CONSISE Laboratory Working Group
Summary of discussions and future plans

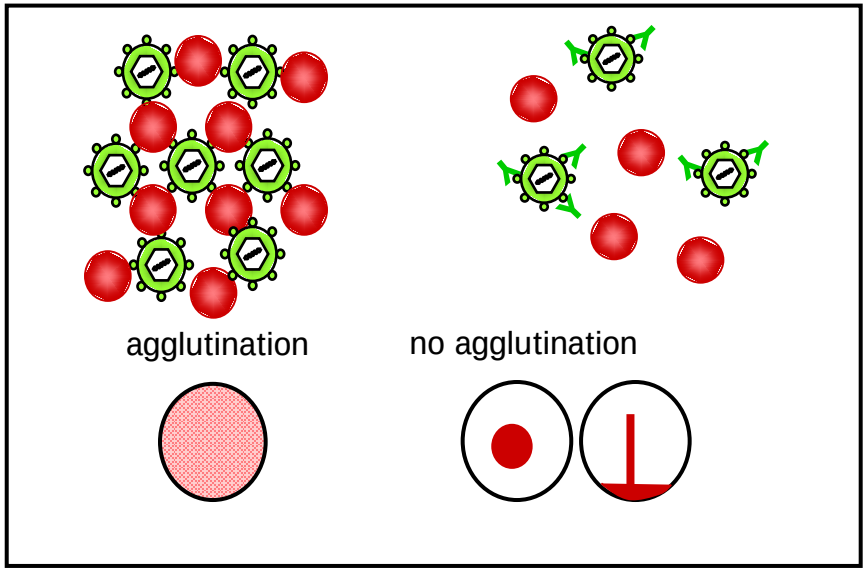
John Wood and Othmar Engelhardt

CONSISE 4th International Meeting, Cape Town South Africa

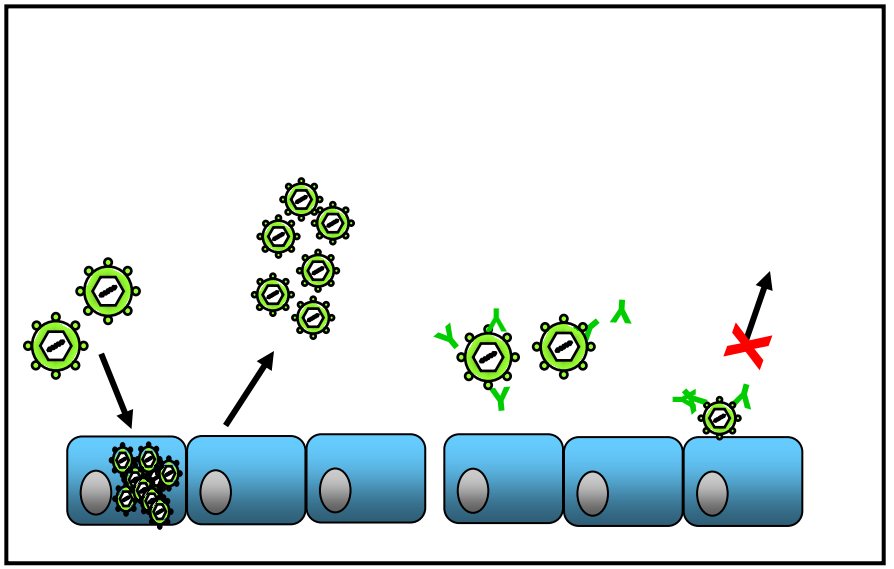
3-4 September 2013

Common assays for influenza serological studies

Haemagglutination Inhibition Assay



Microneutralization Assay



MN assay read-out:
- 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

Update

- Analysis of bias influencing results of first part of MN comparison study
    - Based on information available to date, no evidence for major source of bias in H1N1pdm09 study
- Extension of MN assay comparison (phase 2):
    - Included H3N2 (5 labs) and H5N1 (1 lab)
    - Results from 5 labs submitted to NIBSC (UK) for analysis
    - Ratio of titres between 3-day and 2-day assay similar in most labs
    - Preliminary data confirm the conclusions of phase 1, i.e. there are no underlying reasons that the two assays could not be comparable

Plan

- collect remaining data from additional laboratories
- Prepare report, write manuscript for publication, post consensus assay protocols and report on CONSISE website

HI assay standardization

Background

- Karen Laurie and John Wood coordinated comparison of HI protocols and tried to develop consensus assay
  - Starting point: WHO protocol

Outcome of Cape Town meeting

- Following discussion, consensus reached!
  - Largely in agreement with protocol as in WHO Manual
  - Applicable for H1N1pdm09 for subsequent collaborative study

Plan

- Revise consensus protocol and circulate to WG for approval

(International) antibody standards

Outcome

- Pathway to developing antibody standards presented and approved in principle by WG
- Possible sources of antibody
  - Human serum/plasma
    - Convalescent – help from Epi WG requested to source sera and obtain all required ethical approvals
    - Post-vaccination
  - Animal sera
  - Monoclonal antibodies
  - Human antibodies produced in trans-chromosomal bovines
- Discussion on status of international antibody standards
  - Agreement that formal WHO IS status not required (and too slow) in the first instance
  - Possible post hoc certification by WHO ECBS

Plan

- Revise pathway following discussion and circulate to lab WG and Steering Committee

MN and HI assay collaborative study

Outcome and Plan

- General agreement to look at lab-to-lab variability
  - Compare consensus HI protocol with local HI methods
  - Compare consensus MN protocols with local methods where local methods are different from consensus
  - Either 2-day or 3-day assay can be used
  - To be conducted for H1N1pdm09
  - Small subgroup to develop study protocol
  - NMRC (N Martin) to contribute panels of human sera
- Use the study to evaluate various sources of antibodies as potential antibody standard
  - Existing human IS
  - Monoclonal antibody
  - Pooled ferret antisera
  - Human antibodies from trans-chromosomal bovines

NI assays

Outcome

- 4 laboratories have implemented ELLA assay
- Technical issues with antigen source and some subtypes still to be resolved
- Other assays have been assessed but need more work

Plan

- Small group to plan collaborative study
- Interested labs to contact Maryna Eichelberger to obtain protocol

New serology assays

Update

- Variations of existing assays (MN) being explored, use of different cell line (CaCO2 vs MDCK) and read-out (R Wagner)
- Pseudo particle MN assay being evaluated – correlation with 'classical' MN; NA pseudo particles
- Modified HI assay (stabilised RBCs)
- Protein microarray
- Point-of-care test (dual path platform lateral flow)
- Luminex multiplex platform

Conclusions

- Most assays at early stage, need to wait for further data
  - No recommendation of Lab WG at this point
- Pseudo particle MN assay has potential and needs further work, e.g. standardisation of particle preparation

Thank you

Laboratory Working Group

Presenters

For interesting presentations and lively discussion