

Scoping meeting to identify urgent research needs with respect to human influenza A (H1N1)

Wednesday 24th June 2009 at Wellcome Collection

This meeting was convened by Ian Brown and chaired by Pat Goodwin; a list of attendees is available as Appendix 1.

Following a welcome address and introductions, Ian Brown gave a presentation outlining the background to this current outbreak and summarising what is known about the origins of this new virus. He presented some preliminary results from transmission experiments recently conducted at the VLA designed to understand more about the susceptibility of pigs to pandemic H1N1 2009 infection. Efficient transmission of pandemic H1N1 2009 (using California 7 isolate) has been observed between infected and naive pigs. Clinical disease was induced in infected pigs and whilst variations were observed in the severity of disease there was no mortality. It appears likely, therefore, that pandemic H1N1 2009 could move from humans to pigs, raising two important questions:

- What might the impact and consequences of spread of pandemic H1N1 2009 and establishment in pig populations be?
- Could the pig be used as a model to study pandemic H1N1 2009 in humans?

This presentation, and subsequent updates from Rod Daniels, Nicola Lewis, Wendy Barclay, Oliver Pybus and Kin Chow Chang set the scene for a brainstorming session focussing on identifying urgent high-level research questions that need to be addressed in the short-term. The following points were discussed:

- The potential use of the pig as a model for human infection, and also to generate information about the pig situation, was discussed at length. Clearly pigs have the potential to be infected, as demonstrated by the recent VLA experiments. It was agreed that further challenge studies, in both naïve and pigs with prior exposure to circulating H1N1 strains, could be extremely useful in addressing a range of questions including variations in the virus over time and with transmission, the impact of age of severity of infection, dynamics of infection within individual pigs, innate and adaptive immune responses to infection, assessing the timing of maximum transmissibility of infected individuals etc. These studies would have to be carefully designed to ensure that the maximum amount of data and material could be generated. The design of these experiments should not be biased by knowledge of virus behaviour in previous pandemics.

ACTION: Ian Brown to lead on the development of a concept note for this body of research in collaboration with Brian Charleston, Mick Bailey, Chris Stokes, Nicola Lewis, Kin Chow Chang, Wendy Barclay and epidemiologists.

- The importance of tracking the course of a natural infection, should it occur, on a limited number of farms was raised. However, it was recognised that there is little baseline data available regarding the numbers of UK pig herds, the movements of

herds, the numbers of farmers and abattoir workers involved in this industry etc. If these data were to be collated it would be possible to theoretically quantify some risks including the threat to pig farmers and farm workers if pandemic H1N1 2009 infection were to spread into UK pig herds, rates of spread within and between herds. There is also an opportunity to use this time to develop protocols to study the infection within herds that could be quickly put in place should the virus move into pigs.

ACTION: James Wood will work up a preliminary outline of a proposal focussed on epidemiological analyses in collaboration with pig specialists at regional VLA labs, industry partners, modellers at HPA and Imperial. Opportunities for collaboration with the community-based human study led by Andy Hayward should also be explored.

- Vaccination of pig herds was discussed, but it was generally agreed that the vaccination issue is so complex in this situation that research questions could not be quickly addressed. Furthermore, mass vaccination would only be deployed if a solid evidence base indicated that there was a significant threat to public health.

ACTION: None

- The preliminary data analysis presented by Oliver Pybus indicated that this new strain is most closely related to swine virus isolates circulating in Hong Kong 5 years ago and this viral lineage has not been picked up by surveillance in the intervening period. It was agreed that many researchers have swine flu isolates in storage which, if sequenced, could help to enrich the genetic data and plug some gaps in the phylogenetic analysis. Antigenicity data analysis, by Nicola Lewis and colleagues, could also be enhanced through the study of additional isolates better informing vaccination and diagnostics.

ACTION: Oliver Pybus and Nicola Lewis will liaise with Ian Brown who has access to both UK viral isolate archives and an EU swine flu sample bank to take this forward. Samples could be fed into the flu sequencing pipeline at Sanger - the importance of full genome sequencing was emphasized.

Next Steps:

- The importance of a collaborative and complementary effort from the research community was emphasized by the funders. The programmes of research must address urgent research questions with immediate impact.
- Short outline proposals would be developed, as detailed above, and applicants were advised that the following information should be included:
 - What is your research question(s)?
 - Why does this work need to be done urgently and how will it inform management and control of the pandemic?
 - Approximately how much will it cost?
 - How long will it take; are there any milestones?
 - Who will be involved in the project, and what expertise they will bring?

APPENDIX 1: Attendees for Wellcome Trust meeting

Name	Institute	Attending?
Ian Brown	VLA	✓
Sharon Brookes	VLA	✓
Mark Arnold	VLA - CERA	✓
Pat Goodwin	Wellcome Trust	✓
Alan Archibald	U o Edinburgh	By telecon
Sam Lycett	U o Edinburgh	✓
Wendy Barclay	Imperial College	✓
Azra Ghani (leaving at 12:00)	Imperial College	✓
Lesley Heppell	BBSRC	✓
Bryan Charleston	IAH	✓
Des Walsh	MRC	✓
Kevin Moreton	MRC	✓
Peter Stevenson	Defra	✓
Rod Daniels	NIMR	✓
James Wood	U o Cambridge	✓
Laurence Tiley	U o Cambridge	✓
Nicola Lewis	U o Cambridge	✓
Julia Gog	U o Cambridge	✓
Oliver Pybus	U o Oxford	✓
Kin Chow Chang	U O Nottingham	✓
Chris Stokes	U o Bristol	By telecon
Mick Bailey	U o Bristol	By telecon