HIV & Intestinal Disease
Why is the intestine important in HIV infection?

How do HIV-infected children get intestinal disease?

How do we treat them?
Immunopathology

HIV is an intestinal disease
Immunopathology

• Early depletion of CD4 T lymphocytes after acute infection regardless of the route of infection
• Precedes depletion in peripheral blood and lymphnodes
• Recovery of mucosal CD4 T lymphocytes incomplete with HAART
Immunopathology

- GIT important locus of immune activation
- Increased intestinal permeability
- Bacterial translocation more common in HIV infected patients (even on HAART)
EFFECT OF HIV ON THE INTESTINE
Mucosal Changes

- Increased inflammation
- Villous blunting
- Crypt hyperplasia
- Ulceration
Effect of HIV Infection on Epithelium

• Abnormal enterocyte differentiation
• Paneth cell involvement
• Non-replicative infection of enterocytes
Effect of HIV on Intestine

TAT (Trans-Activator of Transcription)

• Decreased glucose uptake

• Tight junction disruption

Structure of Human Immunodeficiency Virus (HIV)
Effect of HIV on Intestine

GP120

- Increased intra-cellular Ca
- Tubulin depolymerisation
- Decreased ability to maintain ion...
FUNCTIONAL EFFECTS
Intestinal Function in HIV Infection

- Mucosal Absorption
  - Xylose
  - Drug
- Permeability
- Increased endogenous protein loss
- Iron loss
- Motility
- Small bowel bacterial overgrowth
Functional Changes

Sugar Malabsorption

- Lactase deficiency
- AMI
Fat Malabsorption

- Approximately 30% of HIV infected children have increased stool fat
- Mild pancreatic insufficiency is common
- Fat malabsorption independent of pancreatic insufficiency is also common

BUT

- Studies provide cross-sectional data or short-term follow-up
- Most prior to HAART
Fat Malabsorption

• Some patients may benefit from enzyme supplementation

• Modification of diet for children with steatorrhoea and poor weight gain (MCT)
DIARRHOEA
What is the impact of HIV on Diarrhoeal Disease?

- More frequent
- Longer duration
- More PD
- Higher mortality
- OI’s
Causes of Diarrhea are Multifold:

• Infections
  – Childhood diarrhea with usual organisms
  – Opportunistic organisms
Causes of Diarrhea are Multifold

Malabsorption and intolerance secondary to mucosal injury

- Sugar malabsorption
- “post enteritis syndrome” PD
- tropical sprue
- HIV related
Causes of Diarrhea are Multifold

• Bacterial overgrowth
  – Play role in development of prolonged diarrhea

• Non-specific inflammation and small-bowel atrophy

• Medication side effect (also of HAART, especially PI)
Treatment

• c ART

• Specific antimicrobial
Treatment

Diet

• Supportive
• Modify for malabsorption
• Hydrolysed formula
• TPN
Supplements

• Zinc
• Vitamin A
  (not high dose)

• Enterotrophic diets
  – Glutamine
  – Arginine
Probiotics

• HIV disturbs the microbiota
  – Increased potential pathogens
  – Decreased bifidobacteria & lactobacilli
  – Increased intestinal inflammation
Probiotics

• Animal studies
  – Decreased inflammation

• Some human studies show
  – Decreased bacterial translocation
  – Decreased inflammatory cytokines
  – Increased CD4 count

BUT

• Most show no or only modest effect
• Mostly safe
Problem parasites

Microsporidiosis

Cryptosporidiosis

Isosporabelli
Cryptosporidium

- Common cause in all young children
- Self limiting in non-immune compromised children
- Severe diarrhoea in HIV
- Secretory
- AMI
Cryptosporidium

Also causes

- Acalculous cholecystitis or sclerosing cholangitis
- Beading of the common bile duct or papillary stenosis
- Suspect of unexplained cholangitis or raised GGT / ALP
Cryptosporidium

Diagnosis

- Stool microscopy
- Small bowel biopsy
Cryptosporidium

No effective treatment

• Azithromycin
• Paromomycin
• Nitazoxanide
  – high dose, longer course
CMV

- Involves any part of GIT
- Colon most common
  - Dysentery
  - Perforation & strictures
  - IRIS
HIV ENTEROPATHY
Idiopathic AIDS enteropathy

- Chronic diarrheal illness in patients with AIDS, where no cause can be identified despite an extensive evaluation

- Diagnosis of exclusion
Chronic Colitis

- Chronic colitis
- IBD/TB/HIV?
- Perineal fistula
- Recto-vaginal fistula
Develop a General Approach

What are the important questions to ask?
Questions?