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-epidemic” 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.

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 10,000 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).

Meningococcal Carriage* Pattern
* Carriage = asymptomatic pharyngeal colonisation
1. Variation of carriage prevalence according to incidence situations:
   - No systematic variation between endemic and hyperendemic situation (rainy vs. dry season).
   - Substantially higher carriage prevalence of the outbreak strain in epidemic compared to hyperendemic situation (2, 3).
   - 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.

2. Variation in case-to-carrier ratio according to incidence situations (Table 1):
   - The case-to-carrier ratio is a proxy for the invisibility of colonising meningococci in hosts.
   - Substantial increase from endemic to hyperendemic situation (7 - 87-fold).
   - No or few change from hyperendemic to epidemic situation (0.4 - 4-fold, but confidence limits may be large).

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>Situation</th>
<th>Risk of disease given colonisation calculated as weekly cases/carriers (×100)</th>
<th>Increase in risk compared to endemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Navrongo</td>
<td></td>
<td></td>
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<tr>
<td>Endemic</td>
<td>April 2002-4</td>
<td>0.065 - 0.238</td>
</tr>
<tr>
<td></td>
<td>November 2002-4</td>
<td>0.004 - 0.009</td>
</tr>
<tr>
<td>Hyperendemic vs. epidemic situation</td>
<td>7 - 67</td>
<td></td>
</tr>
<tr>
<td>Bobo-Dioulasso region</td>
<td></td>
<td></td>
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<tr>
<td>Hyperendemic</td>
<td>March 2003</td>
<td>4.4 - 0.4</td>
</tr>
<tr>
<td></td>
<td>Epidemic</td>
<td>1.6</td>
</tr>
<tr>
<td>Epidemic vs. hyperendemic situation</td>
<td>0.36 - 3.56</td>
<td></td>
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</tbody>
</table>

Discussion
The model is in line with Lapeyssonnie’s description of meningitis epidemiology, but adds localised epidemics as a distinct and obligatory 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 (e.g., 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.

The model has several applications:
1. A framework for the interpretation of observed epidemiology, e.g., the emergence of serogroup W135 in Burkina Faso during 2001-2003:
   - Epidemic wave caused by a newly entering strain (W135:2a:P1.1,2 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 description of 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.

References
1. Lapeyssonnie L, Bull WHO 1963
2. Mueller JE et al., JID 2006
3. Parent I et al., CID 2005
5. Muller JE et al., JID 2006
7. Parent I et al., CID 2005