Global Measles Control & Outbreak Risk in the US

Jeffrey S. Duchin, MD
Chief, Communicable Disease Epidemiology & Immunization Section
Public Health - Seattle & King County
Professor in Medicine, Division of Allergy & Infectious Diseases
Adjunct Professor, School of Public Health & Community Medicine
University of Washington, Seattle
WHO: Measles deaths decline, but elimination progress stalls in some regions

Improved vaccination rates critical for success

Note for the media

17 JANUARY 2013 | GENEVA - The number of measles deaths globally decreased by 71% between 2000 and 2011, from 542 000 to 158 000. Over the same period, new cases dropped 58% from 853 500 in 2000 to 355 000 in 2011, according to new data released Thursday by WHO, a leading member of the Measles and Rubella Initiative. Although the WHO Region of the Americas has sustained measles elimination since 2002, and the WHO Western Pacific Region is on track to achieve elimination, large outbreaks of measles are jeopardizing progress in the remaining regions that have these goals.

Success of vaccination coverage

WHO recommends that every child receive two doses of measles vaccine. The new data, published in this week's edition of the Centers for Disease Control and Prevention's (CDC) Morbidity and Mortality Weekly Report and then in WHO's Weekly Epidemiological Record, show overall progress in reducing deaths is linked largely to increased vaccination coverage.

Estimated global coverage with a first dose of vaccine increased from 72% in 2000 to 84% in 2011. The number of countries providing the second dose through routine services increased from 97 in 2000 to 141 in 2011. Since 2000, with support from the Measles & Rubella Initiative, more than 1 billion children have been reached through
Measles: The Problem

• Prior to availability of measles vaccine, over 90% of children were infected before 15 years of age.
  – Caused more than 2,000,000 deaths and 15,000-60,000 cases of blindness annually worldwide
  – In the decade before the measles vaccination program began, an estimated 3–4 million people in the US were infected each year, of whom 400–500 died, 48,000 were hospitalized, and another 1,000 developed chronic disability from measles encephalitis.

• In 2000, WHO estimated 535,000 children died of measles, the majority in developing countries, accounting for 5% of all under five mortality.
  – In some developing countries, the case fatality rate for measles among young children may still reach 5–6%.

• In industrialized countries, approximately 10–30% of measles cases require hospitalization, and one in a thousand cases among children results in death from measles complications.
Measles Disease

• Infants susceptible when passively acquired maternal Ab lost.
  – Infants born to women with vaccine-induced immunity susceptible at younger age than those born to women with naturally acquired immunity.

• The age at which people contract measles depends on:
  – Rate of decline of protective maternal antibodies
  – Amount of contact with infected people
  – Level of measles vaccine coverage.
  – Age at vaccination (?)

• Densely populated urban settings with low vaccination coverage: measles mainly affects infants and young children.

• As measles vaccine coverage increases, or population density decreases, the age distribution shifts towards older children (or adolescents, adults).
Measles: Clinical Features

- **Pneumonia** accounts for most measles-associated deaths
  - Risk increased by measles-associated immune suppression as well as immune dysfunction within the lungs.
  - Pneumonia caused by $2^0$ viral or bacterial infections.
  - Measles giant cell pneumonitis in immunocompromised people

- **Other complications:** laryngotracheobronchitis (croup), otitis media, mouth ulcers (stomatitis).
- Diarrhea common, further contributes to under-nutrition.
- Keratoconjunctivitis common, particularly in children with vitamin A deficiency, can cause of blindness.
Measles: CNS Complications

- **Post-measles encephalomyelitis**: 1/1000 cases, mainly older children and adults.
  - Fever, seizures, various neurological abnormalities with onset within 2 weeks of rash.
  - Likely an autoimmune disorder triggered by measles infection

- **Persistent measles virus infections** (months-years after acute infection)
  - **Measles inclusion body encephalitis**: Fatal, progressive neurological deterioration in persons with defective cellular immunity
  - **SSPE**: 1/10,000–100,000 cases; seizures, progressive cognitive & motor deterioration followed by death 5-15 years after infection.
    - Primarily in people with measles before 2 years of age.
    - Measles vaccination programs have led to a dramatic reduction in the incidence of SSPE.73
Measles & Rubella (MR) Initiative

• Led by American Red Cross, the United Nations Foundation, the U.S. CDC, UNICEF, and WHO

• Improving measles vaccination coverage and reducing measles-related deaths = global priority
  

• The infectiousness of measles easily leads to global spread
  
  – Even countries that eliminated indigenous transmission remain vulnerable to outbreaks from importations.
  
  – WHO Region of the Americas successfully eliminated all indigenous transmission of measles viruses in 2002.

  – Since adoption and coverage of measles- and rubella-containing vaccines remain uneven around the world, measles and rubella continue to pose a significant threat everywhere.
Measles & Rubella (MR) Initiative

• MR Initiative (formerly, Measles Initiative) launched in 2001 after success of countries in the Americas in stopping spread of measles
  – Provide technical and financial support for accelerated measles control activities.
• 2003 World Health Assembly resolution urged member countries to reduce measles-attributed deaths by 50% compared with 1999 estimates by the end of 2005.
  – Estimated measles mortality reduced by 60% from 873,000 deaths in 1999 (CI 634,000-1,140,000) to 345,000 deaths in 2005 (CI 247,000-458,000)
  – 23% decline in under-five deaths worldwide between 1990-2008
  – In 2010, measles deaths dropped to approx. 139,000 (74% decrease compared with 2000)
In 2010, there were an estimated 382 measles deaths per day.
During 2000-2011, all regions except India had mortality reductions.
In 2011, measles deaths increased to 158,000.
- 90% of mortality burden in AFR, EMR, India and SEAR countries.
Global Measles & Rubella Strategic Plan

Vision, Goals, Milestones

Goals

• By end 2015
  – Reduce global measles mortality by at least 95% compared with 2000 estimates (535,300 deaths).
  – Achieve regional measles and rubella/CRS elimination goals.

• By end 2020
  – Achieve measles and rubella elimination in at least five WHO regions.
Global Measles & Rubella Strategic Plan

Vision, Goals, Milestones

Milestones

• By end 2015
  – Reduce annual measles incidence to **less than five cases per million** and maintain that level.
  – **Achieve >90% coverage with 1ST routine dose of measles-containing vaccine** (or MR-containing vaccine as appropriate) nationally, and >80% vaccination coverage in every district or equivalent administrative unit.
  – **Achieve >95% coverage with M, MR or MMR during SIAS** in every district.
  – Establish a **rubella/CRS elimination goal** in at least three additional WHO regions.
  – Establish a **target date for global eradication of measles**.
Reported measles incidence per million population, by World Health Organization region and worldwide, 2000–2011
Measles Elimination: Progress

- WHO region of the Americas has eliminated measles
  - Intensive vaccination and surveillance efforts interrupted endemic measles virus transmission
- 4 of 5 remaining WHO regions have set measles elimination targets of 2020 or earlier (except SE Asia)
- Recent progress in reducing measles incidence and mortality in sub-Saharan Africa
  - Increased routine measles vaccine coverage and provision of 2nd dose of measles vaccine through mass measles vaccination campaigns (SIAs)
  - This progress led to the proposal to eliminate measles in the WHO African region by 2020
Current WHO Regional Measles and Rubella Elimination Goals

In 2009, SEAR Regional Committee endorsed a resolution to mobilize support toward measles elimination.

Note: EMRO is in the process of adopting a target for rubella elimination by 2020.
Measles Elimination: Threats

• Recent large measles outbreaks in southern and eastern Africa, including South Africa, Zimbabwe, Zambia, Malawi
  – Measles virus can re-enter communities and cause large outbreaks if high levels of population immunity are not sustained.

• In 2009, 36,000 measles cases reported from 46 countries in Africa.
  – Cases increased to 172,824 in 2010, including large outbreaks in several countries with a history of successful measles control.

• Of the estimated 20.1 million infants who did not receive MCV1 in 2011 through routine immunization services, 11.1 million (55%) were in 5 countries: India (6.7M), Nigeria (1.7M), Ethiopia (1.0M), Pakistan (0.9M), and DRC (0.8M).
Outbreaks

- AFR (2007-’09): 250,000 cases, 1500 deaths
- EUR: 7449 cases 2007, 30,625 in 2009

* Actual # may be 10-50X higher
Measles Elimination: Threats

• During 2011, a total of 222 measles cases (incidence rate: 0.7 per 1 million population) and 17 measles outbreaks were reported in the US, compared with a median of 60 (range: 37–140) cases and four (range: 2–10) outbreaks reported annually during 2001–2010.
  – 90% associated with importations from other countries

• Europe did not meet its goal of regional measles elimination by 2010
  – For 2012, there were 23,871 measles cases reported from among 51 (96%) countries of the WHO European Region.

• During 2012, 223 measles cases were reported from the US and 802 cases were reported from Canada

• Despite very high levels of measles vaccine coverage and population immunity, clustering of susceptible people can lead to measles outbreaks.
Largest Measles Epidemic in North America in a Decade—Quebec, Canada, 2011: Contribution of Susceptibility, Serendipity, and Superspreading Events

Gaston De Serres,1,2 France Markowski,3 Eveline Toth,3 Monique Landry,1 Danielle Auger,3 Marlene Mercier,3 Philippe Belanger,1 Bruno Turnet,3 Horacio Arruda,2 Nicole Boutilier,1 Brian J. Ward,1 and Danuta M. Skowronski5

1Institut National de Santé Publique du Québec, 2Department of Social and Preventive Medicine, Laval University, and 3Ministère de la Santé et des Services Sociaux du Québec, Quebec City, 4Research Institute of the McGill University Health Centre, Montréal, Quebec; and 5British Columbia Center for Disease Control, Vancouver, Canada

Background. The largest measles epidemic in North America in the last decade, occurred in 2011 in Quebec, Canada, where rates of 1- and 2-dose vaccine coverage among children 3 years of age were 95%–97% and 90%, respectively, with 3%–5% unvaccinated.

Methods. Case patients identified through passive surveillance and outbreak investigation were contacted to determine clinical course, vaccination status, and possible source of infection.

Results. There were 21 measles importations and 725 cases. A superspreading event triggered by 1 importation resulted in sustained transmission and 678 cases. The overall incidence was 9.1 per 100 000; the highest incidence was in adolescents 12–17 years old (75.6 per 100 000), who comprised 56% of case patients. Among adolescents, 22% had received 2 vaccine doses. Outbreak investigation showed this proportion to have been an underestimate; active case finding identified 130% more cases among 2-dose recipients. Two-dose recipients had milder illness and a significantly lower risk of hospitalization than those who were unvaccinated or single-dose recipients.

Conclusions. A chance superspreading event revealed an overall level of immunity barely above the elimination threshold when unexpected vulnerability in 2-dose recipients was taken into account. Unvaccinated individuals remain the immunization priority, but a better understanding of susceptibility in 2-dose recipients is needed to define effective interventions if elimination is to be achieved.

Keywords. measles; epidemic; underreporting; surveillance; outbreak; elimination

In 1995, Canada and other countries of the Americas adopted a measles elimination goal [1, 2]. Toward this goal, mass immunization campaigns targeting children receiving the measles-mumps-rubella (MMR) schedule was also introduced at that time [1, 2]. The incidence of measles was 100,000 socially decline in Canada from 803 in
Numbers of all measles cases, imported cases, and cases associated with the initial school outbreak, by week of rash onset in 2011.
Quebec Measles Outbreak
DeSerres. JID 2013:207

• A superspreading event triggered by 1 importation resulted in sustained transmission and 678 cases.
• Overall incidence was 9.1 per 100 000; highest in adolescents 12–17 years old (75.6 per 100 000)
  – Baseline incidence 2001-2010: 0.02-0.31/100,000
• Vaccine coverage (2006, 2008, 2010) showed 1-dose coverage of 97% and 2-dose coverage of 90% by 28 months
• Among adolescent cases, 22% had received 2 vaccine doses.
  – Active case finding identified 130% more cases among 2-dose recipients
  – Attenuated cases in 2-dose recipients not tested/reported
• With 3-5% of population unvaccinated, additional susceptibility in 1- and 2-dose vaccine recipients can push the population towards tipping point for epidemic risk
Figure 3. Vaccination status of case patients, by age group. Unknown/no proof indicates unknown vaccination status or no written proof of vaccination.

DeSerres. JID 2013:207
Long-Lasting Measles Outbreak Affecting Several Unrelated Networks of Unvaccinated Persons

Frédéric Dallaire, Gaston De Serres, François-William Tremblay, France Markowski, and Graham Tipples

1Department of Preventive and Social Medicine, Faculty of Medicine, Laval University, 2Institut National de Santé Publique du Québec, and 3Ministère de la Santé et des Services Sociaux du Québec, Quebec; 4Canadian Field Epidemiology Program, Public Health Agency of Canada, Ottawa, Ontario; and 5National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba

Despite a population immunity level estimated at ~95%, an outbreak of measles responsible for 94 cases occurred in Quebec, Canada. Unlike previous outbreaks in which most unvaccinated children belonged to a single community, this outbreak had cases coming from several unrelated networks of unvaccinated persons dispersed in the population. No epidemiological link was found for about one-third of laboratory-confirmed cases. This outbreak demonstrated that minimal changes in the level of aggregation of unvaccinated individuals can lead to sustained transmission in highly vac-

in May 2007, notifications were sent to emergency departments and first-line physicians asking them to look actively for measles in patients presenting with rash and fever. Suspected cases were investigated by the regional public health units. Information was gathered on clinical presentation, age, any epidemiological link to confirmed cases, travels vaccination status, and laboratory confirmation of measles. History of measles immunization was verified with the patient’s immunization record. The outbreak was considered over after 2 incubation periods without any reported case.

Measles cases were defined as either laboratory confirmed or clinically confirmed. Laboratory-confirmed cases were characterized by either measles virus detection, positive serological test for measles immunoglobulin (Ig) M antibody, or a significant increase in the measles-specific IgG antibody titer between acute and convalescent serum samples. Clinically confirmed cases were defined by fever (temperature, ≥38.3°C), a generalized maculopapular rash for ≥3 days, and either cough, coryza, or conjunctivitis. Clinical cases had to be epidemiologically linked to a confirmed case to be included.

Viruses were isolated by viral culture of pharyngeal and/or urine specimens at the Montreal Children’s Hospital Virology Laboratory. Measles viral RNA in pharyngeal and/or urine speci-
Measles Outbreak
Dellaire. JID 2009

• Mathematical models predicting measles elimination assume random distribution of susceptible persons in the population.
• In reality, unvaccinated individuals are not distributed at random.
• Unvaccinated persons cluster by socio-economic conditions and religious and philosophical opposition to vaccination.
• “The continued propagation throughout many generations of cases raised the possibility that a minimal change in the overall vaccine coverage in the population or in the level of aggregation of unvaccinated individuals can lead to sustained but protracted transmission despite an immunity level near 95.”
88% of cases reported from four countries: Ukraine (53%), Romania (18%), the Russian Federation (8%) and the UK (8%). The 27 EU Member States contributed to 41% of all cases in the Region.
Number of Reported Measles Cases with onset date from Nov 2012 to May 2013 (6M period)

Data source: surveillance DEF file
Data in HQ as of 11 June 2013

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. ©WHO 2013. All rights reserved.
Europe

Measles outbreaks flourish in UK years after discredited research tied measles shot to autism

By Associated Press, May 20, 2013

LONDON — More than a decade ago, British parents refused to give measles shots to at least a million children because of now discredited research that linked the vaccine to autism. Now, health officials are scrambling to catch up and stop a growing epidemic of the contagious disease.

This year, the U.K. has had more than 1,200 cases of measles, after a record number of nearly 2,000 cases last year. The country once recorded only several dozen cases every year. It now ranks second in Europe, behind only Romania.

Last month, emergency vaccination clinics were held every weekend in Wales, the...
Long shadow cast by MMR scare

MMR and measles in England

% of MMR uptake

Confirmed cases of measles, mumps and rubella

Source: NHS IC

It is 15 years since Dr Andrew Wakefield published research suggesting a possible link between the MMR vaccine and autism.
London 2012 Olympics may spark measles outbreak, US warns

America is at risk of a measles epidemic caused by tourists returning home from the London Olympics, according to an official warning issued by the United States Centers for Disease Control.
Measles Elimination: Threats

- WHO projected that the number of measles deaths could reach 1.7 million between 2009 and 2013 if high-risk countries are unable to maintain present recommended strategies for measles control.
Figure 1: Estimated number of measles deaths worldwide 2000–08 and projections of possible resurgence of measles deaths worldwide, 2009–13

Global Measles & Rubella Strategic Plan

*Strategy to eliminate measles (rubella and CRS)*

1. Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.

2. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.

3. **Develop and maintain outbreak preparedness, respond rapidly to outbreaks and manage cases.**

4. Communicate and engage to build public confidence and demand for immunization.

5. Perform the research and development needed to support cost-effective operations and improve vaccination and diagnostic tools.
The graph shows the 1st dose (MCV1) Measles Coverage Globally and in 47 Measles Priority Countries from 2000 to 2010. The coverage increased from 72% in 2000 to 85% in 2010. The number of countries providing MCV2 through routine services increased from 97 (50%) in 2000 to 141 (73%) in 2011.
2. Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress

- **National (integrated) surveillance systems must have complete coverage and be sufficiently sensitivity to detect any ongoing transmission.**
- **High-quality surveys to verify and benchmark vaccination coverage based on service-delivery data or provide coverage estimates if these data are unavailable.**
- **Surveys should also be used to assess the success of communications strategies and to identify reasons for non-vaccination.**
- **Sero-surveys to assess gaps in population immunity and areas for potential outbreaks.**
- **Need reliable systems for monitoring adverse events following immunization (AEFIs).**
5. Research and development to support cost-effective operations and improve vaccination & diagnostic tools

- Epidemiology
- Vaccine efficacy and effectiveness
- Needle free vaccine-delivery methods (e.g. aerosolized or powdered vaccines inhaled through the respiratory tract)
- Improved methods for laboratory testing
- New immunization strategies
- Improved methods to monitor and evaluate measles and rubella vaccination programs
- Development of effective advocacy tools to use with decision-makers and improved messages and strategies to communicate with potential beneficiaries and their families
- Economic analyses of different strategic options
- Mathematical modeling
Challenges to Measles Elimination

Financial risks

• Sufficient predictable, sustainable funds necessary to build strong health system, deliver effective routine immunizations and achieve goals of control, elimination and eradication

• Complacency following initial success of accelerated control activities, intense competition for human/financial resources between global health initiatives (i.e., polio eradication and new vaccine introduction, caused delays in funding for preventive measles SIAs in priority countries.
  – Resulted in a resurgence of measles cases and deaths.
Challenges to Measles Elimination

*High population density and highly mobile populations*

- Measles makes control and elimination very challenging in settings with high population density and along migration routes (including air travel and during mass gatherings)
  - For example, India currently has the largest estimated number of measles cases and deaths due to its relatively low routine immunization coverage, incomplete implementation of a two-dose strategy for measles control and high-density populations.
  - Requires national-level technical consensus on the need for control and elimination
Challenges to Measles Elimination

Weak Immunization Systems and Inaccurate Reporting of Vaccination Coverage

• Resurgence of measles in Africa during 2009-2010 occurred largely due to underlying weaknesses in health systems, including difficulties reaching and sustaining high vaccination coverage.

• Over-reporting of routine and SIA coverage can result in miscalculation of population immunity and the appropriate interval between follow-up SIAs.

• High infectiousness of measles and high rate of clinical disease with infection make measles outbreaks one of the first indicators of program weakness. Strengthening routine immunization systems is critical to attain measles control and elimination and to sustain any gains made.
Challenges to Measles Elimination

Managing perceptions and misperceptions

- Successful vaccination programs can begin to suffer from public misperceptions that any risks associated with the vaccine might outweigh the invisible benefits.

- Currently, pockets of resistance to immunization exist in some countries, most notably in North America and western Europe.
  - This has resulted largely from the efforts of anti-vaccine groups and from highly publicized but completely discredited vaccine safety concerns.
  - This resistance contributes significantly to the ongoing resurgence of transmission in western Europe, to the export of measles virus globally, and also to the large outbreak in 2010 in several countries in southern Africa.
Challenges to Measles Elimination

*Conflict and Emergency Settings*

• Humanitarian crises resulting from armed conflicts or natural disasters adversely affect disease control and eradication efforts
  – population displacement, crowding, interruption of health services, reduced access to health facilities and increased risk of outbreaks, including cross-border transmission.

• In the past, large measles outbreaks in refugee camps have led to extensive deaths, with case-fatality rates of up to 25%.

• With widespread adoption of the SPHERE guidelines, all children affected by humanitarian emergencies should now receive a measles vaccination administered as soon as conditions allow access to affected communities.
Research priorities for global measles control & eradication

*Measles epidemiology*

- What are the epidemiologic characteristics of measles (e.g., incidence, age distribution, case fatality ratios) in various settings in India?
- **What are the causes of measles outbreaks in settings with high reported measles vaccination coverage?**
- **What is the prevalence of measles virus susceptibility among adults in settings with persistent suboptimal measles vaccination coverage?**
- Can adults sustain measles virus transmission in the presence of high child immunity levels thereby making adult vaccination required to reach and maintain elimination?

WHO. Meeting report / Vaccine 30 (2012) 4709– 4716
Research priorities for global measles control & eradication

Measles epidemiology

• At what age do infants lose protection from maternal measles specific antibodies in different epidemiological settings? What are the potential implications of receiving MCV1 at an early age (e.g., prior to 9 months)?

• What is the prevalence of measles virus susceptibility among human immunodeficiency virus (HIV)-infected adults in high HIV-prevalence settings?
Research priorities for global measles control & eradication

*Immunization strategies*

- What are effective strategies for identifying and vaccinating nomadic populations, migrants, refugees, and internally displaced persons in various settings?
- What misconceptions and attitudinal barriers exist among communities and public and private sector health care providers regarding measles- and rubella-containing vaccines, and what communication messages and strategies can increase demand for vaccination in various settings?
- What are the most effective strategies for outbreak response immunization activities?

WHO. Meeting report / Vaccine 30 (2012) 4709–4716
Avian Influenza A(H7N9)
Avian Influenza A(H7N9)

• Human infections first reported in March, 2013
  – Through June 7, 2013: 132 H7N9 human infections and 37 deaths (CFR: 28%).

• Causes severe illness
  – Complications of the infection have included septic shock, respiratory failure, acute respiratory distress syndrome, refractory hypoxemia, acute renal dysfunction, multiple organ dysfunction, rhabdomyolysis, encephalopathy, and bacterial and fungal infections

• More easily transmitted from birds to humans than other avian influenza viruses
Avian Influenza A(H7N9)

- Concern for pandemic potential; limited to no immunity in the population.
- Poultry likely source of infection.
- Unusual age/gender distribution; no evidence of sustained (ongoing) human-to-human spread.
- Monitoring and testing of contacts (>2000 people) of confirmed cases has detected few infections.
- Testing of more than 20,000 people with influenza-like illness (ILI) March-May has confirmed only seven infections with H7N9.
Cases of H7N9 and H5N1 Influenza in China (Same Provinces) by Age-Group (6/10/13)*

*Total cases = 133
Note: ages of 2 cases are unknown
H7N9 virus is more transmissible and harder to detect than H5N1, say experts

Jane Parry

Hong Kong

In the two months since it was first detected, the H7N9 avian flu virus has resulted in almost twice as many confirmed infections in China as the H5N1 bird flu virus caused in a decade. As at 19 April the Chinese authorities had confirmed 87 cases in humans of H7N9 infection, including 17 deaths. “The first case of H5N1 was confirmed in 2003, and there have been only 45 confirmed cases in the whole of China. H7N9 is much more transmissible to humans, and it’s much more difficult to track down,” said Ho Pak-leung, associate professor in the

WHO has sent an international team of experts to Beijing to help the Chinese authorities investigate the outbreak, and the UN Food and Agriculture Organization is also assisting the authorities in the investigation.

Migratory birds have been implicated in the spread of the virus. He Hongxuan, a principal investigator at the Institute of Zoology with the Chinese Academy of Sciences, told state media that the spread of the virus from the Yangtze River delta northwards follows the migration pattern of wild waterfowl. As these birds
• Oseltamivir, even when started 48 h or more after disease onset, was associated with falling viral load in the respiratory tract in most patients with A/H7N9 infection. Therefore, early treatment of suspected or confirmed cases is strongly encouraged.
• The emergence of an NA Arg292Lys mutation in two patients was temporally associated with a rebound of virus load, treatment failure, and a poor clinical outcome.
• The role of corticosteroids in facilitating the emergence of the NA Arg292Lys mutation or even directly affecting viral load and adverse clinical outcome deserves consideration.
Estimated numbers of people residing within two hours' travel time of destination airport calculated using gridded population-density maps and a data set of global travel times.

"A quarter of the global population outside of China lives within two hours of an airport with a direct flight from the outbreak regions, and 70% if a single connecting flight is included".

The US government has declared that H7N9 bird flu "poses a significant potential for a public health emergency", and has given "emergency use authorization" for diagnostic kits for the virus.
Major Challenges in Providing an Effective and Timely Pandemic Vaccine for Influenza A(H7N9)

Michael T. Osterholm, PhD, MPH
Katie S. Ballering, PhD
Nicholas S. Kelley, PhD

The emergence of avian influenza A(H7N9) virus in humans has public health authorities around the world on high alert for the potential development of a human influenza pandemic. As of May 8, 2013, authorities had identified 131 confirmed cases and 32 deaths among residents of 8 provinces and 2 municipalities in China. Three primary scenarios exist for how this A(H7N9) virus outbreak will unfold. First, the virus could disappear in the animal reservoir, ending new human cases. Second, the virus could persist in the animal reservoir, resulting in sporadic human infections. Third, the virus could, through mutation or reassortment, become readily transmissible between 60%-93%). In a study of unadjuvanted A(H1N1)pdm09 vaccine conducted in the United States, effectiveness was 56% (95% CI, 23%-75%). For these studies, most participants were younger than 50 years, with approximately half younger than 18 years.

There is no reason to believe that a yet-to-be-developed pandemic A(H7N9) vaccine will perform any better than existing seasonal vaccines or the A(H1N1)pdm09 vaccines, particularly with regard to vaccine efficacy in persons older than 65 years. To date, the median age of H7N9 cases is 60 years. If a pandemic occurs and this epidemiologic pattern persists, a pandemic A(H7N9) vaccine, even if it includes an adjuvant, will likely have limited to modest effects on the overall morbidity and mortality from the novel strain.

Determining and Measuring Correlates of Protection for A(H7N9) Vaccines

In the United States, vaccine dose for inactivated pandemic...