AGENDA

- Lecture 1 – Bleeding disorders
- Lecture 2 – Neutropenia and Thrombocytopenia

For each of these conditions the following should be addressed
- Clinical presentation
- Initial investigations
- Initial management
- Potential complications
- Therapeutic options
- Indications for referral

Investigations

- Screening investigations
- FBE
- APTT
- PT / INR
- Fibrinogen
- TCT

- PFA – 100
- Blood group
- Von Willebrand’s screen
- Factor XIII

Haemophilia

- What haemophilia was.
- What haemophilia is.
- What are the main problems with haemophilia today.
Haemophilia

- Carrier Woman
- Healthy Man
- Carrier Girl
- Healthy Girl
- Haemophilic Boy
- Healthy Boy

Haemophilia – World Perspective
- An estimated 250,000 patients in the world population.
- Only about 50,000 receive specific treatment.
- Australia has approximately 1800 patients with haemophilia

Haemophilia Management 2008
- Clotting factor replacement is the cornerstone of treatment
- Recent (October 2004) Federal and State Government consensus to fund recombinant FVIII and FIX for all patients with haemophilia in Australia
- Clotting factor needs to be given directly into the veins
- Factor replacement can be given for treatment AND prevention (prophylaxis) of bleeds

Haemophilia Prophylaxis
- Prophylaxis
  - Regular infusions of (recombinant) clotting factor concentrate to prevent joint and muscle bleeds
  - Majority of children begin prophylaxis after the first or second joint bleed
  - The use of early prophylaxis has significantly reduced the complication of joint disease
FVIII and FIX Inhibitors

- Most serious complication
- FVIII or FIX proteins recognised as “foreign”
- Stimulating immune response and formation of IgG
- Occurs in 30% patients severe haemophilia A and 5% patients haemophilia B

Haemophilia 2008

- Whilst inhibitors in haemophilia are still a major problem, the modern management of haemophilia prevents the traditional complications of joint disease
- The availability of recombinant clotting factor concentrate limits the risk of transfusion transmitted viral disease

Structure of Haemophilia Care in Australia

- National Blood Authority provides funds for clotting factor concentrate
  - 30% state / 70% federal
- Management run through haemophilia individual treatment centers
Diagnosis ➔ Transition

< 12 months of age
- Addressing psychological impact of X linked recessive disorder

12 – 24 months of age
- Onset of joint bleeds

2 years – 5 years
- Commencement of home based therapy

> 5 years
- Are boys with hemophilia as active, fit and happy as their peers?

Modern Morbidities of Haemophilia
- Impact on family functioning
- Support of home based therapy
  - Complications of central venous lines
- Activity levels
  - Bone density
  - Maintenance of Healthy Weight
- Maximizing Education Potential

Virchow’s Triad in Haemophilia
- Vessel Wall
- Thrombosis
- Blood Flow
Activity Levels

- In the modern era of haemophilia management, are boys with haemophilia as active as their peers?
- What are the implications of reduced levels of activity in boys with haemophilia?
  - Bone density
  - Maintenance of Healthy Weight

Bone Density

- Importance of musculo-skeletal integrity (including maintaining adequate bone density)
- Patients with haemophilia may be at risk of developing reduced bone density
  - Reduced weight bearing exercise
  - Prolonged periods of immobility

Bone Density

- Maintenance of Healthy Weight
  - Obesity is a major public health problem
    - Greater access to calorie dense foods
    - Reduced activity (greater access to sedentary pastimes)
Risk Factors

Maintenance of Healthy Weight

- Are boys with haemophilia more prone to becoming overweight?
  - Predisposed to becoming overweight on the basis of reduced physical activity

Maintenance of Healthy Weight in Haemophilia

- Implications for patients with haemophilia and obesity significant
  - Complicated venous access
  - Increased clotting factor usage
  - Exacerbation of established joint disease

Changing Morbidities of Haemophilia

- As a result of the major advances in haemophilia care there is the opportunity to focus on a different range of co-morbidities

Von Willebrand disease

- Type 1
  - 80%
  - Mild to moderate quantitative reductions in VWF levels
- Type 2
  - 20%
  - Qualitative defects
- Type 3
  - Virtual deficiency of VWF
Type 1 VWD
- Prospective studies have suggested 1% of population affected
- Tertiary referral centres 1 in 10,000

Type 1 VWD
- VWD is an inherited disease that causes bleeding and type 1 VWD is a quantitative deficiency of VWF.

Type 1 VWD (ISTH)
- All of the following criteria must be met
  - A significant history of mucocutaneous bleeding
  - Laboratory tests compatible with type 1 VWD
  - Either a positive family history or an appropriate genetic mutation

Von Willebrand Disease in the Neonate
- VWF:Ag and CBA increased in the neonatal population
- Reach adult levels by 6 months of age

Royal Children’s Hospital VWD
- Vast majority of patients have Type 1 VWD
  - Type 2 VWD
    - ? 4 patients
  - Type 3 VWD
    - 1 patient

Royal Children’s Hospital Type 1 VWD
- Patients referred from surgical services, adolescent gynaecology and external general practitioners
- Routine investigations
- Family testing performed as routine
- DDAVP challenge performed as routine
**DDAVP challenge**
- Relative contraindication in children less than 2 years of age
- Thirty minute infusion of 0.3 mcg / kg (maximum 20 mcg)
- VWF:Ag at 30 minutes, 1 hour and 4 hours
- Restriction of fluid input over 12 hours following infusion
  - One patient (10 months of age) developed seizures secondary to hyponatremia following treatment with DDAVP

**Management of VWD**
- Non transfusional therapies
  - DDAVP
    - Sustain increase in FVIII / VWF 8 – 10 hours
    - Given 12 – 24 hourly depending on documented response
    - Tachyphylaxis after 4 doses
  - Antifibrinolytics
- Transfusional therapies
  - BIOSTATE (AHF)

**Biostate**
- Plasma derived FVIII / VWF
  - Ratio of FVIII : VWF of 2:3 (product insert suggests Biostate ratio of 1:2)
  - 20 000 units on stock at all times at RCH

**Thrombocytopenia**
- Inherited
- Acquired (ITP)

**Case**
- 3 week old male infant presenting with marked thrombocytopenia in the setting of possible vascular tumour of lower limb
- Antenatal history
  - Largely unremarkable
  - Mother on aspirin for recurrent miscarriages
  - Consanguineous parents

**Case**
- Family history
  - No significant history of bleeding, known platelet disorders
  - Youngest of five children
  - Previous six miscarriages
Case

- Presenting history
  - Presented at birth with large, fleshy vascular(?) lesion affecting the lower limb
  - Referred to paediatrician
    - Possible kaposiform haemangioendothelioma (KHE)
    - Treated with corticosteroids
    - Referred to haematology due to persistent thrombocytopenia

Case

- Initial investigations
  - Slightly anaemic, neutropenic and markedly thrombocytopenic
  - No evidence of coagulation activation
  - Ultrasound showed lesion in right cerebral hemisphere, confirmed on MRI as bleed (antenatal)
  - Managed with platelet transfusion with good response
Case

- Progress
  - Persistent marked thrombocytopenia despite involution of vascular lesion
  - Repeated bone marrow examination showing normocellular bone marrow but (?) decreasing megakaryocytes (confirmed on immunohistochemistry CD61)
  - Patient “well” and not bleeding

Congenital Thrombocytopenia: “Tools” available for assessment

- Platelet count & sizing
- Reticulated platelets
- Electron microscopy
- Bone marrow aspiration and immunohistochemistry
- Flow cytometry for platelet glycoproteins
- Assessment of platelet function
  - PFA 100
  - Aggregometry
  - Molecular markers

Platelet counting and sizing (Coulter principle)

Platelet Counting & Sizing

- Platelet count is not directly measured – derived from platelet histogram
  - Any particle sized between 2 to 20 fl is counted as a platelet
  - Any particle sized outside of 2 to 20 fl is not counted as a platelet
**Reticulated Platelets**

- "Immature platelets"
- Larger mean platelet volume with higher RNA content
- Flow cytometric method using the membrane permeable fluochrome thiazole orange to stain RNA
- Sensitivity improved by using gating techniques incorporating CD61
- Reported as a percentage (lack of widely accepted standardization of normal values)

**Bone Marrow Aspiration**

- Performed under general anaesthetic
- Limited morbidity
- Provides quantitative information with correlation of function with signs of dysplasia / abnormal forms etc.

**Electron Microscopy**

- Provide assessment of platelet ultrastructure
- Somewhat helpful in the assessment of platelet function disorders
- Available in Melbourne through University of Melbourne

**Reticulated Platelets**

- May have a role in the distinguishing patients with ITP / consumptive states from those with decreased platelet production
- May have a role in the predictive value for marrow recovery following chemotherapy
- Not currently available at RCH
Flow cytometry for platelet glycoproteins
- Diagnostic in select group of patients with characteristic disorders
  - Glanzman’s thrombocythaemia (deficient GPIIb/IIIa)
  - Bernard Soulier syndrome (deficient Ib/IX)

Assessment of Platelet Function
- Difficult in Children
- Large volumes of blood required
- Generally require “normal platelet” counts
- Methods available
  - PFA 100
  - Formal aggregometry

PFA-100 Closure Time Measurement
- Quantitative, rapid test of platelet function at high shear rates
- Platelet plug forms under shear stress and occludes the aperture which is detected as the closure time
- Published normal ranges for closure times for children
- Available RCH
Platelet Aggregation

- Gold standard for the investigation of platelet function
- Initially devised 40 years ago (Bonn, Nature 1962)
- Platelet rich plasma placed in an aggregometer cuvette, warmed to 37°C in the heating block of the instrument and stirred by means of a small magnetic stir bar.
- Light transmission through the plasma is monitored continuously on a chart recorder.
- The addition of an aggregating agent results in the formation of increasingly larger platelet aggregates with a corresponding decrease in optical density and is recorded as a tracing by the chart recorder.
- Minimum count in PRP = 100 X10^9/l

Approach to “Congenital” Thrombocytopenia

1. Rule out secondary causes
2. Congenital thrombocytopenia
   a. Syndromic thrombocytopenia
   b. Non - syndromic thrombocytopenia

   Associated with macrothrombocytopenia
   - Bernard Soulier
   - MYH9 related conditions
   Associated with normal sized platelets

Secondary Thrombocytopenia

- Majority of cases of thrombocytopenia occurring in neonates are a result of a clearly apparent underlying systemic illness
- Fetal platelet counts in 59/14 consecutive fetal blood samples
- Thrombocytopenia (<150X10^9/l) present in 247 of these cases (4.1%)

(Fohfeld et al 1994)

1. Syndromic Congenital Thrombocytopenia

- Wiskott Aldrich / Xlinked thrombocytopenia
- TAR
- MYH9 – related disease
- Familial platelet disorder and predisposition to AML (FPD/AML) (Ho et al, Blood 1996)

Non – Syndromic Congenital Thrombocytopenia

- Associated with normal sized platelets
  - CAMT
    - Autosomal recessive
    - Isolated hypomegakaryocytic thrombocytopenia at birth
    - 15 families
    - Deficiency in the expression of TPO receptor
  - Other (?)
Immune Thrombocytopenia Purpura

Case A
- 2 ½ old boy
- Previously well
- Urgent referral to clinic with bruising
- Platelet count < 10 X 10^9/l with otherwise normal blood count
- Examination unremarkable

What investigations need to be performed?
- What treatment is required?
- What advice is given to the parents?

Case B
- 12 year old girl
- Presents from country general practitioner
- Diagnosis of ITP made 6 weeks prior (platelet count 4 X 10^9/l, borderline haemoglobin 114 g/l, normal range 115 – 135) and normal examination
- Moderate bruising but no active bleeding
- Comes following 6 weeks of steroids with Cushingoid features
- Repeat platelet count 10 X 10^9/l with persistent borderline haemoglobin and lymphopenia

What investigations are now necessary?
- What treatment is recommended?
- What advice is given to the patient?

Case C
- 4 year old boy with Down’s syndrome
- Presents with marked bruising, active mucosal bleeding and platelet count < 10 X 10^9/l (and mild normochromic normocytic anaemia with reticulocytosis)
- Develops headache, focal neurological signs and intracranial haemorrhage requiring urgent neurosurgery
Case C

- Why does this patient manifest significant bleeding symptoms despite the “same degree of thrombocytopenia”?
- What treatments are recommended in the setting of urgent splenectomy?

Case D

- 10 month old boy
- Previously well
- Morphologically normal
- Presents with acute onset of increased bruising and marked thrombocytopenia
- Already walking but unsteady

Case D

- Below what age is the diagnosis of ITP less likely?
- The mother wants a helmet – what is your advice?

Case E

- 15 year old girl
- Long standing history of ITP
  - diagnosed at 7 years of age
  - Splenectomy at 7.5 years of age
  - Limited further follow-up
- Presents with exacerbation of menorrhagia associated with iron deficiency anaemia

Case E

- Parents want another splenectomy – what investigations are recommended to identify accessory spleens / splenunculi?
- What treatments are recommended to manage menorrhagia in this patient?

Facts about ITP
Facts about ITP

Randomised study

Imbach et al., Lancet 1985;2:464-68

Annotation

MEDICAL NEMESIS AND CHILDHOOD ITP

Over thirty years ago the physician and clinical immunologist Bick accused the medical establishment of being a major threat to health. He argued that it was responsible for a growing epidemic of immune deficiencies, and referred to this as a form of medical decline (Bick, 1954). His words, however, were largely ignored, and as far as childhood idiopathic thrombocytopenic purpura (ITP) is concerned, he was later proved right.

Classification of Neutropenia

NEUTROPENIA CAUSED BY INTRINSIC DEFECTS IN GRANULOCYTES OR THEIR PROGENITORS

- Reticular dysgenesis
- Cyclic neutropenia
- Severe congenital neutropenia (including Kostmann’s syndrome)
- Shwachman-Diamond syndrome
- Albinism/neutropenia syndromes (including Chédiak-Higashi)
- Familial benign neutropenia
- Bone marrow failure syndromes (congenital and acquired)

NEUTROPENIA CAUSED BY EXTRINSIC FACTORS (Infection / Drugs)

- Autoimmune neutropenia
- Neonatal immune neutropenia with immune dysfunction
- Neutropenia associated with metabolic diseases
- Nutritional deficiencies
- Sequestration
- Bone marrow infiltration
- Chronic idiopathic neutropenia (may also be intrinsic)
- Types of neutropenia are listed in order of discussion in the text.WHIM, warts, hypogammaglobulinemia, infections, myelokathexis.

Neutropenia

- Severe congenital neutropenia (Kostmann’s syndrome)
- Cyclic neutropenia
- Swachman Diamond syndrome
- GSD1b
- Associated with immunodeficiency
Neutropenia - approach

- Age at presentation
- Depth of neutropenia
- Association with bacterial infections

Evaluation of neutropenia

- History and physical examination with emphasis on (1) related phenotypic abnormalities; (2) h/o bacterial infection (including evaluation of the gingiva and perineum); (3) evaluation of lymphadenopathy, hepatosplenomegaly
- Drug exposure, history of periodontitis, dental abscesses, or tooth
- Family history
- Race and ethnic background

Neutropenia: Evaluation

- White blood and differential counts obtained twice weekly for 6 to 8 weeks
- Direct and indirect antiglobulin
- Serum immunoglobulins
- HIV testing
- Other viral studies- CMV, EBV, Parvo
- ANA
- Bone marrow aspiration and biopsy with cytogenetics

Investigations contd..

- Vitamin B12, folate, and copper levels.
- Radiographic studies of the femoral heads, rib cage, and spine may be useful in the diagnosis of Shwachman-Diamond syndrome
- Pancreatic exocrine functions
- Metabolic screening

Principles of Therapy for Neutropenia

- Underlying cause and severity.
- The major concern in neutropenic patients is the development of serious pyogenic infection.
- Fever may often be the only indication of infection as very less local signs
- Organisms involved are usually from the skin or GI tract
FEBRILE NEUTROPENIA

J Age- 4 1/2 yrs
Diagnosis-Acute Lymphoblastic leukaemia (FAB – L2)
Date of diagnosis –26 December 2004
Symptoms- Recurrent fever, Bone pains, Extreme lethargy
3 wks
Investigations- Peripheral smear, bone marrow confirmed diagnosis of acute lymphoblastic leukaemia (FAB L2)

Risk factors- Male, high TLC and significant organomegaly
No lymphadenopathy
Management – Chemotherapy with 4 week, 5 drugs induction protocol.
Marrow on D28 – M1 (remission status)
Next phase - I 2- Radiation
CNS prophylaxis
Standard drugs.
However, 7 days into I 2 phase of therapy he was brought with history of fever, lethargy and refusal to eat. He also had cough and looked toxic.

Examination : Mucositis in the mouth and throat & B/L coarse crepitations in the lungs.
No hepatosplenomegaly.
Investigations: Blood counts, Peripheral blood smear, X-ray, CRP, blood and urine cultures

The smear and count reports were as follows-
- Hb 8 g/L
- Total WBC=1.3 X 10^9/L
- N 08%
- L 78%
- M 08%
- E 06%
- ANC=0.1 X 10^9/L
- Platelets=36 X 10^9/L
- CRP - 96

The peripheral smear of this child is shown below. What can you see in this slide?
The smear shows significant neutropenia.

The large cell on the left is a band form and the one on the right is a myelocyte. Both cells show toxic granulations. This picture suggests a shift to the left indicative of sepsis.

The next slide shows a normal peripheral smear.

Can you make out the difference?

The child was subjected to radiological investigation and the X-ray was as below:

The X-ray shows bilateral soft infiltrates suggestive of bronchopneumonia.

As the recordings of temperature revealed continuous fever of more than 38 degrees C, the child was immediately started on empirical antibiotic therapy.

What would your choice of antibiotics be in this situation?

What are the standard dosages of these drugs?

Febrile neutropenia

- Neutropenia: ANC < 500 cells / cmm.
- Temperature:
  - single observation of > 38.3°C
  - sustained temp > 38.0°C, >1 hr
  - < 36°C with clinical deterioration (HR > 90, RR > 20, BP<90)

Associated risk factors

- Degree of neutropenia (<500/Cmm)
- Prolonged neutropenia ( > 7-10 days)
- Co morbid medical problem- example- Continued cancerous state
**Low Risk Patients**

- Anticipated short duration of neutropenia (<10d)
- No Co morbid Medical Condition
- Controlled oncological status
- **Options:**
  - Oral antibiotics
    - Cefixime
    - Ciprofloxacin + Clindamycin
    - Cipro + Amoxy-clav
  - Parental Monotherapy
    - To continue 7 days as OPD Care
    - If C/S -ve – switch to oral drugs

**High Risk Patients**

- Granulocytopenia >10days
- Proven source of infection
- Co morbid medical condition
- If afebrile by day 14- stop antibiotics
  - If febrile on day 3- repeat Blood C/S on D4

**IDSA Guide Lines- 2002 (Walter et al)**

**Careful Physical Examination**

- Initial evaluation - To risk stratification
  - determine whether Vancomycin is needed in the initial trt.
- Examination sites: - Oral cavity
  - Perianal area
  - Exit sites of lines

**Serial surveillance cultures (Welsh et al Medicine 65, 265, 1996)**

- Not recommended routinely in neutropenia pts.
- Useful in
  - Protracted neutropenia ( > 3-4 weeks)
  - High incidence of virulent organisms

**The blood culture, sample for which was collected at admission, revealed a significant growth of an organism after 48 hrs as seen on the blood agar plate below:**
The organism grown was identified as Haemophilus influenzae which was found to be sensitive to a number of antibiotics. The plate below shows the sensitivity of the organism to ceftazidime.

The general condition of J remained stable for the next five days, but fever persisted. Blood cultures showed the following:
- A repeat count done on D5 after admission revealed Hb of 6gm%
- TLC of 0.9 N4 L88 M02 E06
- ANC = 0.3
- Platelets = 16,000/ cumm

With the counts as above, platelet and RBC transfusions were considered.

What is the role of these transfusions in a situation such as this?
What is the threshold for platelet transfusion in a child whose general condition is stable and who is not bleeding?

However, clinical examination revealed no evidence of bleeding and the mucositis had not worsened. A repeat of the chest X ray did not reveal any further deterioration.

Considering the clinical picture, what steps would one take now?
- What is the role of packed cell RBC transfusion in a child with thrombocytopenia?
- Would you consider empirical antifungal therapy now? Why?
- What drug would you use?

Goals for empirical treatment
To protect against the early morbidity and mortality.

Important Properties of Empirical Regimes
- Broad spectrum of activity that includes Pseudomonas aeruginosa
- Ability to achieve high serum bactericidal levels
- Effective in the absence of neutrophils
- Low potential for the emergence of resistance
- Acceptable toxicity profile
Aminoglycoside-Based Combination Regimes

- Aminoglycoside + AntiPseudomonal β-Lactam
- Additional Anti-Gram-Positive
- Gentamicin
- Tobramycin
- Amikacin
- Tobramycin
- Ticarcillin
- Azlocillin
- Mezlocillin
- Piperacillin
- First generation cephalosporin
- Cefazolin
- Piperacillin
- Ticarcillin
- Oxacillin
- Azlocillin
- Mezlocillin
- Piperacillin
- Carbenicillin
- Nafcillin
- Amikacin
- Ticarcillin
- Oxacillin
- Azlocillin
- Mezlocillin
- Piperacillin
- Cephalosporin
- Cefazolin
- Cefuroxime
- Cefotaxime
- Ceftriaxone
- Cefepime
- Cefpirom
- Aztreonam

Regimen without Aminoglycoside

- Combination of two beta lactam antibiotics
  Example: Piperacillin + Ceftazidime
  Single agent with Aminoglycoside / Extended spectrum penicillin / Vancomycin – should not be used.

Drugs as monotherapy
- Ceftazidime
- Meropenem / Imipenem
- Cefoperazone
- Cefepime / Cefpirom

Defervescence
Ultimate outcome
Comparable


Patients require frequent modifications

- With a documented source of infection
- Protracted granulo cytopenia (> 1 week)
- Continued Oncological status

Use of Vancomycin in the Initial Regimes

- No change in morbidity
- Less use of Amphotericin B
- No change in Febrile episodes
- Increases V R E emergence

CDC Recommendations:
- Not to be included in initial regimes unless culture proven by 3rd day
- Not to be used prophylactically for central line infection

Ref: Karp et al, Am J of medicine 81:237, 1986

Ciprofloxacin

- As monotherapy causes breakthrough infection with streptococcus
- reserved for MDR state

Ref: Meunier et al Antimicrobial agent chemother 35:873, 1991

Would you consider colony stimulating factors? How are they used?

The boy was given a packed cell transfusion
What is the volume of blood to be transfused?
and started on antifungal therapy with fluconazol.

What is the dose of fluconazole? Amphotericin B?
G-CSF was considered but not started.
Why?
Antifungal Treatment

- **Indication:** Persistence of fever on day 5-7
- **Anti-fungals**
  - Itraconazole/Fluconazole
  - Amphotericin B
- **Benefits of empirical antifungals:**
  - Early clinical Defervesence
  - Less morbidity
- **Rationale:**
  - Early treatment of sub-clinical infection
  - Suppression of fungal overgrowth accompanying antibiotics therapy


Colony Stimulating Factors

- **Indications:**
  1. Worsening course
  2. Predicted prolonged neutropenia
- **Effects:**
  - Reduce duration of antibiotics
  - No change in mortality
- **Dosage:**
  - G-CSF: 5ug/Kg
  - GM-CSF: 250/m²
- **Prophylaxis:** (ASCO guidelines - if the chance of FN>40%, prior h/o severe infection)


- Because G-CSF is useful when started early with neutropenia and has a limited role when neutropenia is fully established. Besides, it is expensive.

- The general condition of J gradually improved. He became afebrile after the 9th day of antibiotics and 4th day of antifungals. His mucositis improved and his cough reduced.

- His X-ray done on the 14th day after admission is shown next.

PCP Prophylaxis

- Started in 1980's after isolation of HIV
- Incidence of PCP infection without prophylaxis (Meyer's et al)
  - ALL: 22-43%, RMS: 25%, BMT: 16%
  - SCID: 27%, Solid tumors: 40-50%
- **Standard tri** - TMP-SMX BD - 3times/wk (Ioannidis et al meta-analysis)
- **Others** - Dapson: 2mg/kg
  - Aerosolised Pentamidine - monthly - limited use in children
  - Atovaquone

Granulocyte Transfusion

- In use since 1970
- Lots of studies in favour and against (Higby et al vs Winston et al)
- Donors treated with G-CSF and corticosteroids
- Adequate cell dose - 1×10⁸ PMN cells
- Matched donors (ABO compatible, no need for HLA)
- Needs further study
- IDSA - 2002: Not to be used routinely
Antibacterial Prophylaxis

Controversial

IDSA-Not indicated

When can we consider discharging J?
What is the ANC at which the child can be safely discharged?
What prophylactic therapy would you advise J’s mother to give him at home?
What is the dosage and frequency of administration?
What are the other preventive measures that should be followed?
When would you like to review him again?

Duration of Therapy

- If afebrile by D 3 with ANC >0.5 stop antibiotic on day 7. (To be institutionalized)
- If ANC < 0.5 continue antibiotic
- If has persistent fever and ANC >500/cmm stop antibiotic on D 7.
- If ANC < 0.5 on D 5 – cont for 14 days

Antibacterial Prophylaxis

- Regimens aim at total reduction of endogenous gut flora is not recommended
- Selective gut decontamination (against aerobic and fungal) by Van der et al using TMP/SMX
- Fluoroquinolones – mostly used in adults. Not recommended by IDSA.
- Comparative studies – no overall benefit than simple infection prevention protocols such as hand washing

Duration of antibiotic therapy

- Afebrile by day 3
- Persistent fever

- ANC >500/mm^3 by day 7
- ANC < 500/mm^3 by day 7

- Stop after 7 days
- Low risk
  - Clinically well
  - Neutrophils <200/mm^3
  - Continuous antibiotic

- Stop after 5 to 7 days
-Continue antibiotic

- ANC > 500/mm^3
- ANC < 500/mm^3

- Stop 4-5 days after ANC > 500/mm^3
- Reassess
- Continue 4-2 weeks

- Stop if no disease signs and symptoms

All febrile neutropenia – are infective

Rationale:
No mechanism to differentiate
55% infective pts did not have any source.
Thank you