1. Classification of Bacterial Toxins Associated with Diarrhea...

<table>
<thead>
<tr>
<th>CYTOTOXIC</th>
<th>CYTOTOXIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibrio cholerae</td>
<td>Shigella</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Clostridium perfringens</td>
</tr>
<tr>
<td>LT &amp; ST</td>
<td>Types A &amp; C</td>
</tr>
<tr>
<td>Bacillus cereus</td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td>? Aeromonas</td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>? Other Vibrios</td>
<td>? Salmonella</td>
</tr>
<tr>
<td></td>
<td>? Campylobacter</td>
</tr>
</tbody>
</table>

(c) 2004, Sherwood L. Gorbach, M.D.

2. Mortality Caused by Acute Diarrheal Disease

MORTALITY CAUSED BY ACUTE DIARRHEAL DISEASE

- Shigella 600,000
- Cholera 120,000
- Rotavirus 860,000
- Typhoid 600,000
- ETEC 380,000

Total deaths: 2.5 million

(c) 2004, Sherwood L. Gorbach, M.D.
3. Diagnosis of Diarrhea

**DIAGNOSIS OF DIARRHEA**

**Incidence**
- 1-2 cases/year in the USA
- 3-5 cases/year in developing countries
- twice higher figures in children

**Laboratory Diagnosis**
- 2/3 of outbreaks undiagnosed
- 1/2 of hospitalized cases undiagnosed
- 1/2 of “dysentery” cases undiagnosed
- 4/5 of outpatient cases undiagnosed

4. Eighth Pandemic of Cholera Vibrio Cholerae 0139, Non-01

**EIGHTH PANDEMIC OF CHOLERA VIBRIO CHOLERAE 0139, NON-01**

- Onset in December 1992 in Bangladesh
- By March 1993, over 100,000 cases, 1,400 deaths
- 40-50% of cholera cases in affected areas caused by 0139 strain
- Spread to other parts of India and to Pakistan; imported cases in USA and Europe
- Indistinguishable clinically from classical cholera
- Occurs mostly in adults; prior immunity to cholera is not effective
- Resembles El Tor vibrios, but does not belong to 138 known serogroups
- Produces large amounts of cholera enterotoxin
5. Types of E. Coli Pathogens

**TYPES OF E. COLI PATHOGENS**

- Enteropathogenic        EPEC
- Enterotoxigenic        ETEC
- Enteroinvasive          EIEC
- Enterohemorrhagic      EHEC
- Enteroaggregative      EAaggEC

(c) 2004, Sherwood L. Gorbach, M.D.

6. Virulence Factors in Toxigenic E. Coli

**VIRULENCE FACTORS IN TOXIGENIC E. COLI**

- Toxin production
- Adherence to small bowel mucosa

(c) 2004, Sherwood L. Gorbach, M.D.
7. Toxigenic E. Coli

TOXIGENIC E. COLI

Heat-labile toxin (LT)
- Similar chemically and antigenically to cholera toxin
- Activates adenylate cyclase

Heat-stable toxin (ST)
- Family of toxins in animals and humans
- Activates guanylate cyclase
- Rapid onset, short course

8. Shigellosis

SHIGELLOSIS

- 4 serotypes
  - S. sonnei most common in developed countries
  - S. dysenteriae most severe
- Watery diarrhea most common
- Grossly bloody stool 5-10%
- PMN’s and RBC’s in stool
- Fever and systemic symptoms
- Tenesmus
- Mild disease in children, more severe in adults
- Antibiotic treatment indicated
9. **Enterohemorrhagic E. Coli**

**ENTEROHEMORRHAGIC E. COLI**

- Children and adults
- Bloody diarrhea
- 0157:H7
- Shiga-like toxin
- Vero-cell assay for feces
- Hemolytic-uremic syndrome (HUS)

(c) 2004, Sherwood L. Gorbach, M.D.

10. **Salmonella Syndromes**

**SALMONELLA SYNDROMES**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroenteritis</td>
<td>75%</td>
</tr>
<tr>
<td>- mild (most common) to severe, dehydrating</td>
<td></td>
</tr>
<tr>
<td>- Colitis</td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td>5-10%</td>
</tr>
<tr>
<td>- with/without diarrhea</td>
<td></td>
</tr>
<tr>
<td>- Arthritis</td>
<td></td>
</tr>
<tr>
<td>- Endocarditis</td>
<td></td>
</tr>
<tr>
<td>- AIDS</td>
<td></td>
</tr>
<tr>
<td>Typhoidal (enteric fever)</td>
<td>5-10%</td>
</tr>
<tr>
<td>- with/without diarrhea</td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>5%</td>
</tr>
<tr>
<td>- bone, joints</td>
<td></td>
</tr>
<tr>
<td>- meninges</td>
<td></td>
</tr>
<tr>
<td>- wounds</td>
<td></td>
</tr>
<tr>
<td>- gall bladder</td>
<td></td>
</tr>
<tr>
<td>Carrier state (&gt;1 year)</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

(c) 2004, Sherwood L. Gorbach, M.D.
11. Campylobacter

CAMPYLOBACTER

- C. jejuni - the GI pathogen
- 5-15% of all diarrhea cases
- Chickens most common vehicle
- “Dysentery”-like disease
- 2-phase disease
- Antibiotic treatment questionable

(c) 2004, Sherwood L. Gorbach, M.D.

12. Yersinia

YERSINIA

- Age-related
  - gastroenteritis in children
  - terminal ileitis in adolescents
  - Joints and/or rash in young adults
- Terminal ileum, favorite target
- Acquired from food (animals) and milk
- Antibiotic treatment, questionable
- Causes severe disease in immunocompromised hosts

(c) 2004, Sherwood L. Gorbach, M.D.
13. Incidence of Rotavirus Cases in Children

![Incidence of Rotavirus Cases in Children](image)

14. Fecal Leukocytes Absent in Infectious Diarrhea

![Fecal Leukocytes Absent in Infectious Diarrhea](image)
15. Fecal Leukocytes Present in Infectious Diarrhea

**Fecal Leukocytes Present in Infectious Diarrhea**

<table>
<thead>
<tr>
<th>Present</th>
<th>Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shigella</td>
<td>Salmonella</td>
</tr>
<tr>
<td>Campylobacter</td>
<td>Yersinia</td>
</tr>
<tr>
<td>Invasive E. coli</td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td></td>
<td>Non-cholera Vibrios</td>
</tr>
</tbody>
</table>

(c) 2004, Sherwood L. Gorbach, M.D.

16. Antimicrobial Treatment

**Antimicrobial Treatment**

- Recommended in symptomatic cases
  - Shigella
  - E. coli (infants)
  - C. difficile
  - Typhoid fever
  - Traveler’s diarrhea
  - Cholera
- Not generally recommended, inclusive data
  - Campylobacter
  - E. coli (EHEC, EPEC, EIEC)
  - Yersinia
  - Aeromonas
  - Vibrios (non-cholera)
- Not recommended (except for unusual cases)
  - Non-typhoidal Salmonella
  - E. coli (ETEC)

(c) 2004, Sherwood L. Gorbach, M.D.
17. Treatment of Diarrhea

**TREATMENT OF DIARRHEA**

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>DRUGS OF CHOICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. typhi</td>
<td>Quinolone, or TMP/SMX, ampicillin (sensitive strains)</td>
</tr>
<tr>
<td>Shigella</td>
<td>Quinolone or TMP/SMX (sensitive strains)</td>
</tr>
<tr>
<td>Campylobac</td>
<td>Quinolone, erythromycin</td>
</tr>
<tr>
<td>V. cholerae</td>
<td>doxycycline or ciprofloxacin</td>
</tr>
<tr>
<td>C. difficile</td>
<td>metronidazole or vancomycin</td>
</tr>
<tr>
<td>Giardia</td>
<td>metronidazole, furazolidone, quinacrine, albendazole</td>
</tr>
</tbody>
</table>

(c) 2004, Sherwood L. Gorbach, M.D.

18. Campylobacter Resistance in Minnesota

Campylobacter Resistance in Minnesota

- 1992: 1.3% of isolates were resistant to quinolones
- 1998: 10.2% of isolates were resistant to quinolones
- Temporally associated with licensure of quinolones in poultry

(c) 2004, Sherwood L. Gorbach, M.D.
19. Use of Quinolones in Poultry

**Use of Quinolones in Poultry**

- Campylobacter resistance:
  - In The Netherlands from 1985 to 1989 went from 0% to 11%
  - In Spain from 1989 to 1991 went from 0-3% to 30-50%
- Temporally related to licensing of quinolone use in poultry

(c) 2004, Sherwood L. Gorbach, M.D.

20. In Vitro Campylobacter Resistance in Thailand

**In Vitro Campylobacter Resistance in Thailand**

<table>
<thead>
<tr>
<th>Year</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987-1990</td>
<td>0%</td>
</tr>
<tr>
<td>1993</td>
<td>40%</td>
</tr>
<tr>
<td>1994</td>
<td>50%</td>
</tr>
<tr>
<td>1995</td>
<td>84%</td>
</tr>
<tr>
<td>1996</td>
<td>96%</td>
</tr>
</tbody>
</table>

(c) 2004, Sherwood L. Gorbach, M.D.
21. Nonspecific Therapy of Infectious Diarrhea - 1

**NONSPECIFIC THERAPY OF INFECTIOUS DIARRHEA-1**

- Effective
  - Fluid
    - oral or intravenous
  - Food
    - continue nutrition intake
    - avoid caffeine, lactose & methylxanthines
- Antimotility drugs
  - codeine, paragoric & tincture of opium
  - Diphenoxylate (lomotil)
  - Loperamide (imodium)
- Bismuth subsalicylate (PeptoBismol)

(c) 2004, Sherwood L. Gorbach, M.D.

22. Nonspecific Therapy of Infectious Diarrhea - 1 (cont.)
23. **Nonspecific Therapy of Infectious Diarrhea - 2**

**NONSPECIFIC THERAPY OF INFECTIOUS DIARRHEA-2**

Not effective
- Kaolin, pectin, charcoal
- Anticholinergics
- Cholestyramine
- Lactobacilli
- Hydroxyquinolones (enterovioform, diiodohydroxyquin)

*Warning*: may be harmful

(c) 2004, Sherwood L. Gorbach, M.D.

24. **Control of Diarrheal Diseases**

**CONTROL OF DIARRHEAL DISEASES**

**AVOID FECAL CONTAMINATION**

- Improve food preparation and handling
- Control sewage disposal
- Provided potable water supplies:
  - Piped and chlorinated

(c) 2004, Sherwood L. Gorbach, M.D.