INFECTIVE DIARRHOEA DIAGNOSIS AND MANAGEMENT

Adam Jenney PhD FRACP FRCPA

Clinical Microbiologist / ID Physician
The Alfred Hospital, Melbourne

Thursday, 9th May 2019

Declarations

- Nil conflicts of interest

In this presentation

- Adults - mainly
- Infective causes
- Outpatient diarrhoea

- These are important but not the whole story by any means

Not talking about these

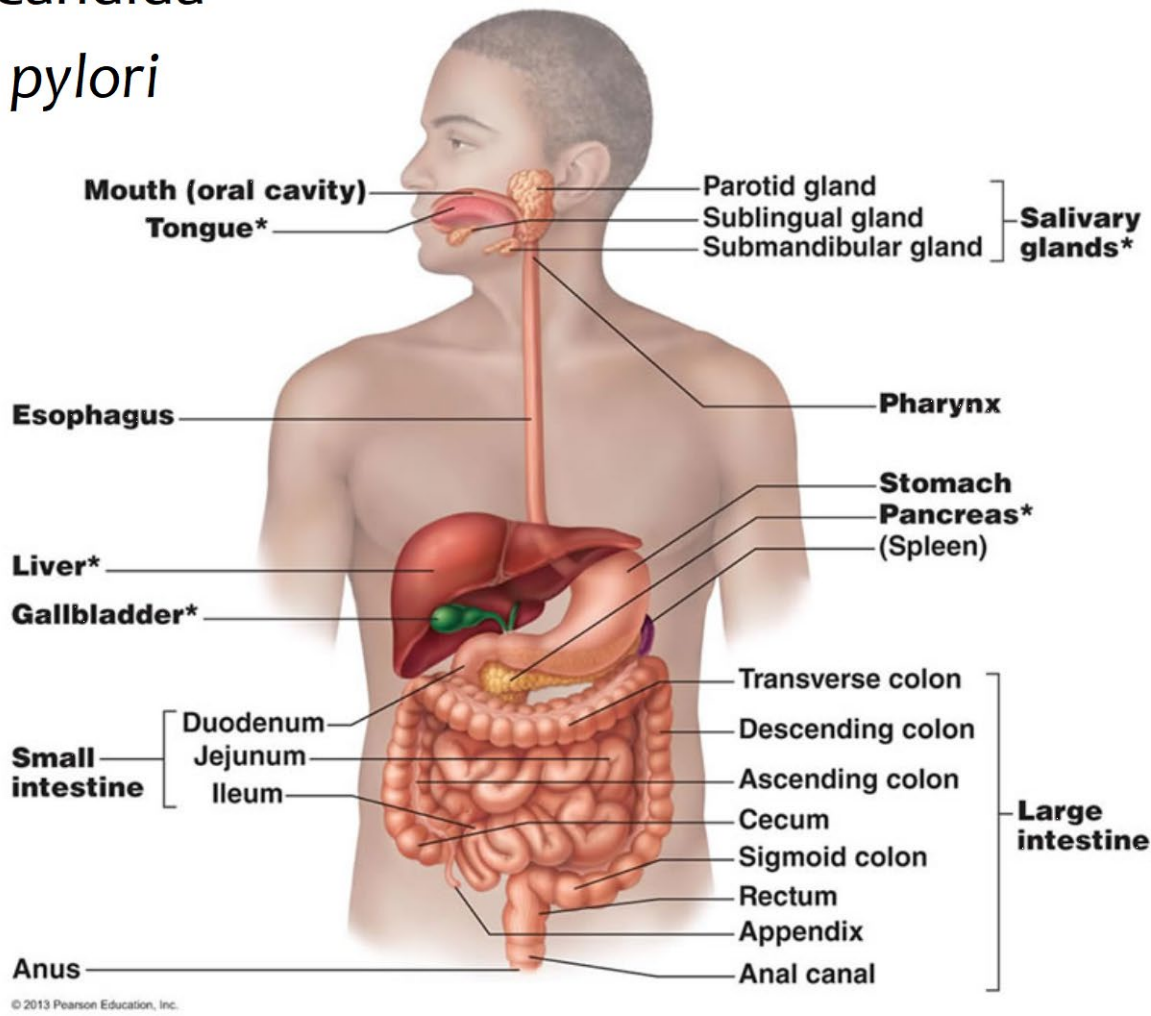
- Hepatitis – though Hep A and E are faecal-oral spread
- Cholecystitis, pancreatitis
- Diverticulitis
- Whipple's Disease
- Typhlitis
- Tropical Sprue
- Mesenteric adenitis
- **Other serious infections with diarrhoea in their symptom profile**
  - **Legionella, malaria**

Non-infective diarrhoea

- Drugs – medication (digoxin, colchicine, ethanol, antibiotics)
- Constipation and overflow
- Malignancy
- Irritable Bowel Syndrome
- Diabetes
- Uraemia
- Addison's
- Hyperthyroidism
- Diet
- Anxiety
- **Inflammatory Bowel disease –** Crohn's, Ulcerative Colitis
- Appendicitis

Infection (inflammation by anatomy)

- Oesophagitis – reflux, Candida
- Gastritis – *Helicobacter pylori*
- **Enteritis**
- **Colitis**
- Proctitis



Presentation of GI infection

- **DIARRHOEA**
- **Vomiting**
- Nausea
- Abdominal Pain -upper abdominal (hypogastrium) vs peri-umbilical vs lower abdomen
- Fever
- Lethargy / Malaise
- Bloating
- Borborygmi

History – very important

- **Symptoms** – which, how prominent, how long?
- **Travel**
- **Exposure to pathogens** – environment, people

- **Immune status** - have the normal barriers been breached
  - Steroids, Chemotherapy, biologics, HIV/AIDS, surgery,

- Drugs – PPIs

Diarrhoea

- What is it?
- >/=3 loose stools in a 24 hour period
  - Strictly speaking - excess stool in terms of mass
  - More frequent, more voluminous, more fluid
- Usually Acute (typically 3-7 days)

- Diarrhoea: 'Assumes the shape of the container'
- In the lab we say: if it rattles we reject it!)

- Blood – Dysentery
- 'Frothy' – mucus

Diarrhoea

- Acute, usually 2-7 days
- ‘Persistent’ - >14 days
- Chronic - >1 month
- Strictly speaking up to 14 days is ‘Acute’ but 2 weeks can seem like a very long time!

Diarrhoea

LARGE BOWEL	SMALL BOWEL
• **Frequent**	• **Less frequent**
• **Small volume**	• **Large volume**
• Blood	• Often no blood
• Tenesmus (painful and unsatisfying)	
‘colitis’	malabsorption

CLINICAL	ANATOMIC	PATHOGENS
Few, voluminous stools	Small bowel origin	*Vibrio cholerae*, enterotoxigenic *E. coli*, *Shigella* (early infecton), *Giardia lamblia*, *V. parahaemolytcus*
Passage of many small volume stools	Large bowel origin	*Shigella*, *Salmonella*, *Campylobacter*, diarrhoeagenic *E. coli*, *Yersinia enterocolitca*, *Entamoeba histolytica*
Tenesmus, fecal urgency, dysentery	Colitis	*Shigella*, *Salmonella*, enteroinvasive *E. coli*, enterohaemorrhagic *E. coli Campylobacter*, *E. histolytica*
Predominance of vomiting	Gastroenteritis	Viral agents (rotavirus, calicivirus) or intoxication (*Bacillus cereus*, *Staphylococcus aureus*)
Predominance of fever	Mucosal invasion	*Shigella*, *Salmonella*, *Campylobacter*, enteroinvasive *E. coli*, viral agents

Vomiting (often with some diarrhoea)

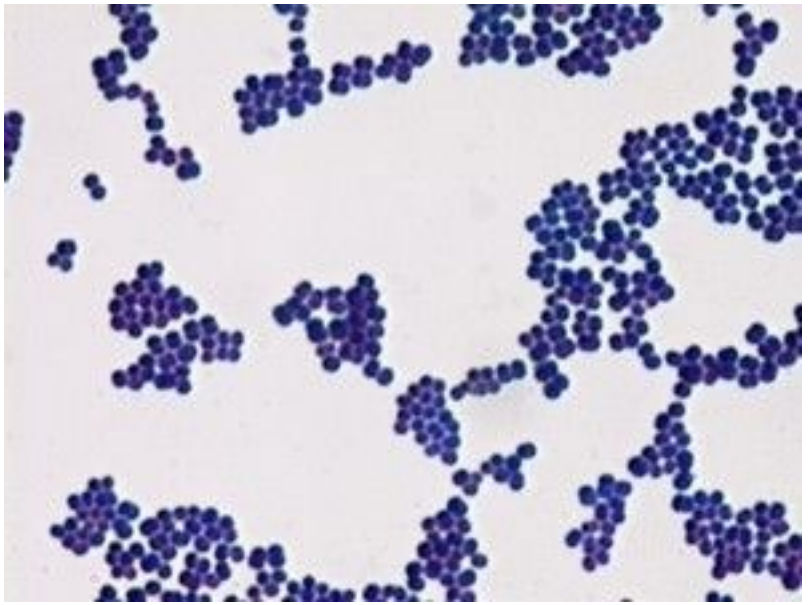
- ‘Food poisoning’
- Associated with some foods that get contaminated

- Some organisms that predominantly cause Upper GI symptoms may cause disease through toxin production:

Staphylococcus aureus

Bacillus cereus

S.aureus



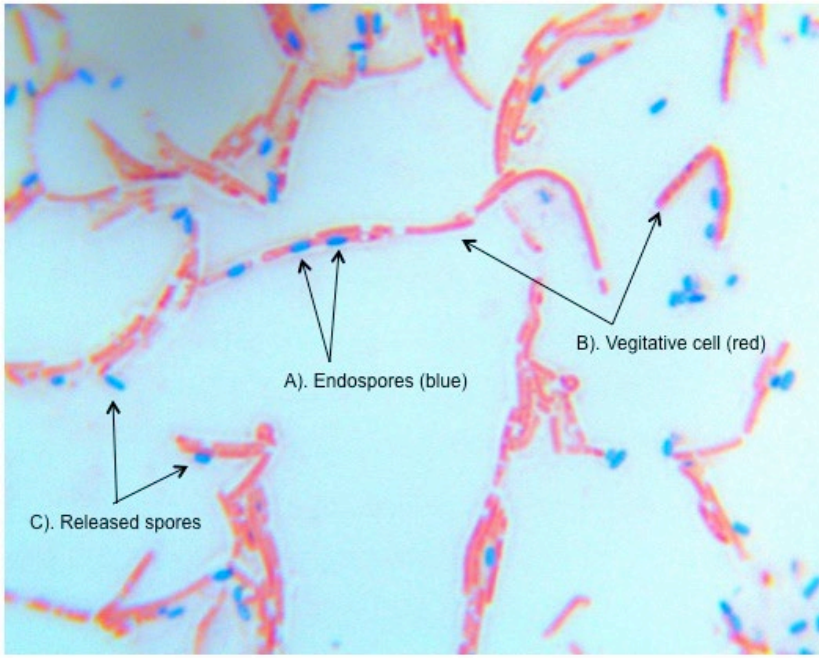
- Replicates in poorly stored food
- Meat and Creamy products
- Forms an Enterotoxin
- Heat stable, water soluble

- Consumed and in 1-6 hours causes vomiting +++
- Maybe a little diarrhoea
- Self-limiting

- (same organism that causes sepsis, skin and bone infections)

Bacillus cereus

- Found everywhere
- Spores – survive heat and then grows in the cold (4°C)
- Toxin– 2 types
- Type 1
  - EMETOGENIC - poorly kept rice/pasta, heat-stable
- Type 2
  - DIARRHOEA-CAUSING –
  - associated with meat
  - and formed in gut
    (heat-labile)



Helicobacter pylori

- Socio-economic status plays a role
- > half the world infected
- 50% in UK at 50 yo

- 90% duodenal ulcers, 50% gastric ulcers (and gastric cancer)
- Gastric Lymphoma

- However not associated with GORD or Barrett's oesophagus

Barry Marshall and Robin Warren won the 2005 Nobel prize in physiology or medicine

Helicobacter pylori

Dx:

- Breath test (urea)
- Biopsy – organism is urease positive
- Culture is tricky

Rx:

- antibiotics (eg. amoxycillin, clarithromycin, metronidazole) in a combination plus PPI.
- Rising Abx resistance

DIARRHOEA

- Viruses
- Bacteria
- Parasites

VIRUSES

- **Norovirus**
- **Rotavirus**

- Adenovirus
- Astrovirus

- CMV

- Outbreaks
- Children

- HIV colitis

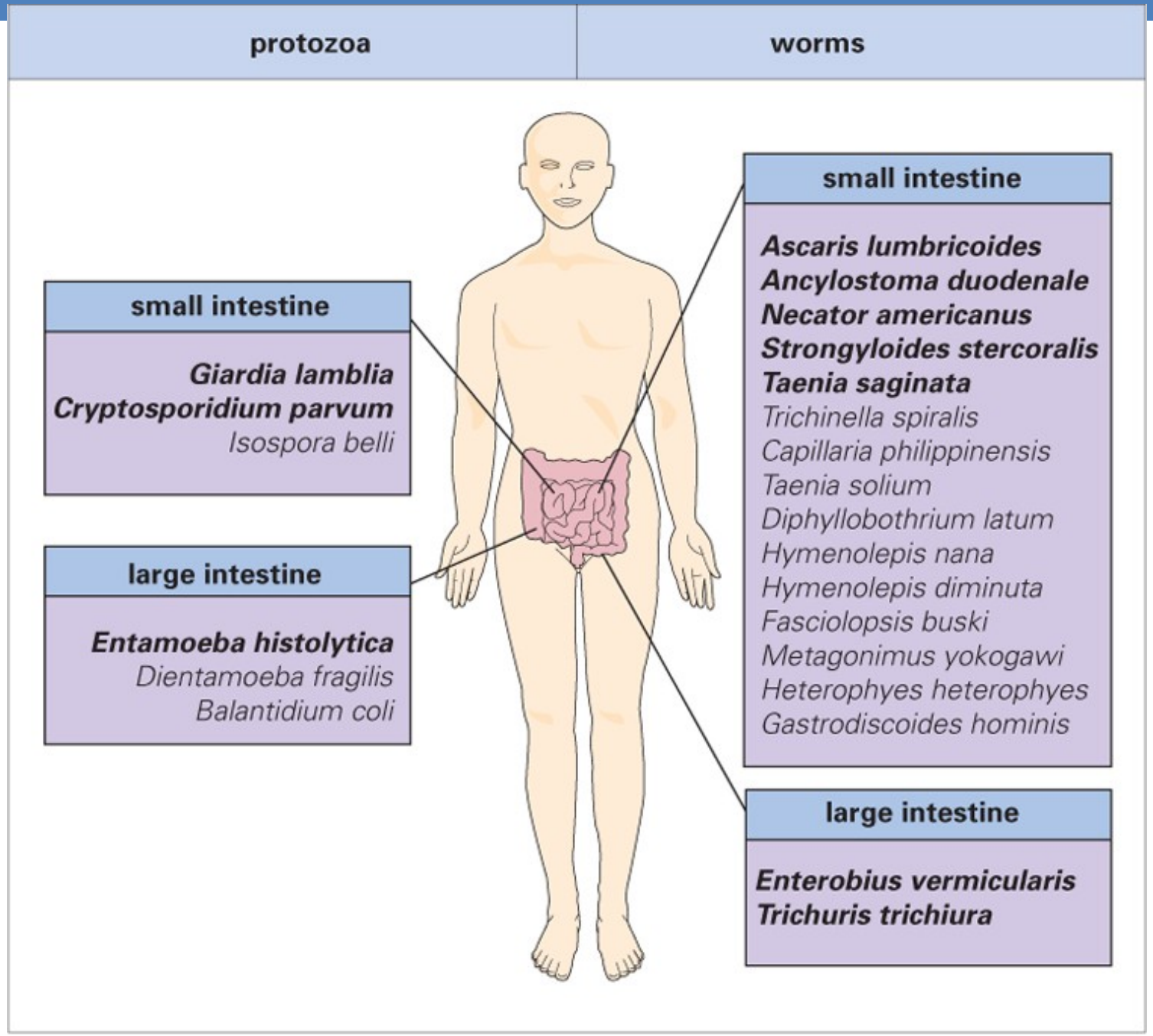
BACTERIA

- ***E.coli***
  - ETEC, EHEC
- ***Campylobacter***
- ***Salmonella***
  - non-Typhi
- ***Shigella***
- *Vibrio cholerae*

- *Yersinia*
- *Aeromonas*

DIARRHOEA

- Viruses
- Bacteria
- Parasites



Enterobacteriaeae

- Escherichia LF
- Salmonella NLF
- Shigella NLF
- Yersinia NLF

Escherichia coli

- ETEC – 'toxigenic'
  - ST toxin - heat-stable enterotoxin increases fluid secretion of SI mucosal cells via GMP
  - LT – toxin – heat labile
- Travellers' Diarrhoea
- Non-bloody

- Self-limiting – usually don't treat

Escherichia coli - EHEC

- EHEC – 'haemorrhagic' *E.coli 057* or *0111*
- Verotoxin or Shigatoxin – target vascular endothelial cells
- The B subunit chaperones the A subunit to the target
- Outbreaks – contaminated meat
- Bloody diarrhoea and renal failure
- Very sick

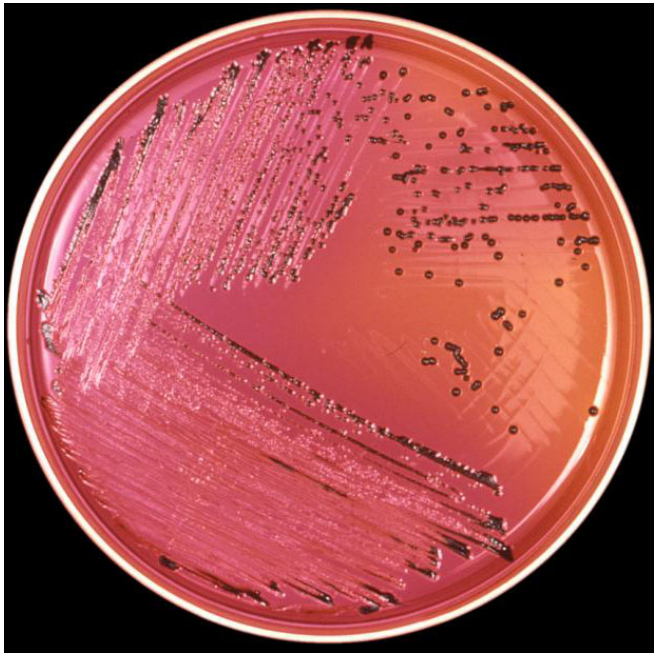
Dx:

- Suspected aa outbreak. Reference lab confirmation by toxin assay on stool and specialized culture

Rx: **Supportive therapy**. Antibiotics can make it worse – FQ release more toxin

Salmonella

- *S.enterica* (lots of subspecies and serovars)
- *eg. Salmonella* Typhimurium (non-typhoidal *Salmonella)*
- Outbreaks, food related, mainly diarrhoea
  - N,V, fever, cramps, myalgia, headache
- IP: 12-48 hours depending on inoculum
- Poultry



- Microbiology
  Non-lactose fermenting
- 'PINK' colonies on XLD
- H_2S – black on the pink on the XLD

- Rx: supportive,

Non-typhoidal Salmonella Antibiotic Rx

- I-C
- Very young, >65 years
- Sepsis
- Prosthetic endovascular graft material
- Haemoglobinopathies

- Macrolide, FQ (oral)
- ceftriaxone (IV)

Shigella

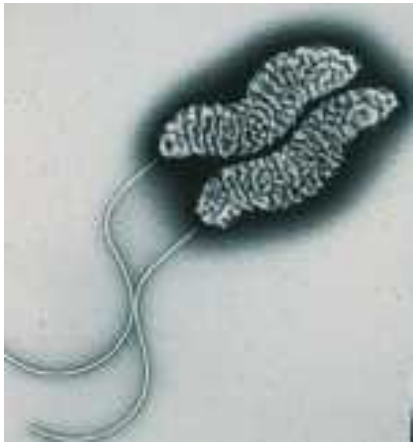
- *S.dysenteriae, S.flexneri, S.sonnei, S.boydii*

- Low inoculum needed (as few as 10 CFUs)
- Survives stomach acid well

- Children can have an acute onset
  - Pain and severe bloody/mucus diarrhoea
- Has a toxin that promotes ulceration, mucus formation and osmotic diarrhoea
- MSM (men-who-have-sex-with-men)

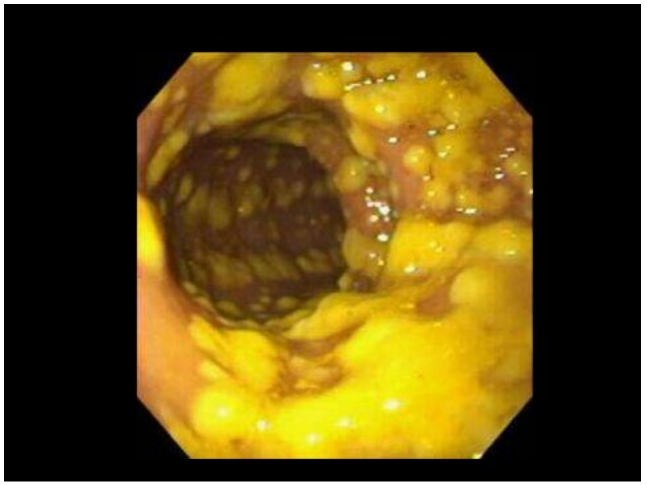
- Rx: self-limiting (Abx only for severe disease)

Campylobacter



- *Campylobacter coli, Campylobacter jejuni*
- Diarrhoea
  - Enterotoxin-mediate
  - Inflammatory – fever, ulceration and blood
- Animal reservoir – eg. chicken
- Culture at 42°C
- Guillain-Barre Syndrome, reactive arthritis – rare complications 2-6 weeks post diarrhoea
- Rx: Supportive treatment usually enough
  macrolide, fluoroquinolone (co-trimoxazole)

Clostridium difficile



- Toxin A and B, Binary toxin

- Toxin A: enterotoxin leads to diarrhoea
- Toxin B: cytopathic
- Binary toxin: found in epidemic strains

- Watery diarrhoea with no fever to pseundomembranous colitis to toxic megacolon

- Treatment:
- STOP THE ANTIBIOTICS
- ORAL Metronidazole (anaerobe), Vancomycin (Gram positive)

- Faecal transplant

Microscopy and Culture of Stool

PCR for Stool

- Quick
- Sensitive
- Diverse targets
  - Viruses
  - Salmonella, Shigella, Campylobacter, Aeromonas, C.difficile
  - Giardia, Entamoeba histolytica, Cryptosporidium, Blastocystis, Dientamoeba

- But there are disadvantages
- Too Sensitive?
- Over-calling
- Non-pathogens
-

Toxin assay

- *C.difficile*
- *C.botulinum*

Serology

- *Strongyloides*
- *Schisosomiasis* in returned travellers

- No real utility for serology for bacteria GI infections eg Typhoid
  Widal test is basically useless

Treatment - principles

- Often don't need specific therapy
- Often diagnosis too late – patients getting better
- The commonest cause of bacterial diarrhoea does not need treatment.

- SUPPORTIVE therapy
- Fluids
  - ORS
  - IV

- Simple analgesia.
- Regular assessment
- Some infections should definitely be treated – eg?

Summary

- Good History
  - Patient exposure
  - Large v small bowel
- Changes in diagnostic algorithms
- Many causes – but most require

Thank you

- Thanks to Dr Iain Abbott, Dr Meredith Hughes