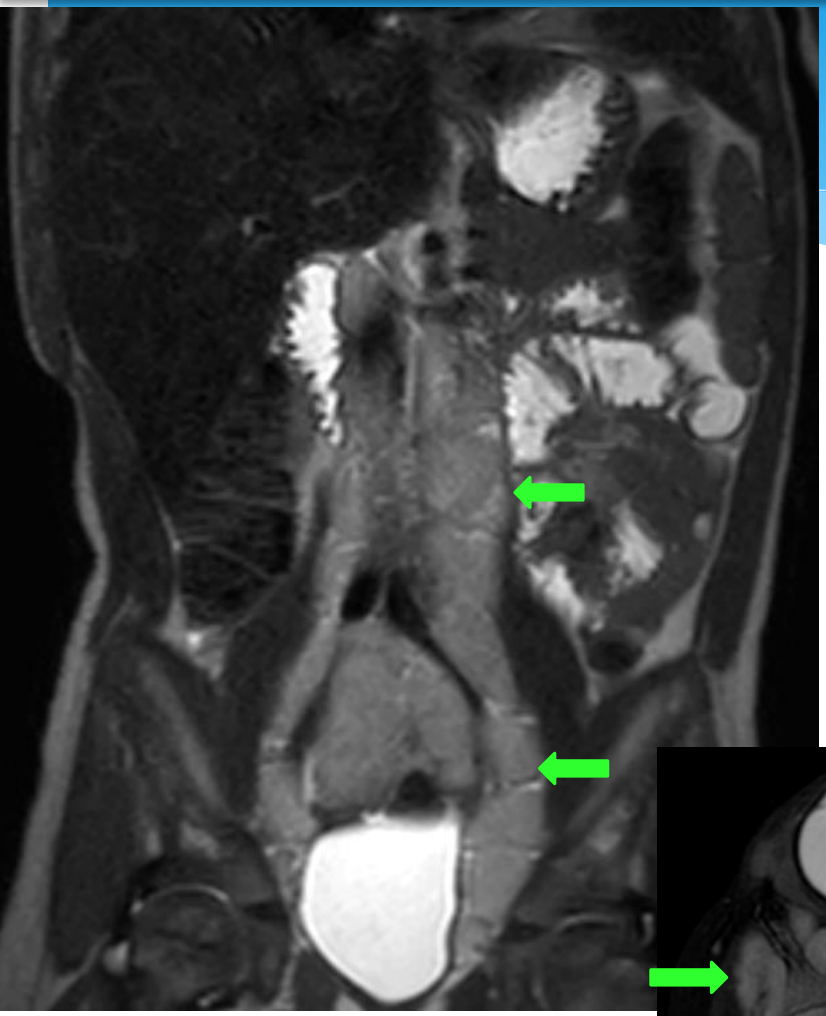
Neuroblastoma Staging

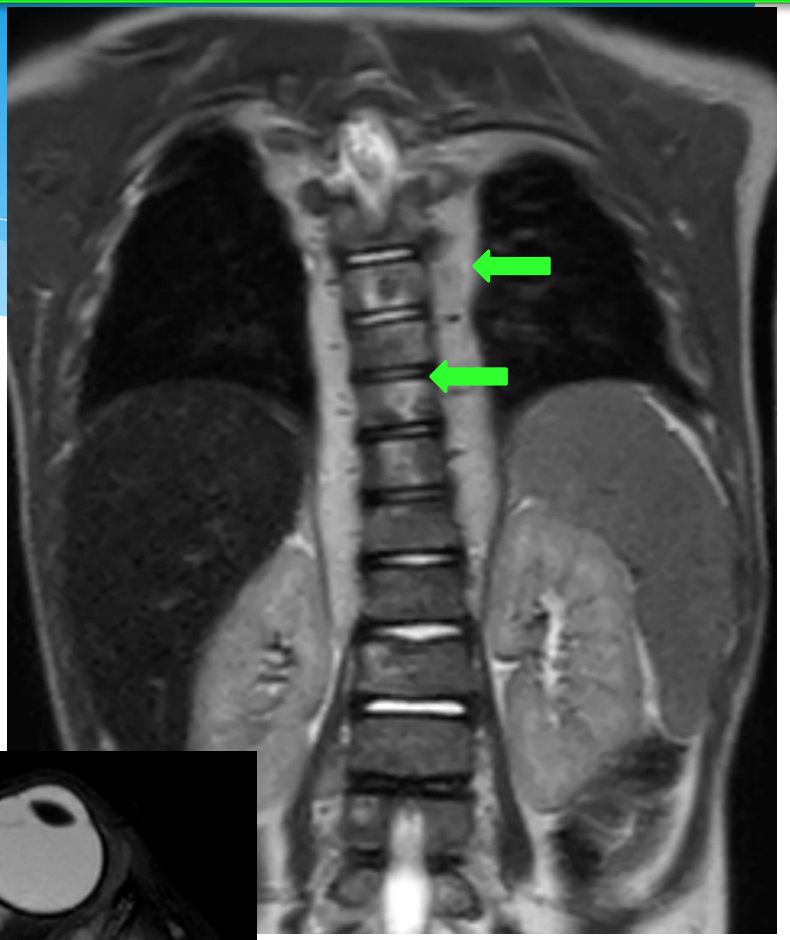


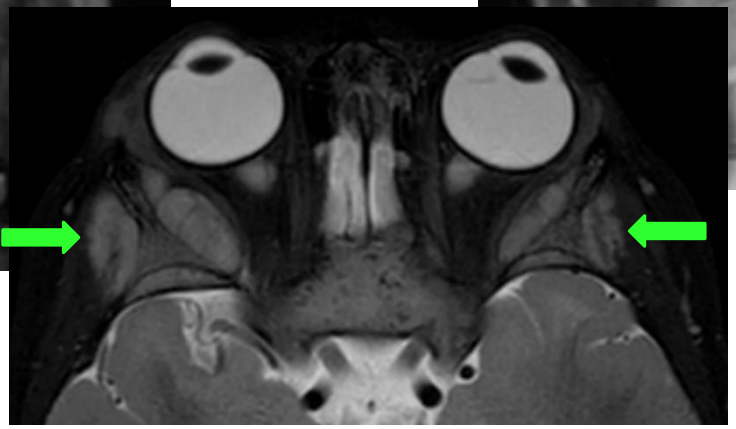
Zs.Sz., 3 yrs, male, NBL Stage 4, MYCN poz.



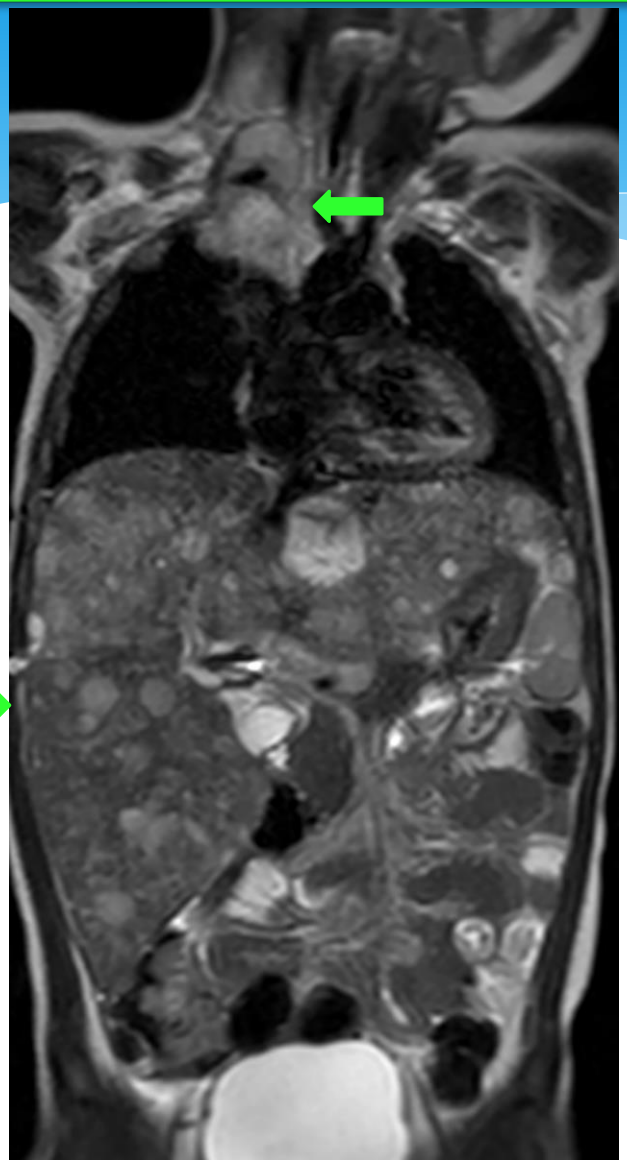
K.N., 3 yrs, female, NBL 4 Stage 4, MYCN neg

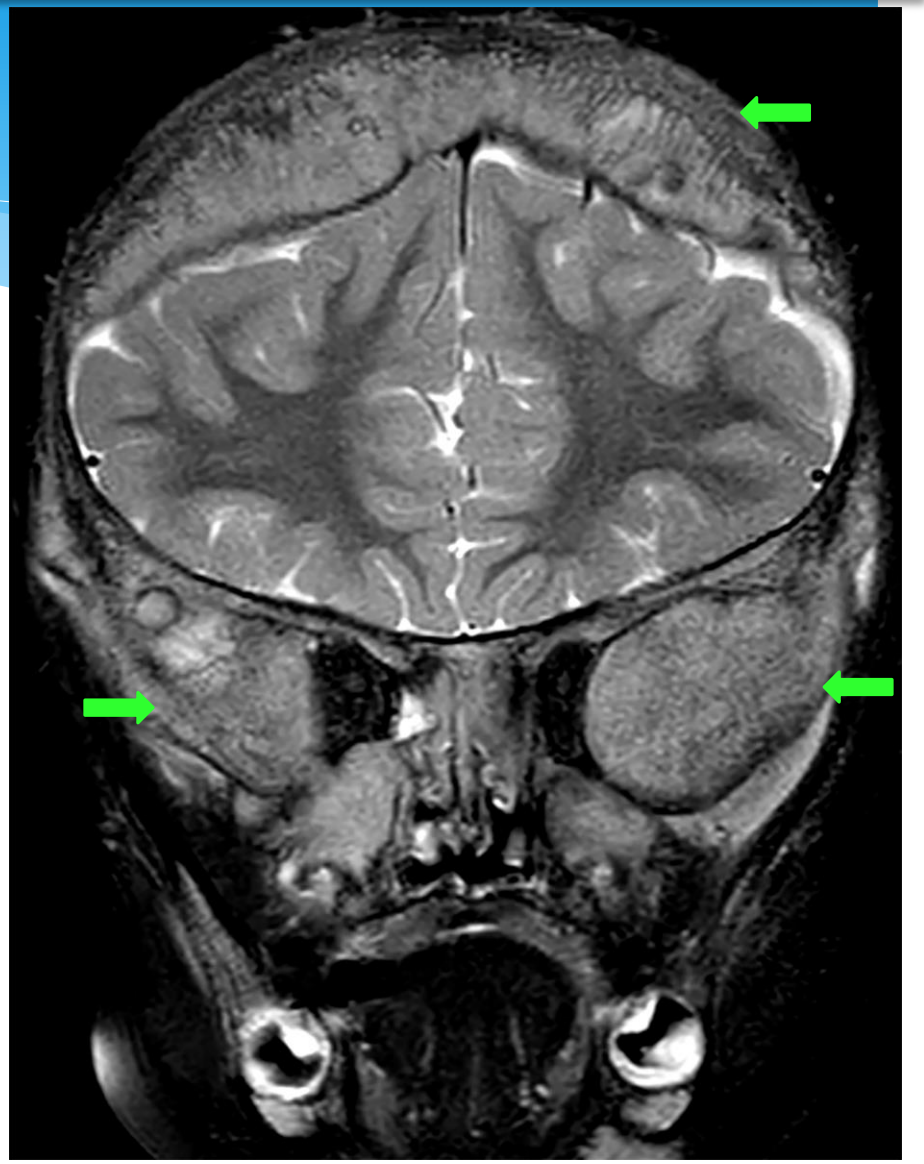






M.C., male, 2 yrs, NBL Stage 4, MCN neg.





Prognosis

- age <1 yr best (75% survival)
- worst for children >2 with stage IV disease (10-20%)
- **N-myc (proto-oncogene) amplification** regardless of age or stage is associated with advanced disease, rapid tumor progression, and a poor prognosis.

Treatment

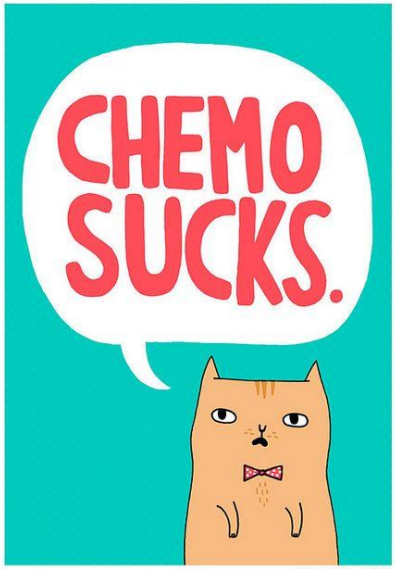
- **Surgery:** debulk or total removal;
  curative in low-stage disease;
  2nd-look after other Rx
- **Chemotherapy** – often platinum based multi-agent ~ stage
- **RT:** to primary tumor site;
  NB cells very radiosensitive;
  before or after surgery;
  emergency relief for cord compression,
  respiratory compromise, proptosis

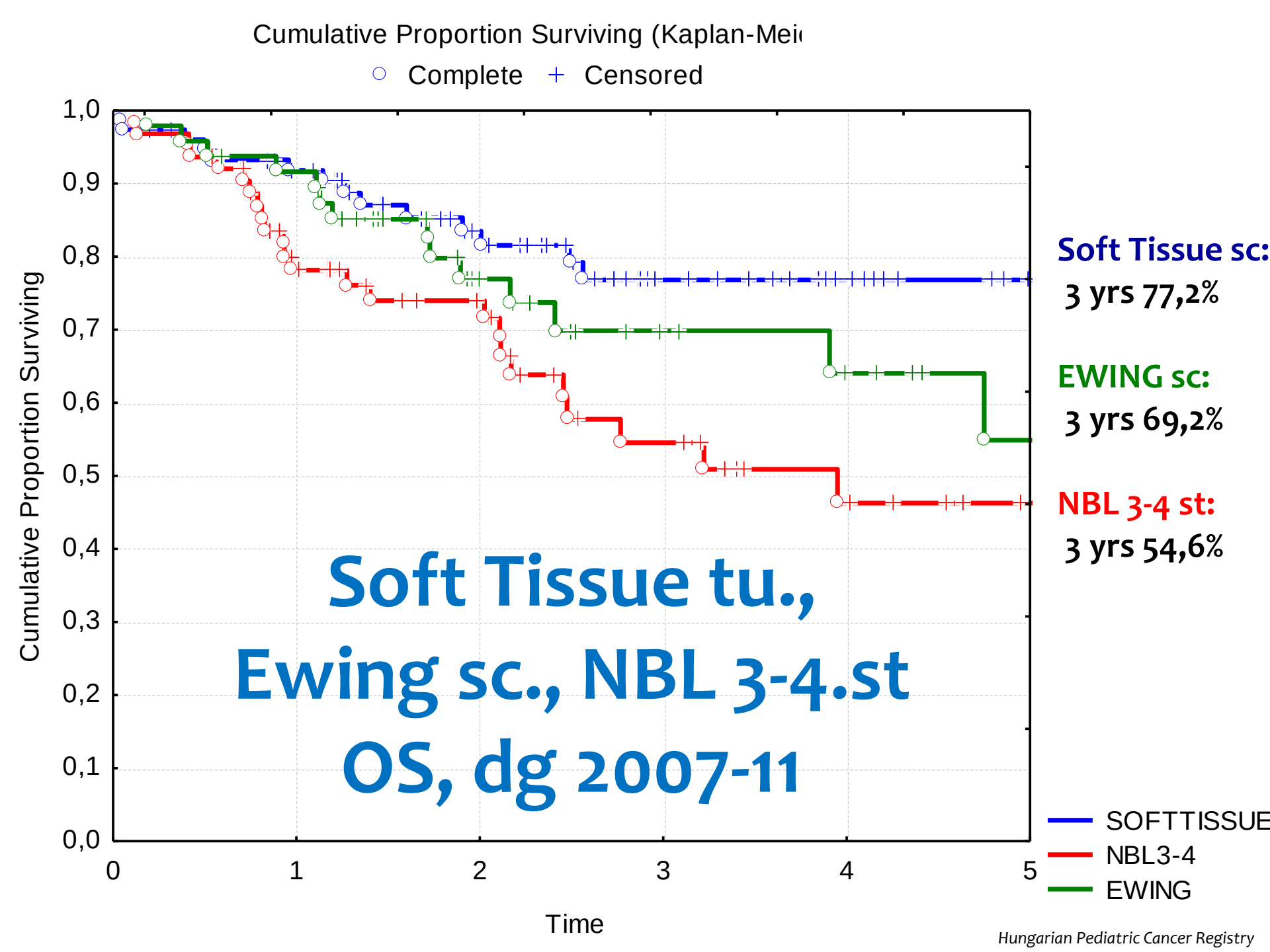
NB Treatment cont'd

BMT

- Children with poor prognosis initially may be treated with high dose chemotherapy with autologous stem cell rescue(s)

- BMT may be used with relapse




Cumulative Proportion Surviving (Kaplan-Mei
Complete
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Cumulative Proportion Surviving
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Time
Soft Tissue sc:
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EWING sc:
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NBL 3-4 st:
3 yrs 54,6%
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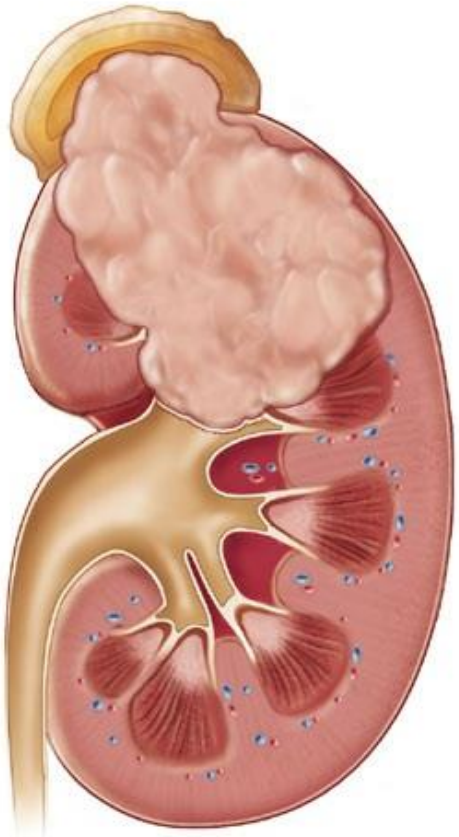
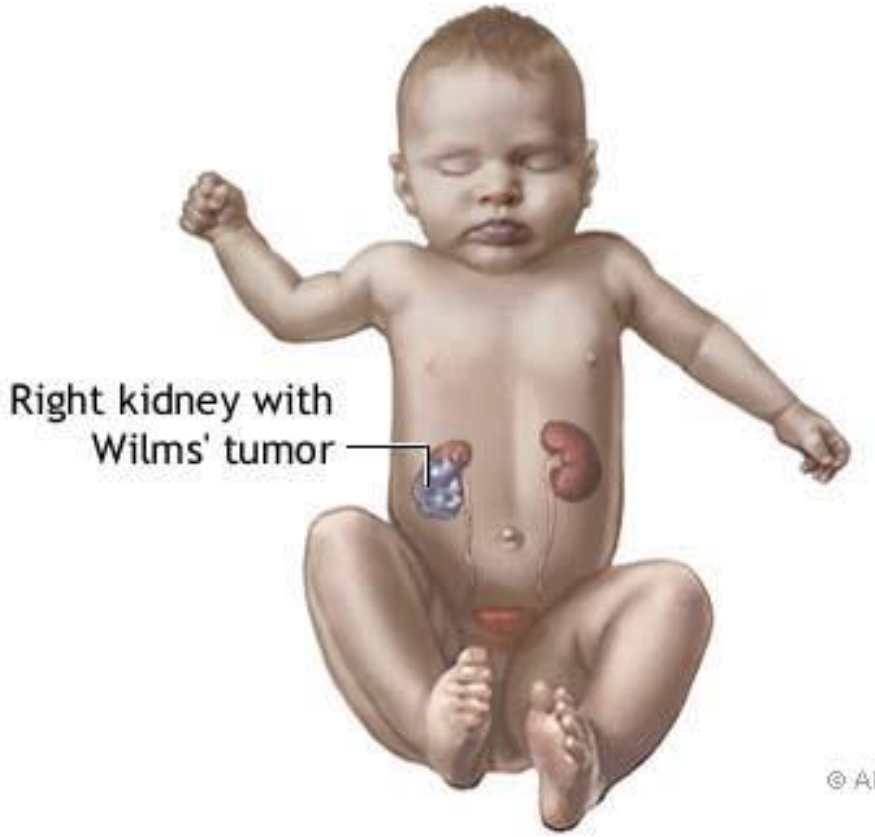
Ewing sc., NBL 3-4.st
OS, dg 2007-11
SOFTTISSUE
NBL3-4
EWING
Hungarian Pediatric Cancer Registry

Tumors of the Kidney

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
- Summary: Exam content outline …

Tumors of the Kidney



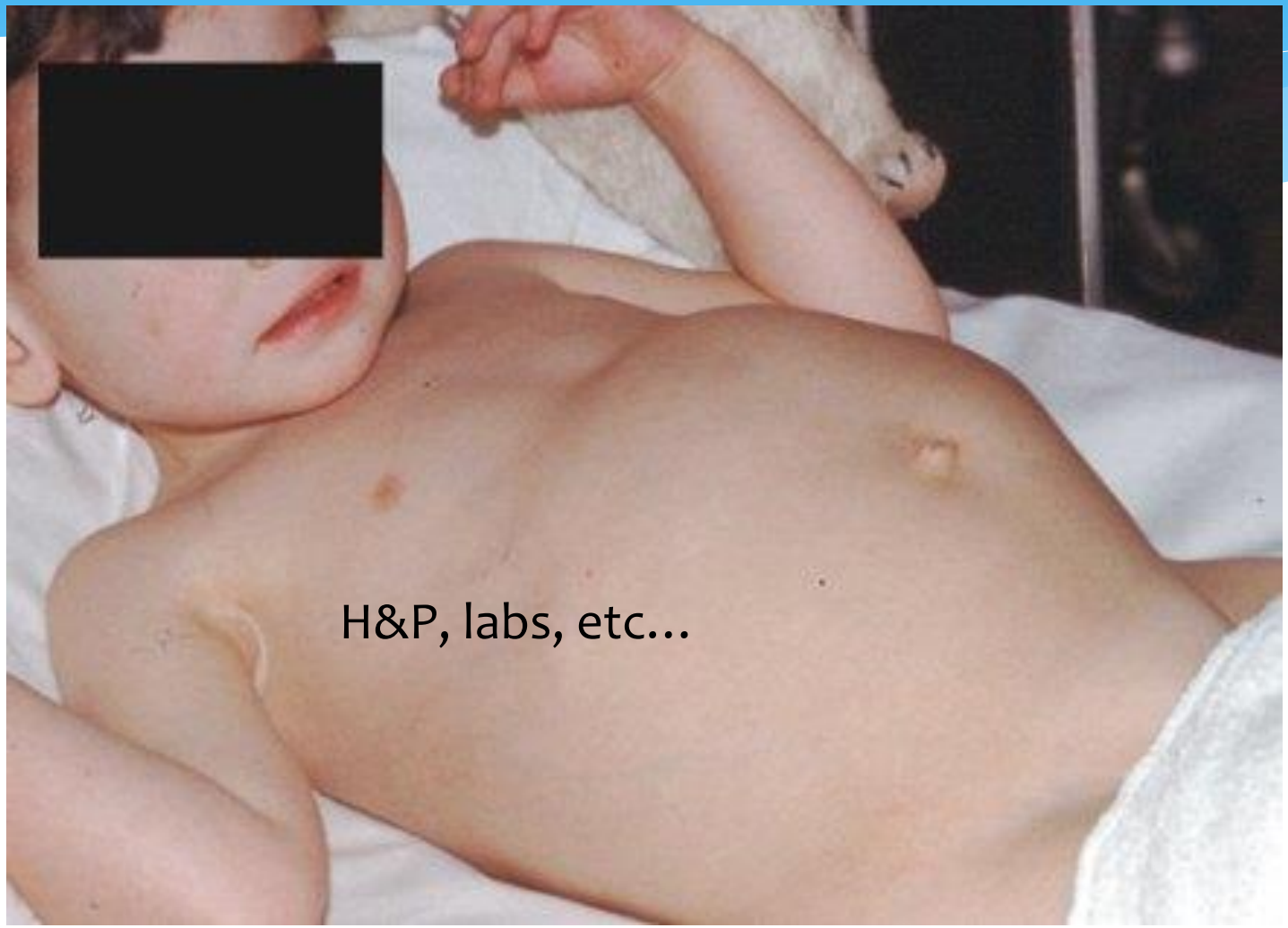


Solid Abdominal Tumor

- 2-year-old boy complains of **abdominal pain** and **loss of appetite.** Physical exam is significant for a large palpable abdominal mass.

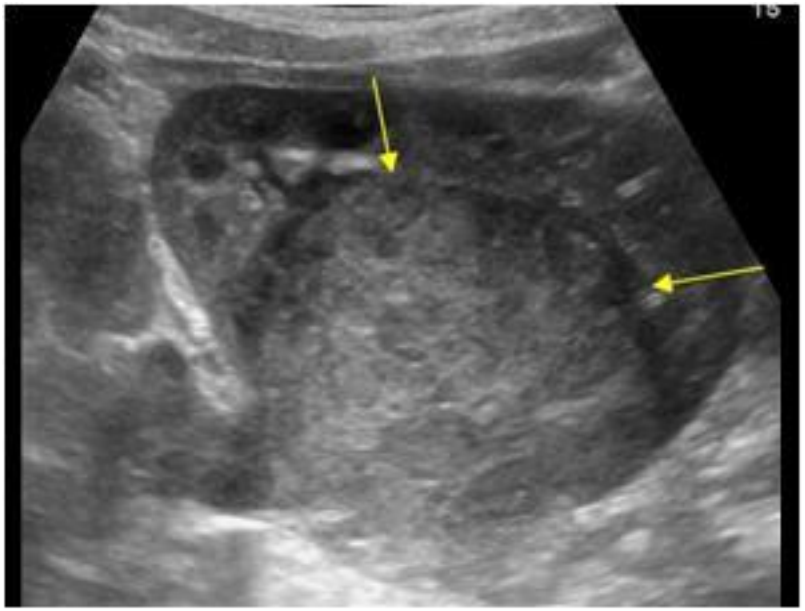
- Differential diagnosis:
  - Neuroblastoma
  - Rhabdomyosarcoma
  - Hepatoblastoma
  - Nephroblastoma (Wilms' tumor)

2-year-old with abdominal pain and palpable mass



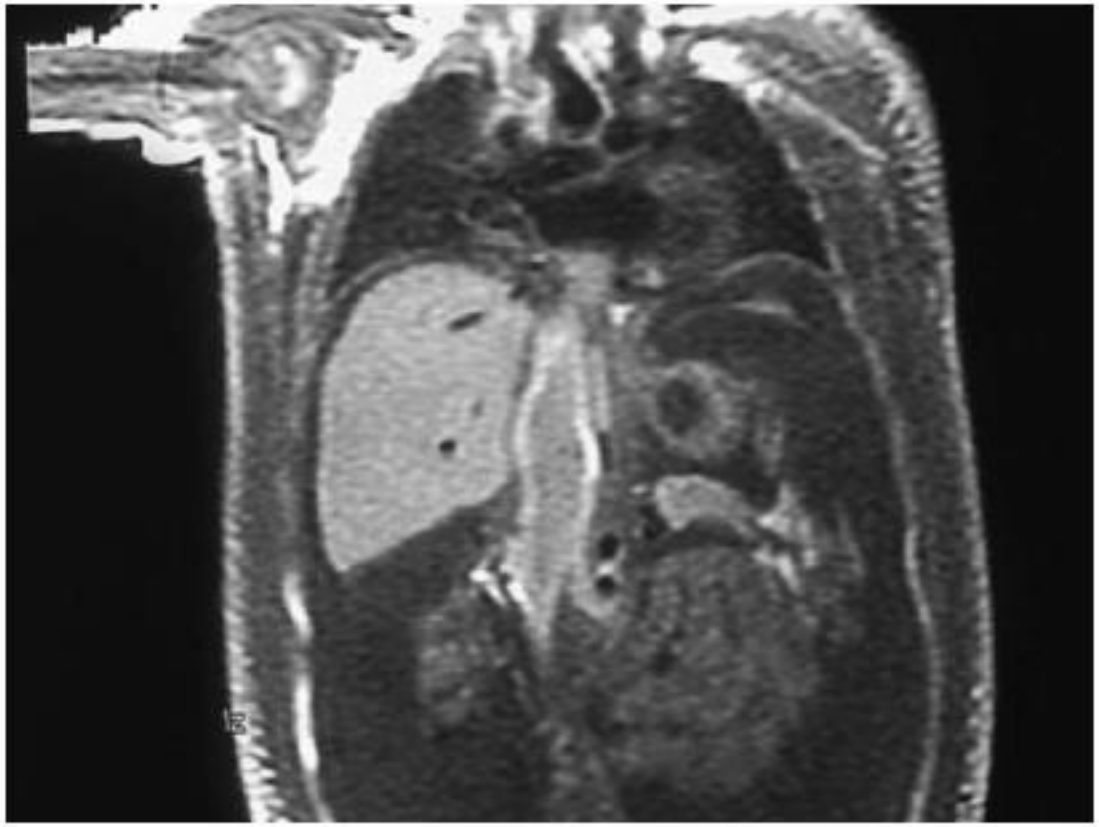
Imaging / US

- **Abdominal ultrasonography** first
  - Solid nature of the lesion, confined to kidney
- **Doppler US** is particularly helpful to exclude intracaval tumor extension
  - If indeterminate, MRI

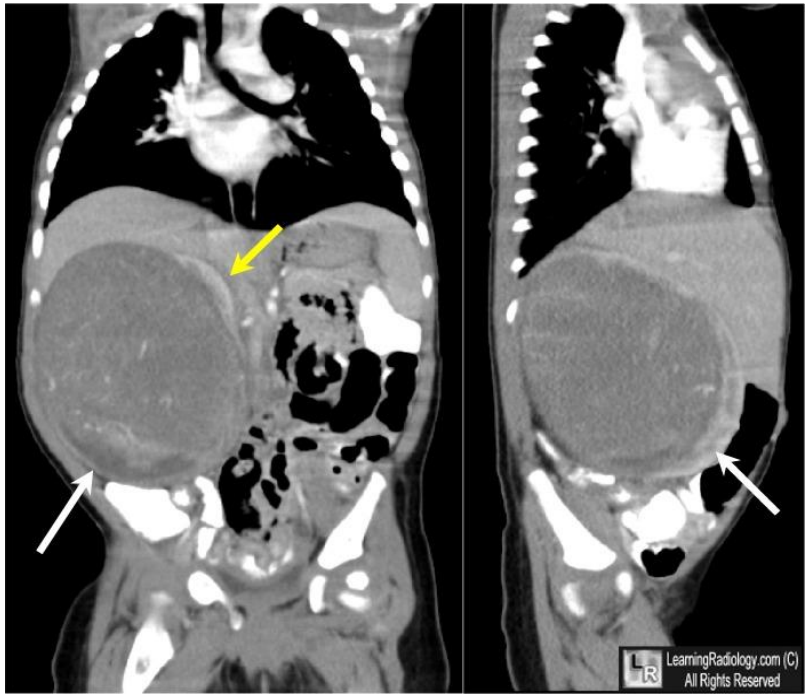


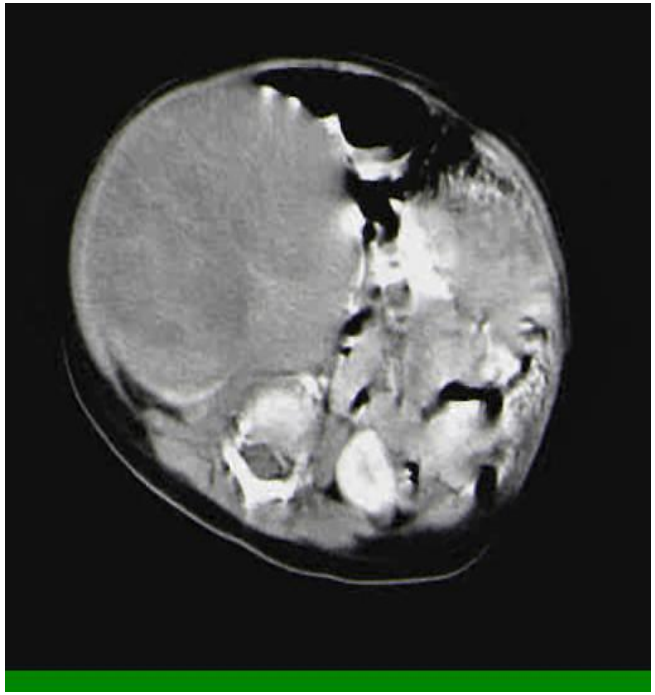
Imaging / MRI Scan

- **MRI** with tumor thrombus extending into IVC



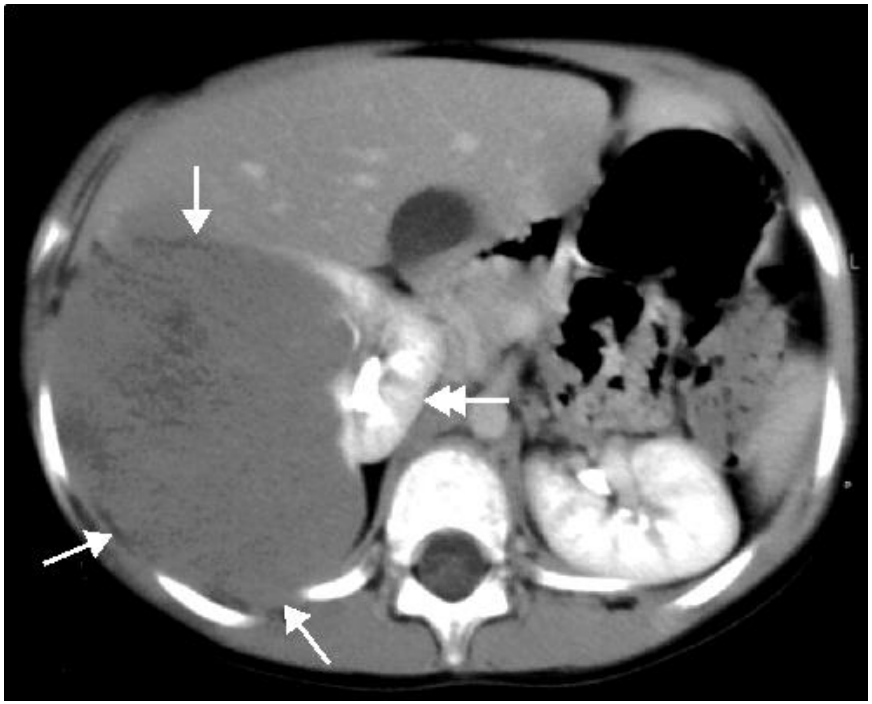
Imaging / CT Scans

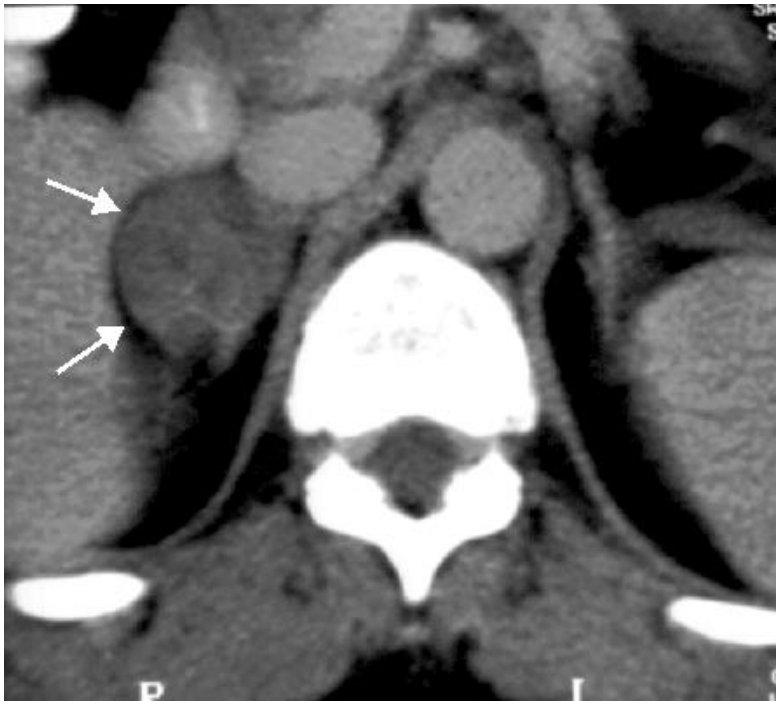




CT Chest/Abdomen/Pelvis can further define the extent of the lesion, pulmonary metastasis

Imaging / CT Scans





Tumors of the Kidney

- **Primary tumors arising from the kidney**, usually Wilms, rapidly growing vascular abdominal tumors; fragile gelatin capsule
- Others: clear cell sarcoma, renal cell CA, lymphoma, PNET, rhabdoid, …
- Wilms tumor pathology may be *favorable* or *unfavorable* depending on degree of anaplasia present;
  prognosis and treatment r/t pathology

Incidence and Etiology

- **Renal tumors represent 5-6% of peds cancer**
- Higher in AA, lower in Asians
- Peak age at 2-3; rare in kids >5;
  M:F 0.9:1.0 (unilateral) 0.6:1.0 (bilateral)
  males younger age at diagnosis
- 1.5% familial in origin; associated with aniridia, hemihypertrophy, GU malforms
- Genetic factors, deletion or translocations

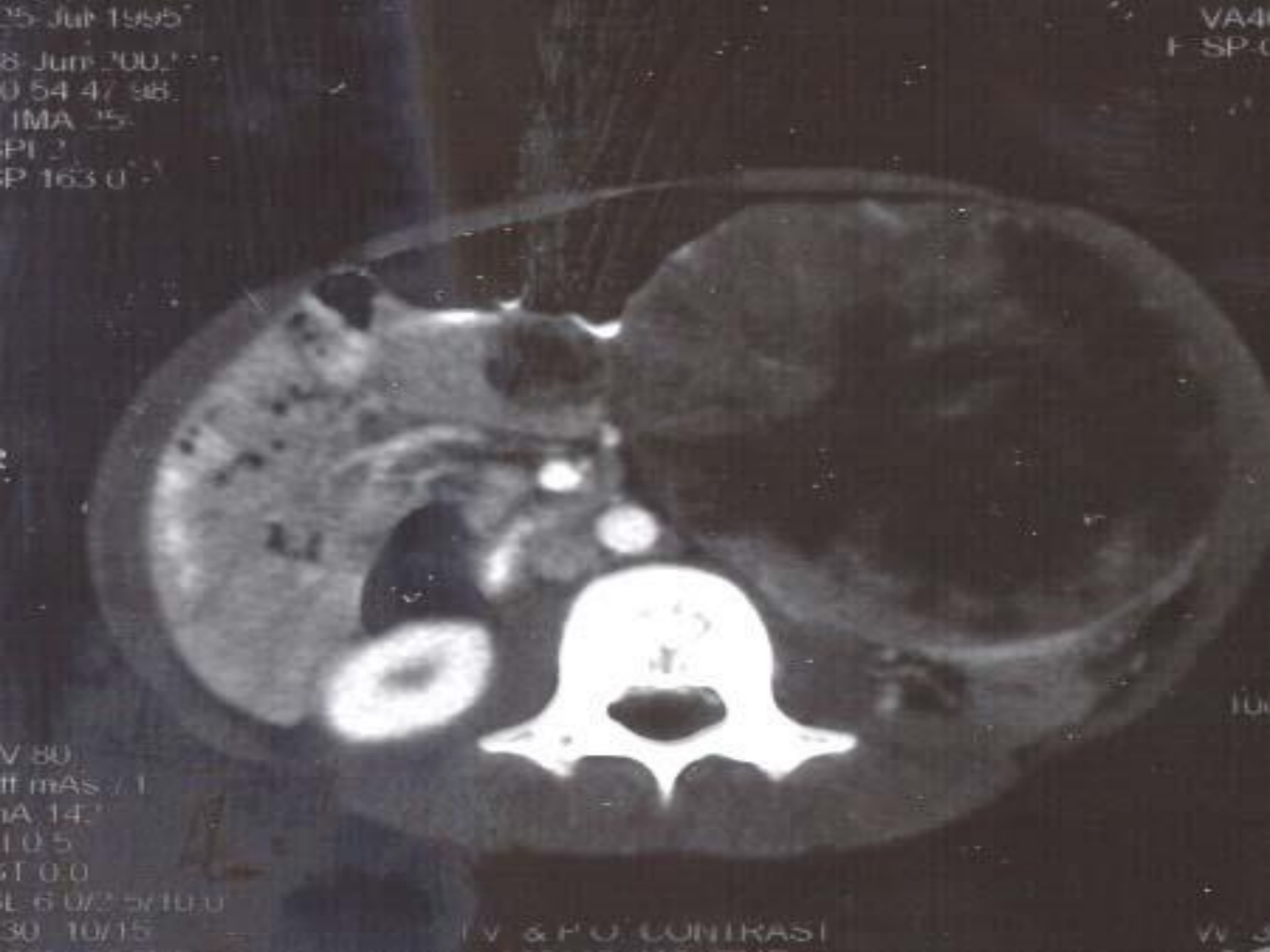
Clinical Presentation

- Asymptomatic abdominal mass found by family or on routine PE
- Pain, malaise, hematuria in 20-30%; 25% with HTN; rare subcapsular hemorrhage, with rapid increase in size, anemia, HTN
- Mets to lungs, liver, regional nodes
- 7% bilateral, at dx or later

- hypertension
- fever

Diagnostic Workup

- H and P
- Labs, renal and hepatic function
- Imaging studies:
  US to determine size and shape, vessel involvement, thrombi in major vessels; chest film/CT to check for mets
- Liver, brain, and bone mets not routinely assessed unless indicated by S/S


I.V. & P.O. CONTRAST

Prognosis

- Histology is most important prognostic factor (favorable histology vs. anaplastic)
- Stage at diagnosis also crucial
- Genetic factors
- Age

Staging of Wilms Tumors

I. Limited to kidney; complete resection
II. Extent beyond kidney, but complete R
III. Residual tumor, confined to abdomen
IV. Hematogenous mets (lung, liver, bone, brain) or lymph nodes outside abdomen
V. Bilateral renal involvement at diagnosis

Tumor spill at time of surgery – considered stage III.

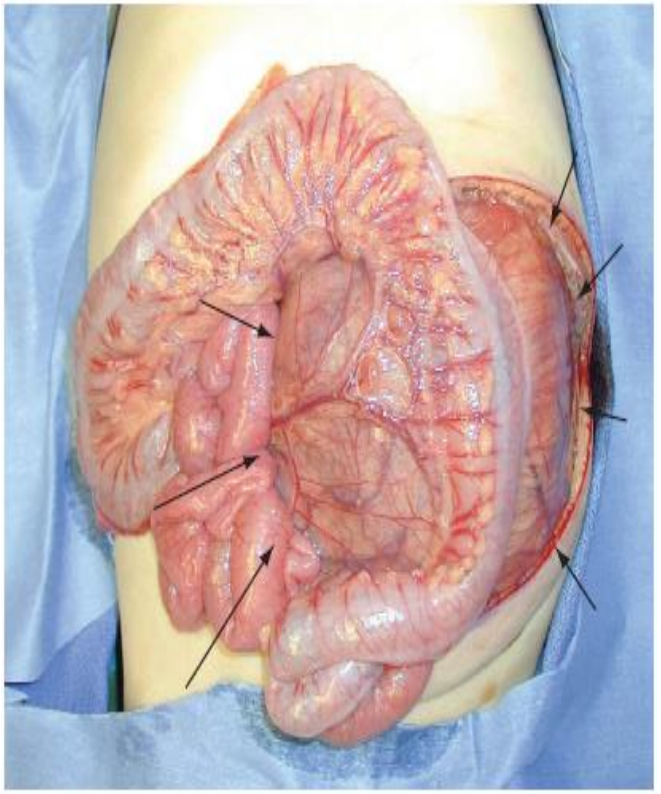
Treatment and Prognosis

- **Surgery initially**, with exam of contralateral kidney;
- **Preop chemotherapy** if intravascular spread or very large invasive tumors; if bilateral;
- NA argument: Preop chemo prevents adequate assessment of staging
- Considered Stage III if imaged only

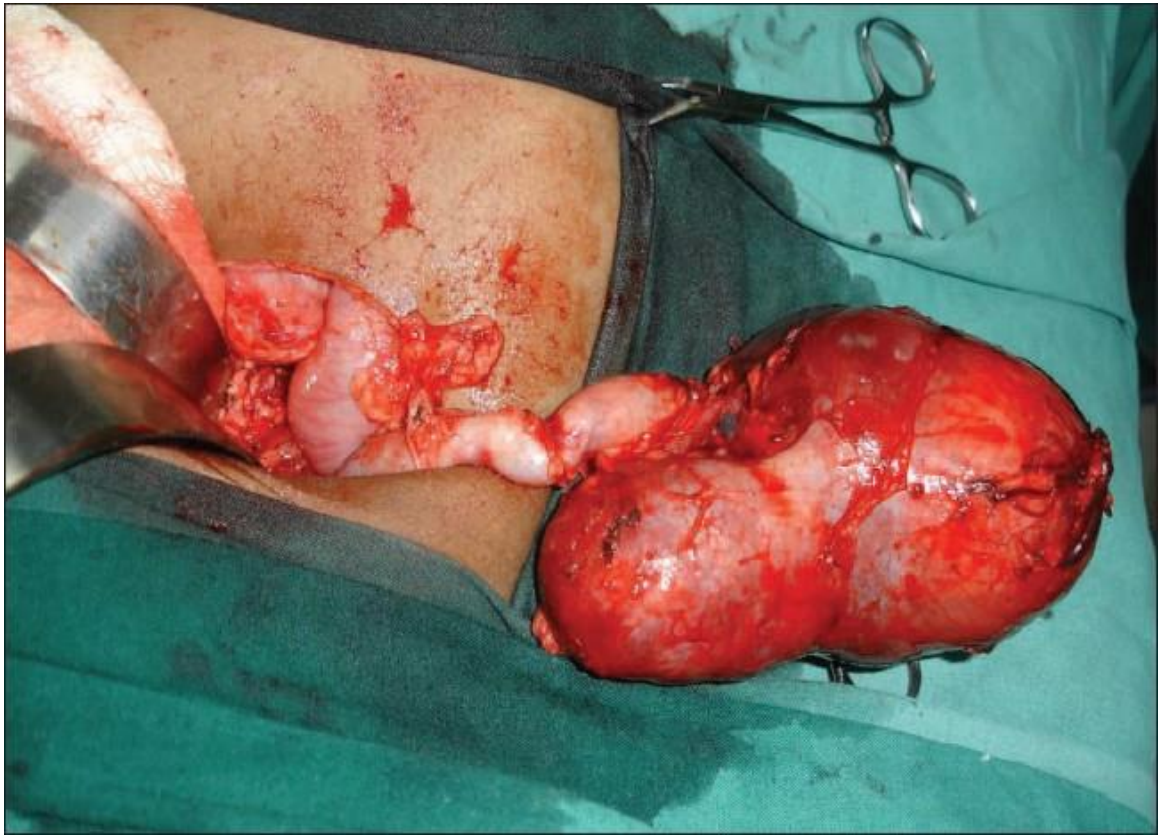
Surgery

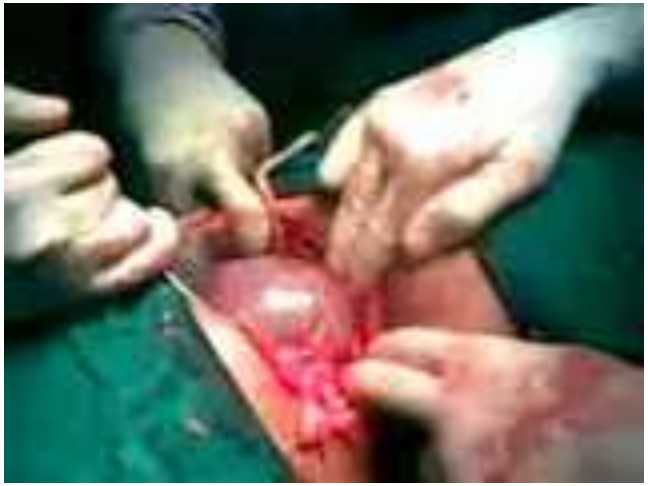
The main responsibility of the surgeon is to:

- Remove the tumor completely, without spillage
- Accurately assess the extent to which the tumor has spread
- Pay particular attention to adequately assessing the lymph node involvement

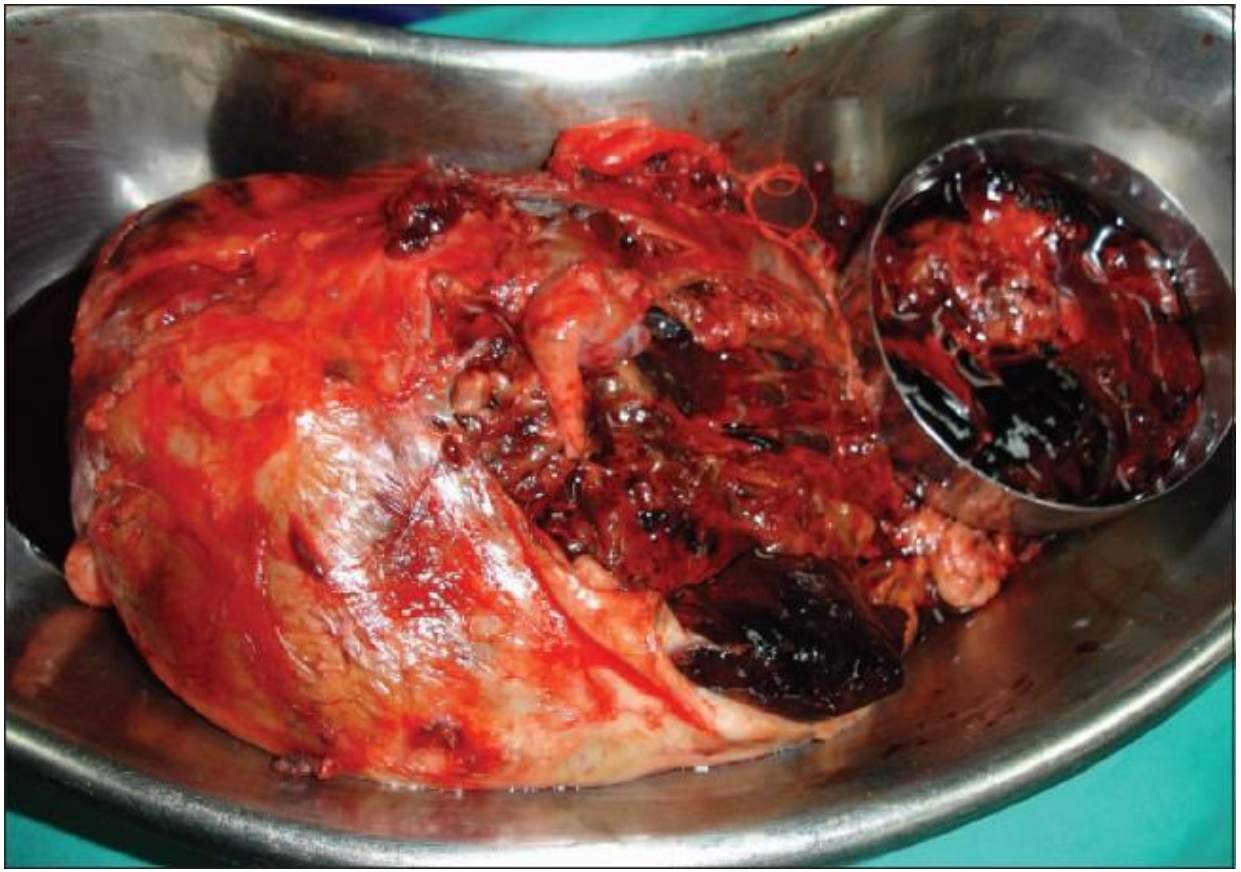


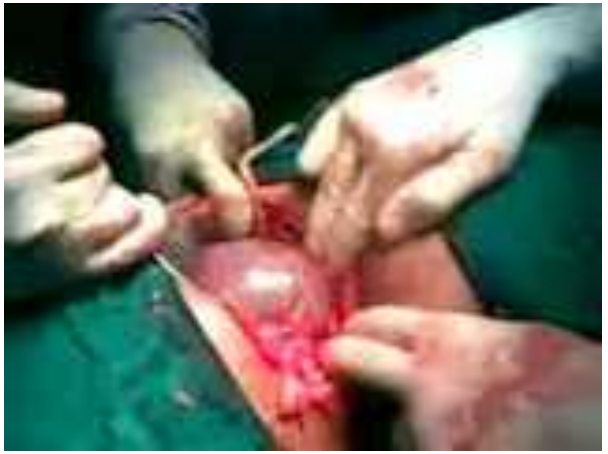
Radical Nephrectomy





Radical Nephrectomy





Tumor spillage associated with recurrence

Treatment and Prognosis cont'd

- Bilateral: preop chemo; nephrectomy of worse side, partial on other
- Chemotherapy: regimens based in national groups
- RT: port extended across midline to prevent scoliosis; if favorable histology, RT only for Stage III and IV; post lung RT, adjust Chemo
- Recurrence: worse if <1 year; on chemo
- Prognosis: <50% - 100% (stage/histology)

Note: *Total body radiation (TBI) may cause short stature due to its affect on the hypothalamic-pituitary axis resulting in a decrease in growth hormone secretion.*

Wilm's Tumor & Congenital Malformations

- Cryptorchidism
- Hypospadias
- Hemihypertrophy
- Aniridia
- "Horsehoe" kidney

(WAGR syndrome: Wilms tumor, aniridia, genitourinary anomalies, and mental retardation sy.)

Malignant Hepatic Tumors

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
- Summary: Exam content outline …

Malignant Hepatic Tumors

- Hepatoblastoma; median age of 1 yr
- Hepatocellular carcinoma
  median age of 12 yrs
  associated with hepatitis B <15 yrs, prolonged use of metabolic steroids

- Nonmalignant: hemangiomas (50% of all hepatic tumors)

Clinical Presentation

- **Hepatoblastoma (80%):**
  asymptomatic abdominal mass; osteopenia
- Hepatocellular Ca (20%):
  abdominal distention, RUQ mass; pain, N & V; jaundice; splenomegaly
- Elevated alphafetoprotein level

Dexter has rash on his stomach…

Dexter has an extended and hard abdomen… complications with his earlier bowel problems and over-eating, we thought.

Dexter was tired… his cerebral palsy and vision impairment would cause him to tire easily, they said.

Can you see the cancer?
Can you see the rash?
Can you see the computer-mouse-sized tumour?

http://lovedexter.weebly.com/blog/see-the-cancer

Treatment and Prognosis

- Preop CTX followed by complete resection

- **Hepatoblastoma:** High cure rates, with cure possible if mets are resected (> 65%)
- **Hepatocellular Cc:** Difficult to resect and difficult to cure even with complete resection (<20%)
- RT of little benefit
  Chemo-embolization?
  Orthotopic liver transplant?

Prognosis

Hepatoblastoma

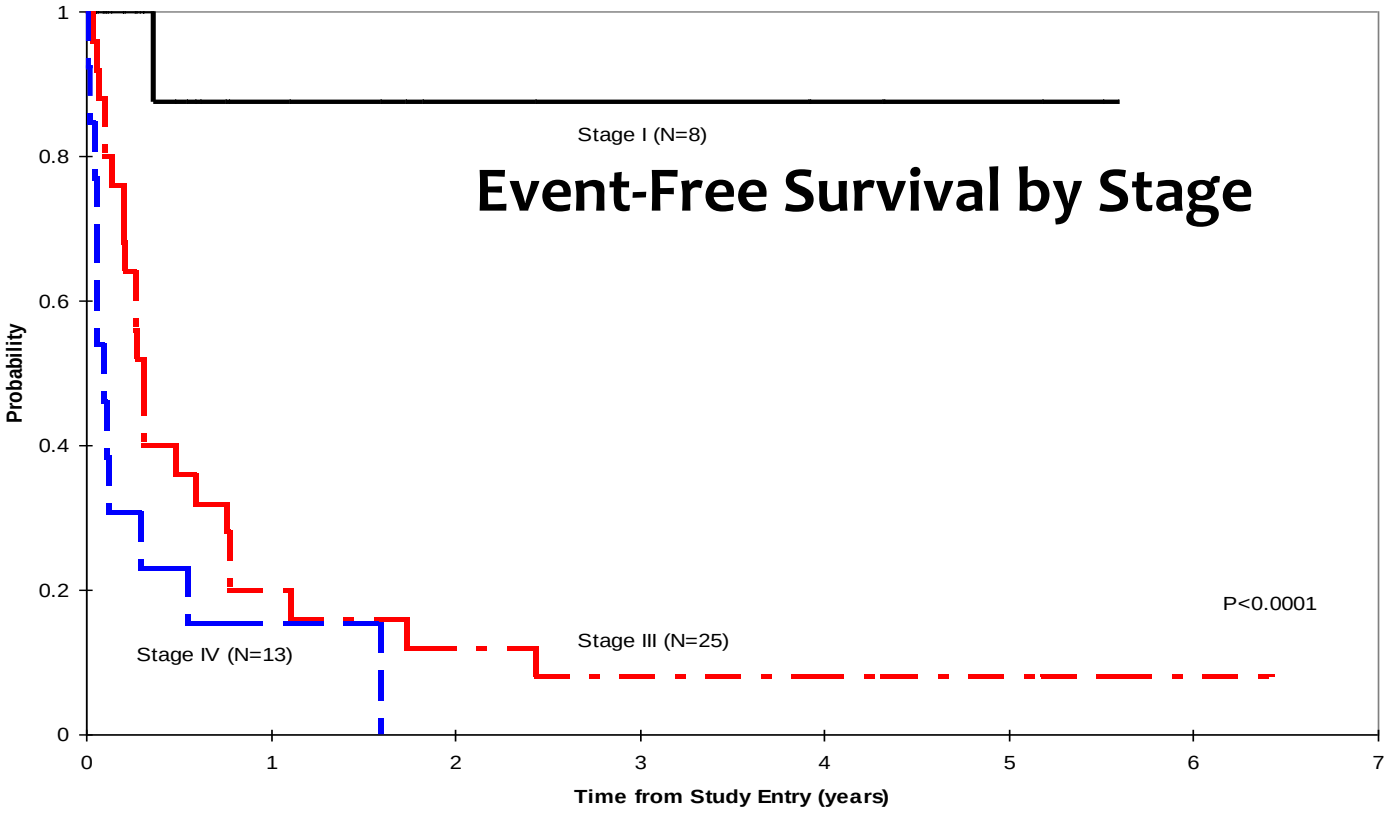
- Resectable tumors
  - At diagnosis (stage I & II) - 90%
  - Following chemo-reduction (III) - 80%
- Unresectable tumors - 50%
- Metastases at diagnosis - 10%

Prognosis

Hepatocellular Carcinoma

- Children with initially resectable HCC have a good prognosis and may benefit from adjuvant chemotherapy.
- The outcome for children with unresectable or metastatic HCC continues to be dismal with current therapies.

Intergroup Study for the Treatment of Childhood Hepatocellular Cc.



Summary

- Abdominal masses
- Differential diagnoses
- Examination of the pediatric abdomen
- Abdominal pain
- General approach to solid tumors
- Neuroblastoma
- Tumors of the kidney
- Malignant hepatic tumors
- Summary: Exam content outline …

Exam Content Outline

- Formulate a differential diagnosis for an abdominal mass
- Know that multicystic dysplastic kidneys and hydronephrosis are the most common causes of palpable abdominal masses in infants
- Recognize that children with hemihypertrophy and somatic overgrowth syndromes should be periodically evaluated for the development of associated embryonal tumors

Exam Content Outline, continued

- Understand that a neuroblastoma usually presents as a nontender abdominal mass
- Understand that urinary catecholamine excretion is increased in most patients with a neuroblastoma and that tests of urine for VMA and VHA are appropriate screening tests for the tumor
- Understand that Wilms tumor usually presents as an abdominal mass and may cause hypertension
- Recognize the tumors that may produce precocious puberty (eg, in liver, CNS, ovary, testes, adrenal glands)

test your knowledge

Infant female with an abdominal mass

aspho
The American Society of Pediatric Hematology/Oncology

http://www.surveygizmo.com/s3/2386255/ASPHO-October-2015-Case-Quiz

An 8-month-old female is referred for evaluation of an abdominal mass. Imaging reveals a large tumor arising from the right kidney. Past medical history is unremarkable. There is no hemihypertrophy, hepatomegaly, or skin rash. Genitourinary exam is normal. Examination of eyes, ears, and mouth is normal. Family history is unremarkable; specifically, there is no history of cancer. The patient undergoes R nephrectomy and pathology confirms Wilms' tumor. Cytogenetic analysis is remarkable for 46 XY karyotype without any loss of heterozygosity. The patient did not have evidence of metastatic disease and was diagnosed with stage II Wilms' tumor. She went on to receive vincristine- and dactinomycin-based chemotherapy.

1. Which tumor predisposition syndrome is most likely in this case?

A. Beckwith-Weidemann syndrome
B. WAGR syndrome
C. Denys-Drash syndrome
D. Li-Fraumeni syndrome

The correct answer is C. Denys-Drash syndrome (DDS) is a rare syndrome associated with Wilms' tumor and gonadal dysgenesis. The key finding here is the XY karyotype in a female patient presenting with Wilms' tumor at a young age. Denys-Drash syndrome and the closely related Frasier syndrome are associated with Wilms' tumor and gonadal dysgenesis. Ambiguous genitalia is a common finding in XY "male" patients with DDS, but depending on the degree of gonadal dysgenesis, an XY patient may have complete feminization of external genitalia. Female (XX) patients with DDS will have normal female genitalia. Beckwith-Weidman and WAGR (Wilms' tumor Aniridia Genitourinary anomalies and mental Retardation) syndromes also are associated with development of Wilms' tumor. However, the patient did not have other findings (hemihypertrophy or organomegaly for Beckwith-Weidemann syndrome, or aniridia or genitourinary anomalies for WAGR) to suggest these syndromes. Li-Fraumeni syndrome is associated with an increased risk of cancer; however, there is no family history of cancer in this case and Wilms' tumor in an infant is not typically associated with Li-Fraumeni syndrome.

2. A germline mutation in which of the following confirms the diagnosis of this syndrome?

A. WT1 gene
B. TP53 gene
C. Imprinting defect on chromosome 11p15
D. PAX6 gene

The correct answer is A. The Wilms' Tumor gene (WT1) is a tumor suppressor located on chromosome 11p13. It is a zinc finger transcription factor critical for kidney development, first identified in patients with WAGR syndrome. Constitutional mutations in WT1 are responsible for DDS, WAGR, and Frasier syndrome. TP53 is a tumor suppressor mutated in Li-Fraumeni syndrome. Genomic imprinting defects on 11p15 are responsible for Beckwith-Weidemann syndrome. The PAX6 gene controls eye development and is located near WT1 on 11p13; it is mutated along with WT1 in WAGR syndrome, explaining the aniridia seen in these patients.

3. What other type of tumor is this patient at risk for?

A. Neuroblastoma

B. Acute myeloid leukemia

C. Hepatoblastoma

D. Gonadoblastoma

The correct answer is D. As may be inferred from questions one and two, the WT1 gene is critical for normal XY gonadal development. XY individuals with DDS or Frasier syndrome have gonadal dysgenesis. There is an increased risk of the development of gonadoblastoma, or rarely malignant germ cell tumors, in the residual gonads. Upon diagnosis of DDS in our patient, pelvic imaging demonstrated the presence of underdeveloped "streak" gonads. She underwent laparoscopic gonadectomy and pathology showed dysplastic gonadal tissue, but no frank conversion to gonadoblastoma or germ cell tumor. Increased risk of hepatoblastoma and neuroblastoma are associated with Beckwith-Weidemann syndrome, but not DDS. Although recurrent somatic mutations in WT1 are seen in acute myeloid leukemia (AML), there is no known increased risk of AML or hematologic malignancy in patients with DDS.

4. What non-oncologic complication is this patient at risk for?

A. Developmental delay/autism

B. Renal failure

C. Cardiomyopathy

D. Stroke

The correct answer is B. The third hallmark feature of DDS (in addition to Wilms' tumor and gonadal dysgenesis) is nephropathy (and ultimately end-stage renal disease) as a result of diffuse mesangial sclerosis. In fact, renal failure early in life (before the age of 6) is the most common presenting feature in patients with DDS. In addition, because of the germline WT1 mutation, patients with DDS are at increased risk for developing Wilms' tumor in the contralateral kidney. Our patient had progressive renal insufficiency. After much discussion with the family, nephrologist, and kidney transplant team, our patient underwent nephrectomy followed by orthotopic, living related-donor kidney transplant.

Learning points: The diagnosis of DDS should be considered in female patients who develop Wilms' tumor when younger than 18 months. In particular, in female Wilms' tumor patients with ambiguous genitalia or with renal insufficiency (elevated creatinine for age, proteinuria), the diagnosis should be strongly suspected and sequencing for WT1 gene mutations should be undertaken. Confirmation of WT1 mutation has important implications for management of and guidance for the patient. Our patient already had dysplastic changes in the remnant gonads, which were resected prior to transformation to gonadoblastoma. The diagnosis also influenced the timing and decision making regarding kidney transplant. Our patient had progressive renal insufficiency, in spite of appropriate medical management. Given that end-stage renal disease was inevitable in our patient, the decision was made to proceed with transplant prior to her becoming dialysis dependent, in part to avoid these comorbidities and also so she could undergo nephrectomy prior to the development of Wilms' tumor in the remaining kidney, which would have precluded her from transplant for at least 2 years and significantly complicated therapy.