Pandemic influenza testing at the coalface: time for reassessment?

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ABSTRACT

- Australian federal and state governments were advised several years ago that an influenza pandemic would overwhelm Australian public reference laboratories.
- It was proposed at the time that currently underused capacity in the private sector be used to enhance pandemic responses.
- The current outbreak of pandemic influenza has confirmed the predictions of advisors from the private sector.
- Future official pandemic plans should be adjusted to take into account these observations.

MJA 2010; 192: 102–104

The 2009 pandemic of H1N1 influenza, which involves a virus strain that has standard virulence but is readily transmissible, has provided health systems with a unique opportunity to test and fine-tune pandemic health plans before the arrival of a more devastating pandemic strain.

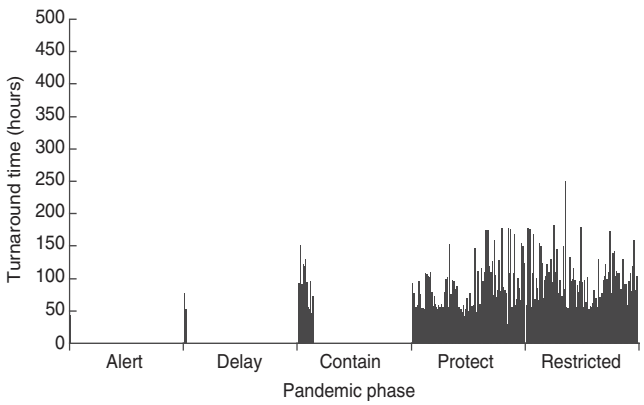
Australia has been seriously planning for a pandemic since 2005, when there was concern about the pandemic potential of the H5N1 strain of avian influenza (a virus strain that turned out to have enhanced virulence but was *not* readily transmissible to humans), with the development of various federal[1,2] and state[3-10] pandemic plans. With the exception of Queensland (which signed a memorandum of understanding with private pathology laboratories and funded them for testing infrastructure), all jurisdictions decided that a central public reference laboratory testing protocol would be the best response in a pandemic. All guidelines specified that the presence or absence of influenza A infection should be notified to the managing clinician within 24 hours of receipt of a sample to assist in clinical management.[1-10] A further 24 hours was specified as the benchmark for determining whether an influenza A specimen represented the pandemic strain. Polymerase chain reaction (PCR) testing was favoured over antigen testing (which is offered by many private sector and peripheral public sector laboratories) because of an assumed superior sensitivity of the former test in an outbreak situation. The public sector Communicable Diseases Network Australia also promulgated similar guidelines.[11]

The Australian Government commissioned a study by the Health Infrastructure Assurance Advisory Group on private pathology laboratory surge capacity, to determine whether the private sector could provide support during national disasters such as pandemics. The report on the study found that the private sector had considerable underused capacity for molecular diagnosis of influenza and recommended that its resources be included in pandemic plans.[12] The ability of the private sector to do this is currently hampered by the Medicare Benefits Schedule's policy of only reimbursing (at close to cost price) testing for a maximum of three nucleic acids (item 69496). This is not economically viable for most private laboratories, especially if testing for the usual panel of seven to eight viruses is requested (influenza A, influenza B, parainfluenza 1–3, adenovirus, respiratory syncytial virus, and human metapneumovirus). Many guidelines also advise simultaneously requesting PCR assays for atypical agents such as *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydophila psittaci*, *Legionella pneumophila*, *Legionella longbeachae*, and *Coxiella burnetii* in some circumstances, as clinical manifestations are rarely characteristic of a particular aetiology. This makes pathology testing even less commercially viable. An expanded panel is nevertheless important because, in managing patients with possible pandemic influenza, identifying an alternative diagnosis is just as helpful in clinical management as determining the pandemic influenza strain status (enabling specific therapy and making patient triage and isolation more efficient).

In December 2007, the public sector Public Health Laboratory Network had a face-to-face meeting with private pathology laboratories to discuss these issues. But, despite these discussions, none of the jurisdictions with plans for centralised testing changed their plans, and pandemic funds were channelled solely to public sector reference laboratories.[4-12]

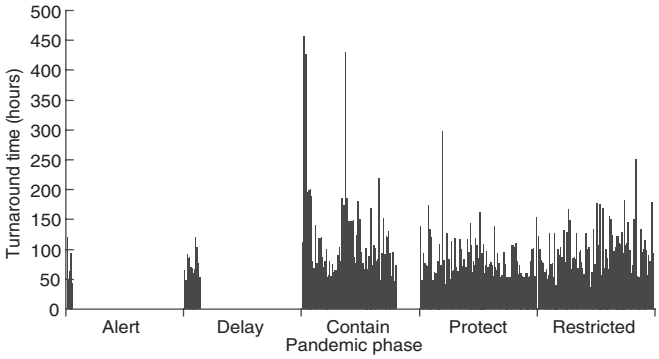
The experience of our laboratory (a private pathology service in Western Australia and the Northern Territory) during the current pandemic may be helpful in determining whether such centralised strategies have been successful thus far. To date, since the declaration by the Australian Government Department of Health and Ageing of the "Alert" phase on 25 April 2009, we have referred over 5500 specimens from patients with suspected influenza to a reference laboratory for diagnostic testing. Of these, 220 have been reported back as positive for influenza A (191 for the pandemic H1N1 strain, three for seasonal H1 influenza A, and 26 for H3 influenza A). Turnaround times for results, calculated from the time of specimen collection to the time of electronic download of the result into our computer system, are charted in Box 1. (These are best-case scenario estimates, as the results also need to be

1 Turnaround time for 220 specimens that were positive for influenza A*



* Australia had been in Alert phase since the avian influenza scare of 2005; the Delay phase commenced on 28 April 2009, the Contain phase on 22 May 2009, and the Protect phase on 17 June 2009; the "restricted" phase (our term) began on 22 July 2009, when the reference laboratory asked referrers to restrict specimens to high-risk patients only. ◆

2 Turnaround time for a random sample of 409 specimens that were positive or negative for influenza A*



* Australia had been in Alert phase since the avian influenza scare of 2005; the Delay phase commenced on 28 April 2009, the Contain phase on 22 May 2009, and the Protect phase on 17 June 2009; the "restricted" phase (our term) began on 22 July 2009, when the reference laboratory asked referrers to restrict specimens to high-risk patients only. ◆

delivered to the requesting doctor by phone, hard copy or electronic transfer.) Although the number of positive results was very low in the initial two phases of the pandemic, it is clear that the turnaround time rose progressively with each phase and that the target turnaround time of 48 hours was only ever achieved in the first phase. Acknowledgement that the reference laboratory (PathWest Laboratory Medicine WA) was not coping with the demand was confirmed by communiqués released on 12 June 2009 (discouraging testing for uncomplicated cases) and 22 July 2009 (notifying doctors that specimens from high-risk cases only would be processed). This later period is represented by the last column in Box 1 (the "restricted" phase). In spite of these measures, there has not yet been any improvement in test turnaround time. During this period, the thermocycler (PCR machine) in our laboratory (and presumably in many other private pathology laboratories) was relatively underused. It would appear that similar experiences were noted in other jurisdictions,[13] but it would be interesting to know whether the Queensland experience was modified by their different approach.

For illustrative purposes only, total turnaround times for a random sample of 409 influenza A-positive and -negative specimens are displayed in Box 2. These data showed a similar pattern to the positive-only specimens, with rising turnaround times as the pandemic phases progressed, except that the benchmark was not achieved even during the first phase. This is presumably because patients at the highest risk of disease (who were the most likely to test positive for influenza A) had specimen transport facilitated by use of a taxi as well as better coordination with the recipient laboratory's testing runs.

These data suggest that PathWest was being used in an inefficient manner — spending a huge amount of precious time and expertise processing an enormous number of specimens that would subsequently be reported as negative (96% of the total) while the private pathology laboratories were referring a large number of specimens (requiring packaging and transport by courier) that they were technically equipped to process. After the first phase of the pandemic, reporting did not meet the benchmark turnaround time and was no longer clinically helpful in making management decisions.

We propose that a more efficient approach for pandemic influenza diagnosis could be developed by implementing a "hub and spoke" system (now universally used for detection of HIV and hepatitis C virus), whereby specimens are screened for influenza A nucleic acids by the receiving laboratories and only positive specimens are referred for further characterisation. This would free up a vast amount of resources at both laboratory sites for efficient processing. This could be achieved by one of two means: (i) directing some pandemic funding to private laboratories for specific pandemic influenza screening tests (as in the Queensland model); or (ii) adjusting the Medicare Benefits Schedule PCR reimbursement item (number 69496) to make such testing economically viable in the private sector (by allowing up to nine PCR targets).

These recent experiences confirm the advice given by the private sector in correspondence with the Australian Government Office of Health Protection in response to the then-current version of the federal pandemic plan on 27 April 2008:

> [T]here is no clear articulation [in the document] of the fundamental need for close interaction between public and private sectors to address the threat posed by a pandemic.

The Australian Government was also advised at the time that

> Given that most health interactions in Australia occur in the community (where community general practitioners consult and send appropriate laboratory requests to private pathology laboratories), the initial cases in a pandemic will almost certainly present there. In addition, very shortly after the establishment of a pandemic in Australia, the public hospital system and their diagnostic laboratories will effectively be overwhelmed and potentially grind to a halt.

Ah, "The best laid schemes o' mice and men gang aft agley!" (Robert Burns).

Acknowledgements

We would like to thank Dr Desmond Chih and Ms Sylvia Gandossi for assistance with data collection and graphics.

Competing interests

We are both employees of Symbion Health, a private sector pathology company.

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(Received 17 Aug 2009, accepted 13 Oct 2009) ❑