Lessons from the 2009 Swine Flu Pandemic, Avian Flu, and their Contribution to the Conquest of Induced and Natural Pandemics

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MITIGATION OF TERRORIST ACTS
Scientific Contributions to Biosecurity and Mitigation of Terrorism
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The PMP for Mitigation of Terrorist Acts, now co-chaired by Sally Leivesley and Alan Leigh Moore, has long studied the mitigation and even the prevention of pandemic disease from terrorist acts. In this effort we have benefited from experience and motivation of natural epidemics such as smallpox, SARS, and seasonal and specific influenza disease.

For fighting disease,

- limit occasion for infection—personal protective measures ,
- vaccine to build immune response to prevent infection
- pharmaceuticals to prevent symptoms or to kill bacteria or microbes in the body

Emphasizing personal protective measures, the 2006 Report[1] of that PMP (sub-panel at that time) reads,

> *Since 2002, the Mitigation Subgroup has considered measures to reduce the impact of potential terrorist use of biological agents against humans; included have been improved air filtration, vaccination, and pharmaceutical intervention against the agent causing the disease or, in some cases, the toxins responsible for severe illness or death. Over the past year, much public attention has focused on pandemic influenza, such as might arise from reassortment of the Type A (H5N1) avian flu that has been spreading from Southeast Asia, but expert consensus is stronger that a flu pandemic is likely than is the judgment that it will derive from H5N1. Even a recurrence or an image of the 1917-18 H1N1 "Spanish flu" that killed some 50 million people world wide would be a disaster in the modern age of specialization and globalization, and such a pandemic that occurred in the next few years could not be much eased by available stocks of vaccine or antiviral drugs.*
>
> *Because mitigation of a natural flu pandemic can teach us much about defense against some bioterror agents, because there is a receptive audience to measures against pandemic, and because we have some novel and important perceptions to counter this serious and likely threat to health, life, and society, in the attached paper, "Conquering Pandemic Flu by Practical Measures," we present our analysis and recommendations for countering pandemic flu by nonpharmaceutical means.*

[1] PERMANENT MONITORING PANEL ON TERRORISM (PMPT), FOURTH MEETING, Erice, 18-22 May 2006, FINAL REPORT

We speak of an epidemic in terms of a single reproductive factor R_0 ("R-naught") and a serial interval v ("nu "). For the SARS epidemic, R_0 is about 3 and v about 8 days. For smallpox, R_0 is about 3 and v ≈ 14 days. And for influenza, R_0 ~ 1.7-2.4 and v ≈ 4 days. In our paper we take for flu $R_0 = 2$, although we recognize that it will vary from society to society and in various groups within society. Unchecked, an epidemic that begins with N "index cases" would give rise v ≈ 4 days later to 2N additional cases, v days later to 4N more, 8N more, and so on, so that after M serial intervals there will be $N (1 + R_0 + R_0^2 + R_0^3 + ... + R_0^M)$ cases altogether, until the susceptible population is exhausted and a substantial fraction of the population is resistant or even dead.
[emphasis added]

The paper proposes a set ofpractical Personal Protective Measures —PPM-- that, in principle and if practiced by almost everyone in the population of a large group or society, could essentially eliminate the damages ofpandemic flu in that group or society, by reducing the reproduction factor below 1.0 and thus limiting the number of flu infections per index case to the finite sum of the above series—namely to 1/ (1- R_0) cases. If such measures reduce an initial R_0 = 2 to R_0 = 2/3, a 3-fold reduction, each index case would then correspond to a total of 3 infections—not to 2000 in 40 days and doubling every 4 days thereafter. To have any prospect of such benefits, the great majority of individuals must practice modest protective measures; if all complied perfectly except 33%, the number of cases from index case would no longer be finite.

Even if the efficacy of PPM were demonstrated in a test evaluation, which is not yet the case, it is clear that relatively few in society would be ready to use such measures if the necessity presented itself, in the absence of sound information as to what to do and how to do it. The information does not move itself; major staff resources and effort would need to be expended to evaluate the effectiveness not only of the PPM but of the means of communication and persuasion that could be used via schools, place of employment, clubs, pharmacies, and faith-based organizations to persuade people that they should equip themselves and practice the PPM.

Pandemic influenza is unlikely to be a terrorist weapon, both because of its potential for worldwide destruction, even of the society for which a potential bioterrorist some esteem, but also because it is likely to spread worldwide in any case. Avian flu itself, in the form that does not spread from human to human, is a more likely weapon of terrorism, which might be used to do serious damage to the commercial poultry sector of a target country.

Thus, a successful counter to human pandemic influenza does not eliminate a bioterror weapon of concern, but the measures that individuals and groups take to protect against pandemic flu are themselves directly relevant to real bioterror threats such as the smallpox epidemic that would result from human-to-human transmission in a population in which vaccination ceased in 1972 when the elimination of smallpox as a naturally occurring disease was in sight. Furthermore. ***the availability to individuals and groups of practical***

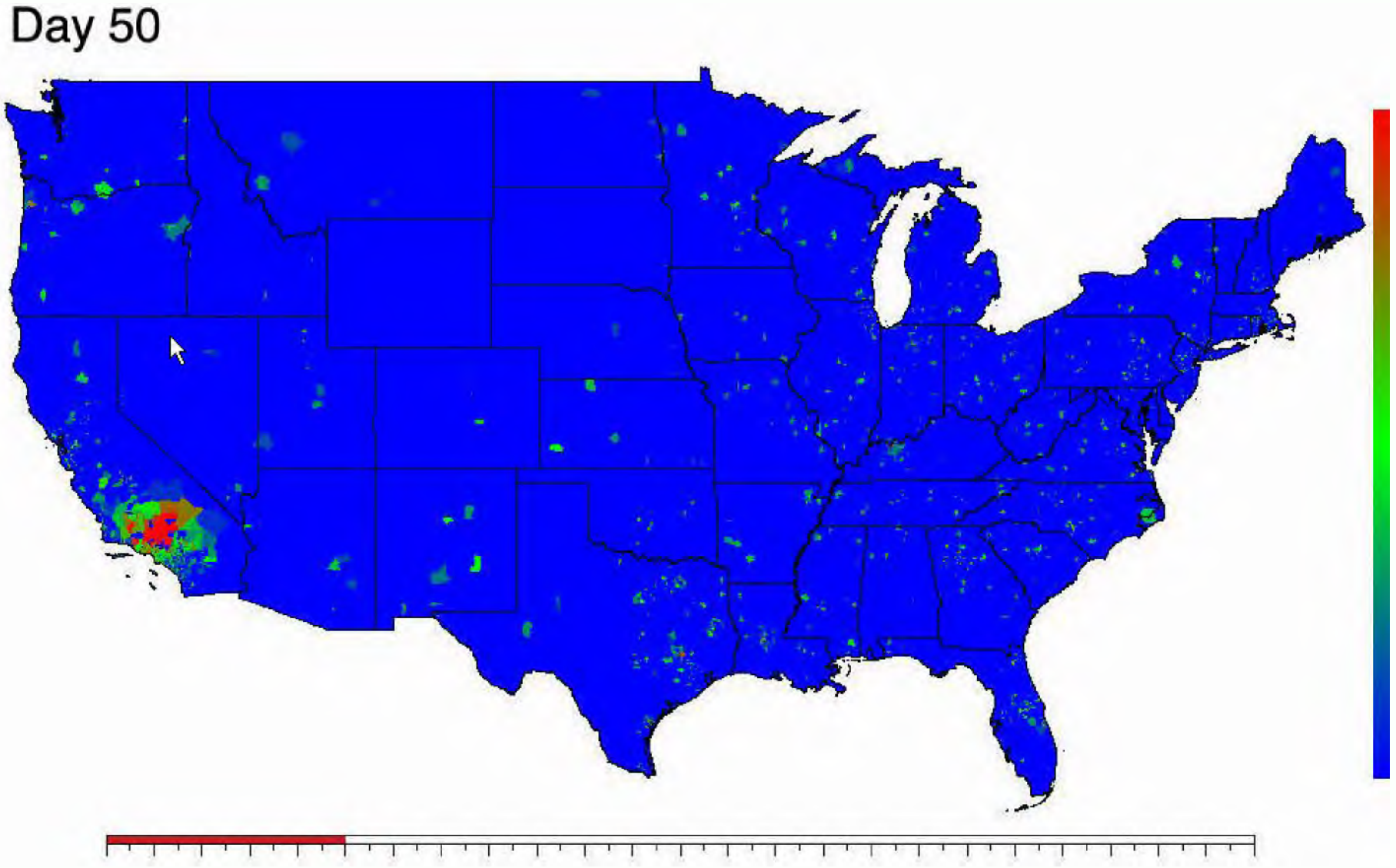
measures such as hand washing, disposable and improvised masks, elbow bumps instead of handshakes, and improved air filtration, and the frequent practice of such measures to prepare for an eventual flu pandemic, can provide effective tools for reducing the incidence of sickness and death from the more commonly expected bioterror weapons such as anthrax or tularemia *. The direct empowerment of individuals and groups, would be an important supplement to measures that may be taken by government, such as an alert that bioterror germs may have been liberated into the atmosphere or building lobby*

> *There are major differences between protection against pandemic flu and against an anthrax bioterror attack on a city. Protective measures against diseases without significant human-to-human transmission do not have the prospect for reducing casualties by factors of 1000 or more, but only by the protective factor that might be 3 or 5. Against bioterror attack, warning is of greater importance, and those close to the atmospheric release point may not be able to protect themselves against breathing the agent. Still, for an attack on a large city, a factor 3 reduction in casualties might save hundreds of thousands of people. Those who care about mitigating the potential damage from bioterror attacks should welcome the benefit that would come from a capability in-being to use personal protective measures against pandemic influenza.*

“It's probably not going to be practical to contain a potential pandemic by merely trying to limit contact between people (such as by travel restrictions, quarantine or even closing schools), but we find that these measures are useful in buying time to produce and distribute sufficient quantities of vaccine and antiviral drugs,” said Germann of Los Alamos’ Applied Physics Division.

“Based on our results, combinations of mitigation strategies such as stockpiling vaccines or antiviral agents, along with social distancing measures could be particularly effective in slowing pandemic flu spread in the U.S.,” added Longini.

(Timothy C. Germann, Kai Kadau, Ira M. Longini, Jr., and Catherine A. Macken, Mitigation strategies for pandemic influenza in the United States, *PNAS 2006 103:5935-5940; published online before print April 3, 2006)*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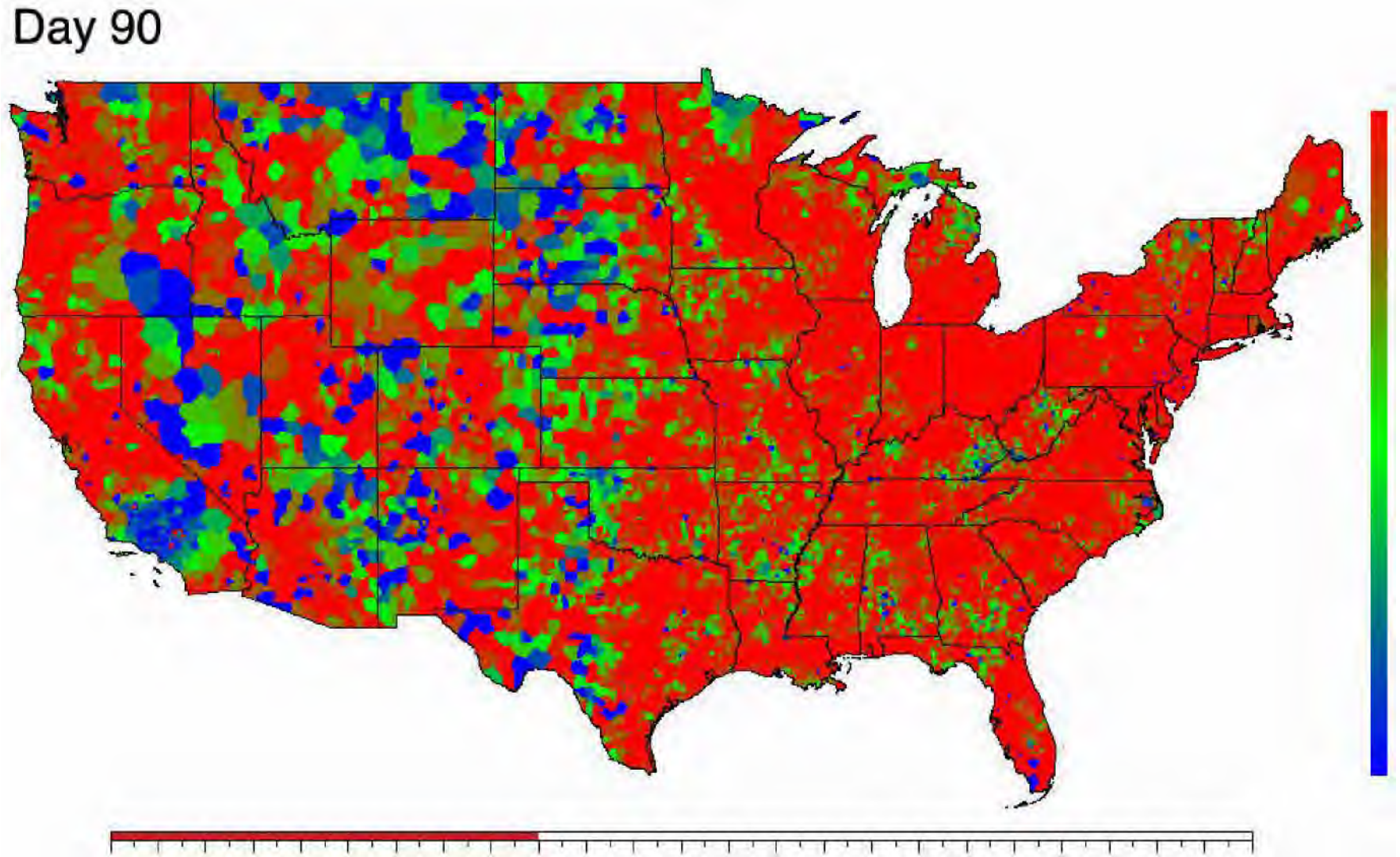
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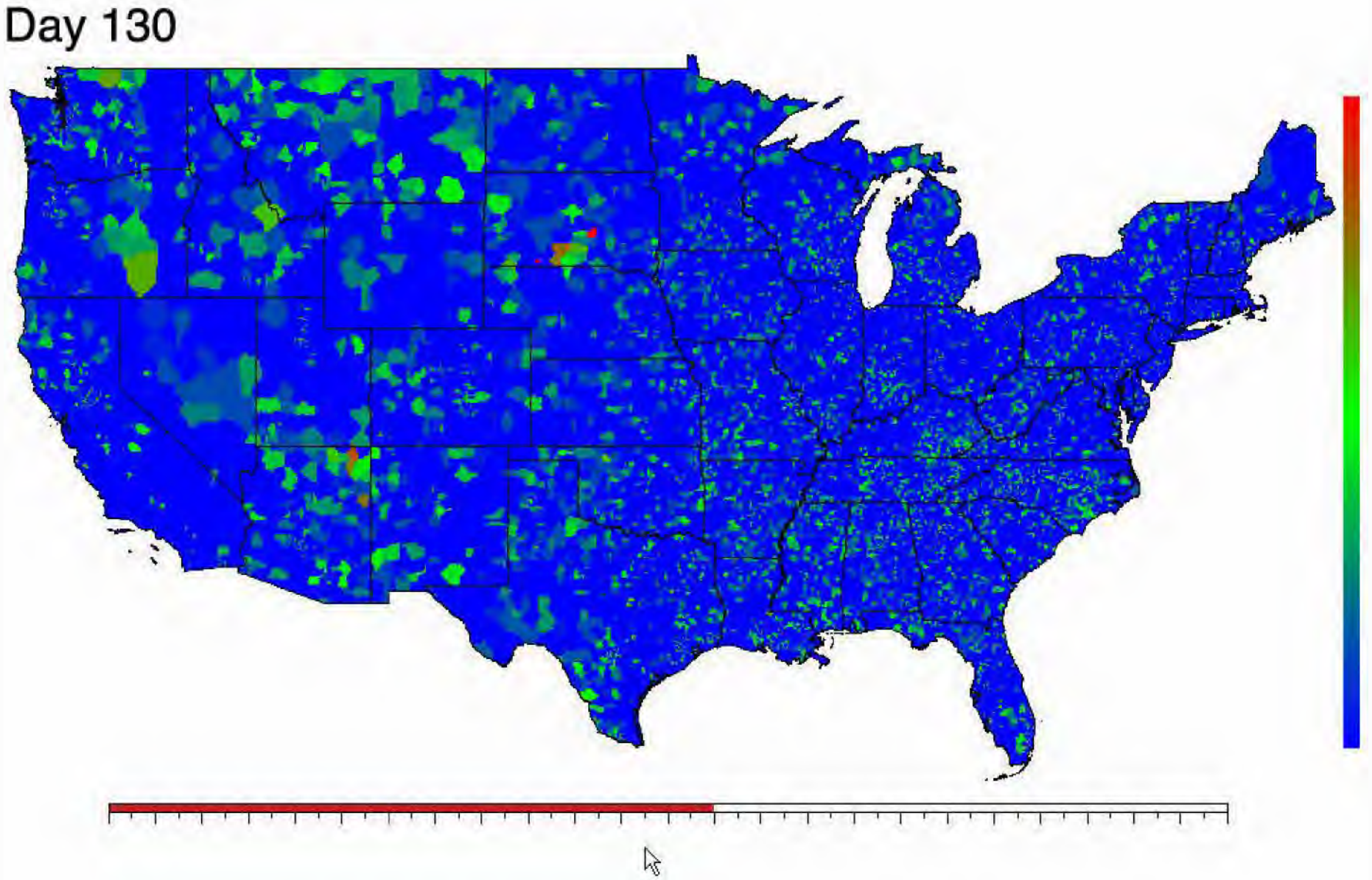
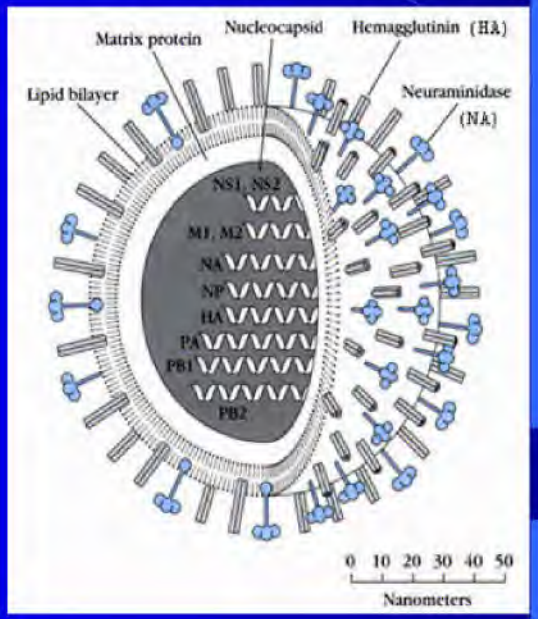

Day 130

Les virus de la grippe A

(A. Osterham)

Subtype divisions of influenza A viruses made on basis of HA (1-15/16) and NA (1-9) antigens
Genomic nucleic acid consists of 8 RNA segments, allowing gene reassortment during mixed infection
Virulence of influenza virus depends on presence of series of basic amino acids adjacent to cleavage site of HA polypeptide



subtype	Humans	Swine	Horse	Birds
H1	+	+	-	+
H2	+	-	-	+
H3	+	+	+	+
H4	-	-	-	+
H5	(+)	-	-	+
H6	-	-	-	+
H7	(+)	-	+	+
H8-H15	(H9+)	-	-	+

NB: H16 just been identified (Fouchier et al., PNAS 200

subtype	Humans	Swine	Horse	Birds
N1	+	+	-	+
N2	+	+	-	+
N3	-	-	-	+
N4	-	-	-	+
N5	-	-	-	+
N6	-	-	-	+
N7	-	-	+	+
N8	-	-	+	+
N9	-	-	-	+

WHAT HAVE WE LEARNED?

- Emerging infections
- Influenza H5N 12003, high mortality, low transmissibility (among humans)
    - Result: global preparedness
- H 1 N 1, Mexico, April 2009: rapid spread, detected early, could not be stopped, Peaked in Oct-Nov 09
    - Mortality low, mild symptoms, affected healthy young people
    - "30 July 2010 -- As of 25 July 2010, worldwide more than 214 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H 1 N 1 2009, including over 18398 deaths." [Annual deaths from normal "seasonal flu" about 250,000 worldwide—so 7%]

Lessons learned:

- Detection mechanisms worked
- Response was national; information reliably available through WHO
- Vaccine *development* went well
    - Vaccine distribution and vaccination varied among and within countries

Perceived failures:

- International Health Regulations (IHR) and the WHO
  - Moving from Phase 5 to Phase 6 pandemic
  - Undue influence of laboratories and pharmaceutical manufacturers?
- Resulting overemphasis on antivirals and vaccine, vs. personal protection

Successes:

- Detection and monitoring
- Technological advances
  - Vaccine developed and tested in 3 months
  - Inhalable vaccine
- International commitment and collaboration
- Absence of panic in public response

Lessons for the future:

- Technical developments
  - Early diagnostics, pre-symptomatic assay of classrooms, offices...
  - Cell-based vaccine production to delay commitment to full stock
  - Develop vaccines against conserved elements of flu viron
  - Emphasize learning details of transmission of particular strain

- Develop and tune models reflecting detailed transmission means e.g., via droplets, aerosols, fomites (surfaces to hand to mouth, nose, etc)

- Plan for interaction of security and health structures in case of infection spread by terrorists
- Evaluate potential for personal protective measures masks, bleach, hand sanitizer, elbow bumps.
- Change criteria for declaration of Phase 6 pandemic severity as well as geographic spread.
- Recognize non-identity of public health goals and pharmaceutical company profits.

I thank Diego Buriot for his contributions