CONSISE Activities Overview and Update Laboratory Working Group

John Wood and Othmar Engelhardt

CONSISE 4th International Meeting, Cape Town South Africa

3-4 September 2013

CONSISE Steering Committee – Laboratory Working Group

Eeva Broberg,

Katja Hoschler,

Jackie Katz,

Malik Peiris,

Wenqing Zhang

Othmar Engelhardt

Olav Hungnes,

Karen Laurie,

John Wood

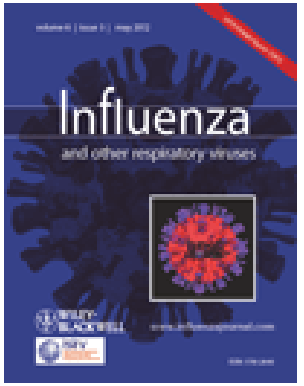
Background:

1st International Influenza Seroprevalence Meeting, Ottawa, Canada, February 9-10 2011

- *Influenza serological studies to inform public health action: best practices to optimise timing, quality and reporting*

- Several conclusions and actions agreed
  - Formed the basis for subsequent discussions
- Meeting report

  Laurie et al. (2012) Influenza and Other Respiratory Viruses



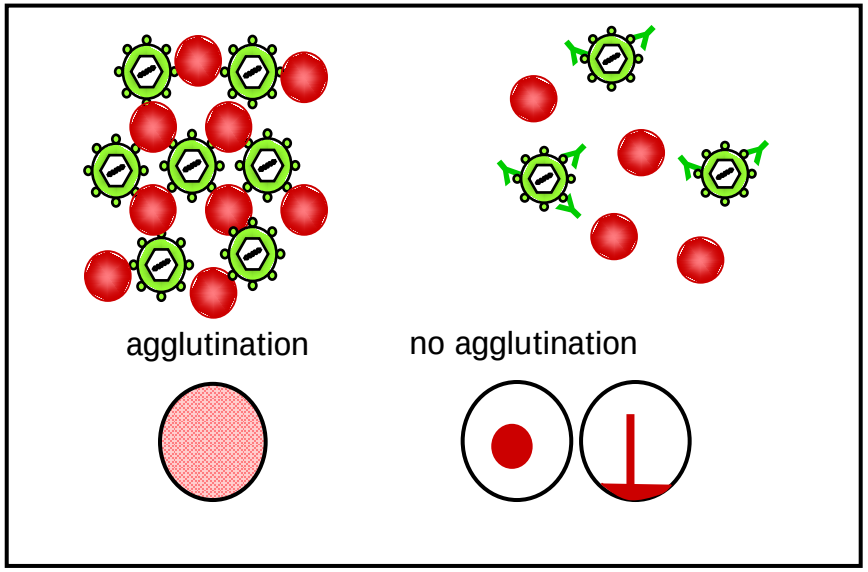
One of conclusions

Co-ordinate and standardise the international laboratory response

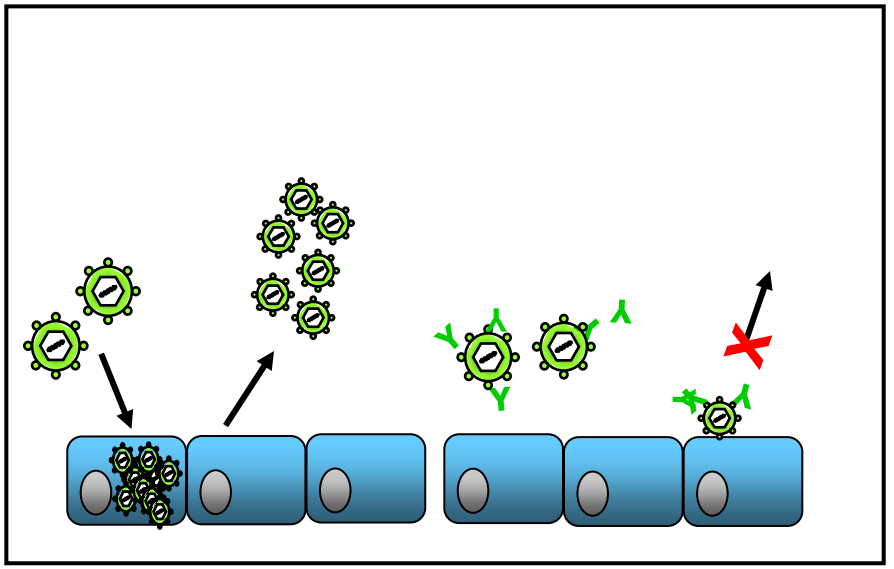
- develop an international network of laboratories for conducting serological studies and ensuring a common approach to generating comparable sero-epidemiological data
- establish commitment for production of international antibody standard and control panels
- establish collaboration/coordination between laboratory, clinical and epidemiological partners to access serum and virological samples rapidly in outbreak

Common assays for influenza serological studies

Haemagglutination Inhibition Assay



Microneutralization Assay



MN assay read-out:
- 7 day assay CPE on monolayer
- 3 day HA detection
- 2 day ELISA detection (WHO protocol)

In collaborative studies HI/MN assay variability between laboratories can be substantial

How can they be standardized?

MN assay comparison

Background

- Karen Laurie (WHO CC, AUS) coordinated comparison of 2d ELISA WHO and 3d HA protocols – consensus protocols developed
- Laboratory comparison exercise for H1N1 pdm09 assays began 4 October 2012
    - Comparison of two methods where labs used their own serum samples
    - Results from 11 labs submitted to NIBSC (UK) for analysis
    - Ratio of titres between 3-day and 2-day assay similar in most labs
    - Therefore, there were no underlying reasons that the two assays could not be comparable
    - As conclusions were based on only one subtype, plans were made to extend study with data for seasonal H3N2 and H5N1

MN assay comparison

Plan for Cape Town meeting

- Examine whether data from H1N1pdm09 study may have been biased due to factors such as:
  - Inexperience with one assay format
  - Age group(s) of serum samples
  - Use of wild-type vs reassortant virus
  - Titre ($TCID_{50}$) of virus stocks
- Karen Laurie and Othmar Engelhardt to present preliminary analysis of MN H3N2/H5N1 extension study
- Discuss results and plan next steps

HI assay standardization

Background

- Group is strongly in favour of keeping HI as the primary serology assay, but will assess how it can be better standardized.
- HI assay variability between labs can be substantial and in collaborative studies no clear relationship between protocol used and inter-lab variability has been seen
- Karen Laurie and John Wood coordinated comparison of HI protocols and tried to develop consensus assay
  - Starting point: WHO protocol

Plan for Cape Town meeting

- Discuss whether a consensus HI assay protocol is feasible

MN and HI assay standardization

Plan for Cape Town meeting

- A new collaborative study using panels of sera will be designed for implementation after Cape Town meeting
  - laboratory comparison between consensus and local HI and MN methods
  - Evaluation of animal sera and Mab as antibody standards

International antibody standards

Background

- Previous collaborative studies have shown that use of antibody standards can significantly reduce variability between laboratories

Plan for Cape Town meeting

- John Wood to discuss pathway to developing antibody standards
- Othmar Engelhardt to discuss resources needed to prepare International Standards including presentation from Nick Martin (NMRC)

Quality assessment

Background

- A small group from CONSISE met with Dr Vivienne James from UK NEQAS
- Value of EQA is understood and appreciated by CONSISE Lab WG
- Consensus that formal EQA would be premature at the moment
  - CONSISE still exploring variables
- More emphasis currently on developing consensus protocols and standardisation
- Use of shared serum panels as a more realistic option at this point

NI assays

Background

- Some labs have begun evaluation of sera from influenza vaccine trials using ELLA assays with encouraging results. Some of the difficulties related to the source of NA
- All CONSISE labs have been encouraged to evaluate the ELLA assay.

Plan for Cape Town meeting

- Update on NI assays from Maryna Eichelberger (FDA) and Kim Westgeest (Erasmus University)
- Share experience on use of NI assays including those of Ralf Wagner (PEI)
- Discuss the next steps

New serology assays

Background

- At Hong Kong meeting CONSISE members indicated that new MN serology assays using virus pseudotypes were being evaluated
- It was agreed that the CONSISE group should review the new serology assay being used

Plan for Cape Town meeting

- Presentations by Ralf Wagner (PEI), Emanuele Montomoli (U of Siena), Jackie Katz (CDC) on new serology assays followed by discussion
- Group to review the new serology assay**s**

CONSISE involvement with influenza A (H7N9) and MERS-CoV serology assays

H7N9

- CONSISE TC in May 2013 led to posting of H7N9 HI/MN assay protocols from China CDC on CONSISE website
- A further CONSISE TC in July 2013 led to posting of CDC H7N9 modified HI assay protocol using horse erythrocytes on CONSISE website
- Link to WHO website for information on number of human cases http://www.who.int/influenza/human_animal_interface/influenza_h7n9/en/index.html

MERS-CoV

- WHO TC in June to assess MERS-CoV laboratory diagnoses included serology assays – CONSISE represented
- A variety of serology assays - need for serum panels

Thank you

CONSISE Steering Committee – Laboratory Working Group

Eeva Broberg, Katja Hoschler, Olav Hungnes, Jackie Katz, Karen Laurie, Malik Peiris, Wenqing Zhang

Also

Maria Van Kerkhove, Angus Nicoll from the epi working group