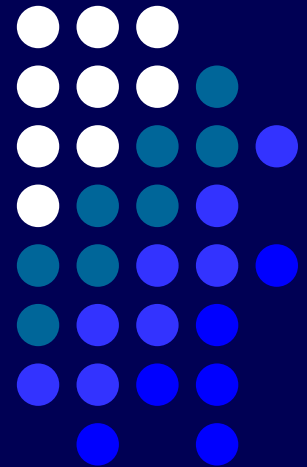
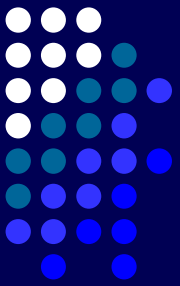


Clostridium difficile: A New Face to an Old Foe



Bob Habicht, MD
14 May 2008

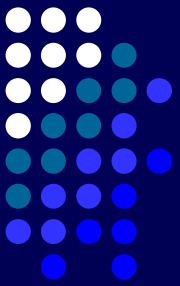




Objectives

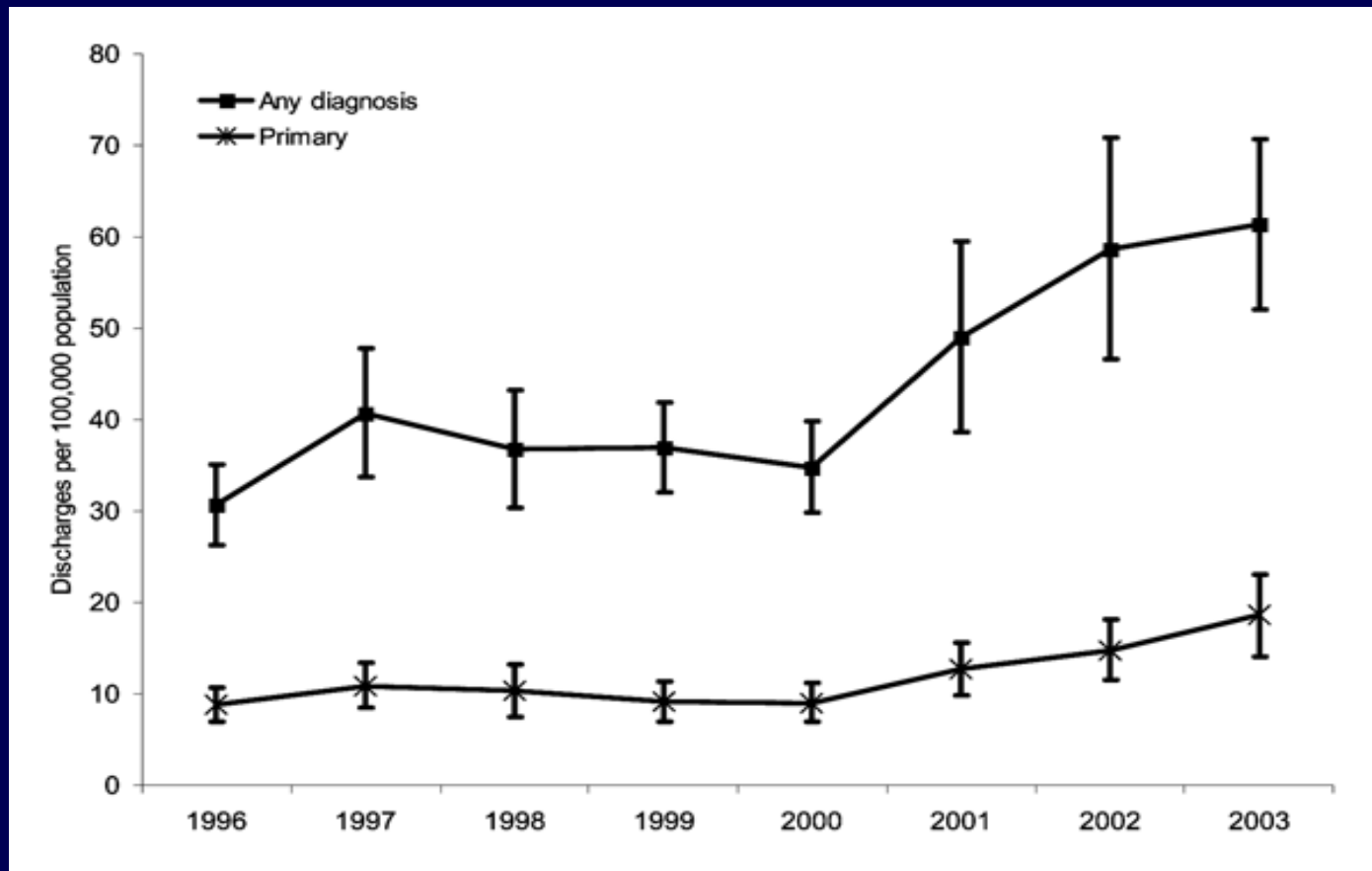
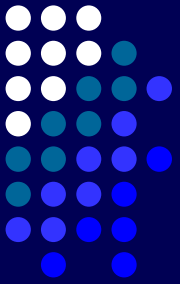
- Recognize the changing epidemiology of *Clostridium difficile*
- Review current knowledge about the new strain of *Clostridium difficile* including risk factors and pathogenicity
- Discuss new approaches to diagnosis, disease stratification and treatment

Clostridium Difficile: An Historical Perspective

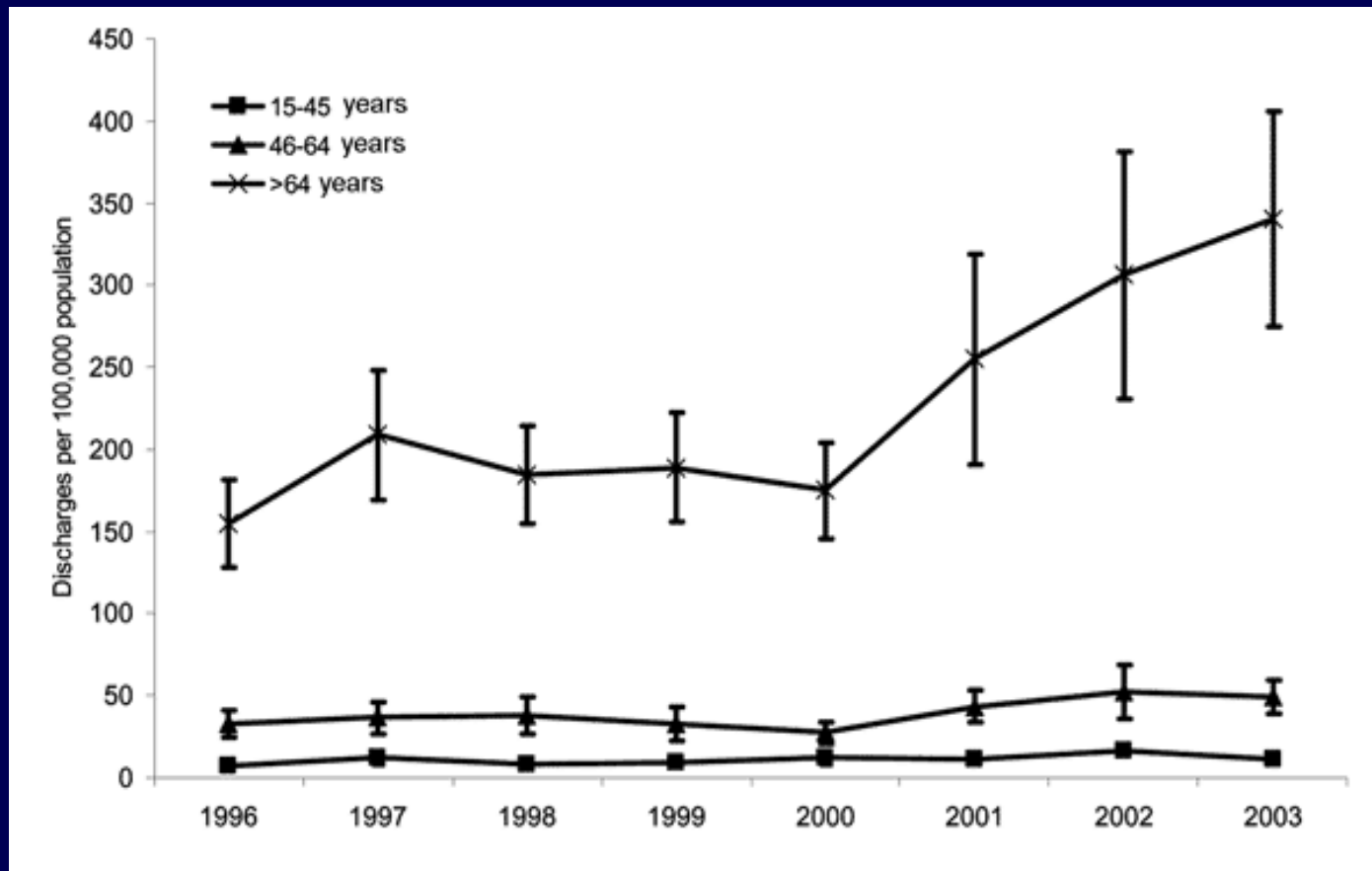


- 1935- first identified as “*Bacillus difficile*”
- 1970’s- antibiotic associated diarrhea
initially thought to be secondary to
S. aureus
- 1978- *C. difficile* toxins identified in humans

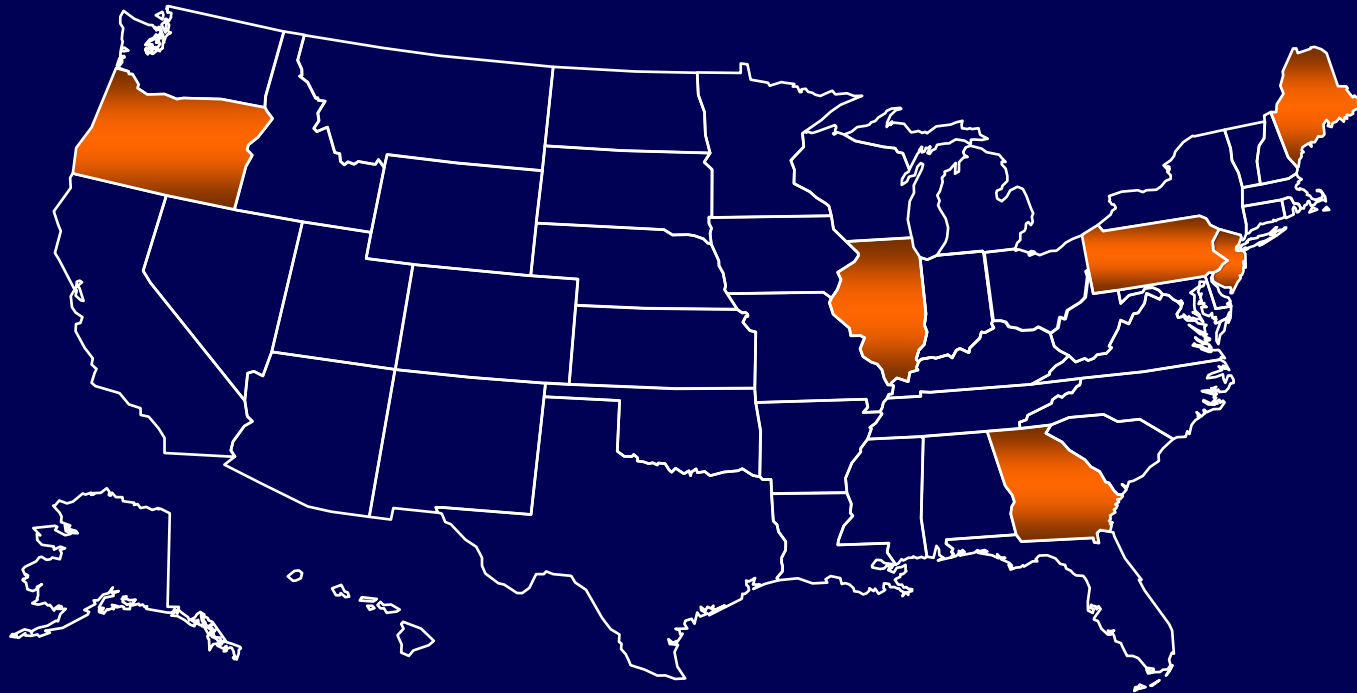
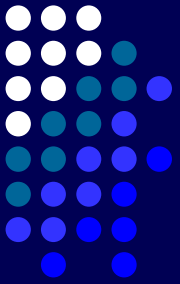
Incidence of *C. difficile*



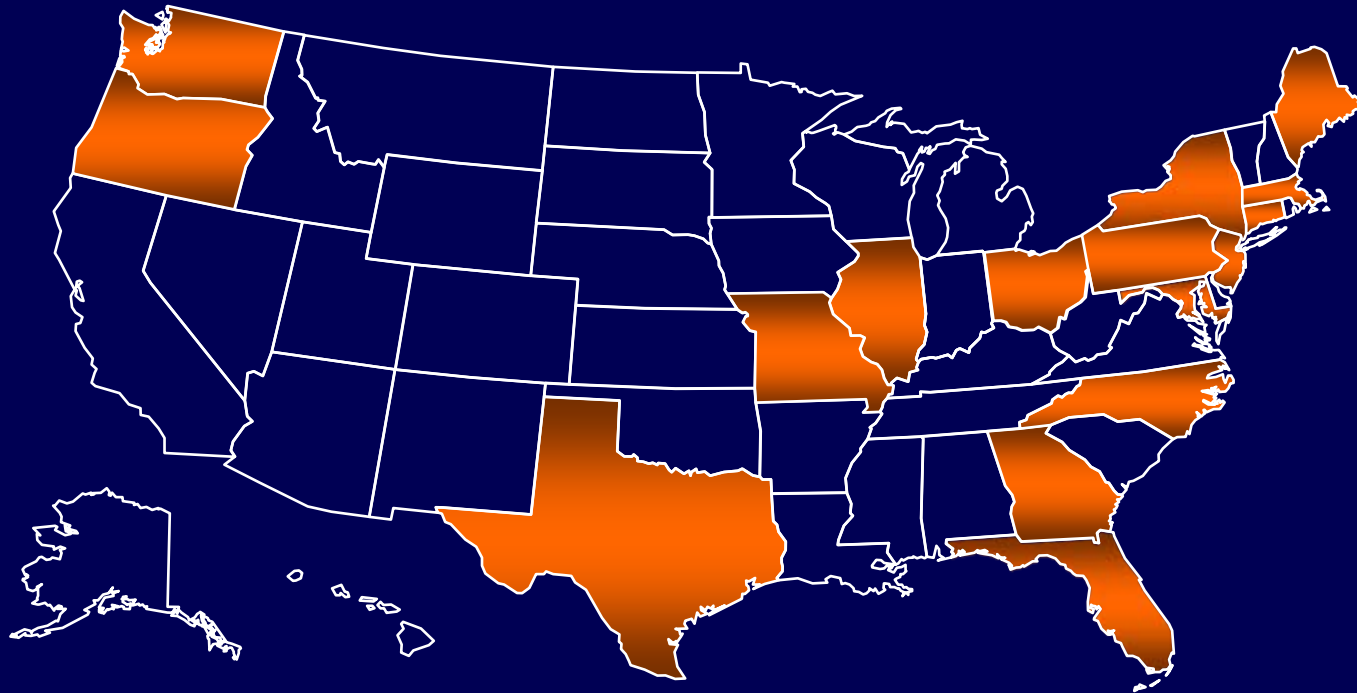
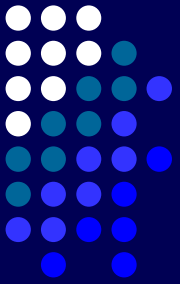
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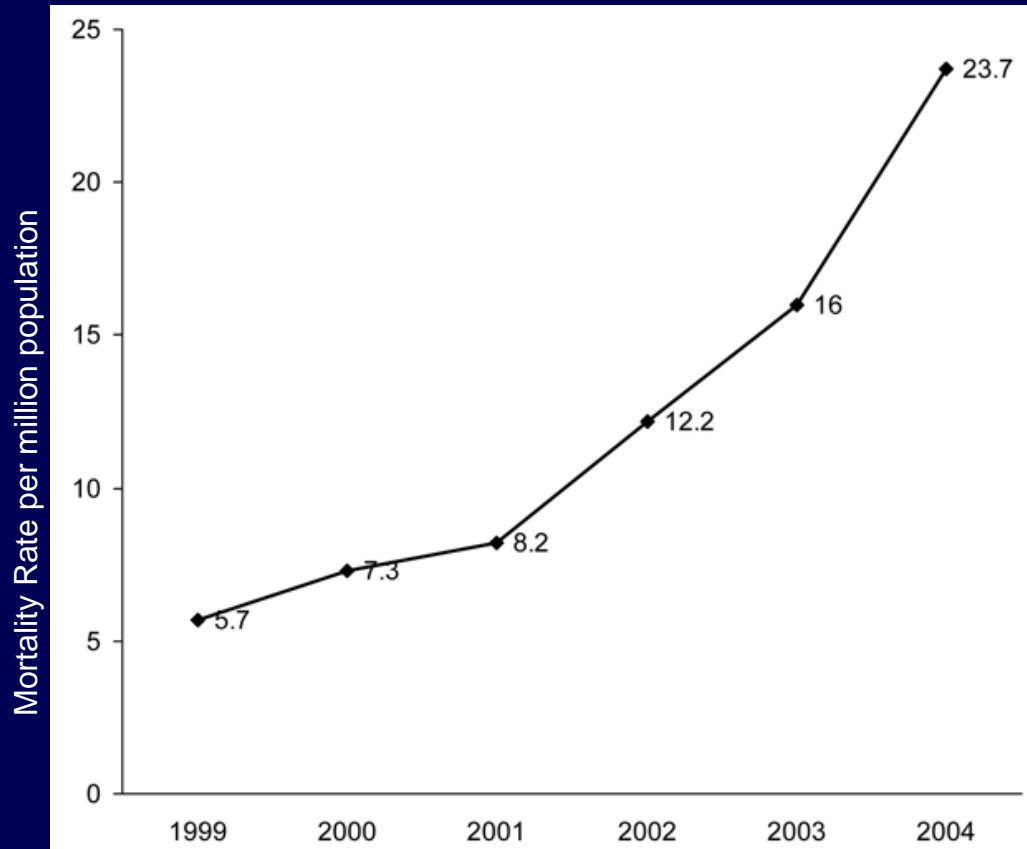
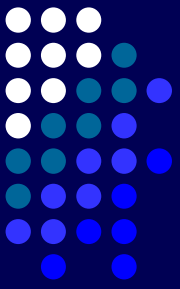
Spread of epidemic strain of *C. difficile*: 2001-2004



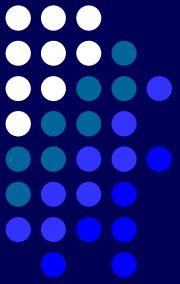
Spread of epidemic strain of *C. difficile*: November 2005



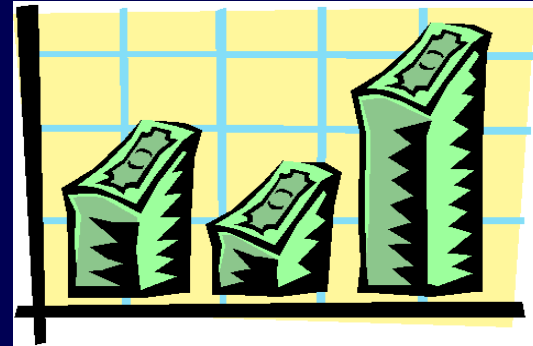
Mortality Associated with *Clostridium difficile*

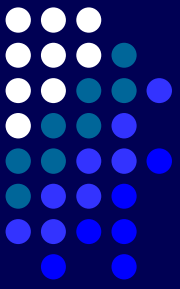


Financial Burden of *C. difficile*



- 2000- Pittsburgh outbreak
- 2002- Quebec outbreak
- Additional \$2,380-2,950 attributable cost per CDAD episode
- Additional \$5,042-\$7,179 attributable inpatient costs over 180 days for inpatient care



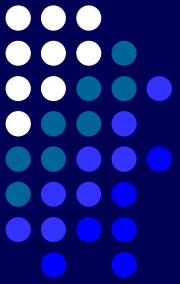


New Populations at Risk

- Young patients without serious underlying disease
- Peripartum women

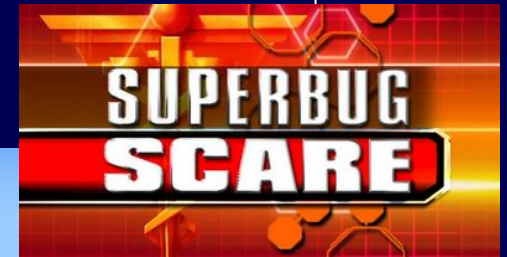


NAP-1 Prevalence:



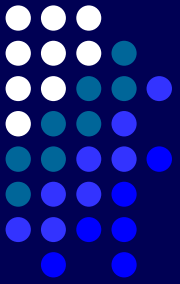
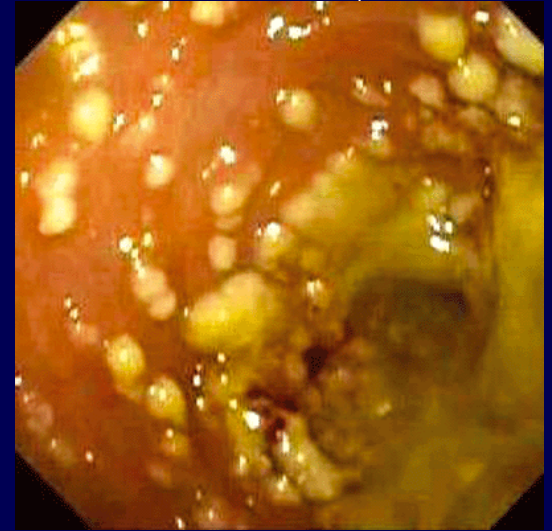
- Connecticut Report 2006
 - 241 residents diagnosis with CA-CDAD
 - 110 hospitalized
 - 33% of total cases and 27% of those hospitalized without any predisposing healthcare interaction or underlying health condition

- APIC Study 2008



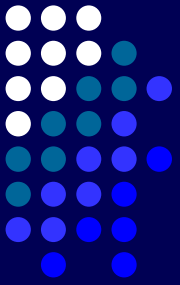
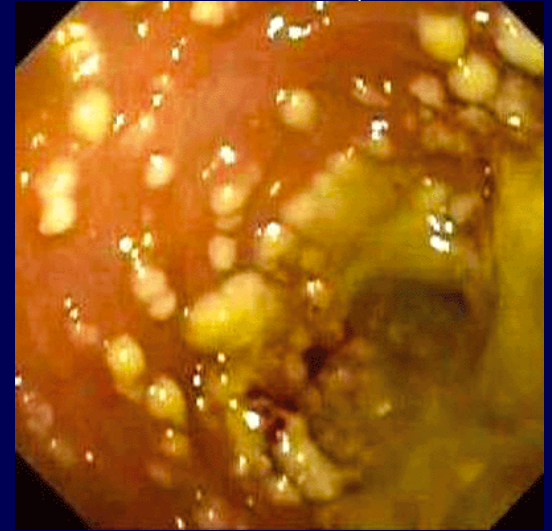
Spectrum of disease

- Asymptomatic colonization
- Diarrhea (mild to severe)
- Colitis +/- pseudomembranes
- Toxic megacolon
- Colonic perforation/peritonitis
- Sepsis and acute abdomen without diarrhea (ileus)

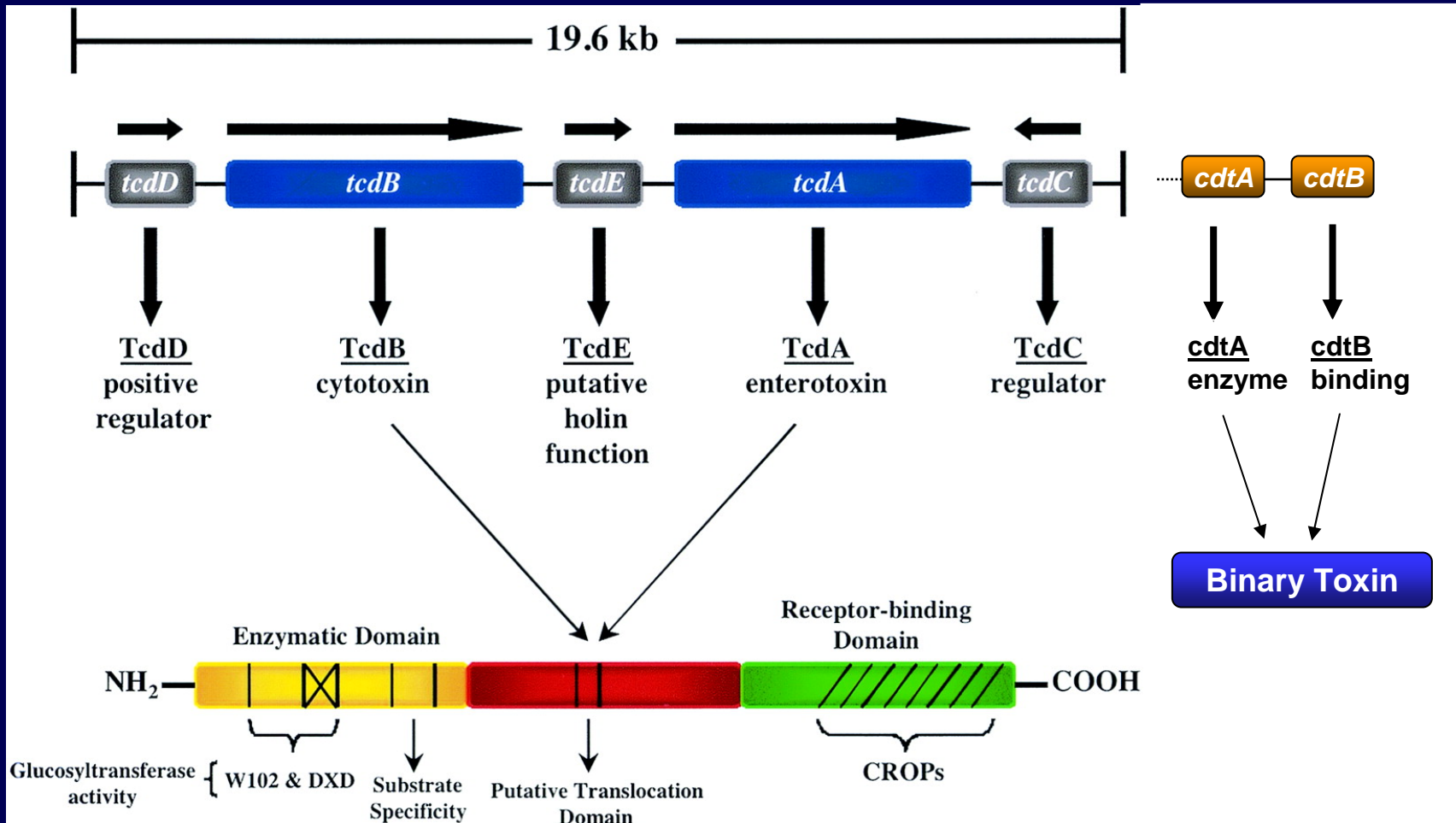
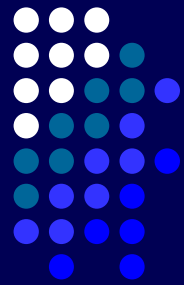


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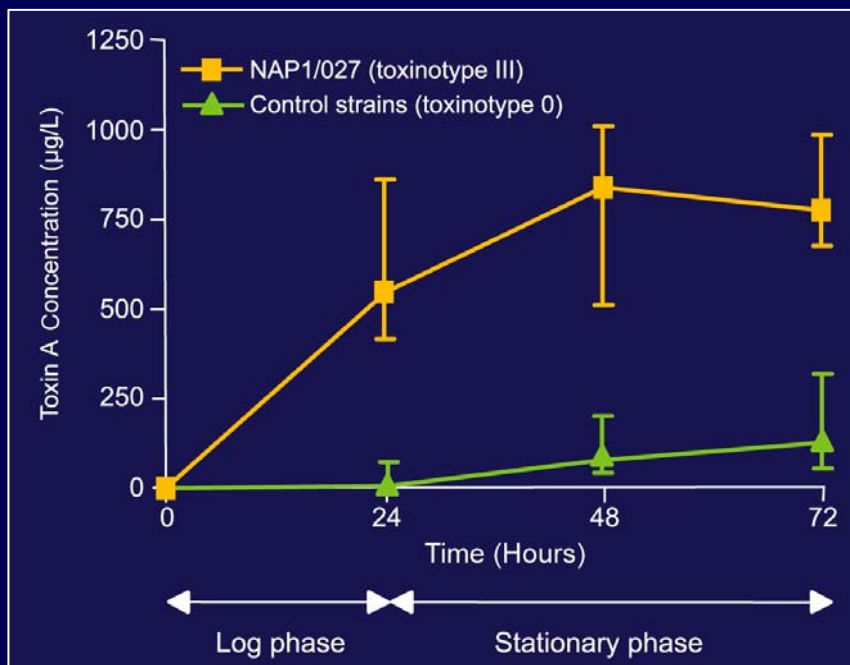
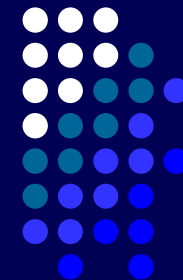
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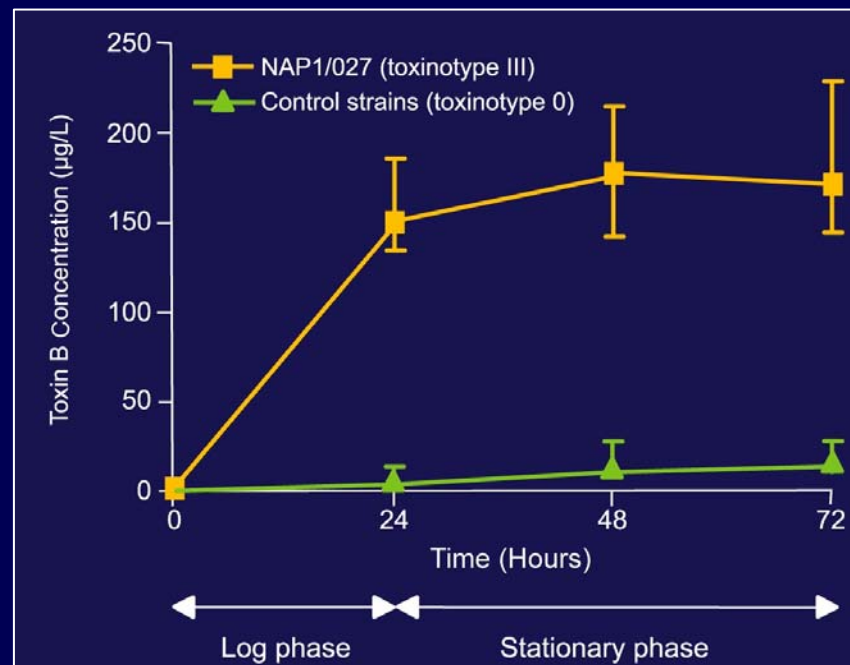
Genetic Loss of Regulation: NAP1/BI/027



NAP1 Toxin Production



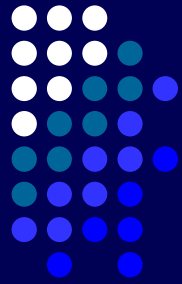
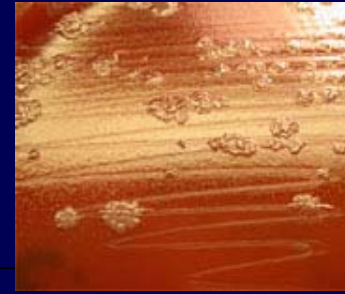
***In vitro* production of toxin A**



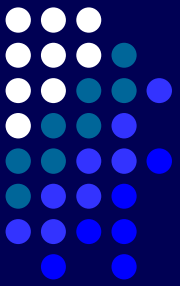
***In vitro* production of toxin B**



Diagnostic Modalities



Test	Sensitivity (%)	Specificity (%)
Endoscopy	51	~100
Culture	89-100	84-99
Cell culture cytotoxin test	67-100	85-100
EIA toxin test	63-99	75-100

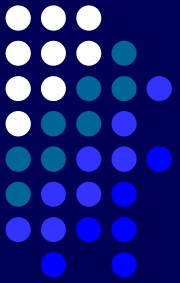


Risk Factors

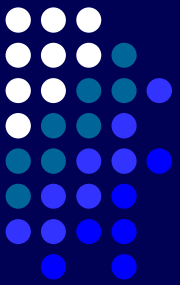
- Hospitalization or chronic care facility
- Recent antibiotic exposure
- Advanced age
- Less common or controversial RF's:
 - Exposure to gastric acid neutralizing agents
 - Immunosuppression
 - Gastrointestinal surgery
 - Gastrointestinal endoscopy

Risk Factors

HOSPITAL →



- Hospitalization or chronic care facility
- Recent antibiotic exposure
- Advanced age
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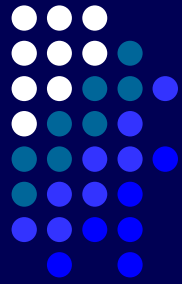


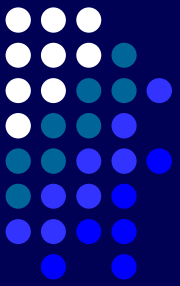
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Risk Factors: Antibiotics

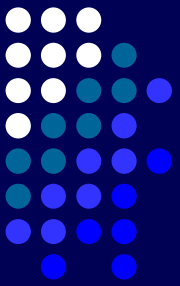
- 1970s- “clindamycin colitis”
- Cephalosporins- 1980’s.
- Fluoroquinolones- 2000’s.





Risk Factors

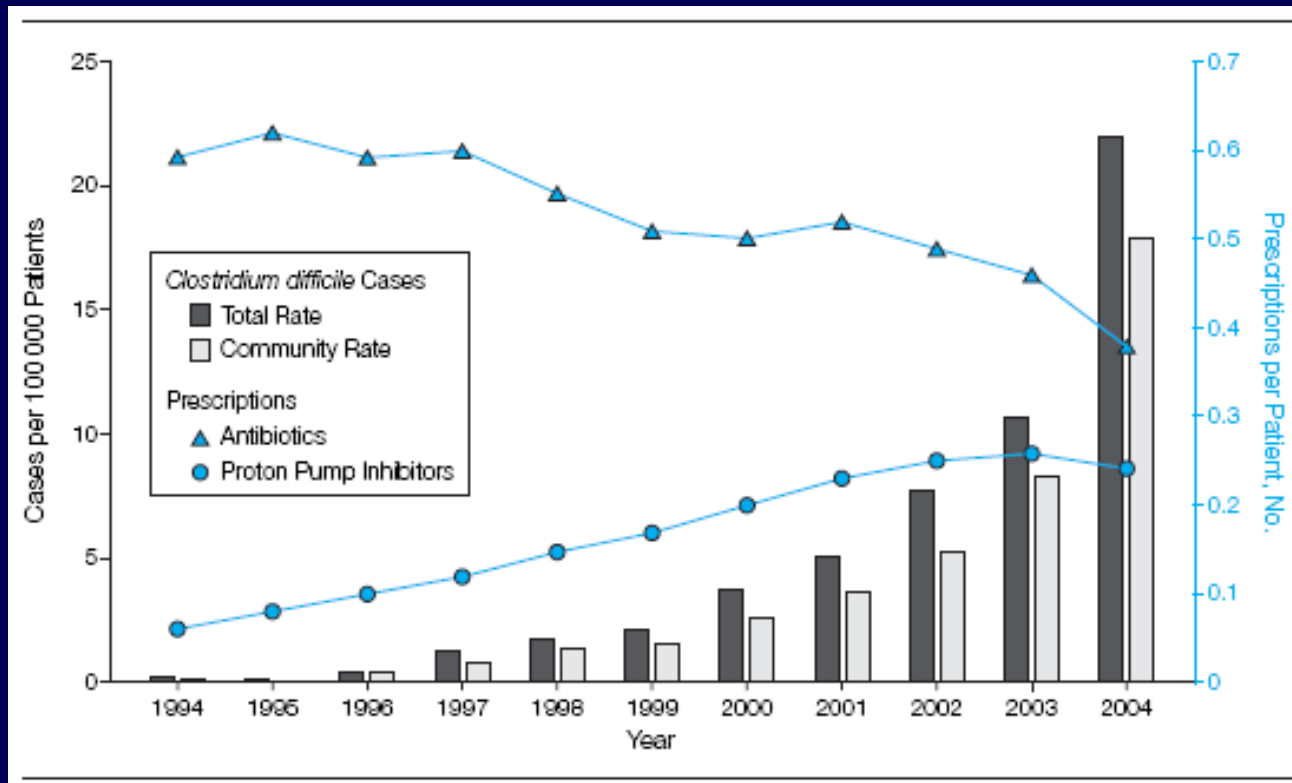
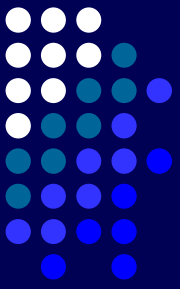
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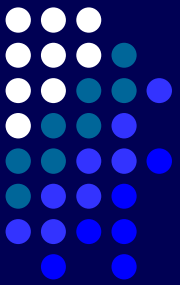


Risk Factors

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Stomach Acid Suppressing Medications and CA-CDAD

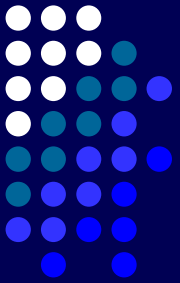




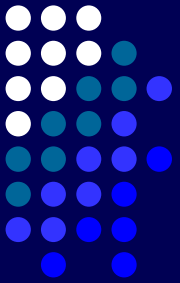
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- Hospitalization or chronic care facility
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 - **Immunosuppression**
 - Gastrointestinal surgery
 - Gastrointestinal endoscopy

Treatment



- Initiate strict infection control
 - Surveillance programs for CDAD
- Stop offending antimicrobial or gastric acid suppression agent if possible
- Stratify
- Start therapy while awaiting test results if clinically indicated

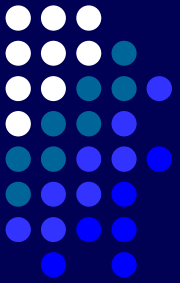


Disease Stratification

TABLE 1. PROPOSED TREATMENT RECOMMENDATIONS FOR CDAD⁶

Disease Classification	Drug Regimen
Mild to moderate WBC < 15,000 cells/mm ³ or unchanged or normal serum creatinine	Metronidazole 500 mg PO TID for 10–14 days
Severe uncomplicated WBC ≥ 15,000 cells/mm ³ or increasing serum creatinine level 50% higher than the level prior to <i>C. difficile</i> infection	Vancomycin 125 mg PO QID or via nasogastric tube for 10–14 days
Severe complicated Above criteria plus hypotension or shock, megacolon, perforation, severe colitis on CT	No ileus: Vancomycin 500 mg PO QID <i>plus</i> metronidazole IV 500–750 mg every 8 hr With ileus or megacolon: Vancomycin 500 mg via NG tube or PO <i>plus</i> metronidazole 500–750 mg IV every 8 hr <i>plus</i> vancomycin rectal instillation
First recurrence	Same as initial episode
Second or further recurrence	PO vancomycin taper, ± pulse regimen: Taper: 125 mg QID for 10–14 days 125 mg BID for 7 days 125 mg daily for 7 days Pulse: 125 mg every 2–3 days for 2–8 weeks

±=With or without; BID=twice a day; CT=computed tomography; IV=intravenous; PO=oral; QID=four times a day; TID=three times a day; WBC=white blood cell count.

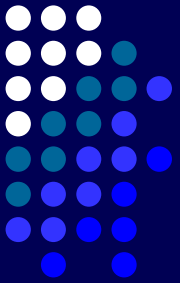


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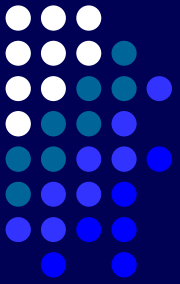


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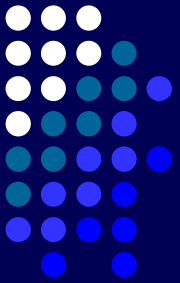


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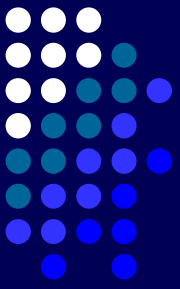


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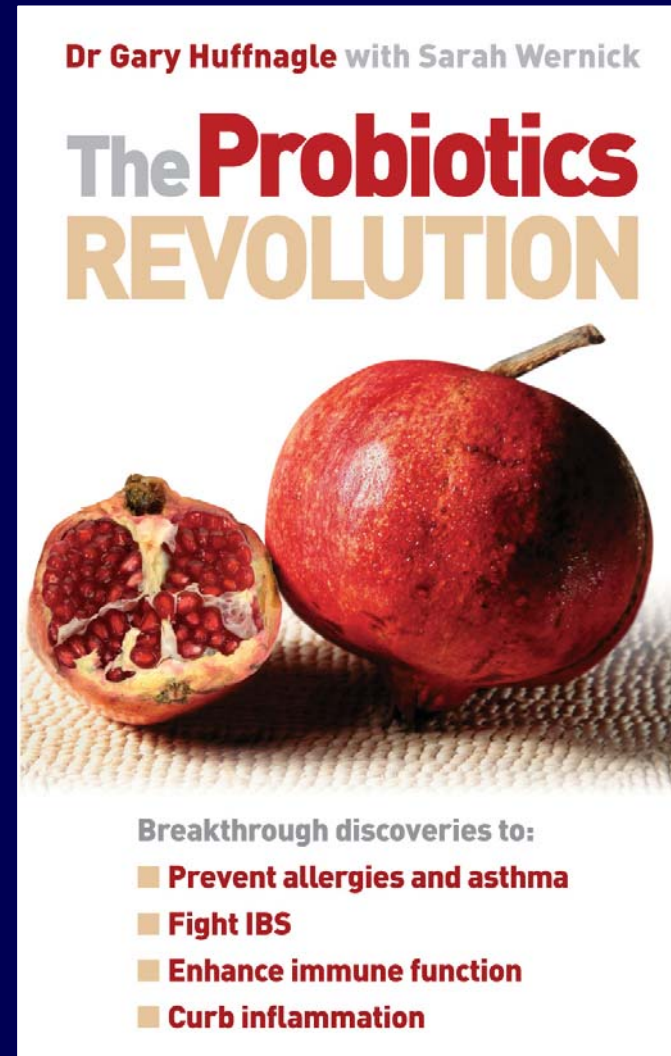
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Future Directions

- Probiotics
- Rifaximin
- OPT-80
- Tolevamer
- Nitazoxanide
- Fecal Replacement Therapy
- IVIG
- *Clostridium difficile* toxoid vaccine



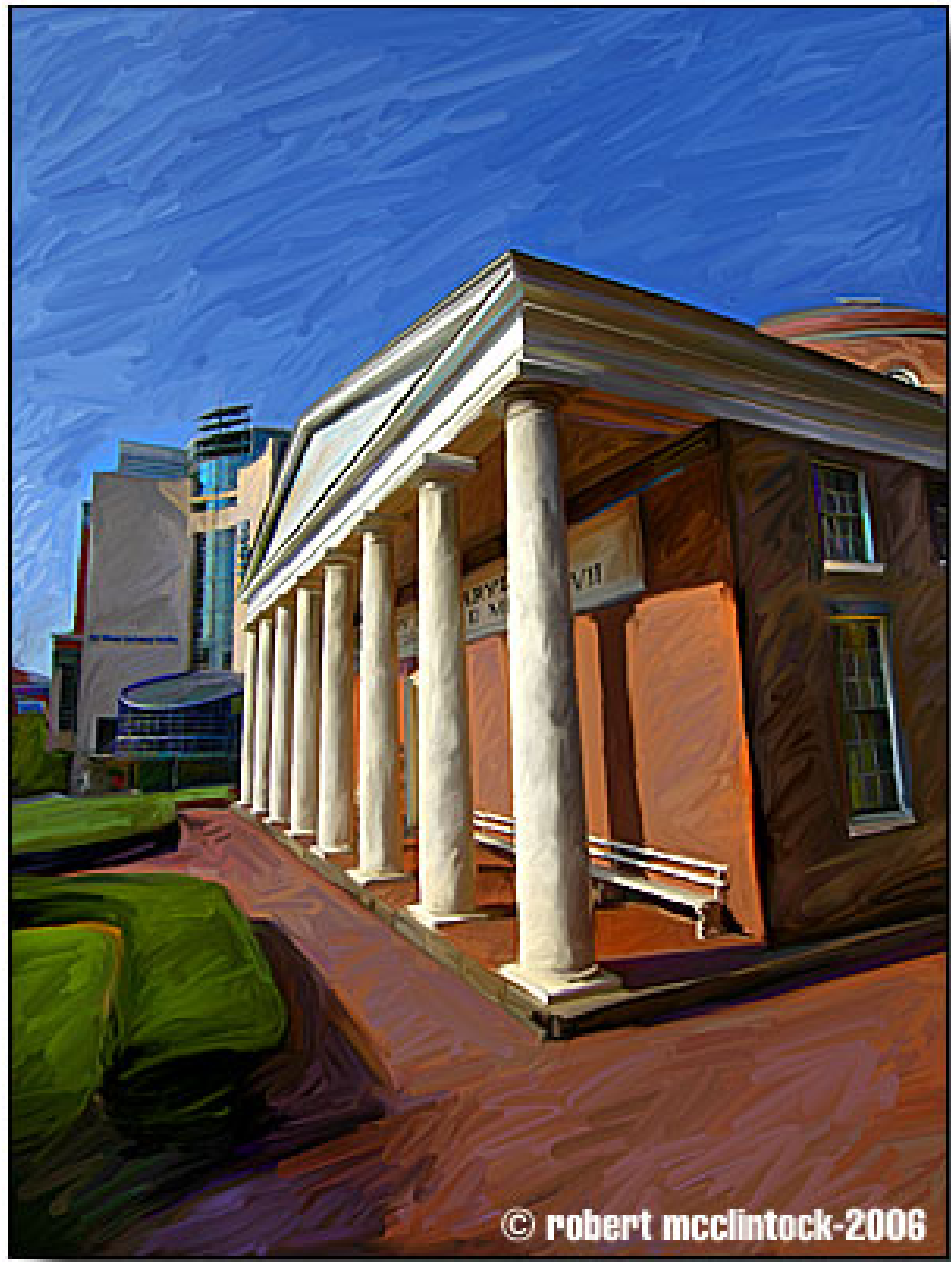
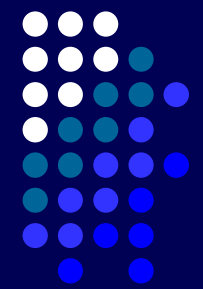
Dr Gary Huffnagle with Sarah Wernick

The Probiotics REVOLUTION



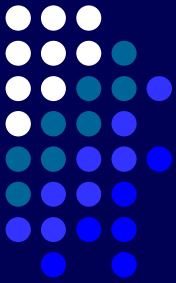
Breakthrough discoveries to:

- Prevent allergies and asthma
- Fight IBS
- Enhance immune function
- Curb inflammation



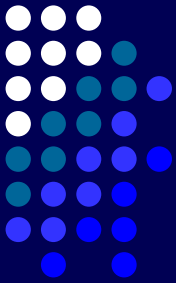
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