Dengue: the disease and epidemiology

Annelies Wilder-Smith
Consultant, Vaccines for Arboviral Diseases, WHO-IVB
Lee Kong Chian School of Medicine, Singapore

SAGE meeting April 2018
Dengue

- Rapidly expanding arboviral disease transmitted by Aedes mosquitoes
- 50 fold increase in past 50 years
- Four antigenically distinct serotypes (DENV1-4)
- Clinical spectrum:
  - 80% asymptomatic
  - Self-limiting febrile illness
  - Severe dengue (~2-4% of symptomatic)
  - Secondary infections are associated with higher risk of more severe dengue
  - CFR 0.1—1%

Homotypic and heterotypic immunity

Epidemiology

Table 1 | Estimated burden of dengue in 2010, by continent

<table>
<thead>
<tr>
<th></th>
<th>Apparent (Millions (credible interval))</th>
<th>Inapparent (Millions (credible interval))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>15.7 (10.5–22.5)</td>
<td>48.4 (34.3–65.2)</td>
</tr>
<tr>
<td>Asia</td>
<td>66.8 (47.0–94.4)</td>
<td>204.4 (151.8–273.0)</td>
</tr>
<tr>
<td>Americas</td>
<td>13.3 (9.5–18.5)</td>
<td>40.5 (30.5–53.3)</td>
</tr>
<tr>
<td>Oceania</td>
<td>0.18 (0.11–0.28)</td>
<td>0.55 (0.35–0.82)</td>
</tr>
<tr>
<td>Global</td>
<td>96 (67.1–135.6)</td>
<td>293.9 (217.0–392.3)</td>
</tr>
</tbody>
</table>

Bhatt et al, Nature 2013. doi:10.1038/nature12060
Temporal and spatial heterogeneity of dengue transmission

Spatial heterogeneity at small scale

Salje et al. Dengue diversity across spatial and temporal scales. Science 2017


Spatial heterogeneity dependent on socioeconomic factors, population density, ecological factors:

Kamphaeng Phet, Thailand, school based cohort study:

Seroprevalence differences within 5-10km: 1255 children, aged 9: 67 to 92%
For all school children: 46 to 94%
(Tim Endy, Katie Anderson, personal communication)

Heterogeneity of seroprevalence between and within countries

**Thailand.** Vongpunsawad et al. PLoS ONE 2017


**Singapore** Ang et al, Epi News Bulletin 2014

https://mrcdata.dide.ic.ac.uk/_dengue/dengue.php
Dengue Vaccine
(http://www.who.int/immunization/research/vaccine_pipeline_tracker_spreadsheet/en/)

Phase I
- DPIV
  - GlaxoSmithKline, Biomanguinhos, WRAIR

Phase II
- DEN-80E
  - Merck

Phase IIb

Phase III
- TV003/TV005
  - US National Institutes of Health
  - Butantan

Registration
- CYD-TDV
  - Dengvaxia™
  - Sanofi Pasteur

- DENVax
  - Takeda

- TLAV-TPIV
  - WRAIR

- YFV 17D-204
  - 5'

- C prM
  - E
  - NS1
  - NS2A
  - NS2B
  - NS3
  - NS4A
  - NS4B
  - NS5

- CYD-TDV
  - SANOFI PASTEUR

- 3'