The rational clinician in a pandemic setting

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ABSTRACT

- Pandemic (H1N1) 2009 influenza has generated many controversies in Australia around case definitions, laboratory diagnosis, case management, medical logistics and travel restrictions.
- Our experience as clinical advisers in the Victorian Department of Human Services Emergency Operations Centre suggests the following:
  - Case definitions may change frequently, and will tend to become more clinically specific over time.
  - Early in a pandemic, laboratory diagnosis plays a critical role in case finding and pathogen identification.
  - Later in the pandemic, standardised case management applied to well crafted case definitions should reduce reliance on the diagnostic laboratory in clinical management. The diagnostic laboratory will remain critical to monitoring disease surveillance, pathogen virulence, and drug susceptibility.
  - Medical logistics will continue to challenge pandemic managers as the health sector struggles to do the most good for the greatest number of people.
  - Travel restrictions remain scientifically controversial public health recommendations.
  - Issues of scalability (escalation and de-escalation of the response) relating to virus lethality need to be resolved in current pandemic planning.

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Australia has experienced the first pandemic of the 21st century. Early in the pandemic, Australia harboured the highest rate of disease transmission of laboratory-confirmed pandemic (H1N1) 2009 influenza in the world, and Victoria was at the centre of the outbreak. Since the first laboratory-confirmed case in Australia on 8 May 2009, the pandemic has precipitated evolving guidance from national and state health authorities. This has included the development of a new pandemic phase, "Protect",[1] that was not previously envisioned in the Australian Health Management Plan for Pandemic Influenza (AHMPPI).[2] Furthermore, the pandemic has elicited considerable professional controversy.[3,4]

Having served as clinical advisers in the Victorian Department of Human Services (DHS) Emergency Operations Centre, which for several days received over 1500 calls daily to the flu hotline from health professionals and the public, we wish to address issues generating persistent professional controversy: clinical case definitions, laboratory diagnosis, case management, medical logistics and travel restrictions.

Case definitions

The early case definition was criticised for not being an "accurate model for the swine flu epidemic"[3] and for missing the main target group for measuring community spread.[4] Moreover, it was asserted that "the case definition should be used to guide clinicians, not the laboratory testing strategy" because otherwise it does not identify the real extent of disease spread until it is too late.[3]

Outbreak investigation protocols are well established in public health literature. A working case definition, which may include additional criteria on the time, place and population at risk, is constructed from clinical and laboratory evidence. In the early stages of an outbreak, sensitivity is preferred over specificity — a case definition is purposefully kept broad to limit false negatives.[5] During the course of the pandemic in Victoria, with enlarging geographic spread of the disease, emergence of community transmission and increased clinical clarity, more than four case definitions were provided to clinicians. These definitions were progressively more clinically focused and specific. In this way, the state health authorities conformed to best practices as they dealt with the evolving pandemic.

The rational clinician can expect clinical case definitions in a pandemic to become increasingly age- and symptom-specific (albeit less sensitive) and to reflect evolving insights about disease presentation.

Laboratory diagnosis

The initial laboratory testing strategy was extensively criticised:

> … initial laboratory testing to confirm a case of swine flu was only allowed if a sick patient fitted the specific case definition … Tests on all other patients who had a clinical illness suspected of being swine flu were initially refused or given low laboratory priority. This is the opposite of what should have occurred. To understand the full extent of disease spread, widespread testing without assumptions needs to occur so that the accuracy of the proposed case definition can be tested.[3]

However, testing the accuracy of the case definition is not the key issue early in a pandemic. Knowing that the disease was imported, and in the belief it could be contained, the key issue in this pandemic was active case finding and contact tracing.

The DHS arranged for test specimens that met the current case definition to be sent by courier to the Victorian Infectious Diseases Reference Laboratory (VIDRL). Specimens originated from sentinel reporting sites, as well as general practices and hospital clinical departments. Two weeks into the pandemic in Australia, the degree of infectivity remained unclear. Testing of suspected cases linked epidemiologically to a suitable travel history continued. However, by early June, community transmission provided convincing evidence of containment failure. On 3 June, Victoria transitioned to a "Modified Sustain" pandemic phase. Published guidance for health professionals emphasised that laboratory testing for pandemic (H1N1) 2009 influenza was not required for all patients presenting with influenza-like illness and should be limited to symptomatic patients with severe disease or a high risk of complications, and vulnerable populations.[6] This guidance

directed clinicians to send swabs from these patients to their routine pathology services for influenza A testing. VIDRL remained available for H1N1 subtyping of confirmed influenza A specimens, as well as for influenza A testing where this was otherwise unavailable.

Reports of secondary cases linked to a confirmed case, as well as new cases lacking a relevant travel history, had emerged in the community in May. These cases suggest that community transmission and containment failure existed well before the pandemic phase change on 3 June, and that this evidence should have uncoupled testing strategy from patients' travel and contact history. The earlier implementation of a testing strategy focusing on high-risk patients would have decreased the testing burden for VIDRL. Moreover, we believe that laboratory findings from sentinel surveillance merited early analysis and dissemination, but this did not occur until 19 June.[7]

Nonetheless, the use of a dedicated reference laboratory with proven quality control early in the pandemic remains consistent with best practices in outbreak investigation and led to Australia's detection of the highest intensity of disease transmission among affected countries. After the epidemic curve is well defined, use of a diagnostic laboratory should focus limited resources on high-risk or vulnerable populations, particularly those with an uncertain diagnosis, such as may arise from failure to meet the given case definition.

Case management

At issue for the informed clinician is clinical decision making based on the laboratory data that are available at the time. Early in the pandemic, circulating seasonal influenza strains predominated. Indeed, laboratory analysis from 19 June 2009 demonstrated that the positive predictive value of influenza-like illness for novel pandemic (H1N1) 2009 was less than 5%.[7] However, pandemic (H1N1) 2009 influenza virus increasingly predominated as the pandemic unfolded. Unfortunately, laboratory results for the novel virus were not available to influence early clinical decision making for any given patient. Lacking patient-specific laboratory data, some practising infectious disease physicians managed their patients "not in quarantine and … generally not receiving antiviral therapy".[3] This approach ignores important aspects of community-based influenza management.

A World Health Organization expert reference group, acknowledging the global insufficiency of vaccine and antiviral agents against influenza caused by novel human subtypes, has published two sentinel articles on non-pharmacological interventions for pandemic influenza. These emphasise reliance on population-based recommendations including home-based care, social distancing, deferral of non-essential travel, strict respiratory and hand hygiene, and attention to disinfection of contaminated household surfaces.[8,9] A pandemic setting always places some practising physicians in a resource-constrained context. Standard case management relying on a clinical case definition in the absence of laboratory data remains completely consistent with best practices in communicable disease control in such settings and, indeed, it is expected.

However, practitioner calls to the DHS Emergency Operations Centre swine flu hotline revealed commonly shared concerns over using antiviral therapy (the category B1 drugs oseltamivir and zanamivir) in some high-risk populations, especially pregnant women. We believe the Victorian public health guidance on category B1 drugs[10] does not sufficiently recognise the evidence for the adverse consequences of influenza infection during pregnancy. These complications include increased rates of neural tube defects, spontaneous abortion, premature rupture of membranes, intensive care unit admission, and maternal death. Health authorities internationally have made unequivocal calls for the use of oseltamivir in pregnant patients with confirmed, probable or suspected pandemic (H1N1) 2009 infection.[11]

Medical logistics

Medical logistics underlie many of the problems reported in the swine flu pandemic. For the disaster medicine community, problems in communication, transportation and commodity distribution are predictable consequences of inadequately tested disaster plans. We embrace the calls of our infectious disease and general practitioner colleagues for enhanced multidisciplinary pandemic planning.[3,4] As an example, calls to the swine flu hotline at the DHS Emergency Operations Centre peaked at 1892 calls per day, but clinical support for the hotline itself was an afterthought not initially envisioned by the Victorian Human Influenza Pandemic Plan.[12]

Travel restrictions

Restrictions on travel, especially in view of the close contact generally involved (< 1 m separation for > 15 min), may appear consistent with social distancing measures intended to reduce exposure to disease. The pandemic influenza border plan cited in the AHMPPI[2] involves positive pratique, thermal imaging, mandatory questionnaires, interviews and quarantine,[13] all intended to slow the spread of pandemic disease. However, health authorities internationally have dismissed such border control measures. In the United States, academic scientists, commenting on proposed changes to quarantine rules, reported:

> The basic premise of the proposed revision, that the identification and quarantine of airline passengers showing symptoms of influenza infection will significantly diminish the spread of pandemic flu, is highly questionable and unsupported by data … The assumption that we can stop a pandemic illness of SARS [severe acute respiratory syndrome] or influenza by monitoring air travel is not correct.[14]

In Canada, where SARS had higher transmissibility and case-fatality than the current pandemic strain of influenza, health authorities reported that "Canadian screening results raise questions about the effectiveness of available screening measures for SARS at international borders".[15] The WHO continues to reject travel bans as part of pandemic (H1N1) 2009 disease control.[16]

We believe border control measures undertaken for the swine flu pandemic in Australia have little scientific justification. Given the domestic response to both international travellers and Victorians travelling interstate, exemplified by calls to restrict both domestic and international travel, we believe the political imperative to take action exacerbates public health mythology. It also heightened interstate and international tensions. The modern traveller has unwittingly become cast as the enemy of the people.

Planning implications

Overall, the dimensions of the current pandemic oblige substantial further changes to national and state pandemic plans. Central to

these changes is detail about scalability (escalation and de-escalation) in response to new pandemic circumstances — such as whether virus lethality differs from that anticipated, as is currently the case, or otherwise progresses within an unfolding pandemic, as occurred when the pandemic of 1918 comprised repeated epidemics with an increasingly virulent virus. The lessons to date from case definitions, laboratory diagnosis, case management, medical logistics and travel restrictions should be promptly integrated into present plans.

Competing interests

None identified.

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