Meningococcal Disease: Global Problem, Local Solutions

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- Studying the burden of disease due to vaccine-preventable infections in India, Sri Lanka, Bangladesh, and Nepal
- Developing diagnostic tests to better determine the etiology of pneumonia and meningitis infections
- Assessing the strategy of immunizing mothers to prevent disease in their infants
- Evaluating the best use of limited oxygen supplies in therapy of pneumonia
Outline—Meningococcus

- Causes severe disease with sudden onset and severe outcomes
- Disease patterns differ around the globe
- Use of vaccine to prevent disease
- Vaccine development program in Africa
Section A

Introduction
Neisseria meningitidis *Nomenclature*

- Meningococcus
- Abbreviation: Nm
- Now obsolete
  - Cerebrospinal meningitis (CSM)
  - Spotted fever
  - Diplococcus meningitidis
Peripheral Blood Smear and Buffy Coat Gram Stain

Peripheral blood smear (Wright’s stain) and buffy coat gram stain of 14-year-old with fatal meningococcemia.
Petechiae in Septicemia

Photo Source: CDC
Bacteremia without sepsis
  - Occult bacteremia: no mortality

Meningococcemia, without meningitis
  - Clinical sepsis, rash: high mortality 15–40%

Meningitis with or without meningococcemia
  - Intermediate mortality 5–15%; 20% sequelae

Also: pneumonia, arthritis, urethritis
Serious Outcomes of Meningococcal Disease

Meningococcemia
- Skin scars from necrosis
- Limb loss from gangrene
- Renal failure
- Septic arthritis
- Pneumonia
- Epiglottitis
- Pericarditis

Up to 40% fatality rate

Meningitis
- Spastic quadriplegia
- Hearing loss
- Cerebral infarction
- Cortical venous thrombophlebitis
- Cerebral edema
- Cranial nerve palsies
- Mental retardation
- Hemiparesis

3%–10% fatality rate

Comparison of meningococcal disease: one decade (1990–1999)

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Deaths</th>
<th>Conjugate vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.K.</td>
<td>10,000</td>
<td>1,000</td>
<td>New group C, (3 suppliers)</td>
</tr>
<tr>
<td>U.S.A.</td>
<td>22,000</td>
<td>2,000</td>
<td>New group A,C,Y, W conjugate</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>700,000</td>
<td>100,000</td>
<td>None</td>
</tr>
</tbody>
</table>
Section B

Epidemiology of Disease Due to *Neisseria meningitidis*
Agent—Neisseria meningitidis

- Gram-negative diplococcus
- Capsular polysaccharide antigens differentiate serogroups (A,B,C,X,Z,29-E, and W135)
- Serogroups A,B,C (W-135) associated with epidemics
- Subtyping identifies certain strains (clones) with increased virulence and epidemic potential
  - Serogroup A, III-1; serogroup B, ET-5
Reservoir

- Humans only
- Asymptomatic carriage in the nasopharynx is common (5–15% in children, 1% in adults)
Mode of Spread

- Person to person by aerosol or direct contact with respiratory secretions of infected people
- Most cases acquired through exposure to asymptomatic carriers
- Relatively few cases acquired through direct contact with patients with meningococcal disease
Meningococcal Disease Transmission

- **Aerosol**: via air droplets of respiratory secretions, no physical contact
- **Direct contact**: with infected persons, e.g., kissing, sexual contact, mouth-to-mouth resuscitation
- **Indirect contact**: oral contact with shared items, including cigarettes, drinking glasses, utensils, etc.
Meningococcal Disease Transmission

C = Carrier
D = Disease
→ = Transmission
↓ = Invasion
Effect of Crowding in British Army Guards Depot

Caterham, 1916

- Barracks built for 800 men, but with WW I mobilization, up to 13,000 were housed in barracks, huts, tents
- Military rule for bed separation was three feet, but “…there were great temptations to…hygienically unprincipled authorities to put in more beds”
  — Glover, 1920
# Estimating Carrier Rates With a Ruler

<table>
<thead>
<tr>
<th>Feet (Scale ½)</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inches 3</td>
<td>6</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>9</td>
<td>0</td>
</tr>
</tbody>
</table>

- Beds less than 9” apart. Carrier Rate = 30% or more.
- Beds less than one foot apart. Carrier Rate = 20% or more.
- Beds 1’ 4” apart (The usual distance in mobilization standard strictly observed) Carrier Rate = 9:½
- Beds 2’ 6” apart (as in “spacing out” Caterham) Carrier Rate = under 5%
- Beds 3 feet apart. Carrier Rate = under 2%
Nasopharyngeal Carriage

- Five to ten percent of the population are carriers
- Carriage is usually transient
- Level of carriage does not predict the course of an outbreak
- Less than one percent of persons exposed who become carriers will develop invasive disease
- Carriage is believed to increase immunity to the bacteria
Host Factors

- Risk of invasive disease due to *N. meningitidis* is higher in children, decreases with age
- All humans are susceptible, but disease risk is higher in persons with terminal complement deficiency, splenectomy, viral respiratory infections
Incubation Period

- One to ten days
- Usually less than four days
## Risk Factors for Meningococcal Disease in the U.S.

<table>
<thead>
<tr>
<th>Clinical definition</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sporadic cases</strong></td>
<td></td>
</tr>
<tr>
<td>Household intimate contact</td>
<td>500–800&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dormitory residence</td>
<td>10.7&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Outbreaks</strong></td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>7.8&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bar patronage</td>
<td>16.7&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Acquisition of new NP carriage</strong></td>
<td></td>
</tr>
<tr>
<td>Alcohol ingestion (&gt;15 per week)</td>
<td>3.8&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td>Bar patronage (last 2 weeks)</td>
<td>1.9&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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<sup>1</sup>(1976). J Infect Dis, 134, 201./JAMA, 235, 261.<br/>
<sup>2</sup>Froeschle et al., Connaught Laboratories, unpublished data.<br/>
<sup>3</sup>Imrey et al. (1996). Am J Epidemiol.<br/>
Stages of Meningococcal Infection and Disease

- **Exposure** to carrier
  - [Transmission]
- Mucosal **colonization** (carriage)
  - [Invasion]
- Invasive **disease**: septicemia, meningitis, other
  - [Epidemiogenic transformation]
- **Endemic** to **epidemic** disease
Incidence of Meningococcal Disease in the U.S.

Incidence of Meningococcal Disease in the United States
(1920-1995)

Cases per 100,000 Population

Year

Adapted by CTLT from Wenger JD, Perkins BA. Patterns in the emergence of epidemic meningococcal disease.
Incidence of Meningococcal Disease—U.S.

- By age group—selected U.S. areas, 1989–1991

Adapted by CTLT from MMWR 1993, 42:SS2;21.
Annual Incidence of Meningococcal Disease—Maryland

By age group—Maryland, 1992–1997

Incidence (Cases per 100,000)

Inset: Incidence (Cases per 100,000)

Age (Years)


Adapted by CTLT from JAMA.
Annual Incidence of Meningococcal Infection—Students

- Maryland college students, 1992–1997

Annual Incidence of Meningococcal Infection, Maryland College Students, 1992-1997

Rate (Cases per 100,000)

- Four Year College: 1.74
- Dormitory (Four Year): 3.24
- Non-Dormitory (Four Year): 0.96
- Two Year College & Non-College: 1.49

Dormitory v. non-dormitory, p=0.05
## N. Meningitidis Serogroups

<table>
<thead>
<tr>
<th>Serogroups</th>
<th>Most disease</th>
<th>Epidemics</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>B</td>
</tr>
<tr>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>D</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>E&lt;sub&gt;29&lt;/sub&gt;</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>--</td>
<td></td>
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<tr>
<td>I</td>
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<tr>
<td>K</td>
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<td></td>
</tr>
<tr>
<td>L</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>W&lt;sub&gt;135&lt;/sub&gt;</td>
<td>W&lt;sub&gt;135&lt;/sub&gt;</td>
<td>W&lt;sub&gt;135&lt;/sub&gt; (since 2001)</td>
</tr>
<tr>
<td>X</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Z</td>
<td>--</td>
<td></td>
</tr>
</tbody>
</table>
Epidemiology Is Serogroup Specific

- **Serogroup A**
  - Major and most explosive outbreaks, now in meningitis belt

- **Serogroup B**

- **Serogroup C**

Source: WHO
Section C

Approaches to Control and Policy Considerations
Prevention and Control of Meningococcal Epidemics

- Epidemic response: mass vaccination campaigns
- Routine Immunization of children
Mass Vaccination Campaigns

- Within weeks halt epidemics due to serogroups A or C
- Polysaccharide vaccine types A,C,Y, and W135 are usually effective
- Group B vaccine is problematic, but is used in Norway and Cuba
Routine Immunization

- With polysaccharide vaccine (used in school children and adults)
- With conjugate vaccine (infants)
- U.K. began group C conjugate vaccine for all infants in 2000
- In U.S., some states recommend group A/C vaccine for college entry
- New conjugate vaccine means new U.S. policy: universal for 11-year-olds
## Comparison of Meningococcal Disease

- **Epidemiology and policy**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High-income regions</th>
<th>Low-income regions; Meningitis Belt</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serogroups</strong></td>
<td>B,C</td>
<td>A, C, now W135</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td>Endemic, winter</td>
<td>Endemic/epidemic, dry season</td>
</tr>
<tr>
<td><strong>Incidence (per 100,000)</strong></td>
<td>1–5</td>
<td>20/600</td>
</tr>
<tr>
<td><strong>Peak age</strong></td>
<td>College</td>
<td>School age</td>
</tr>
<tr>
<td><strong>Case fatality</strong></td>
<td>5–15%</td>
<td>15% or more</td>
</tr>
</tbody>
</table>
Meningococcal Vaccines

- Polysaccharide vaccine
  - Meningococcal capsular polysaccharides
    - A/C/Y/W-135: (Menomune®)

- Conjugate vaccines
  - Meningococcal capsular polysaccharides covalently linked to carrier proteins
    - C-conjugate: many producers; used in the U.K. and most of Europe, Canada, Brazil, and Australia
    - A/C/Y/W-135-conjugate: (Menactra™), (U.S. FDA approved 2005)
    - A/C bivalent from MVI for meningitis belt
Surface of Meningococcus

Group A Vaccine

- Higher molecular weight PS is more immunogenic
- Immunogenic with booster response in infants
- Finland (1975): 100% efficacy in children from 3 months to 5 years old
- New Zealand (1985): 3–23 months 100% protected with two doses
Group C Vaccine

- Poor response of infants, and poor booster response
- Decreased response with repeat doses
- 90% efficacy in U.S. military bases (1969)
- In Brazil (1974), no protection at 6–23 months, 67% efficacy at 24–36 months
- Canada (1993), 79% efficacy, lower in under-fives
- Used for outbreaks in U.S. colleges
Antibody Response to Group A or C Polysaccharide

Antibody Response to Group A or C Polysaccharide

- **Group A**
  - Nonimmunized: Red line
  - Immuneized: Orange line

- **Group C**
  - Nonimmunized: Red line
  - Immuneized: Orange line

- Protective Range: Shaded area
- Immunizations: Arrows
T-Cell–Dependent Immune Response

- Total Ab
- IgM Ab
- IgG Ab

Ab Titer vs. Time After Immunization

1° Ag
2° Ag
Group B Vaccine

- Group B PS is cross-reactive with sialic acids in childhood CNS human tissue, hence “self Ag,” and not immunogenic
  - Outer membrane proteins (OMP) used to make vaccines in Norway and Cuba
- In Norway (1991): OMP product had 57% efficacy in older children
- In Brazil (1990): Cuban OMP vaccine 74% effective at 4–6 years
Section D

Vaccine Policy
## National Immunization Policy: Examples

<table>
<thead>
<tr>
<th>Country</th>
<th>Income (GNP per capita USD)</th>
<th>Incidence per 100,000</th>
<th>Vaccine policy</th>
<th>Vaccine used</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.A.</td>
<td>25,850</td>
<td>1.1</td>
<td>College age</td>
<td>PS, Cj</td>
</tr>
<tr>
<td>U.K.</td>
<td>16,561</td>
<td>5</td>
<td>Universal</td>
<td>Cj</td>
</tr>
<tr>
<td>Egypt</td>
<td>1,200</td>
<td>~8</td>
<td>School age</td>
<td>PS</td>
</tr>
<tr>
<td>Benin</td>
<td>380</td>
<td>65.9</td>
<td>Epidemic response</td>
<td>PS</td>
</tr>
</tbody>
</table>

Monovalent C PS-conjugate vaccine licensed in the U.K. in 1999 for all school children, then all infants, part of routine schedule

Safety and immunogenicity studies were done, but no efficacy studies before licensure
77–97% reduction in disease over two years

Meningococcal C Disease Reports, UK

Meningococcal Disease: Endemic and Cyclical in the U.S.

Meningococcal Disease is Endemic and Cyclical in the United States

Serogroup Distributions Have Changed in the U.S.

- *N. meningitidis* serogroup distributions have changed in the U.S. (all age groups)

Age-Specific Fatalities from Meningococcal Disease

Age-Specific Fatalities from Meningococcal Disease, United States, 1997-2001

Deaths

<table>
<thead>
<tr>
<th>Age Group (Year)</th>
<th>0</th>
<th>50</th>
<th>100</th>
<th>150</th>
<th>200</th>
<th>250</th>
<th>300</th>
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<tbody>
<tr>
<td>&lt;1</td>
<td>139</td>
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<td></td>
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<tr>
<td>1-4</td>
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<td>5-14</td>
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<tr>
<td>15-24</td>
<td>266</td>
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<td>25-34</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>93</td>
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<tr>
<td>45-54</td>
<td>102</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>55-64</td>
<td>48</td>
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<td></td>
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<tr>
<td>65-74</td>
<td>56</td>
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<td>75-84</td>
<td>57</td>
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<td></td>
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<tr>
<td>85+</td>
<td>48</td>
<td></td>
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</tr>
</tbody>
</table>

Most cases in adolescents and young adults are potentially vaccine preventable.

Serogroup Distribution by Age Group, United States, 1994-1998

- 0-2 years: 48% B, 48% C
- 2-5 years: 65% C
- 6-11 years: 71% Y
- 12-17 years: 70% Y
- 18-23 years: 79% W-135
- 24-54 years: 87% W-135
- ≥55 years: 87% W-135

Adapted by CTLT from CDC. 
Meningococcal disease is serious but preventable in adolescents and young adults

Maryland Residents Diagnosed with Invasive Meningococcal Disease, 1 January 1990 to 31 December 1999

<table>
<thead>
<tr>
<th></th>
<th>All ages n/total</th>
<th>&lt;15 years n/total</th>
<th>15–24 years n/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40/294 (13.6%)</td>
<td>5/109 (4.6%)</td>
<td>16/71† (22.5%)</td>
<td></td>
</tr>
<tr>
<td>Potentially vaccine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>preventable</td>
<td>193/257* (75.1%)</td>
<td>64/94 (68.1%)</td>
<td>53/64‡ (82.8%)</td>
</tr>
</tbody>
</table>

†P = 0.001, <15 years vs. 15–24 years
‡P = 0.04, < 15 years vs. 15–24 years
*Serogroup information not available for all cases

Product Approval Information - Licensing Action

Proper name: Meningococcal Polysaccharide (Serogroups A, C, Y and W-135) Diphtheria Toxoid Conjugate Vaccine
Tradename: Menactra
Manufacturer: Aventis Pasteur, Swiftwater, PA, License #1277
Indication for Use: For active immunization of adolescents and adults 11-55 years of age for the prevention of invasive meningococcal disease caused by Neisseria meningitidis serogroups A, C, Y and W-135
Approval Date: 1/14/2005
Type of submission: Biologics license application

Approval Letter - [Text]

Package Insert - [PDF]
Meningococcal Conjugate Vaccine
Meningococcal (Groups A, C, Y and W-135) Conjugate Vaccine (MCV-4)
February 10, 2005

ACIP Recommends Meningococcal Vaccine for Adolescents and College Freshmen

The Advisory Committee on Immunization Practices (ACIP) to the Centers for Disease Control and Prevention (CDC) this week recommended that children 11-12 and teens entering high school, as well as college freshman living in dormitories receive a newly licensed meningococcal vaccine.

Source: CDC’s National Immunization Program.
### History of Meningococcal Vaccines, 2002

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Producer</th>
<th>Price</th>
<th>Since</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Aventis</td>
<td>NA</td>
<td>1978</td>
</tr>
<tr>
<td>A + C</td>
<td>Aventis</td>
<td>NA</td>
<td>1978</td>
</tr>
<tr>
<td>A, C, W135, Y</td>
<td>Aventis, Merck [95*]</td>
<td>$60+ (U.S. college market)</td>
<td>1981</td>
</tr>
<tr>
<td>A, C, W135, Y</td>
<td>GSK</td>
<td>~$5 (Hajj)*</td>
<td>1980s</td>
</tr>
</tbody>
</table>

*Not licensed in the U.S.
# History of Meningococcal Vaccines, U.S., 2005

<table>
<thead>
<tr>
<th>Antigen</th>
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<td>GSK</td>
<td>~$5 (Hajj)*</td>
<td>1980s</td>
</tr>
<tr>
<td>A, C, W135</td>
<td>GSK</td>
<td>$1.50 (W. Afr.)*</td>
<td>2003*</td>
</tr>
<tr>
<td>A, C, W135, Y (Cj)</td>
<td>Sanofi (Aventis)</td>
<td>~$60</td>
<td>2005</td>
</tr>
</tbody>
</table>

*Not licensed in the U.S.*
Section E

African Disease
La ceinture de la méningite cérébro-spinale par Lapeyssonnie

Source: WHO
Meningococcal Meningitis Belt

- Only here: repeated, frequent, severe Nm epidemics, mostly group A
- 170 million population at risk for hyperendemic and epidemic disease
- Hyperendemic incidence: 3 to 60 per 100,000
- Epidemic incidence: 200 to 600 per 100,000
- In 1996–1997 epidemic
  - 214,000 cases
  - 21,800 deaths
- At least 1 million deaths over last 40–50 years
Meningococcal Meningitis Belt

- Defined by Lapeyssonnie in 1963: Ethiopia to Senegal
- Parts of 16 Sahel (Sub-Saharan) countries
- Belt is dry grassland and scrub, with subsistence farming (millet, sorghum, peanuts, and grazing)
- GNP per capita: U.S. $100–820 (least developed category)
African Meningitis Belt

- La ceinture de la méningite cérébro-spinale par Lapeyssonnie

Source: WHO
Meningitis Belt Is a Changing Environment with Droughts

Photo by aheavens via flickr.com. Some rights reserved.
Meningococcal Meningitis Belt

- Climate features
- Mostly semi-arid Sahel with 100–200 mm of rain per year, mostly in one season (May–November)
- Northern boundary—Sahara Desert (moving boundary)
- Southern boundary—humid savannah and rain forest
- Few epidemics in local regions within isohyet 1,100 mm or mean humidity greater than 10 gm/m$^3$
Major epidemics occur every 5–10 years
Between epidemics, incidence of infection falls markedly but remains several times higher than that found in industrialized countries
Periodicity of Nm Outbreaks

Annual Number of Cases of Meningitis, Burkina Faso, 1940-1993

Adapted by CTLT from WHO.
Seasonality of Epidemics in the Meningitis Belt

Seasonality of Nm Epidemics in the Meningitis Belt, 1995-1999

- **Ghana (1996-1997)**
- **Sudan (1998-1999)**

Adapted by CTLT from WHO.
African “Meningitis Belt” Outbreaks

- West African outbreaks of CSM are usually enormous.
- In the 1996–1997 outbreak, over 213,658 cases reported, with 21,830 deaths reported.
- Underestimates because reporting systems are not sufficient.
- Attack rates of 1:10 in individual communities reported.
- Up to 5% of patients may be secondary or co-primary infections.
Intercontinental Spread of Serogroup A

Adapted by CTLT from WHO.
Seasonality of Outbreaks

- Epidemics usually start in the early part of the dry season
- Stop abruptly at the onset of rains
- New epidemic during the following dry season
Seasonality of Nm epidemic, Zaria, Nigeria

Seasonality of Nm Epidemic, Zaria, Nigeria

Cases

Absolute Humidity

Mean Max. Temperature

Adapted by CTLT from Greenwood, 1984
Characteristics of Meningitis Belt

- Environmental conditions at the end of the dry season damage respiratory mucous membranes
  - High temperature
  - Low humidity
  - Harmattan (a dusty wind that blows from the Sahara)
Meningococcal disease, Uganda – update

From 28 December 2005 to 3 February 2006, 301 suspected cases of meningococcal disease including 23 deaths have been reported from the districts of Nakapiripirit (258 cases including 19 deaths) and Moroto (43 cases including 4 deaths) in north-eastern Uganda. Laboratory tests have confirmed Neisseria meningitidis A.

The International Coordinating Group (ICG) on Vaccine Provision for Epidemic Meningitis Control has provided 250 000 doses of bivalent vaccine for a mass vaccination campaign as well as 10 000 doses of oily chloramphenicol for case management. The immunization campaign has started in both districts. Reports of suspected cases in 5 neighbouring districts are also being investigated.

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1 See No. 5, 2006, p. 43.

Ménингокoccie, Ouganda – mise à jour

Du 28 décembre 2005 au 3 février 2006, on a signalé 301 cas suspects de méningococcie, dont 23 mortels, dans les districts de Nakapiripirit (258 cas dont 19 décès) et Moroto (43 cas dont 4 décès), au nord-est de l’Ouganda. Les tests de laboratoire ont confirmé Neisseria meningitidis A.

Le Groupe international de coordination pour l’approvisionnement en vaccin antiméningococcique (ICG) a fourni 250 000 doses de vaccins bivalents pour une campagne de masse et 10 000 doses de chloramphénicol huileux pour la prise en charge des cas. La campagne de vaccination a commencé dans les deux districts. On enquête également sur des cas suspects signalés dans 5 districts voisins.

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1 Voir N° 5, 2006, p. 43.
Factors for Nm Epidemics in the Meningitis Belt

- Nasopharyngeal carriage
- Waning immunity
- Environmental factors
- Demographic factors
- Socioeconomic factors
- Concurrent infections
Summary

The diagram illustrates the changes in meningococcal carriage and herd immunity over time. It shows two types of immunity: immunity against panclonal antigens (e.g., polysaccharide) and clone-specific non-polysaccharide immunity. The y-axis represents meningococcal cases, while the x-axis represents years from 1970 to 1990.

Clones I-1, IV-1, and III-1 are marked on the graph, each with its respective carriage levels. The diagram also highlights periods A, B, C, D, and E, indicating different phases in the data.
Section F

African Solutions
Meningococcal Disease and Epidemics

- We do not understand
  1. What triggers invasion after colonization
  2. What triggers epidemics in population
  3. Timing and distribution of serogroup-specific disease
Vaccine technology to prevent Nm epidemics exists, but has not been used effectively in West Africa, though used in the U.K. and U.S.

Political commitment and resource constraints are a problem

Resources to speed development of group A conjugate vaccine are needed

Resources to improve delivery of vaccine are needed
Obstacles to Prevention and Control (Meningitis Belt)

- Lack of adequate surveillance information
- Lack of a widely available, effective vaccine for young children
- Inadequate vaccine stock
- Poor logistics and infrastructure
- Lack of funding and support for mass campaigns
Group C conjugate vaccine now routinely used in the U.K. and U.S., where incidence rates were much lower than those in Africa

Who will make similar group A vaccine available to children in West Africa?
## History of Meningococcal Vaccines, U.S., 2005

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Producer</th>
<th>Price</th>
<th>Since</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Aventis</td>
<td>NA</td>
<td>1978</td>
</tr>
<tr>
<td>A + C</td>
<td>Aventis</td>
<td>NA</td>
<td>1978</td>
</tr>
<tr>
<td>A, C, W135, Y</td>
<td>Aventis, Merck [95*]</td>
<td>$60+ (U.S. college market)</td>
<td>1981</td>
</tr>
<tr>
<td>A, C, W135, Y</td>
<td>GSK</td>
<td>~$5 (Hajj)*</td>
<td>1980s</td>
</tr>
<tr>
<td>A, C, W135</td>
<td>GSK</td>
<td>$1.50 (W. Afr.)*</td>
<td>2003*</td>
</tr>
<tr>
<td>A, C, W135, Y (Cj)</td>
<td>Sanofi (Aventis)</td>
<td>~$60</td>
<td>2005</td>
</tr>
</tbody>
</table>

*Not licensed in the U.S.*
Meningococcal Vaccine Initiative

- The Bill and Melinda Gates Foundation will work with WHO to eliminate meningococcal epidemics in the African Meningitis Belt before 2010
- $70 million for 10-year development program
- Indian manufacturer has developed group A conjugate vaccine with agreement to provide 25 million doses per year at less than $1.00
Meningitis Vaccine Project

Mission

The Meningitis Vaccine Project’s mission is to eliminate meningitis as a public health problem in sub-Saharan Africa through the development, testing, introduction, and widespread use of conjugate meningococcal vaccines.

Objectives

- To develop meningococcal conjugate vaccines that are appropriate for use in Africa
- To create pathways for the licensure of vaccines
- To assure production in sufficient volume at a price that facilitates wide use in Africa
- To monitor the effectiveness and safety of the vaccines in controlled clinical trials
- To investigate innovative ways to finance the procurement of vaccines through local, country, and other global programs
- To introduce the vaccines through mass and routine immunization in synergy with other public health programs.

Photo Credit: Benoit Lange (left); Benoit Lange (right)

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World Health Organization
Meningococcal Disease Is Challenging

- Persistent global health problem
- Causes endemic and epidemic disease
- Early disease can be easily misdiagnosed
- Signs and symptoms may be hard to distinguish from common viral illness
- Displays rapid onset and progression
- High morbidity and mortality, despite effective therapy