Avian Influenza: why do we need to share genetic data?

Ilaria Capua
OIE and FAO Reference Laboratory for Newcastle Disease and Avian Influenza, Istituto Zooprofilattico Sperimentale delle Venezie Legnaro – Padova, Italy
Highly Pathogenic Avian Influenza, Italy 1999-2000
One WHO Expert on SARS Finds Flu More Frightening

Grippe aviaire : l’épidémie devient extrêmement dangereuse

LOCK UP ALL OUR CHICKENS

Aviares, pericolo per l’umanità? Influenza killer

Gli esperti europei di influenz riuniti a Malta. Il nostro Paese deve aumentare le scorte di antivirali, pronto il piano di emergenza

«Il virus dei polli colpirà 16 milioni di italiani»

Crovari: epidemia inevitabile. Le previsioni: 150 mila vittime. Un commissario in ogni Asl
Spanish influenza 1918-1919
20-40 million dead
Pandemic potential

• Direct infection of humans with AI
• Generation of a new pandemic virus through genetic reassortment between an avian and mammalian virus
H5N1 epidemic—a disease of global relevance

• H5N1 has become endemic in poultry in several parts of the world
• It is capable of infecting a variety of birds (@50 species) and 10 species of mammals
• For every human that is infected, at least 1 million animals are infected
• It represents a threat for food security in developing countries
H5N1: evolution of a panzootic
“Atypical” characteristics of the H5N1 epidemic

• Involvement of waterfowl
• Spill-over to wild birds
• Billions of susceptible birds in certain affected areas
• Peculiarity of husbandry/social practices
• Infection of mammals
• Human health implications
Raw duck blood pudding - Vietnam
Chicken carcases placed over pond on catfish farm in Indonesia
Catfish feeding on chicken carcass
H5N1: unprecedented eco/epidemiological situation

- Industrial poultry
- Other species
- Wild bird reservoir
- Rural poultry
- Live bird markets
- Poultry reared in the open
Spread from East Asia
Early 2006 – H5N1 reaches Africa
HPAI – in Africa

• Is reducing one of the primary sources of protein to the undernourished population
• Is spreading in an uncontrolled manner (10 countries have notified infection in one year)
• Concern about human health implications in HIV infected, poverty stricken population
First appearance of H5N1 in Africa

- IZSVe was the first laboratory to isolate the H5N1 African strain
- Genetic characteristics of the first African isolates would shed light on H5N1 epidemiology and pathogenicity
- We declined offer to deposit sequence in password protected database (only 15 labs had access) and deposited the full sequence in GenBank
As H5N1 Keeps Spreading, A Call to Release More Data

PARIS—An impassioned call by a prominent Italian influenza scientist has renewed the debate about how to balance global health against scientists’ needs to publish and countries’ demands for secrecy. On 16 February, Ilaria Capua of the Italian Zoosanita Cattivissima dragged the tricky issue back into the spotlight. WHO, FAO, and OIE encourage countries to send virus samples to specialized reference labs that can confirm the outbreak and study the virus further. Some have been reluctant to do so because they worry about intellectual property rights or not showing their cards. Capua says she will submit H5N1 sequences from her lab to public databases immediately.

Capua counters that just isolating and sequencing a virus that comes in the mail does not give researchers the right to sit on the data—especially not at a government lab. “Most of us are paid to protect human and animal health,” she says. “If publishing one more paper becomes more important, we have our priorities messed up.” Governments can often be persuaded to release the sequences, adds Capua, who repeated her call at an OIE meeting in Paris on Monday and also plans to submit it to ProMED, an e-mail list about emerging infectious diseases.

WHO agrees that in an ideal world, scientists would share their data widely and voluntarily, says Wenqing Zhang of the agency’s Global Influenza Programme. But because that’s not happening, the agency created a special secured section at the Influenza Sequence Database at Los Alamos National Laboratory in New Mexico in 2004. Currently, some 15 labs have passwords to access these data, says Zhang, including WHO’s eight reference labs. The system is invaluable for WHO, she adds, as it helps the agency track the virus and adjust risk assessments if necessary.
Scientists around the world, racing to discover how avian influenza is spreading and whether it is evolving toward a pandemic strain, face a dilemma: Should they share their interim findings widely, show them only to a select set of peers, or keep them to themselves until they can publish papers, often critical to their careers?

Now, a lone Italian researcher has cast a harsh spotlight on the WHO's system, suggesting that it places academic pride over public health - and snubbing it by posting prized bird-flu data in plain view.

Ilaria Capua, a 39-year-old Italian veterinarian working on avian influenza in a government lab, last month received a sample of the virus in the mail from Nigerian health authorities. The virus had just attacked birds in Nigeria, the first confirmed case of the disease in Africa. The sample was something of a prize, a chance to study a specimen and explore how it spread from its stronghold in Asia.

Within days of isolating the virus, Dr. Capua says, she got an offer from a senior scientist at the WHO in Geneva, whom she declined to name, to enter her finding in the closed system. She could submit the virus's genetic information, or sequence, to the database. In exchange, she would be given the password to the WHO's massive stash of data. A spokesman for the WHO confirmed that the offer was made.

Instead, Dr. Capua posted the gene sequence in a public database accessible on the Internet. She also sent a letter on Feb. 16 to around 50 of her colleagues urging them to do the same with their bird-flu samples.

"If I had agreed" to the WHO's request, she said in an interview, "it would have been another secret sequence."
At a time when health authorities are racing to head off a possible avian flu pandemic, it is distressing to learn that the World Health Organization is operating a secret database that holds the virus's genetic information. A lone Italian scientist has challenged the system by refusing to send her own data to the password-protected archive. Instead, she released the information publicly and urged her colleagues to do the same. She is surely right. The limited-access archive should be opened or bypassed immediately to encourage research on this looming health menace.

The campaign by Ilaria Capua, an Italian veterinarian who works on avian influenza, was spotlighted in recent articles in the journal Science and The Wall Street Journal. The hidden data could be of immense value in determining how the virus is evolving and in developing effective vaccines or drugs. The possibility of breakthroughs can increase only if many more scientists can analyze the data.
Dreams of flu data

The lack of an accessible store of information is undermining the fight against avian flu.

"Confidentiality of sensitive national outbreak surveillance data assured?" This prominent guarantee on the website of the South East Asian Nations Infectious Diseases Outbreak Surveillance Network says it all. Open sharing of data often ends when it could compromise trade or other national interests.

Three cheers, then, to Ilaria Capua of the Tri-Veneto Region Experimental Animal Health Care Institute in Italy, who last month threw down the gauntlet to her colleagues by refusing to put her latest data on NIAID and Italy in these private networks. Instead she uploaded them to the Avian Flu Bank and called on her colleagues worldwide to do likewise. Only in this way can researchers establish and track the global pattern of the evolution of the bird-flu virus.

Imagine scientists anywhere being able to log on to a publicly available, searchable, Internet database, updated in real time, with full clinical and sequence data on each human case, and accurate and complete poultry data. Dream on. The WHO's chunky online Global Health Atlas, which gives rough, aggregated data for many diseases, doesn't have a

"The world badly needs a database for outbreaks of avian flu."

Shared data are key to beating threat from flu

SIR — We fully support Ilaria Capua in her call for avian-influenza researchers to release data to the public, rather than store them in restricted databases, as reported in your Editorial "Dreams of flu data" (Nature 440, 255–256; 2006). Keeping sequences secret, whatever the motivation, slows down scientific progress and hinders efforts to protect public health. The influenza genome sequencing project (www.niaid.nih.gov/dmid/genomes/mscs/influenza.htm) has, in the past year, sequenced more than 1,000 complete genomes of human influenza and

Bird Flu Fears Ignite Debate on Scientists' Sharing of Data

By David Brown
Washington Post Staff Writer
Thursday, May 25, 2006; A20

The issue gained public attention in February when Ilaria Capua, a 40-year-old virologist at the Tri-Veneto Region Experimental Animal Health Care Institute in Italy, sequenced the first H5N1 sample from Africa, isolated from a chicken farm in northern Nigeria. Someone at WHO invited her to contribute it to the Los Alamos data, but she declined and instead filed it in GenBank.

Action stations

The time for sitting on flu data is over.

Concern about the accessibility of data on flu strains remains an acute issue, which research administrators and political leaders should step forward and address.

Indonesia has become the hot spot of avian flu, with the virus spreading quickly in animal populations, and human cases occurring more often than elsewhere. Yet from 51 reported human cases so far — 39 of them fatal — the genetic sequence of only one flu virus strain has been deposited in GenBank, the publicly accessible database for such information.

And last week in China, researchers belatedly published details of the appearance of human-to-human transmission. In the Sumatra event, the transmission did not spread beyond the family.

Yet scientists outside the WHO networks have no access to these data. The problem last year spurred the US National Institutes of Health (NIH) to create a consortium to sequence and make public thousands of flu strains from humans and birds.

“H5N1 sequences should be promptly deposited in a publicly accessible database.”

Very quickly, this more open approach led to the useful discovery that viruses swap genes with each other more frequently than had been previously thought.

Some political leaders are drawing the appropriate conclusions. Dennis Kucinich (Democrat, Ohio) and Wayne Gilchrest (Republican, Maryland) are circulating a letter in the House of Representatives.
A global initiative on sharing avian flu data

The global spread of the H5N1 avian influenza virus has already seriously threatened economic wellbeing and food safety in affected countries. The speed with which the virus has spread across continents has been unprecedented for a virus of this nature. The virus can infect humans and pose a potential for a pandemic. For these reasons, GISAID abbreviates for Global Initiative on Sharing Avian Influenza Data, has been initiated to ensure that the spread and evolution of the virus is monitored and the information is shared in a timely manner. This is turn demands that scientists work together to develop data sets that can be used by governments and organizations at national and international levels. The virus poses severe threats to animal and public health and data from both sectors are needed.

Several countries and international agencies have recently taken vigorous actions towards containing the virus. However, the situation is complex and the data sets are not yet available in a usable format. Several countries have not placed restrictions on exports and the risk of further international spreading of avian influenza virus and its potential impact is high. The GISAID Initiative has been initiated to share these data sets and make them available to the scientific community. The initiative is based on the understanding that open access to information is critical to contain the virus and prevent the spread of the disease. The initiative will allow researchers to share data sets and allow for rapid dissemination of information.

Signatories:

Nature Correspondence 24 Aug, 2006

70 leading scientists, 6 Nobel Laureates

Open access, free database which will contain human and animal influenza virus sequences and protects intellectual property
Veterinary initiatives promoting genetic data sharing to support the global H5N1 crisis

- OIE/FAO: support and promote data sharing
- OFFLU network – collects strains and sequences and promotes deposit in open access databases
- EPIZONE: EU Network of Excellence, WP 6.2 aims at understanding AI epidemiology through the generation and analysis of sequence data
- WHO is now supporting sequence data sharing
H5N1 improving our understanding

• Control in the animal reservoir is a prerequisite to the management of the pandemic potential

• The comparison between strains is essential to increase knowledge on AI epidemiology and human health implications

• Consensus from health officials to release sequences must be sought
Phylogenetic analysis and molecular changes: results for HA gene

• All the sequences of the Egyptian strains cluster together.
• The first isolate from Ghana clusters with recent Ivory Coast strains.
• Unique amino acid changes in the HA molecule were identified in viruses circulating in a given country or geographical area.

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>AA SUBSTITUTION</th>
<th>HA sequences available in GenBank (No.)</th>
<th>HA sequences with characteristic substitution (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudan</td>
<td>R329G</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Egypt</td>
<td>P239S</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Ghana, Ivory Coast,</td>
<td>S4G</td>
<td>1 Ghana 6 Ivory Coast 8 Burkina Faso</td>
<td>1 Ghana 6 Ivory Coast 8 Burkina Faso</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Global Initiative on Sharing Avian Influenza Data

- all users agree to share their own data, as well as clinical, epidemiological, biosafety and regulatory information
- all users agree to credit the use of others' data and acknowledge the source of genetic resources
- all users agree to analyze findings jointly and publish results collaboratively
- all users agree to maintain common access to technology derived from the data so that it can be used not only for research but for development of products such as diagnostics and vaccines.

This is different from many publicly funded databases, where there is no agreement to share the capability to use the data and to collaborate on it.

However, under the agreement all the sequence data are also made available to a variety of publicly funded databases with a maximum delay of six months.
WHY is this so important?

Because it can serve as a model for future epidemics threatening mankind – we would have a system in place to react promptly and maximise the outcome of research efforts.
GISAID- where are we?

- Created a foundation (www.gisaid.org)
- Sourced software, currently upscaling to satisfy number of users
- Drafted user access agreement
- Obtained worldwide consensus
- WE NEED FUNDS!!!
“One Health”

Birds of a feather should flock together... a little more