A Hypothetical Model for Epidemic Meningococcal Meningitis in the African Meningitis Belt

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MERIT Meeting, December 2008
Background and Objective

- In 1963, L. Lapeyssonnie described the particular epidemiological pattern of meningococcal meningitis in an area spanning from Senegal to Ethiopia, which he named the “Meningitis Belt” (1). He described an “endemo-sporadic” incidence beyond that observed on other continents, with “seasonal re-enforcement” and regular epidemic waves.

- Progress in surveillance and biological methods has allowed better understanding of this phenomenon and development of vaccination strategies. However, the epidemic pattern still cannot be explained, which is required to mathematically model the impact of vaccine strategies and to predict epidemics.

- This paper presents a hypothetical explanatory model for epidemic meningococcal meningitis. The typical incidence and carriage patterns will be presented before assembling them into a model.

1. Lapeyssonnie L, Bull WHO 1963
Meningococcal Meningitis Incidence Pattern

Four incidence situations can be discriminated:

1. **Endemic situation:** during June to October (dry season in the meningitis belt), the incidence is similar to other regions of the world (e.g., average weekly incidence rate of meningococcal disease in France: up to 0.1 per 100,000) *(Figure 1a)*.

2. **Hyperendemic situation:** incidence increases in all communities and during all dry seasons to 1 per 100,000 and higher *(Figure 1a)*.

3. **Localised epidemics:** occur sporadically in some communities (one village may be concerned while the neighbouring one is not). Weekly incidence rates of 500 per 100,000 or higher, which increases the incidence in the whole district *(Figure 1b)*.

4. **Epidemic waves:** increased total annual case number during some years in a country or a region *(Figure 2)*.
Figure 1. Example of weekly incidence rates (per 100,000, 4-week moving average) of notified suspected meningitis cases and air humidity in the meningitis belt. Sanitary districts Secteur 15 (400,000 inhabitants) and Houndé (250,000 inhabitants) in western Burkina Faso, 1997-2008. Data: Direction régionale de santé des Hauts-Bassins, Burkina Faso.

a) Scale of y-axis up to 5 per 100,000.
   All districts experience hyperendemic incidences of about 1 per 100,000 during all years.
   Hatched line, relative air humidity measured at the Bobo-Dioulasso airport during 2006.

b) Scale of y-axis up to 80 per 100,000.
   Epidemics were declared at the district level only during some years.

Figure 2. Annual total number of reported suspected meningitis cases, Burkina Faso, 1940 to 2008. Data: Ministry of Health, Burkina Faso.
Figure 1a. Hyperendemicity during dry season

Figure 1b. Localised epidemics on the community level
Figure 2. Epidemic waves on the country/regional level
Meningococcal Carriage Pattern

1. Variation of carriage prevalence according to incidence situations:
   - No systematic variation between endemic and hyperendemic situation (rainy vs. dry season)
   - No absolute serogroup-specific carriage prevalence that is associated with epidemic risk
   - Substantially higher carriage prevalence of the outbreak strain in epidemic compared to hyperendemic situation (2, 3):
     serogroup A: 16% vs. 0% (2, 4); serogroup W135: 25% vs. 3% (3)

2. Variation in case-to-carrier ratio according to incidence situations (Table 1):
   - The case-to carrier ratio is a proxy for the invasiveness of colonising meningococci in hosts
   - Substantial increase from endemic to hyperendemic situation (7- to 67-fold)
   - No or few change from hyperendemic to epidemic situation (0.4- to 4-fold, but confidence limits may be large)

3. Raghunathan P et al., JID 2006
Table 1. Estimates of risk of serogroup A meningococcal meningitis given serogroup A colonisation, across endemic, hyperendemic and epidemic situations. Data: Navrongo, northern Ghana as published in (6), and Bobo-Dioulasso region, western Burkina Faso (2,4,5).

<table>
<thead>
<tr>
<th>Epidemiologic situation</th>
<th>Month</th>
<th>Risk of disease given colonisation calculated as weekly cases / carriers (x100)</th>
<th>Increase in risk between situations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Navrongo</td>
<td>Hyper-endemic</td>
<td>April 2002-4 0.065 - 0.238</td>
<td>Hyperendemic vs. endemic situation: 7 - 67</td>
</tr>
<tr>
<td></td>
<td>Endemic</td>
<td>November 2002-4 0.004 – 0.009</td>
<td></td>
</tr>
<tr>
<td>Bobo-Dioulasso region</td>
<td>Hyper-endemic</td>
<td>March 2003 4.4 - 0.4</td>
<td>Epidemic vs. hyperendemic situation: 0.36 – 3.56</td>
</tr>
<tr>
<td></td>
<td>Epidemic</td>
<td>March 2006 1.6</td>
<td></td>
</tr>
</tbody>
</table>

4. Mueller JE et al., JID 2006
5. Parent I et al., CID 2005
Figure 3. Structure of the hypothetical model for meningococcal meningitis in the African meningitis belt.

Dry season
- Persistent dry, dusty climate
  - "Epidemic cofactor", e.g.: viral respiratory infection epidemic
  - "Epidemic wave factor", e.g.: waves of "epidemic cofactors" - meningococcal strain variations

Rainy season
- Epidemic wave factor - meningococcal strain variations
  - Invasiveness
    - Incidence x 10-100
    - Carriage
      - Incidence x 10-100
  - Hyperendemicity
  - Localised epidemic
    - Incidence x 3-10
    - Expansion and intensity of localised epidemics
      - Incidence x 3-10

Community level
- Endemic incidence
  - Incidence x 10-100

Regional level
- Regular meningitis season(s)
- Epidemic wave
Model Structure

- Incidence situations are model states, their transitions imply a multiplication of incidences.

- As illustrated in figures 1 and 2, the transitions to hyperendemic and epidemic situation each imply a 10- to 100-fold increase of weekly incidence rates on the community level.

- The transition to an epidemic wave implies a further 3- to 10-fold increase of annual case number on the country or regional level.
Factors Causing Transition

- The transition from endemic to the hyperendemic situation can be explained by the 10- to 100-fold higher risk of disease given colonisation during the dry season (Table 1). This is most likely a damaging effect of persisting dry and dusty climate on the pharyngeal mucosa, favouring bacterial invasion.

- The transition to the localised epidemic can be explained in large parts by a surge in carriage prevalence (in the order of 10- to 50-fold). Such epidemic co-factors could include respiratory infections that potentially stimulate bacterial transmission and adhesion to the mucosa (2).

- The transition to an epidemic wave occurs if new meningococcal strains escape pre-existing immunity or if co-factors occur in a larger geographical area.

Discussion

- The model is in line with Lapeyssonnie’s description of meningitis epidemiology, but adds localised epidemics as a distinct and obligatory the feature.

- The model’s advantages:
  - allows combining observed meningococcal incidence and carriage patterns with known related factors such as climate, viral infections, and strain biology.
  - other potential causal factors (eg, crowding in refugee camps, waning population immunity) can be integrated in specific steps of the model.

- This hypothetical model requires validation with health centre-level incidence data and calls for further evidence on
  - variations of case-to-carrier ratio and carriage prevalence across incidence situations
  - differences between epidemic and non-epidemic situations (identification of co-factors)
  - impact of viral respiratory and systemic infections on serogroup-specific meningococcal colonisation, transmission and invasion in vitro and in vivo.
Applications

1. A framework for the interpretation of observed epidemiology, eg, the emergence of serogroup W135 in Burkina Faso during 2001-2003:
   - epidemic wave caused by a newly entering strain (W135:2a:P1.5,2 ST-11)
   - occurrence of localised epidemics in some districts not related to strain expansion, but to epidemic co-factors

2. Mathematical modelling:
   - attempts to predict epidemics based solely on meteorological or district-level data not likely to succeed
   - models should include the described four incidence states and various assumptions about the vaccine impact on transition probabilities.

3. Prevention strategies: interventions that limit the harmful links
   - between the dry season and seasonal increase of meningitis (by, e.g., indoor air humidification)
   - between epidemic co-factors and epidemic meningitis (e.g., using vaccines against respiratory pathogens)
   - are of importance for serogroups like X or W135, against which no preventive vaccine strategy exists