Rôle et activités d’un Centre Collaborateur de l’OMS : le CC-OMS sur les méningites

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Invasive Bacterial Infections
CNR des Meningocoques et Haemophilus influenzae
WHOcc for meningitis
Institut Pasteur
Paris

2ème journée CNR – LNR
17 Novembre 2017
Current mandate and Terms of Reference

Four-years mandate Nov2016-Nov2020

- TOR 1 : To support WHO in meningitis outbreak investigation and documentation by providing detailed laboratory confirmation and molecular analysis.

- TOR 2 : To support WHO in strengthening countries’ meningitis laboratory diagnostic capacity.

Conducted Activities:

- Capacity building: Transfer of technologies, teaching and training
- Conducting Interlaboratory studies of quality assurance.
- Developing new bedside diagnostic tools
- Typing of meningococcal isolates
- Exploring Vaccine Failure
Diagnosis and typing

- Implementation of molecular typing methods for the three agents Nm, Sp and Hi
- Development of bedside tests
- Molecular typing

2016-2017 n=183 samples (primary samples and isolates)
Typing of *Neisseria meningitidis* for changing epidemiology

**Genotyping**
- MLST: polymorphism of several genes.
- Whole Genome sequencing (WGS)

**Phenotyping**
- Capsule (12 serogroups)
  - A, B, C, W, Y, X 99% of cases
  - E, H, I, J, L, Z Rare among invasive isolates in immune-competent patients

**Monitoring population biology**
- Naturally competent for transformation
- Frequent horizontal DNA exchanges

*Maiden et al., 2013 Nat Rev Microbiol.*
Teaching and training

- One-week course from 29 May to 2 June 2017 at the Institut Pasteur
- Funding: TOTAL Foundation
- Both theoretical and practical courses
- Five participants from Cameroon: CAR, Côte d’Ivoire, Niger and Morocco
- Diagnosis and typing of Neisseria meningitidis
  - PCR-based diagnosis both on primary samples and cultured isolates
  - RDT
  - Antibiogram
  - MALDI-TOF
  - WGS bioinformatics training
EQA June 2016

Distribution of 8 samples (spiked CSF) to participating laboratories

- Institut Pasteur (Abidjan, Côte d’Ivoire)
- Institut Pasteur (Bangui, CAR)
- CERMES (Niamey, Niger)
- Institut Pasteur (Casablanca, Morocco)

<table>
<thead>
<tr>
<th>Laboratory results</th>
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<tr>
<td></td>
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<tr>
<td>% species identification consensus</td>
</tr>
<tr>
<td>L14: 62.5</td>
</tr>
<tr>
<td>L15: 100</td>
</tr>
<tr>
<td>L17: 100</td>
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<tr>
<td>L18: 87.5</td>
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<tr>
<td>% genogroup identification consensus</td>
</tr>
<tr>
<td>L14: 50</td>
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<tr>
<td>L15: 100</td>
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<td>L17: 100</td>
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<td>L18: 83.3</td>
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Rapid beside diagnostic tools for Nm

Capture control line antibodies against NmX

Capture line antibodies against NmX

Gold-labeled binding antibodies against NmX

<table>
<thead>
<tr>
<th></th>
<th>Sp</th>
<th>Sn</th>
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<tbody>
<tr>
<td>A</td>
<td>98 (96-99)</td>
<td>91 (77-98)</td>
</tr>
<tr>
<td>C</td>
<td>100 (99-100)</td>
<td>64 (45-80)</td>
</tr>
<tr>
<td>Y</td>
<td>100 (99-100)</td>
<td>75 (35-97)</td>
</tr>
<tr>
<td>W</td>
<td>95 (91-98)</td>
<td>97 (92-98)</td>
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<tr>
<td>X</td>
<td>99 (96-100)</td>
<td>100 (89-100)</td>
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</table>

Transfer to an industrial partner for industrial production

A kit of three cassettes to detect serogroups A, C, Y, W and X

in field testing during 2017-2018 season
Meningococcal isolates from countries in the African Meningitis Belt 2004-2010

Serogroup distribution (%)

Niger (N=124)

Mali (N=132)

Burkina Faso (N=283)

Chad (N=53)

773 isolates (2004 and 2010)

13 sub-Saharan countries

Caugant et al. PLoS ONE 2012
### Agents of acute bacterial meningitis sub-Saharan Africa (2014)

<table>
<thead>
<tr>
<th>Country – Pays</th>
<th>No. CFS samples - Nombre d'échantillons de LCR</th>
<th>No. CSF positive fluid samples - Nombre d'échantillons de LCR positifs</th>
<th>Neisseria meningitidis serogroup A</th>
<th>Neisseria meningitidis serogroup B</th>
<th>Neisseria meningitidis serogroup C</th>
<th>Neisseria meningitidis serogroup X - Neisseria meningitidis serogroup Y</th>
<th>Neisseria meningitidis serogroup W135</th>
<th>Other Neisseria meningitidis</th>
<th>Other pathogens - Autres pathogènes</th>
<th>Haemophilus influenzae type b - Haemophilus influenzae type b</th>
<th>Streptococcus pneumoniae</th>
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<td>Benin – Bénin</td>
<td>79</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
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<td>Burkina Faso</td>
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<td>0</td>
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<td>15</td>
<td>404</td>
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<td>Cameroon – Cameroun</td>
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<td>0</td>
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<td>Democratic Republic of the Congo*</td>
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<td>0</td>
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<td>1</td>
<td>27</td>
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<td>Gambia – Gambie</td>
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<td>–</td>
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<td>Niger</td>
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<td>0</td>
<td>8</td>
<td>0</td>
<td>14</td>
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<td>Nigeria – Nigéria</td>
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<td>Senegal – Sénégal</td>
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<tr>
<td>Sudan – Soudan</td>
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<td>1</td>
<td>4</td>
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<td><strong>Total</strong></td>
<td>3387</td>
<td>860</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>12</td>
<td>5</td>
<td>231</td>
<td>28</td>
<td>505</td>
<td>22</td>
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</tbody>
</table>

* Data for epidemic season (weeks 1–26). – Données pour la saison épidémique (semaines 1-26).
Vaccine failure

- Molecular analysis of the isolates
- Level of the expression of the capsule and sequence insertion in the promoter \textit{cps} region
- Serological analysis of the bactericidal antibodies induced by the vaccine.
- Complement analysis in patients
Epidemic *Neisseria meningitidis* Serogroup C: Nigeria and Niger since 2013

Core genomeMLST loci-based Neighbour-net phylogenetic network

ST-10217

C:P1.21-15,16:F1-7:NA (ST-10217)

cc11

cc865

Sidikou et al., 2016 Lancet Infect Dis; Kretz et al., 2015. Emerg Infect Dis
Cameroon 2017

- Community-acquired case

- Meningococcal meningitis epidemic within a prison in Yaoundé

- 7 isolates and 11 CSF samples

  W:P1.5,2:F1-1:cc11 (ST-11)

  C:P1.5-1,2-36:F5-1:cc175 (ST-2881)
NmC Cameroon 2017 in Africa

- Cameroon cc175 (C) 2017
- ST-10217

cc11

cc865
Could the multicomponent meningococcal serogroup B vaccine (4CMenB) control *Neisseria meningitidis* capsular group X outbreaks in Africa?

Eva Hong, Marzia Monica Giuliani, Ala-Eddine Deghmane, Maurizio Comanducci, Brunella Brunelli, Peter Dull, Mariagrazia Pizza, Muhamed-Kheir Taha

*Vaccine* 31 (2013) 1113–1116
Undiagnosed illness - Liberia

A cluster of sudden deaths of unknown aetiology in Sinoe County Liberia between 23 April and 7 May 2017, a total of 31 cases including 13 deaths.

- Fever, abdominal pain, diarrhea, vomiting, and mental confusion. Some patients presented with purpura and/or petechiae.

- *Neisseria meningitidis* group C by PCR in clinical specimens (31 cases) and serological results of 3 cases

- Toxicological investigations were not suggestive of intoxication

- The importance of the inclusion of meningococcal septicemia in routine surveillance.

The Liberian national reference laboratory in Margibi County

CDC Atlanta, USA, The National Institute for Communicable Diseases (NICD) and the National Institute of Occupational Health (NIOH) in Johannesburg, South Africa, The Institut Pasteur in Paris, France. Center for Analytical Chemistry in Vienna, Austria,
Changing epidemiology in Sub-Saharan Africa

- Decline NmA (cc5)
- Emergence of W (cc11) in 2001-2002
- After the decline of serogroup W between 2003 and 2005, a new increase in W is observed since 2010
- NmC in Nigeria and Niger since 2013
Ala-Eddine Deghmane
Eva Hong
Aude Terrade
La Plateforme de Microbiologie Mutualisée (P2M) du PIBnet de l’Institut Pasteur

Centre d’enseignement de l’Institut Pasteur

Xin Wang CCOMS CDC  
Atlanta USA

Dominique Caugant CCOMS NIPH Oslo, Norway

Katya Fernandez and Olivier Ronveaux WHO, Geneva Switzerland

MRF
Fondation TOTAL
Distribution of cc175 isolates (n=370)

Y (228 - 61.62%) (+2 Cameroon)
W (78 - 21.08%) (+12 Cameroon)
meningitis (191 - 51.62%)
septicaemia (48 - 12.97%)
carrier (71 - 19.19%)
other (1 - 0.27%)
meningitis and septicaemia (2 - 0.54%)
invasive (unspecified/other) (14 - 3.78%)
No value/unassigned (43 - 11.62%)
No value/unassigned (21 - 5.68%)
B (10 - 2.70%)
NG (18 - 4.86%)
C (7 - 1.89%)
A (3 - 0.81%)
E (2 - 0.54%)
X (2 - 0.54%)
W/Y (1 - 0.27%)
Cameroon 2017 against NmW in Africa

- Hajj cc11 (W)
- South American-UK cc11 (W)
- Cameroon cc11 (W)
- Cameroon cc175 (C)
Possible global spread of NmX cc181?

Meningococci of Serogroup X Clonal Complex 181 in Refugee Camps, Italy

Stefanelli et al., Emerg Infect Dis 23, 870 (May, 2017).