

Jesse Hennum, MD & M. Cristina Pacheco, MD
Case Presentation:
"When vigilance is not enough: A 5-year-old girl with back pain and fever"

Viewing Time

The program will take up to one hour to complete.

Target Audience

This program is designed for primary care physicians.

Other health care professionals working with patients and their families may also find this program of interest.

Faculty Disclosure

It is the policy of Children's Hospitals and Clinics of Minnesota to ensure balance, independence, objectivity, and scientific rigor in all its educational programs. Our faculty have been asked to disclose to our program audience any real or apparent conflicts of interest related to the content of their presentation. They have also been requested to let you know when any product mentioned in their presentation is not labeled for the use under discussion or is still under investigation.

Faculty Disclosure

Jesse Hennum, MD, and M. Cristina Pacheco, MD, have disclosed no actual or potential conflict of interest in relation to this educational activity.

During this educational activity **Drs. Hennum and Pacheco** will not be discussing the use of any commercial or investigational product not approved for any purpose by the FDA.

Case Presentation:
**"When vigilance is not enough:
A 5-year-old girl with back pain and fever"**

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Pathologist
Children's Hospitals and Clinics of Minnesota

Case Presentation:
**"When vigilance is not enough:
A 5-year-old girl with back pain and fever"**

A lecture presenting a case that was seen in a local community hospital, discussing the workup and diagnosis of the case and reviewing the literature pertinent to the discussion.

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Program Objectives

Upon completion of this program, participants should be able to:

- Inform participants of unusual presentations of common pediatric problems.
- Identify specific difficulties in the diagnosis of specific problems.
- Discuss potential difficulties in the management of pediatric problems.

Disclaimer

Children's Hospitals and Clinics of Minnesota accepts no responsibility for the materials presented through these Grand Rounds seminars. Each professional host assumes all responsibility for maintaining confidentiality or obtaining authorization, in accordance with all applicable laws.

Accreditation


Children's Hospitals and Clinics of Minnesota is accredited by the Minnesota Medical Association to provide continuing medical education for physicians. Children's Hospitals and Clinics of Minnesota designates this educational activity for a maximum of 1 AMA PRA Category 1 Credits™ toward the AMA Physician's Recognition Award. Each physician should only claim those credits that he/she actually spent in the activity.


Receiving CME Credit

To receive CME credit you must view the entire program and complete the evaluation form at the end.

When vigilance is not enough...

Grand Rounds
Children's Hospitals & Clinics
Feb 5 & 7, 2008

Jesse Hennum, MD 
Chief Resident

Cristina Pacheco, MD 
Pathologist



In the winter, a fall...

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 Case Presentation:
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Emergency Dept: 5am

- 5 year old previously healthy girl
- CC: Back pain
- "Daddy pushed me down because he was mad at me."
- Yesterday her father accidentally "clotheslined" her while trying to get her to calm down (she was running around the house). She fell onto her buttocks, landing onto the wood floor.
- Started complaining of back pain 2 hours later; pain has been unrelenting and she refused to get out of bed today

Further history

- Developed a temperature of 104 F last night, fever persisted overnight and into this morning despite antipyretics
- Also, 3 days ago she fell out of a chair and seemed to have a greater than expected amount of pain for a few hours in her legs.
- Back pain is worsened by bearing weight, moving back or moving lower extremities
- Denies any weakness or sensory changes
- No bowel movement for 2 days, no urine since night before

Further history

- PMH: Physiologic jaundice at birth requiring phototherapy. Healthy, normal development and growth. Immunizations: Has not received 5 year old shots, otherwise up-to-date.
- SH: Lives in suburban Twin Cities with parents. No sick contacts. No travel history. Not in daycare or school.
- FH: Paternal GF with diabetes, Maternal aunt with multiple sclerosis

Physical Exam

- HR 140, T 99.1F, RR 26, BP 112/76 WT 17.5 kg
- General: Well-appearing, smiling, comfortable, talkative, but refuses to move, laying flat on her back
- HEENT: Atraumatic, Sclera nonicteric, oropharynx clear
- Neck: Supple
- Lungs: Clear to auscultation
- Heart: Regular rate and rhythm
- Abdomen: non tender, no hepatosplenomegaly
- Skin: No petechiae or bruising
- Back: Generalized tenderness, no CVA tenderness, no point tenderness.
- Neuro: Strength 5/5 feet and toes, does not move legs otherwise. DTR 2+ at patella. Babinski bilaterally downgoing
- External anus: Normal

Differential Diagnosis

A 5 year old girl with severe back pain and fever

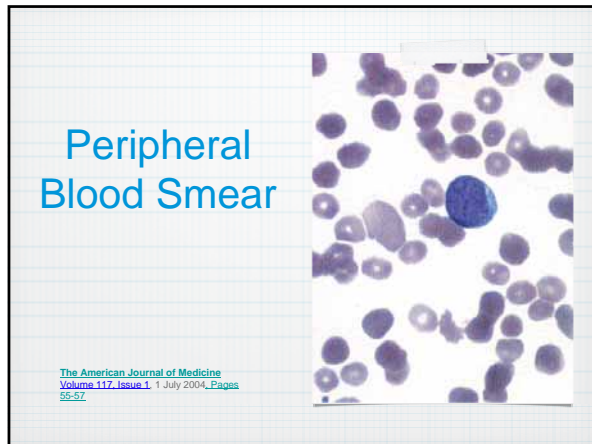
- Traumatic
 - Spondylolysis
 - Spondylolisthesis
 - Disk degeneration
 - Vertebral compression fracture
 - Muscular strain
- Structural
 - Scoliosis
 - Scheuermann disease
- Neoplastic
 - Osteoid osteoma
 - Leukemia
 - Lymphoma
 - Metastatic tumor
 - Neurofibroma
 - Osteoblastoma
 - Aneurysmal bone cyst
- Referred pain
 - Pyelonephritis
 - Pneumonia
 - Pancreatitis
 - Cholecystitis
- Infectious
 - Diskitis
 - Vertebral osteomyelitis
 - Epidural abscess
 - Paraspinous abscess
 - Appendicitis (retrocecal)
 - Psoas abscess
- Rheumatologic
 - Ankylosing spondylitis
 - Reactive arthritis
 - Juvenile rheumatoid arthritis

Lab/Radiology results

- Plain films of thoracic, lumbar spine, sacrum and coccyx; MRI of cervical, thoracic, and lumbar spine are all within normal limits

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2.8	8.0	7.9												
22.6														
133	97	13												
3.7	26	0.4												
MCV 91 RDW 14.8														
Neut 25% Band 7% Lymph 62% Mono 1% Blasts 5%														
Bilirubin 0.4 CRP 39 Albumin 3.5 Protein 7.1														
Alk Ph 107 AST 38 ALT 25 LDH 386 ESR														
111														
UA: SG 1.020, LE neg, Nitrite neg, WBC 2-5/hpf, RBC 0, Many amorphous urate crystals														

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Back pain & Leukemia?

- Musculoskeletal pain is often a presenting sign of leukemia or other cancers.
- Studies have demonstrated 0.25-1% of musculoskeletal complaints of children evaluated in clinic are actually neoplasms.
- ALL is the most common cancer that presents with musculoskeletal complaints.
- Characteristics that are concerning:
 - Predominantly nocturnal pain
 - Fever (the most predominant systemic symptom)
 - Hepatomegaly/splenomegaly
- CBC may be normal at the onset of symptoms.

Sao Paulo Med. J. 2005. 123(1) J Pediatr. 1990;117(2 Pt 1):233-7

Oncology Consult

- 5 year old girl with acute onset of back pain, pancytopenia with peripheral blasts
- Plan for bone marrow biopsy and aspiration, admission for acute leukemia
- Start Cefazidime

A photograph of a pink flower with green leaves, likely a Hibiscus, used as a decorative element.

Hospital Day #1-2

- Bone Marrow aspiration and biopsy performed under sedation.
- IV fluids started with urine alkalization.
- IV ceftazidime begun, blood, urine cultures -> negative
- Bone marrow reveals: Precursor B-lymphoblastic leukemia
 - Flow Cytometry- CD10, CD19, and Tdt positive
 - Bone marrow 84.6% blasts
 - 10% overall cellularity
 - Cytogenetics: Gains of Ch 4,6,10,14,18,21
 - "High hyperdiploid ALL with trisomy 4 and 10 is associated with a good prognosis"
- Port-a-cath placed on hospital day #2

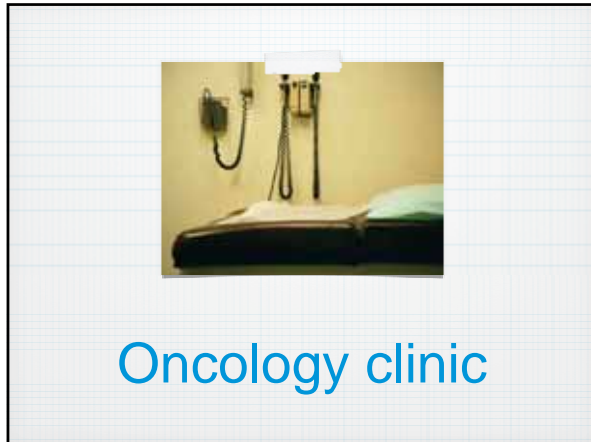
Hospital Day #3-6

- Classified as "standard risk" pre-B cell ALL
- Induction therapy begins with intrathecal cytarabine, vincristine, PEG-asparaginase and dexamethasone
- Ranitidine for ulcer prophylaxis
- Trimethoprim/Sulfamethoxazole twice weekly

Hospital Discharge

- The patient had progressive improvement in back and leg pain and was able to ambulate normally.
- No fevers since admission. Blood cultures remained negative. Cefazidime discontinued at discharge.
- Chemotherapy administered without complication.
- Discharged on hospital day# 6; Day 4 of induction chemotherapy.
- Medications: Dexamethasone, Trimethoprim-Sulfamethoxazole (Monday and Tuesday), Ranitidine BID, Miralax and ondansetron prn.
- Discharge note "Follow-up in 4 days for Day 8 evaluation. Needs to find primary care physician."

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Oncology clinic #1

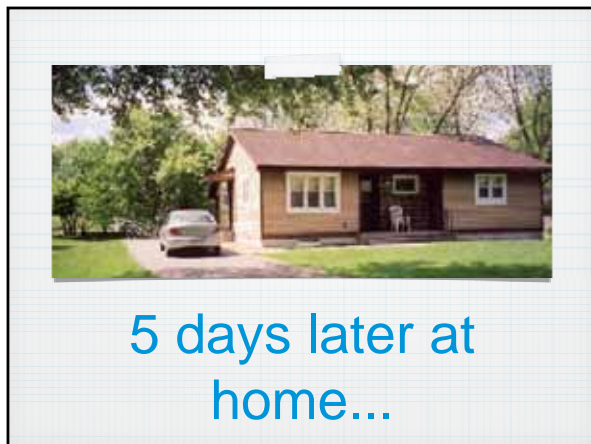
- Since hospital discharge: No fevers, occasional "tummy-aches," constipation improving with Mira-Lax, decreased appetite.
- WBC 1,300 (M3% L 49%, N 48% - ANC 624); Hgb 10.1; Platelets 94,000.
- Lumbar puncture (CSF negative cytology) and bone marrow aspiration (1.4% blasts, 30% cellularity) done for day # 8 evaluation.
- Vincristine and intrathecal methotrexate given.
- Continue dexamethasone at home for 28 days total.
- Continue TMP/SMX and ranitidine

Oncology clinic #2

- Day 15 of induction chemotherapy.
- Pt is reportedly doing well.
- WBC 1,100; Hgb 8.7; Platelets 127,000
- Vincristine given.
- Continue dexamethasone at home for 28 days total.

Oncology clinic #3

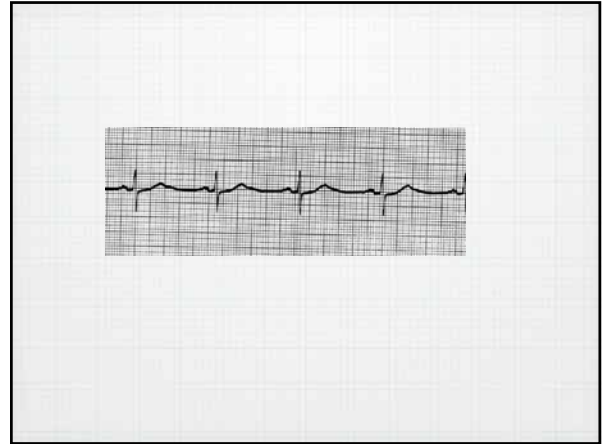
- Day 22 of induction chemotherapy.
- Now has diarrhea with intermittent abdominal pain. No fever, chills or vomiting. No chest pain, cough, or shortness of breath.
- WBC 1,000 (ANC 524); Hgb 9.3; Platelets 89,000.
- Vincristine given today. Continue dexamethasone.
- Return in 1 week. Loperamide prn for diarrhea.



Phone call to oncologist

- **21:08** Mother reports: Pt is sick. Started night before. Has been breathing faster and harder and now child has developed temp to 102.7. Also has had tan-colored stools with blood on TP. No vomiting. Oncologist recommends prompt visit to ED, informs ED of impending arrival.
- **22:50** No sign of patient. Oncologist calls family for status. They plan to leave soon, dad is filling up the tires (they had a flat). Patient is having a lot of back pain, but walking and talking.
- **23:50** Patient arrives in the ED.

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Emergency Department

- 01:10 HR 52. O2 sat: *Undetectable*. Pulses absent.
- Chest compressions initiated. PICU staff arrives.
- 01:15 PEA. Labs: pH 7.33, pCO2 17, K 3.8, AG 21.
- Atropine (0.2 mg/kg) and epinephrine (0.1mg/kg) given. CPR continues.
- 01:20 Bagging difficult- air leak detected.
- Endotracheal tube changed to cuffed tube. PRBC 15 mL/kg and D15 32mL given. Epinephrine dose repeated.
- 01:23 Asystole. Compressions continue.
- Epinephrine drip ordered and bolus repeated.
- 01:30-40 Albumin, bicarb, PRBCs. Epinephrine drip started.

Emergency Department

- 01:40 Left radial arterial line placed. Transducer readings flat.
- 01:45 Transcutaneous pacing with sync attempted, unable to capture rhythm. Epinephrine continuous infusion started.
- 01:50 Continued boluses of bicarbonate, epinephrine, calcium chloride
- 01:55 Cardiac ultrasound confirms no cardiac motion.
- 02:01 Labs: pH <6.79, pCO2 113, PO2 < 24, Potassium 7.2
- 02:04 Resuscitative efforts ceased.

Sepsis!!

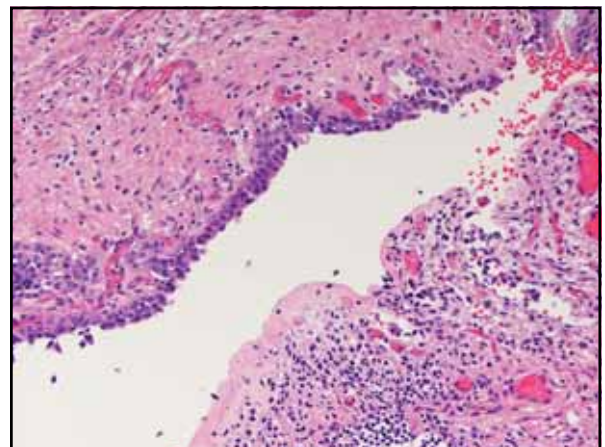
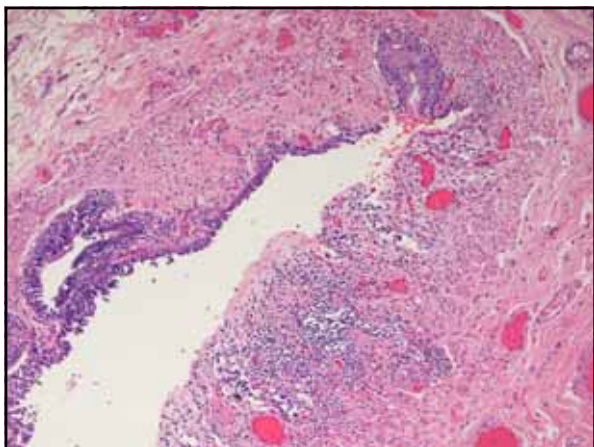
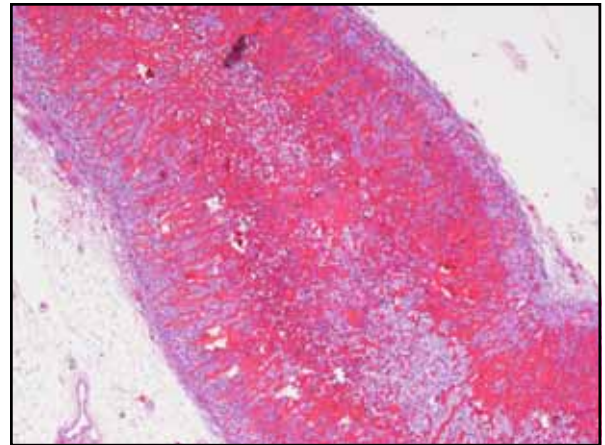
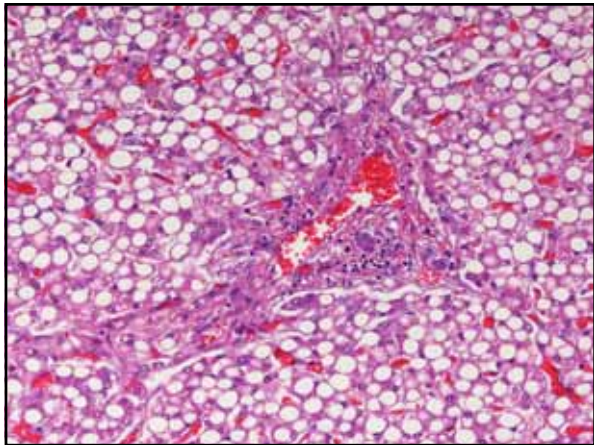
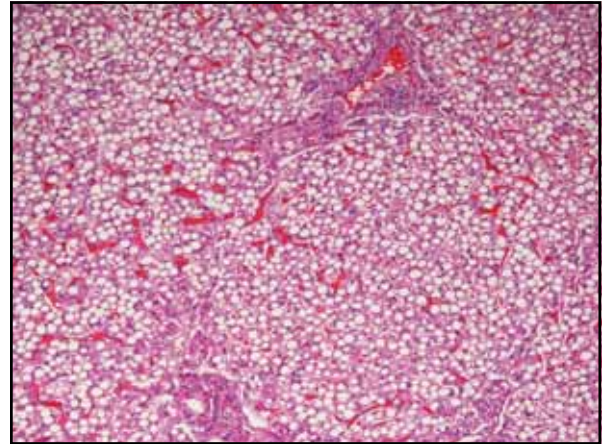
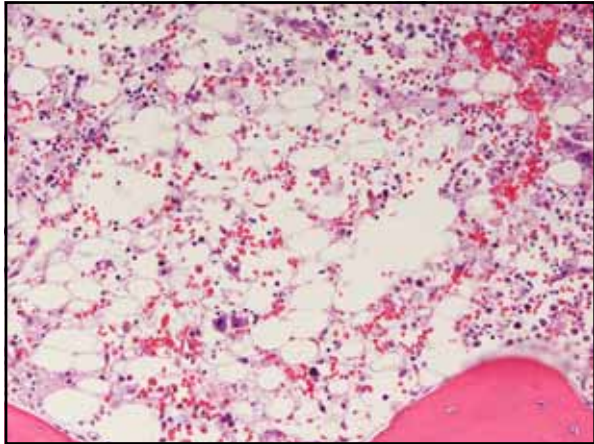
Within five hours, blood cultures were reported to be growing gram negative rods, ultimately identified as *escherichia coli*.

A scanning electron micrograph (SEM) showing a cluster of Escherichia coli bacteria. The bacteria are rod-shaped and appear to be attached to a textured surface.

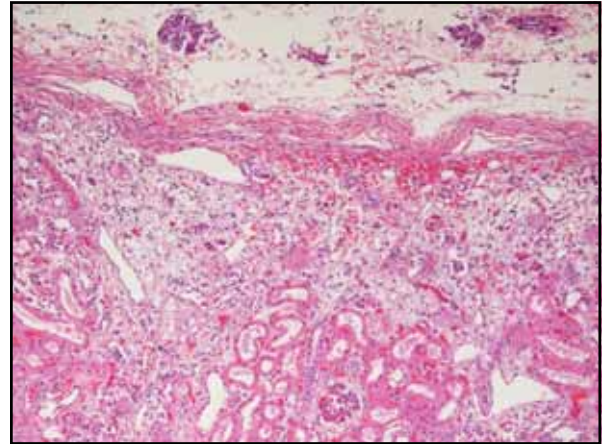
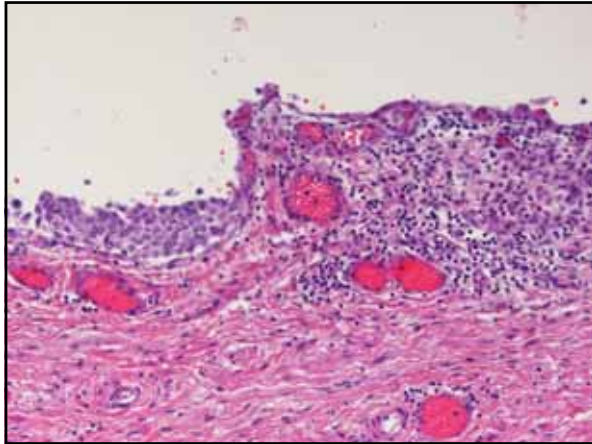
Autopsy examination

Dr. Pacheco

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Final Anatomic Diagnosis

- 5 year old female with recently diagnosed precursor B ALL:
 - E. coli sepsis (premortem blood culture positive)
 - Mild chronic cystitis
 - Subcapsular segmental sclerosis suggestive of chronic reflux
 - Erosion of surface anal mucosa with chronic inflammation and gross erythema
 - Marked hepatomegaly (wt 1228 gm vs 596 expected)
 - Severe macro and micro vesicular steatosis
 - Bilateral pulmonary congestion, right lung greater than left
 - Bilateral adrenal hemorrhage
 - Marked thymic atrophy
 - Hypoplastic marrow, variable cellularity (10-30%)
 - No evidence of residual leukemia
- Death in this case is due to E. coli sepsis. The source of sepsis could be due to bacterial seeding from the anal erosions due to diarrhea or from chronic subclinical reflux.

Taking a closer look...

Could this have been prevented?

- 98% of pediatric ALL patients survive to induction of remission.
- Overall, 90% of young children will achieve clinical cure of ALL (5-year survival).
- 96-99% of patients survive febrile neutropenia.
- While septic shock due to gram negative organisms had a 97% mortality in the 1960s...
- ...today, up to 91% of patients survive.

Journal of Clinical Oncology, Vol 24, No 36 (December 20), 2006: pp. 5750-5762

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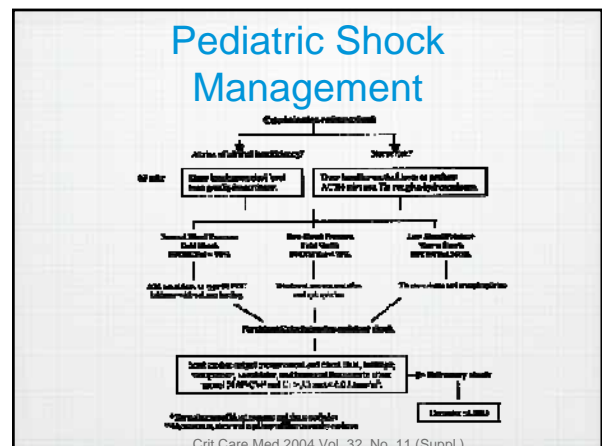
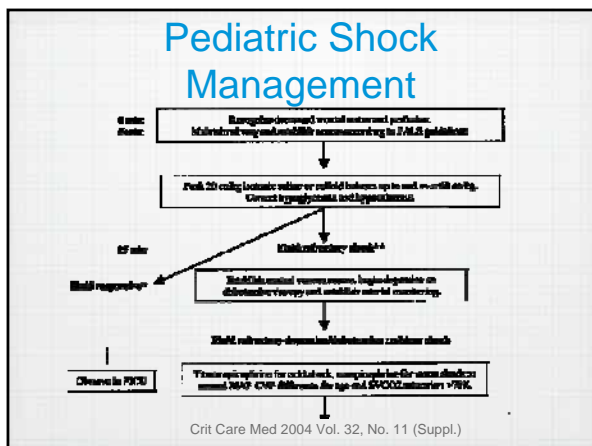
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Early Goal-Directed Therapy of Pediatric Septic Shock

- Sepsis is defined as the Systemic Inflammatory Response Syndrome (SIRS) in the presence of proven or suspected infection.
- Tissue oxygen demand is high during sepsis. When oxygen delivery does not meet demand, tissue hypoxia develops.
- Early recognition and treatment of septic shock has been shown to dramatically improve mortality rates (38 vs 9% in one study)
- Treatment involves improving oxygen delivery through cardiac output and maximizing arterial oxygen content through ventilation and transfusion, temp and pH management.
- Goal-directed therapy involves monitoring of oxygen consumption (often mixed venous oxygen saturation).

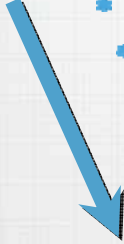
Crit Care Med 2002; 30:1365-1378 Israeli Journal of Emergency Medicine. 2007. 7(2):5-10.



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Pediatric Shock Management

- Access (ABC's)
- Saline (Ca Glu)
- Dopamine/Dobutamine
- Epinephrine/Norepinephrine
- Adrenal insufficiency
- Dilator (vasodilator or PDE-inhibitor)



Crit Care Med 2004 Vol. 32, No. 11 (Suppl.)


Summary

- Musculoskeletal complaints may be secondary to malignancies, especially leukemia.
- Induction chemotherapy remains highly toxic, and vigilance to adverse reactions and complications probably explains the low mortality rate.
- Early recognition and treatment of septic shock improves outcomes. Follow the guidelines.

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