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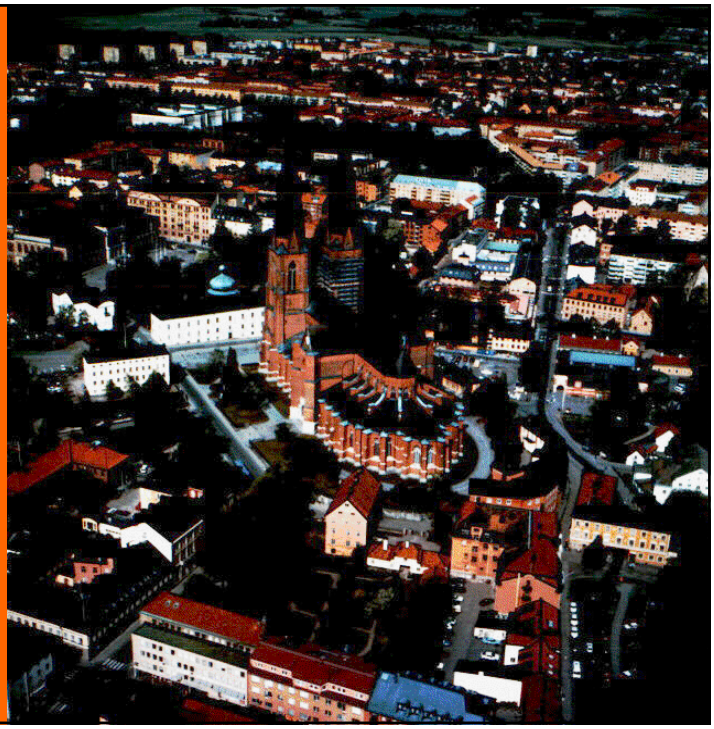


Cancer Pain -

Pain in Children with Cancer

- Past
- Present
- Future

- April 2007 Skien

Pain in pediatric oncology

- PAST
  - 30-40 years ago almost all children with cancer died; today 75-80% survive
  - No central lines/ports - more pain and anxiety
  - Supportive care less developed, e.g. pain management, antiemetic therapy, antibiotics, etc.
  - However, treatments were less intensive; less adverse effects and treatment related pain but more cancer pain

Pain in children with cancer

- PRESENT
  - Diagnostics
    - Epidemiology & etiology
  - Treatment
    - Special oncological cases

Pain still common in children with cancer

- Pain as the presenting symptom
  - 62% — Miser A et al. Pain 1987;29:85-90
- Pain at diagnosis
  - 78% — Miser A et al. Pain 1987;29:85-90
  - 49% — Ljungman G et al. Pediatr Hematol Oncol 2000;17(3):211-21
- Pain in cross sectional studies
  - 50% of inpatients report pain (33%Ljungman G - 85%Collins J)
  - 35 % of outpatients report pain
  - Risk factors: reduced physical condition, in-patient status, co-morbidity; surprisingly neither disease state nor type of malignancy.

    Zernikow B et al. Eur J Pain 2005;9:395-406

- Pain is a symptom much feared by children and parents;

  the most feared for younger children.

Lansky SB et al. Pizzo et Poplack eds. Pediatric Oncology 1989:1127-39

Enskär K et al. J Pediatr Oncol Nurs 1997;14:18-26

The pain experience complex in children with cancer

- Cancer pain - threat of relapse/death
- Increased fear - anxiety
- Increased pain

The Measurement of Symptoms in Children with Cancer; MSAS 10-18

Collins J J Pain Symptom Manage 2000;19:363-377

- Pain compared to other symptoms
- Determines symptom prevalence, characteristics, and distress in children with cancer during the previous week
- Most prevalent symptoms (%)
  - lack of energy 49.7
  - pain 49.1 (most common S in inpatients 84.4, outp 35.1)
  - drowsiness 48.4
  - nausea 44.7
  - cough 40.7 etc.
- Of symptoms prevalent in >35%; highest distress (% quite a bit to very much)
  - feeling sad 39.5
  - pain 39.1
  - nausea 36.6
  - lack of appetite 35.8
  - feeling irritable 34.7

MSAS 10-18

Collins J J Pain Symptom Manage 2000;19:363-377

- Multidimensional assessment
- Pain

	Prevalence	Intensity moderate to very severe	Frequency a lot to almost always	Distress quite a bit to very much
Total	49.1	80.8	35.9	39.1
Inp	84.4	86.8		52.8
Outp	35.1	75		26.3

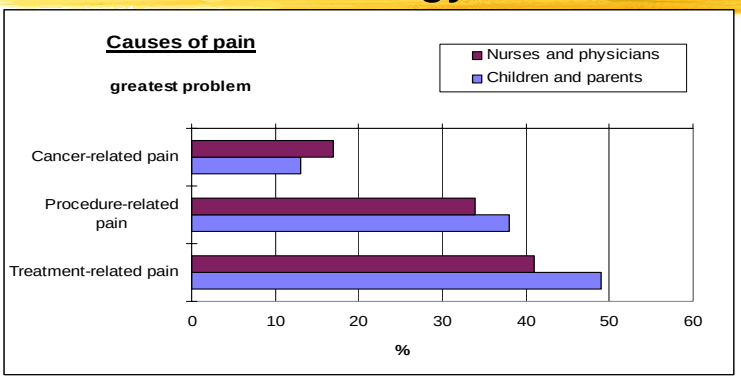
The Measurement of Symptoms in Children with Cancer; MSAS 7-10

Collins J J Pain Symptom Manage 2002;23;10-16

- Multidimensional assessment

		Degree when symptom was present		
%	Prevalence	Intensity a lot	Frequency almost all the time	Distress very much
pain	32.4	56	54	37
tiredness	35.6	51	64	5
insomnia	31.1	-		39
itch	25.0	56	54	38
appetite↓	22.3	-	52	12
worry	20.1	43	43	30
nausea	13.4	-	45	65
sadness	10.1	60	53	50

Pain in children with cancer - Etiology



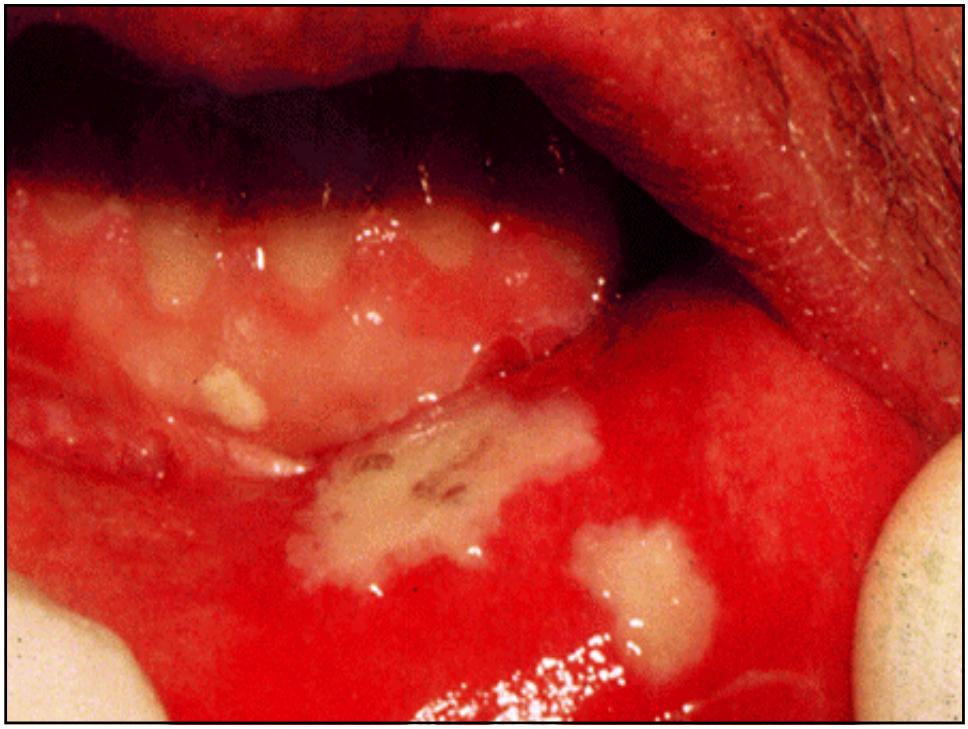
Ljungman G et al. Acta Paediatr1999;88:623-630
Ljungman G et al. Pain 1996;68(2,3):385-394

Also shown by:
McGrath PJ et al. J Psychosoc Oncol 1990;8(2/3):109-124
Elliott S et al. Clin J Pain 1991;7:263-268
Zernikow B et al. Eur J Pain 2005;9:395-406

Pain in children with cancer - Etiology

- Treatment related pain
  - mucositis
  - neuropathic leg- and jaw pain and intestinal neuropathy /constipation
    - vinca-alkaloids, ifosfamide, phantom limb pain
  - post op
  - infection with inflammation
  - epigastric pain
  -

Ljungman G et al. Pain 1996;68(2,3):385-394
Ljungman G et al. Acta Paediatr 1999;88:623-630



Clinical History: 15-year-old female with neutropenia and right-sided abdominal pain and diarrhea.

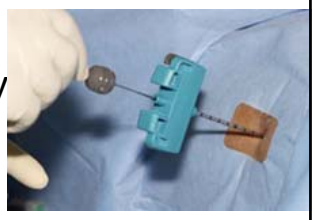
Findings: CT scan demonstrates bowel wall thickening and enhancement involving the cecum and ascending colon.

Diagnosis: Typhlitis.

Discussion: Typhlitis is a necrotizing inflammation of the colon and ileum seen in neutropenic patients. The cecum is the most frequently involved. The pain in the right lower quadrant may mimic appendicitis.

Pain in children with cancer - Etiology

- Procedure related pain
  - Port needle, iv sampling & cannulation, finger pricks
  - LP
  - bone marrow aspiration/biopsy
  - fine needle biopsy
  - pleurocentesis
  - brachytherapy, etc.



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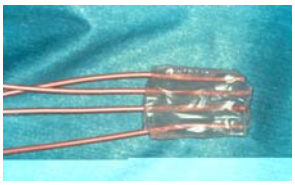
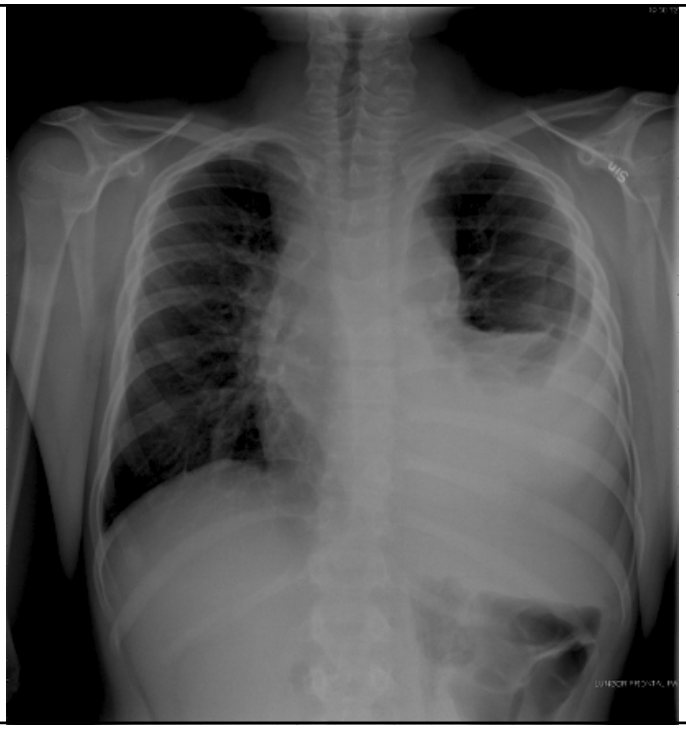


Brachytherapy

Pain in children with cancer - Etiology

- Cancer related pain
  - skeletal pain; BM- or skeletal involvement
  - inflammatory pain caused by tumor release of cytokines
  - pain caused by involvement of soft tissue, distension of organs, obstruction of the intestine, etc.
  - pain caused by invasion/compression of CNS or PNS
    - raised ICP
    - spinal cord compression
    - polyneuropathies



Control of Severe Pain in Children with Terminal Malignancy

Collins J et al. J Pediatr 1995;126:653-7

- Identified characteristics of patients who required massive opioid infusions (>3 mg/kg/h (3.8-518); 12 in Boston 1989-1993)
  - The need for massive opioid infusions for 11 of 12 patients - solid tumors metastatic to:
    - spinal nerve root
    - nerve plexus
    - large peripheral nerve
    - spinal chord compression
    - PAG
    - 4/12 satisfactory analgesia; 3/12 spinal/epidural; 5/12 sedation

Regional anesthesia for pain associated with terminal pediatric malignancy

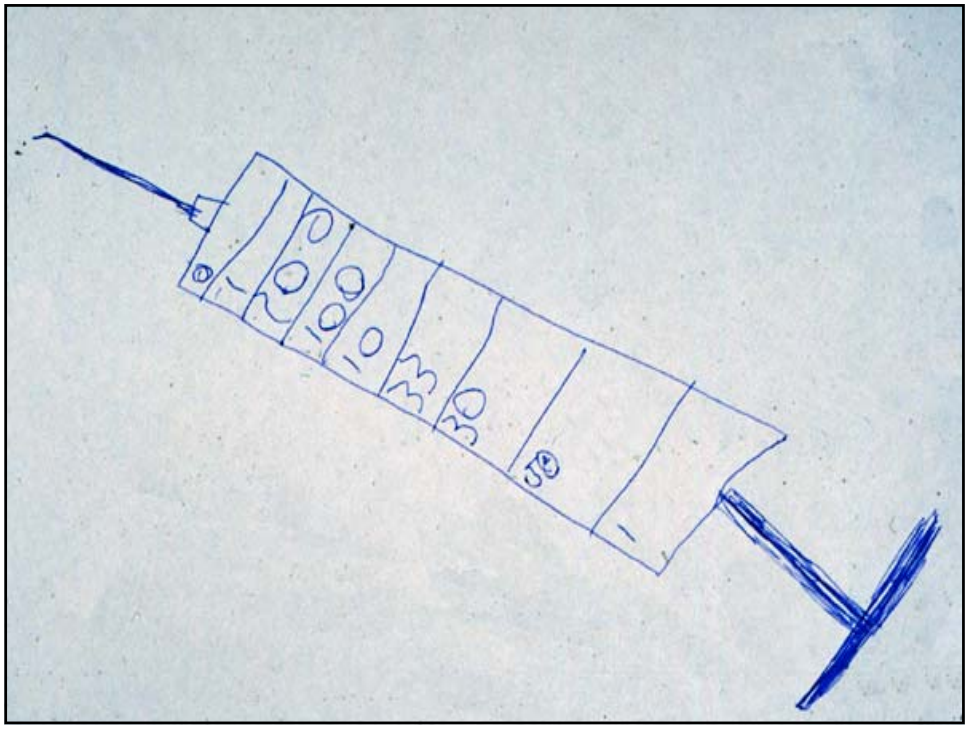
Collins J et al. Pain 1996;65:63-69

- Identified characteristics of patients who required regional anesthesia for terminal pain (11 in Boston 1986-1994)
  - Indications
    - limiting side effects of opioids
    - neuropathic pain unresponsive to massive opioid infusions
    - analgesia for thoracocenteses for pleural effusion
  - Analgesia satisfactory in all cases
  - 5 patients nursed at home with epidural or subarachnoid infusions

Pain in palliative end-of-life care

Wolfe et al. N Engl J Med. 2000;342:326-33.

- pain common symptom
- 89% suffered a lot or a great deal from at least one symptom in their last month of life, most commonly pain, fatigue, or dyspnea
- treatment successful in
  - 27% pain
  - 16% dyspnea



The analgesic ladder for cancer pain treatment (WHO)

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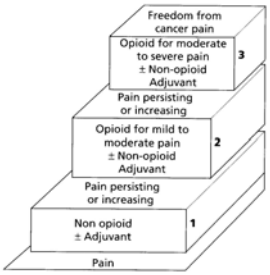


☒Paracetamol

- 15 mg/kg x 4-6 po
- 20 mg/kg x 4-6 pr

☒NSAIDs

- ASA >3 år 10-15 mg/kg x 6
- Ibuprofen 5-10 mg/kg x 3-4
- Naproxen 10-15 mg/kg x 2
- Ketoprofen 1- 2 mg/kg x 3-4 iv/po
- Naproxen 5 mg /kg x 2-3 po
- Diclophenac 1 mg/kg x 3-4 iv/po

The analgesic ladder for cancer pain treatment (WHO)

- 2
  - Codeine 0.5-1 mg/kg x 4-6
    - Fixed combination with paracetamol often ok
  - Tramadol 1-2 mg/kg x 3 iv/po
    - triple action: µ1-opioid receptor agonist + increases serotoninergic and noradrenergic tone in descending inhibitory tracts
    - potentially effective against neuropathic pain
- 3
  - Opioids
    - morphine (”gold standard”) 0.2-0.5 mg/kg po; 0.1 mg/kg iv
    - oxycodone
    - hydromorphone
    - fentanyl
    - methadone

The analgesic ladder for cancer pain treatment (WHO)

- Zernikow B et al. Eur J Pain 2005 Oct 19 Epub ahed of print.
- German multi-center quality improvement study 224 patients; 2265 treatment days
- WHO guidelines closely followed
- Seemed to provide effective analgesia
- However, in this study no evidence that combination of opiod with non-opioid is more effective; selection bias cannot be excluded.

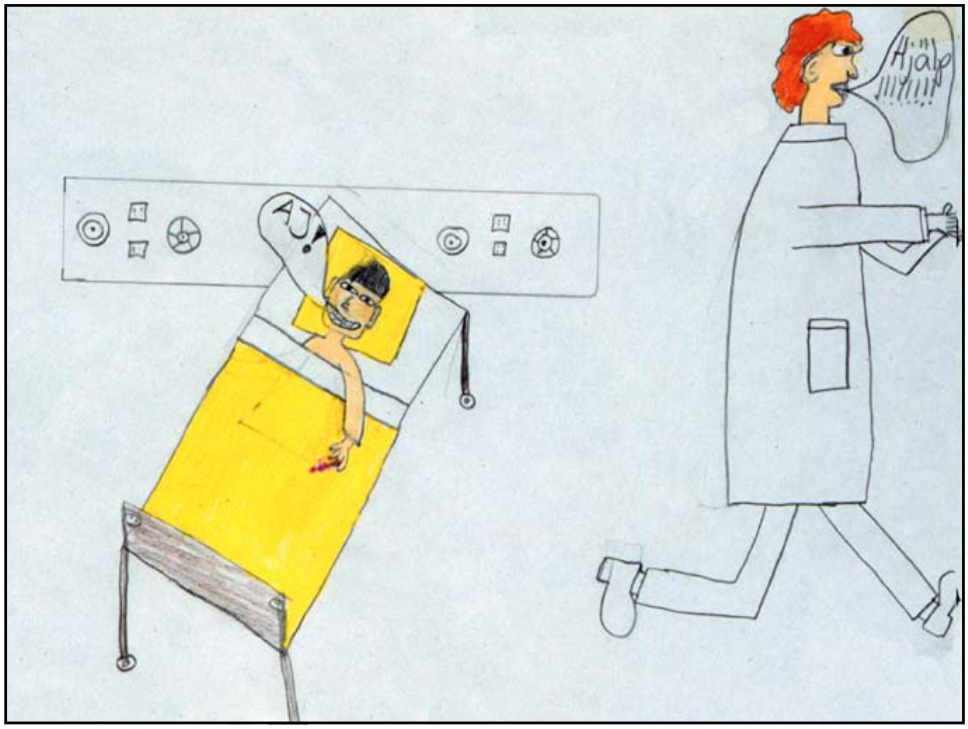
When morphine is not sufficient

- Opioid rotation — oxycodon, ketobemidon
- Development of tolerance
- Side-effects, pruritus, nausea, constipation, etc. — antiemetics, laxantives, naloxone
- Renal failure
- Neuropathic pain — low dose ketamine + reduction of opioid

Low dose ketamine

- Alternative when
  - neuropathic component
  - development of tolerance against opioids
    - often radical improvement in intractable terminal pain
    - NMDA receptor antagonist
    - 0.1-0.2 mg/kg
    - often combined with a benzodiazepine
    - reduction of opioids 50% initially

– Fine PG. J Pain Symptom Manage. 1999;17(4):296-300.



Treatment - special cases in pediatric oncology

- Steroids
  - reduce swelling
  - antileukemic & antilymphatic effect
  - increased well being
- Radiation
  - reduced tumor/distension
  - skeletal metastases
- Chemoth.
  - reduced tumor/distension
- NSAIDs
  - skeletal metastases

Non-pharmacological treatment

- TENS
- (Acupuncture)
- Massage

- Education / information
- Relaxation
- Distraction
- Hypnosis

Treatment - neuropathic pain

- TENS

- Antidepressants amitriptylin
- Anticonvulsants gabapentin, carbamazepine

- Neveblocks
- Spinal/epidural/intrathekal adm.
- Neurosurgery
- Dorsal column stimulation

Pain in pediatric oncology

- FUTURE
  - New targeted therapies: immunological, antiangiogenic, enzyme inhibitors; less adverse effects
  - More individualized or ”tailored” therapies
  - Improved practices for pain diagnostics and treatment
  - Hopefully less pain

Conclusions

- Still a lot of pain and suffering in pediatric oncology
- Most of the pain inflicted by treatment and procedures
- Obligation to reduce this pain and suffering as much as possible

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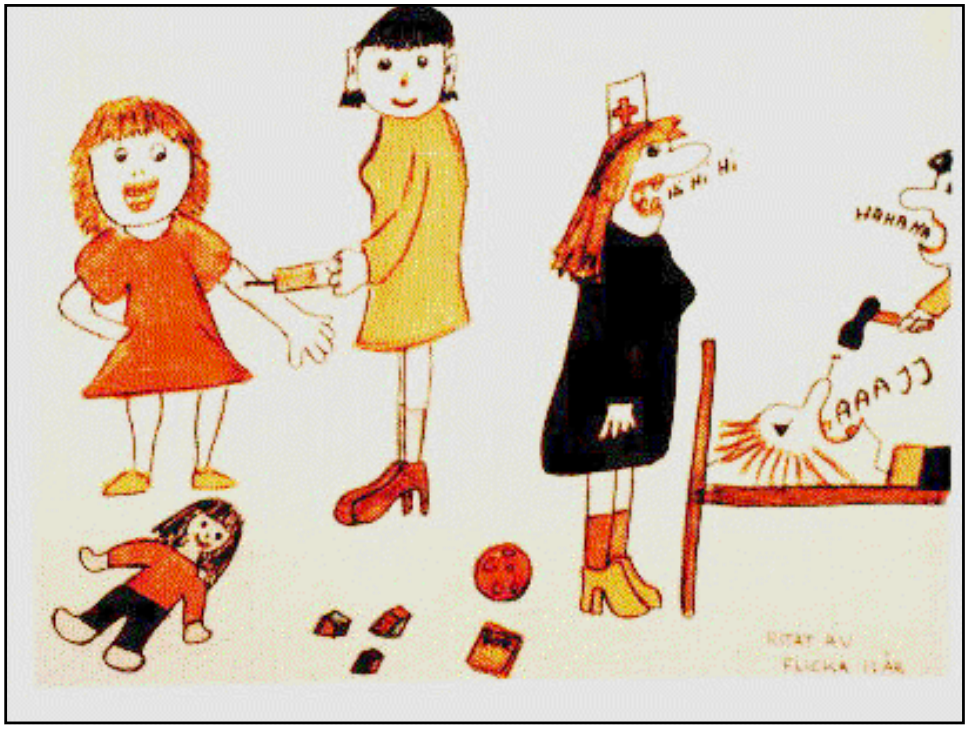
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