25 August 2009

This supplement has been prepared to present scientific and technical news items that may be of more interest to technical personnel at RDT&E activities and the labs, or the medics rather than the broader readership of the basic CB Daily. Due to the nature of the material, the articles, if available online, are usually only available through subscription services thus making specific links generally unavailable. Thus, usually only the bibliographic citation is available for use by an activity's technical library.

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Chem-Bio News – Pandemic Influenza Edition #75

1. SWINE FLU COULD INFECT HALF OF U.S: *"Presidential Panel's Estimate Is First To Gauge Possible Impact of Pandemic."*

2. ASIA WAY SHORT OF VACCINE TO FIGHT SWINE FLU: WHO: *"Asia is going to be way short of the new H1N1 vaccine to fight swine flu when the next surge of infections hits during the cold season this year, a spokesman for the World Health Organization said on Tuesday."*

3. PRESIDENTIAL PANEL CALLS FOR PLANNING CZAR, FASTER VACCINE: *"A White House expert advisory group today released a report calling for the Obama Administration to accelerate novel H1N1 vaccination preparation for high-risk Americans and appoint a White House pandemic preparedness point person, among other recommendations."*

4. US HOSPITALS URGED TO TAKE SURVEY ON VENTILATOR NUMBERS BY SEPTEMBER 10: *"The US Department of Health and Human Services (HHS) contracted with the American Association for Respiratory Care (AARC) to perform a comprehensive inventory of mechanical ventilators in every hospital in the country."*

5. FIRST ESTIMATION OF DIRECT H1N1PDM VIRULENCE: *"When assuming that half of ARDS [acute respiratory distress syndrome] are of lethal outcome, we may assume that H1N1pdm may generate 1 case of ARDS every 5,000 infections. ARDS is always treated in ICUs, and three weeks of treatment is probably an average period to be taken into account. In case of attack rates of 30% to 50% this fall and winter in Northern Hemisphere [6], these figures may help refining preparedness."*

6. PANEL URGES HHS TO PREPARE FOR H1N1 VACCINE SAFETY CONCERNS: *"The National Vaccine Advisory Committee (NVAC) unanimously passed a recommendation that HHS "develop, and where possible test in advance, a strong and organized response to scientific and pubic concerns about vaccine safety that may emerge during the 2009 H1N1 vaccination campaign."*

7. SWINE ORIGIN INFLUENZA A (H1N1) VIRUS AND ICU CAPACITY IN THE US: *"We calculate that 46 million people will contract the infection, resulting in 2.7 million hospitalizations, 331,587 episodes of ARF-MV [acute respiratory failure – mechanical*

ventilation] and nearly 200,000 deaths, suggesting that the US may require the ability to provide MV at a volume approximately 33% over the current annual use."

8. A CELL-BASED H7N1 SPLIT INFLUENZA VIRION VACCINE CONFERS PROTECTION IN MOUSE AND FERRET CHALLENGE MODELS: *"We have extended to the H7 subtype the finding that protective efficacy may not be directly correlated with the pre-challenge levels of serum antibodies, a finding which could be of great importance in assessing the potential effectiveness of pandemic influenza vaccines.."*

9. BELFAST PUTS EXTRA GRAVES AT THE READY SHOULD SWINE FLU PANDEMIC WORSEN: *"Up to 10,000 burial plots are currently being held in reserve at Roselawn Cemetery after the land was purchased by Belfast City Council for its future grave provision. Currently there is unused space for around 4,000 burials in and around Belfast."*

CB Daily Report

Chem-Bio News

SWINE FLU COULD INFECT HALF OF U.S
By Rob Stein
The Washington Post
August 25, 2009

"Presidential Panel's Estimate Is First To Gauge Possible Impact of Pandemic."

"Swine flu could infect half the U.S. population this fall and winter, hospitalizing up to 1.8 million people and causing as many as 90,000 deaths -- more than double the number that occur in an average flu season, according to an estimate from a presidential panel released Monday.

The virus could cause symptoms in 60 million to 120 million people, more than half of whom might seek medical attention, the President's Council of Advisors on Science and Technology estimated in an 86-page report to the White House assessing the government's response to the first influenza pandemic in 41 years.

Although most of the cases probably would be mild, up to 300,000 people could require intensive care, which could tie up all those beds in some parts of the country at the peak of the outbreak, the council said.

"This is going to be fairly serious," said Harold E. Varmus of Memorial Sloan-Kettering Cancer Center in New York, co-chair of the 21-member council. "It's going to stress every aspect of our health system."

The estimates mark the first time experts have released specific calculations about the possible U.S. impact of the pandemic. The "plausible scenario" is based on previous pandemics and how the swine flu behaved in the United States this spring and during the Southern Hemisphere's winter over the past few months, said Marc Lipsitch of the Harvard

School of Public Health, who helped prepare the estimate."

The full article can be found at: http://www.washingtonpost.com/wp-dyn/content/article/2009/08/24/AR2009082401733.html

Return to Top

ASIA WAY SHORT OF VACCINE TO FIGHT SWINE FLU: WHO
By Tan Ee Lyn
Reuters
August 25, 2009

"Asia is going to be way short of the new H1N1 vaccine to fight swine flu when the next surge of infections hits during the cold season this year, a spokesman for the World Health Organization said on Tuesday.

Australia and China are due to begin producing the vaccines in September, but these would be used domestically and the rest of the region is unlikely to benefit.

"Nowhere is ready ... there is going to be massive underproduction of vaccines as compared to the needs and demand," said Manila-based WHO spokesman Peter Cordingley."

.....

"Nobody is going to do very well, it'll be a long time before production comes up to even answering Australia's problems."

In Japan, the flu season has already arrived while its drug companies have not even started producing the new vaccine.

Cordingley said the lack of vaccines in developing countries was of particular concern.

"They don't have resources, they have populations that are at such high risk in cramped conditions in squatter villages, with no health services, no access to a doctor, lots of pregnant women, we are very worried about it."

The full article can be found at: http://www.reuters.com/article/healthNews/idUSTRE57O24K20090825

Return to Top

PRESIDENTIAL PANEL CALLS FOR PLANNING CZAR, FASTER VACCINE
By Jim Wappes
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
August 24, 2009

“oint a White House pandemic preparedness point person, among other recommendations.

The group said the federal government's preparations for a likely fall wave of novel H1N1 influenza have been well organized and scientifically grounded, according to the report by the President's Council of Advisors on Science and Technology (PCAST).

But some preparedness steps, the report said, should be improved or accelerated.

In a press release today, PCAST listed these primary recommendations:

* Accelerate preparation of flu vaccine for distribution to high-risk individuals
* Clarify guidelines for the use of antiviral medicines
* Upgrade the current system for tracking the pandemic's progress and making decisions about allocating resources
* Accelerate development of communication strategies—including electronic social networking tools—to broadcast public health messages to help mitigate the pandemic's impact
* Identify a White House point person with primary authority to coordinate key decisions across the government as the pandemic evolves

The full article can be found at: http://www.cidrap.umn.edu/cidrap/content/influenza/swineflu/news/aug2409whitehouse.html

Return to Top

US HOSPITALS URGED TO TAKE SURVEY ON VENTILATOR NUMBERS BY SEPTEMBER 10
RTMagazine.com
August 21, 2009

“The US Department of Health and Human Services (HHS) contracted with the American Association for Respiratory Care (AARC) to perform a comprehensive inventory of mechanical ventilators in every hospital in the country. A survey is being taken to gain an accurate account of the number of ventilators that would be available in the event of a nationwide pandemic.

The Office of Preparedness and Response requested this inventory information “as the nation braces for the nH1N1 virus that may affect record numbers of Americans,” according to an announcement from AARC. The announcement goes on to explain, “Initial experience shows that many individuals are placed on ventilators as a result of this flu.”

All information gained from the survey will be kept in confidence and will not be available through the Freedom of Information Act. The AARC clarifies that no relocation of ventilators will be performed as a result of this survey; the information is sought so that the government can acquire or assist in augmenting current ventilator capacity.”

The full article can be found at: http://www.rtmagazine.com/news/2009-08-21_01.asp

Return to Top

FIRST ESTIMATION OF DIRECT H1N1PDM VIRULENCE
By Antoine Flahault
PLoS Currents – Influenza
August 24, 2009

“We provide rough estimates of direct lethality from ARDS due to H1N1pdm from two independent sources of data, one from New Caledonia where 30,000 infections are assumed to have occured and 3 deaths reported to be attributable directly to the pandemic virus. Another source is Mauritius where 70,000 infections are estimated to have occured, and 7 reported death from ARDS (5 of them are currently confirmed). These surveillance data allows for first estimation of direct lethality due to H1N1pdm to be 1 per 10,000 infections, about 100 times more than regular seasonal influenza.”

“Influenza lethality is due to three main causes: First, direct viral origin, leading to viral pneumonia of high severity, with an acute respiratory distress syndrom (ARDS), associated with 30 to 50% lethality in intensive Care Unit (ICU) [1]; Second, bacterial surinfection, due to pneumococal, staphylococal, streptococal, or meningococal pneumonia, usely curable with appropriate antibiotics, provided they are administered early enough; and Third, decompensation of severe underlying conditions, often in elderly people or in vulnerable chronic patients. The last one is the predominant cause of death attributable to seasonal influenza in developed countries, and has reached for years now, despite of the use of mass immunization in elderly, a level around 1 death per 1,000 infections. This cause of lethality is rarely reported as attributed to influenza in death certificates, and therefore is not easily assessable during outbreaks, and is usely measured as excess mortality when time series of mortality become available, sometimes in real time, most often several months after the season [2]. The second cause, i.e. bacterial surinfections, is much less seen in developed countries due to antibiotics availability. However, in the developing world, it may still be a cause of concern, since bacterial pneumonia may rapidely become lethal if treatment is not given appropriately in time. The direct lethality due to viral pneumonia gives probably the best estimate of influenza strains' virulence, since it may vary from strain to strain, and is not due to the level of health development of a country. Furthermore, ARDS always leads to ICU, and is easy enough to diagnose and to report.

Death from ARDS due to seasonal influenza

There are not many assessments available with regards with the incidence of death from ARDS due to seasonal influenza in the litterature. Empirical evidence suggests in France that less than 5 to 10 of such cases are identified each year, when an average of 6 million seasonal infections are estimated from the French Sentinelles system [3]. We may therefore assume, waiting for better estimates in the future, that deaths from ARDS due to seasonal influenza is an exceptional event, which occurs once every million infected patients.

Death from ARDS due to H1N1pdm

It is too early to provide precise figures of deaths of ARDS due to the new strain of pandemic influenza. In the USA there are a too large uncertainty reported on the denominator (i.e. number of influenza infections), when in the UK or Argentina too. In smaller areas, and in particular in islands such as French New Caledonia or Mauritius, we may have first rough estimates which may be more relevant and easier to catch.

French Government estimated last week that 20,000 cases of influenza had occured in New Caledonia in the emerging outbreak, leading to a rough estimate of 30,000 infections and by August 21st, 3 deaths of confirmed cases were reported, in patients aged 8 yr, 27 yr, 58 yr [4].

Mauritius Government estimated last week that 15,000 cases of influenza had occured in the last two weeks in Mauritius, however some reports from the media and recent personal communication from local doctors lead me to estimate that about 50,000 cases actually occured, and therefore about 70,000 infections, taking acount mild illnesses. By August 19th, 7 deaths had occured, 5 of them were already virologically confirmed in patients aged 4, 6, 28, 46, 53 [5].

New Caledonia and Mauritius figures are consistant to a rough estimate of about 1 death from ARDS due to H1N1pdm per 10,000 infections, i.e. a virulence of an order of magnitude of 100 times that observed for seasonal strains.

We acknowledge that we are producing very rough estimates of direct lethality associated to H1N1pdm. However, it may be useful to deliver such estimates as early as possible in the course of this pandemic, with the purpose of helping health authorities to check availability of ICUs and artificial ventilation devices in their countries, in case of a wave of similar virulence this fall in the Northern Hemisphere. When assuming that half of ARDS are of lethal outcome, we may assume that H1N1pdm may generate 1 case of ARDS every 5,000 infections. ARDS is always treated in ICUs, and three weeks of treatment is probably an average period to be taken into account. In case of attack rates of 30% to 50% this fall and winter in Northern Hemisphere [6], these figures may help refining preparedness.

This work is funded by EHESP School of Public Health, Rennes, France
The author has declared that no competing interests exist."

The full article can be found at: http://knol.google.com/k/antoine-flahault/first-estimation-of-direct-h1n1pdm/2nsp4xxomyqub/1?collectionId=28qm4w0q65e4w.1&position=1#

Return to Top

PANEL URGES HHS TO PREPARE FOR H1N1 VACCINE SAFETY CONCERNS
By Robert Roos
CIDRAP News (Center for Infectious Disease Research & Policy – University of Minnesota)
August 24, 2009

“An advisory committee today called on the Department of Health and Human Services (HHS) to be ready to respond quickly to safety concerns that may emerge during this fall's novel H1N1 influenza vaccination campaign.

The National Vaccine Advisory Committee (NVAC) unanimously passed a recommendation that HHS "develop, and where possible test in advance, a strong and organized response to scientific and pubic concerns about vaccine safety that may emerge during the 2009 H1N1 vaccination campaign."

"The challenge will be to communicate effectively and to differentiate rapidly between adverse events that may be causally related to the vaccine and those which would be expected by chance alone," states the recommendation.

The 17-member committee said HHS could prepare in two specific ways:

* Assembling information on background rates in the general population of anticipated adverse events following immunization. An HHS official at the meeting said such events might include, for example, heart attacks and shortness of breath.
* Organizing drills or practice scenarios for how the government will respond to concerns about adverse events temporally—but not necessarily causally—related to H1N1, including identifying data resources and strategies for communications messages

The recommendations are specifically intended for Assistant Secretary for Health Dr. Howard Koh, to whom the committee reports.

The recommendation comes as clinical trials of H1N1 vaccines are just getting under way. HHS expects to launch the vaccination campaign in mid October, when only preliminary trial results will be available.

Planners are mindful of the 1976 swine flu vaccination campaign, which reached more than 40 million people but was associated with an increase in cases of Guillian-Barre syndrome, a temporary paralytic condition. Officials say vaccine safety and purifications steps are much more advanced today than at that time.

The NVAC also approved a separate recommendation today that HHS develop a detailed overall plan for communicating about the H1N1 vaccination program. The group urged HHS to develop a comprehensive plan for achieving at least the following aims:

* Delineating the difference between seasonal flu and pandemic H1N1 flu
* Reaching out to healthcare providers who do not usually supply vaccination services, such as obstetricians/gynecologists and internists
* Identifying high-risk groups and groups that are targeted for both seasonal flu and pandemic flu immunization, and explaining why these groups may differ
* Discussing and responding to emerging news and events, such as vaccine supply and vaccine safety concerns”

The full article can be found at: http://www.cidrap.umn.edu/cidrap/content/influenza/

swineflu/news/aug2409nvac.html

Return to Top

SWINE ORIGIN INFLUENZA A (H1N1) VIRUS AND ICU CAPACITY IN THE US
By Marya D. Zilberberg, Christian Sandrock, Andrew Shorr
PLoS Currents – Influenza
August 22, 2009

“We developed a model simulating the potential impact of influenza H1N1 pandemic on the volume of acute respiratory failure requiring mechanical ventilation (ARF-MV) and the accompanying mortality rate in the US. We calculate that 46 million people will contract the infection, resulting in 2.7 million hospitalizations, 331,587 episodes of ARF-MV and nearly 200,000 deaths, suggesting that the US may require the ability to provide MV at a volume approximately 33% over the current annual use.”

“INTRODUCTION

In March of 2009 a novel strain of swine origin influenza A (H1N1) virus (S-OIV) was detected in Mexico. It has now spread to the rest of the world. With over 170,000 laboratory-confirmed cases worldwide, the World Health Organization (WHO) has declared a global pandemic[1]. In the United States, current estimates suggest an attack rate of approximately 6-8% in affected communities, which according to officials from the Centers for Disease Control and Prevention (CDC) may more than double during the traditional flu season[2]. Although reports of both severe illness and fatalities are uncommon, concern exists about the potential for this virus to cause severe acute respiratory failure necessitating mechanical ventilation (ARF-MV) with specialized methods[3]. Since H1N1 is predicted to affect a significant proportion of the population, even a low incidence of concomitant ARF-MV may overwhelm the already-stretched emergency department and intensive care unit (ICU) resources[4]. To estimate what the S-OIV may portend for the ARF-MV in the US, we developed a model simulating its potential impact on the volume of ARF-MV and the accompanying mortality rate.

METHODS

Because the situation is evolving rapidly and information is scant, in addition to peer-reviewed studies we relied on other sources of credible estimates and reasonable assumptions for model inputs (Table). We employed data from the CDC to estimate the H1N1 incidence and mortality in the US population, and those from the Mexican experience for our baseline rates of hospitalization and ARF-MV[5]. We explored a range of potential values for model inputs given the uncertainties surrounding them, and each outcome was subjected to 10,000 Monte Carlo simulation trials.

RESULTS AND DISCUSSION

In the base case, we calculate that 46 million people will contract the infection, resulting in 2.7 million hospitalizations, 331,587 episodes of ARF-MV and nearly 200,000 deaths (Table),

suggesting that the US may require the ability to provide MV at a volume between 23% and 45% over the current use[4] (Table). Tornado diagrams for each outcome indicated that the estimates are equally sensitive to all corresponding inputs (data not shown).

Our model is limited by the accuracy of the input parameters. As the flu season progresses, more precise inputs may become available. Additionally, we did not model the impact of an effective vaccine on the attack rates or the outcomes; however, because of the uncertainties surrounding the timing and the number of doses available, and its effectiveness, this too will require updating when the information becomes available. Finally, the applicability of data from Mexico is uncertain[5]. Differences in the delivery of and access to healthcare between the US and Mexico may alter both rates of progression to ARF-MV and mortality.

These limitations notwithstanding, the model is informative in several ways. First, our findings represent an attempt to quantify the potential need for surge capacity in our ICUs in response to this evolving pandemic. We should point out that, although we modeled the burden over the entire epidemic period, the vast majority of the cases will likely occur during the peak flu months, thus straining the ICU and MV capacity even more intensely over a shorter period of time. For this reason, our estimates emphasize the need for careful planning and prioritization schemes as they relate to the allocation of scarce ICU resources. Second, in light of the recent report of severe ARF-MV cases requiring advanced MV modes available only in specialized centers and requiring special equipment not commonly stockpiled at the state and federal levels, planners must explore the feasibility of regionalizing S-OIV-related ARF-MV care[3]. Third, as this infection will likely disproportionately affect areas of higher population density, regional response plans are urgently needed.

CONCLUSION

In summary, estimates of what may be expected with S-OIV should help ICU directors, hospital administrators and other policy makers allocate appropriate resources for an effective coordinated response. In addition to education and prevention, efforts must focus on planning for the impact of this virus on ARF-MV."

The full article can be found at: http://knol.google.com/k/marya-d-zilberberg/swine-origin-influenza-a-h1n1-virus-and/3htiswudddv6h/1?collectionId=28qm4w0q65e4w.1&position=2#

ANALYST NOTE: The full article also contains a table of model input parameters and outcome estimates.

Return to Top

A CELL-BASED H7N1 SPLIT INFLUENZA VIRION VACCINE CONFERS PROTECTION IN MOUSE AND FERRET CHALLENGE MODELS
Preventive Medicine Week
August 30, 2009

"We have investigated the immunogenicity and protective efficacy of a cell based candidate

pandemic influenza H7 vaccine in pre-clinical animal models."

"Mice and ferrets were immunised with two doses of the split virus vaccine (12-24 mu g haemagglutinin) with or without aluminium hydroxide adjuvant and challenged 3 weeks after second dose with the highly pathogenic A/chicken/Italy/13474/99 (H7N1) virus. The H7N1-specific serum antibody response was also measured. After challenge, viral shedding, weight loss, disease signs and death (only mice) were recorded. Low-to-modest serum antibody titres were detected after vaccination. Nevertheless, the vaccine induced significant protection from disease after challenge with the wild-type virus. In the murine lethal challenge model, vaccination effectively prevented death and, furthermore, formulation with adjuvant reduced excessive weight loss and viral shedding. In ferrets, vaccination reduced viral shedding and protected against systemic spread of the virus."

"We have extended to the H7 subtype the finding that protective efficacy may not be directly correlated with the pre-challenge levels of serum antibodies, a finding which could be of great importance in assessing the potential effectiveness of pandemic influenza vaccines.."

The full article can be found at: (R.J. Cox, et. al., "A cell-based H7N1 split influenza virion vaccine confers protection in mouse and ferret challenge models". Influenza and Other Respiratory Viruses, 2009;3(3):107-117). Link not available.

Return to Top

BELFAST PUTS EXTRA GRAVES AT THE READY SHOULD SWINE FLU PANDEMIC WORSEN
By Matthew McCreary
The Belfast Telegraph
July 25 2009

"Up to 10,000 burial plots are currently being held in reserve at Roselawn Cemetery after the land was purchased by Belfast City Council for its future grave provision. Currently there is unused space for around 4,000 burials in and around Belfast.

But the extra tract of land at Roselawn could be brought forward for the burial of thousands of corpses in the event that swine flu sweeps across the province."

The full article can be found at: http://www.belfasttelegraph.co.uk/news/local-national/belfast-puts-extra-graves-at-the-ready-should-swine-flu-pandemic-worsen-14430649.html

Return to Top

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