Emerging Disease Threats: Public Health Surveillance and Immune Intervention

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Global public health problems loom large. Apart from the continuing spread of HIV/AIDS and other infectious diseases, Avian influenza, Ebola and Middle East respiratory syndrome (MERS) have followed one after another. This has not only caused worldwide panic, but also affected social stability and economic growth.
1. Threats

Society

MERS infections in S. Korea rise to 35 with 5 tertiary contagions

A woman waits past a quarantine tent for people who may be infected with the virus causing MERS at Seoul National University Hospital in Seoul, South Korea, on June 2, 2015. Feared for the Middle East Respiratory Syndrome (MERS) reached a peak in South Korea as the first two deaths and tertiary infection were reported Tuesday, according to Yonhap News Agency.

The number of South Koreans diagnosed with the Middle East Respiratory Syndrome (MERS) kept rising to 35 Thursday since the first patient was tested positive on May 20, the health ministry said.

Five new cases were reported as three people, who had contact with the patient zero, were confirmed positive for the deadly viral disease, according to the Ministry of Health and Welfare.
1. Threats

The Ebola Epidemic in DRCongo 2018-2019

Latest numbers as of 6 March 2019
Total cases: 913
- Confirmed cases: 848
- Probable cases: 65
Deaths: 574
- Confirmed: 509
- Probable: 65

The Lassa Fever Epidemic in Nigeria 2018-2019

1. Threats

West Africa

Nigeria

https://www.who.int/emergencies/diseases/lassa-fever/en/
1. Threats

Flu in History

Gao et al, Cell, 2018

Virol Sinic, 2018
Why so many emerging and re-emerging infectious diseases?

......—SARS—FLUs—MERS—Ebola—Zika—........
Emerging and Re-emerging Infectious Diseases

- natural disaster
- man-made calamity
- Both?
2.1 EcoHealth

Ecology of EVD

Bat → Other mammals → Human

天然宿主/储存库
中间宿主
人
人际传播
2.1 EcoHealth

Ecology of influenza

Shi and Gao et al., 2014, Nature Reviews Microbiology
2.1 EcoHealth

One world one health

One Health

Environment

Medicine

Veterinary/Animal Medicine/Agriculture
It is not just polar bears and penguins that are at risk.
Change of human behavior
2.2 human behavior

Population mobility and disease transmission

The global airline

2013 global airline

SARS  H5N1流感  手足口病  血小板伴发热综合征  H7N9  H10N8  H5N6


H1N1流感  MERS  埃博拉出血热  寨卡热
3. Prevention and Control

Identification

左：列文·虎克和显微镜；右：伽利略和望远镜
3. Prevention and Control

TEM image of a liver tissue of an S. suis infected patient


TEM image of Influenza viruses

Song

The Nobel Prize in Chemistry 2017

The Nobel Prize in Chemistry 2017 was awarded to Jacques Dubochet, Joachim Frank and Richard Henderson "for developing cryo-electron microscopy for the high-resolution structure determination of biomolecules in solution".

Rao, PNAS, 2017

TEM image of Influenza viruses

Song

MERS-CoV和SARS-CoV S三聚体与受体结合模型图

Gao, Nat Commun, 2017
3. Prevention and Control

Surveillance

Chinese National Influenza Center (CNIC)

Enhanced surveillance
Through field investigations for each novel influenza virus infection
Genomic Surveillance of EBOV in SLE, Sep-Nov 2014

Nature, 2015
Intra-host Ebola viral adaption during human infection

- Dynamic intra-host substitutions of the virus during acute infection: samples collected during the early phase of infection possessed Ts at these nucleotide sites, whereas they were replaced by Cs in samples collected in the later phase, suggesting that these short stretches of T>C mutations could emerge independently.

- Our study showed the dynamic intra-host adaptation of EBOV during patient recovery and gave more insight into the complex EBOV-host interactions.

Liu W.J., et al, Biosafety & Health, 2019
Clinical and Laboratory Follow-up of a Female Patient With EVD: Sierra Leone Ebola Virus Persistence Study

The last case in Sierra Leone during the 2014-16 Ebola epidemic

Table 1. Signs Reported by a Female Ebola Patient During Admission in the Ebola Treatment Unit and During Follow-up in the Ebola Virus Persistence Study. Sierra Leone

<table>
<thead>
<tr>
<th>Days After Onset of Symptoms</th>
<th>In ETU</th>
<th>ETU Discharge</th>
<th>Post ETU Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Fever</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Anorexia</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Generalized body weakness</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Generalized body pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Headache</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Chest pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Joint pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cough</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Difficulty breathing</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Sore throat</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Red eyes</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Nausea</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Confusion</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Agitation</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Inomnia</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Itching</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Other signs after ETU discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depersonalization</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Nightmares</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Eye pain</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Weight loss</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cutaneous lesions</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Other signs assessed systematically and never reported for this patient during admission in the ETU: vomiting, coma, bleeding, sneezing, hiccuping, signs of shock, peripheral edema.

Liu W.J., et al, Open Forum Infect Dis, 2019
HIV prevalence in suspected Ebola cases during the 2014–2016 Ebola epidemic in Sierra Leone

Among suspected EVD cases from the Sierra Leone-China Friendship Biological Safety Laboratory during the epidemic in Sierra Leone, HIV and HCV antibodies were tested in 678 EVD-negative samples by enzyme-linked immunosorbent assay. A high HIV prevalence (17.6%) and low HCV prevalence (0.22%) were observed among the suspected cases. Notably, we found decreased HIV positive rates among the suspected cases over the course of the epidemic. This suggests a potentially beneficial effect of an improved public health system after assistance from the World Health Organization and other international aid organizations.

Liu W.J., et al, Infect Dis Poverty, 2019
On the ground in Sierra Leone

When you arrive in Sierra Leone, things look pretty normal. Life goes on as usual in many respects. In Freetown, the streets are still busy, and people still go to the market. In the villages, people are doing the same things they always do: sitting and chatting, wandering, playing football. But there is nothing normal about the work we are doing here. We have been in Sierra Leone for more than a month, with a China-based team running a mobile testing laboratory and a holding center for Ebola cases. When you arrive at a clinic or a holding center here, you see immediately how devastating Ebola is and how inadequate the resources are. The local public health system is weak. People die in fields outside of clinics. Many more die inside their homes.

With 4868 deaths from 9911 cases as of 22 October, according to the World Health Organization, the Ebola outbreak in West Africa—including Guinea, Sierra Leone, and Liberia—shows no signs of diminishing.

Getting Ebola under control is a problem for the world because, as we have seen, viruses do not require a visa to travel. Cases have surfaced in Senegal, Nigeria, and Mali, and Ebola has even extended its reach to Europe and North America. Ebola was long thought to affect only people living in poverty, so it has been neglected by the world. We have too few virologists and vaccinologists working in relevant areas and too little money invested in relevant research. Even if we get this outbreak under control soon—and we believe we will—the health workers to help implement these measures; and educators to work with the public and improve communications. Only when all this has been implemented in a coordinated way are we likely to see the transmission chain in West Africa cut; hopefully this will happen before Ebola becomes a big problem elsewhere. All this is needed now, on the ground, in every community and village.

Looking to the future, we call on the world to build up an effective public health system in West Africa. The first and obvious need is for strong government leadership to coordinate the region’s public health affairs. But more is needed: A younger generation from developed countries must be trained to specialize in African communicable diseases. Some of these people must be trained in disease surveillance and outbreak response, while others are needed to run laboratories. Most and most urgently, training must be given in infection control and in the prevention and cure of Ebola. These must be the priorities.
In 1980, WHO announced the eradication of smallpox through vaccination.
George’s “surface” work
Recombinant Chimpanzee Adenovirus Vaccine AdC7-M/E Protects against Zika Virus Infection and Testis Damage

The HA-specific T-cell responses to 2009 pH1N1 split-virus vaccine

JVI, 2018; Vaccine, 2017
3. Prevention and Control

Immune Intervention: mAb

Human MAbs against RVFV

Patent: 201910116927

Wang et al. Nature Microbiology, 2019
Structures of phlebovirus glycoprotein Gn and identification of a neutralizing antibody epitope.

Phlebovirus Gn presents a novel fold

Epitope of neutralizing antibody MAb 4-5 binding to SFTSV Gn

SFTSV

RVFV

Wu, Y et. al., 2017, PNAS
A humanized neutralizing monoclonal antibody against MERS-CoV targeting the receptor binding domain of the spike protein

➢ 4C2 and 2E6 are two neutralizing antibodies against MERS-CoV

➢ the structure of 4C2/MERS-RBD complex elucidates the neutralizing mechanism: blocking virus binding to receptor via steric hindrance and interface residue competition

➢ Humanized 4C2h can protect mice against MERS virus

Patent: 201410050894.5
Patent: 201410812405.5

4C2, a humanized MAb, protects mice against MERS-CoV infection in both prophylactic and post-exposure settings

Cell Res, 2015
Human MAbs against ZIKV

Patent: 201610649447.0
Patent: 201610527710.9
Patent: 201611108858.5

Wang et al., Science Translational Medicine, 2016
Human MAbs against H7N9

H7N9-specific neutralizing MAb

Broadly neutralizing MAb

Huang et al., Nature Microbiology, 2018

Wu et al., Nature Communications, 2015

Xiao et al., Cell Discovery, 2019
Double Lock of a Human Neutralizing and Protective Monoclonal Antibody
Targeting the Yellow Fever Virus Envelope

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**Figure A:** Comparison of response units over time for different concentrations of a compound.

**Figure B:** Comparison of response units over time for different concentrations of another compound.

**Figure C:** Plot showing the percentage of neutralization of the virus as a function of concentration.

**Figure D:** Plot showing the percentage of neutralization of VFP with varying concentrations.

**Figure E:** Graph depicting percentage survival over days post-infection.

**Figure F:** Graph showing body weight changes over days post-infection.
Preexisting immunity against H7N9 Virus in healthy population

Conserved CD8 epitopes in H7N9: 50%

Immune intervention: T-cells

FACS

CD4

IFNγ

0.2

5.5

2.5

2009 pH1N1

H7N9

No preexisting Abs

T-cells

J Infect Dis, 2016; Curr Opin Virol, 2014
Biased preexisting immunity against AIVs (H5, H6, H7 and H9)

Universal Vaccine for flu?
Prolonged establishment of memory T cell immunity in H7N9 survivors

Cohort (n=45): prospective study

Min Zhao, et al, JVI, 2018
To fully understand viral pathogenesis and develop effective medical countermeasures, we must strengthen current surveillance and basic research efforts!
Since 2005, China CDC has deployed professionals for responding to global public health emergencies:

1. Indonesia Tsunami
2. Polio: STOP (Nigeria, Namibia, Pakistan, Ethiopia)
3. West Africa Ebola, 2014
5. Africa CDC establishing, 2015
6. Angola Yellow fever, 2016
7. Madagascar Plague, 2017
8. DRC Ebola, 2018
9. Uganda Ebola, 2019
China - Africa Public Health Cooperation

Xi Jinping, the Chinese President announced to implement the China-Africa cooperation public health plan in Johannesburg Summit of Forum on China-Africa Cooperation, which was held in South Africa on December 2015.

- China will support Africa to strengthen public health system and capacity building.

- China will participate actively in Africa CDC establishing and assist to improve laboratory and technology capacity building.
Forum on China-Africa Cooperation: what it means for health

At this year’s Forum on China-Africa Cooperation (FOCAC), Beijing pledged to build on previous commitments to improve health care on the continent, including promises to upgrade medical facilities, to invest in the Africa Centers for Disease Control and Prevention (Africa CDC), and to train medical staff, according to the China investor’s primary focus of health care on the African continent.

The cooperation between 20 African and Chinese health institutions has become more pronounced in recent years. The China CDC has invested in the Africa CDC and supported its work in establishing a more comprehensive health system. Additionally, China has pledged to upgrade medical facilities and train medical staff in Africa. The cooperation has been beneficial for both sides, as it has improved health care in Africa and helped Chinese medical staff gain experience in working in Africa.

Forum on China-Africa Cooperation: what it means for health

Geoge F Gao: Head of China CDC signals a more global outlook

Geoge F Gao: Head of China CDC signals a more global outlook

In the action plan that emerged at the end of the meeting, Beijing acknowledged that the recently ended Ebola outbreak in west Africa has spurred China’s efforts to improve disease surveillance and preparedness. At the meeting, which was hosted by the World Health Organization (WHO), China made a contribution to the WHO’s mission to end the Ebola outbreak and pledged to improve its disease surveillance and response capacity.

Ebola, an infectious disease specialist from Cameroon who has worked with the Chinese government for several years, acknowledged that there is a sense of responsibility among Chinese scientists to improve disease surveillance and response capacity, and to work with the WHO and other international organizations to improve global health security.

Ebrima Tamba, a professor of international relations at the University of Oxford, addressed the issue of global health security. He noted that the current crisis of the novel coronavirus has exemplified the need for a comprehensive and inclusive response, and that China’s leadership in this area is crucial.

The meeting emphasized the importance of cooperation and coordination among countries and international organizations in dealing with global health issues. It also highlighted the need for increased investment in research and innovation to address emerging health threats.

The meeting concluded with a commitment to continue working together to improve global health security and to address the challenges posed by emerging health threats.
China-Africa High-level Meeting on Health Cooperation

17 August, 2018

Africa CDC Development and China-Africa Public Health Cooperation: Opportunities and Challenges
Public health priorities for China–Africa cooperation

In September, 2018, the heads of State from 53 African countries and world dignitaries gathered in Beijing (China) for the seventh triennial Summit of the Forum on China–Africa Cooperation (FOCAC). The outcome of the Summit was the adoption of the FOCAC Beijing

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Chinese Center for Disease Control and Prevention, Beijing 102206, China (GFG); Africa Centres for Disease Control and Prevention, Addis Ababa, Ethiopia (JNN);
Let’s make a flu day!
Flu: the most important virus/pathogen!
谢谢！
Welcome to
Chinese Center for Disease Control and Prevention