REMAP-CAP

“ The Genesis”

For the 48th Annual Meeting of the Japanese Society of Intensive Care Medicine

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World Health Organization

Declaration

- I, Nahoko Shindo, have no conflict of interest to declare for this presentation.
- The views presented in this presentation are mine and not necessarily representing the World Health Organization's.

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Timeline

Major infectious threats in the 21st Century & collaboration mechanisms to fight against them

MAJOR EPIDEMIC THREATS SINCE 2000

- Yellow fever (Central Africa, Brazil)
- Zika
- H7N9
- Ebola (West Africa)
- H1N1
- H5N1
- MERS-CoV
- SARS
- Cholera (Haiti)
- Cholera (Yemen)
- Plague (Madagascar)

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018

COVID-19

INTERNATIONAL COLLABORATION EFFORTS TO FIGHT EPIDEMIC THREATS

GAVI

Gavi, the Vaccine Alliance, is an international organisation that was created in 2000 to improve access to new and underused vaccines for children living in the world's poorest countries.

GOARN

The Global Outbreak Alert and Response Network (GOARN) is a technical collaboration of existing institutions and networks who pool human and technical resources for the rapid identification, confirmation and response to outbreaks of international importance.

IHR (2005)

The International Health Regulations (2005) or IHR (2005) are an international law which helps countries work together to save lives and livelihoods caused by the international spread of diseases and other health risks. The IHR (2005) aim to prevent, protect against, control and respond to the international spread of disease while avoiding unnecessary interference with international traffic and trade.

PIP Framework

The Pandemic Influenza Preparedness (PIP) Framework brings together Member States, industry, other stakeholders and WHO to implement a global approach to pandemic influenza preparedness and response. Its key goals include:

- to improve and strengthen the sharing of influenza viruses with human pandemic potential; and
- to increase the access of developing countries to vaccines and other pandemic related supplies.

PIP Review

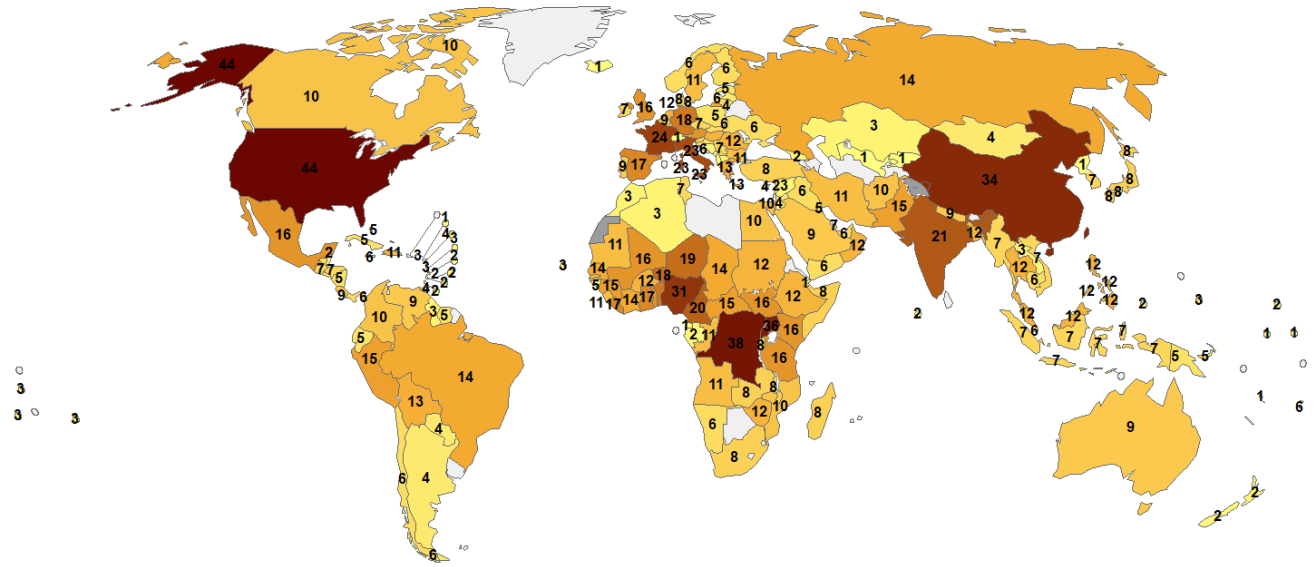
IHR Review

LEGEND

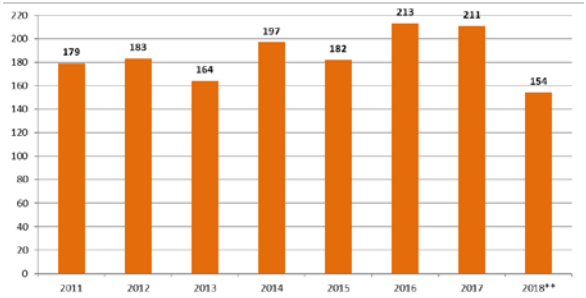
- Epidemic
- Pandemic

Epidemic events* globally, 2011-2018**
a total of 1,483 epidemic events, in 172 countries

In average, there are 180-190 events per year



Number of epidemic events* by year**



**WHO/IHM data as of March 2019 (note: 2018 data are not complete)
Source: data reported to WHO and in media

* Analysis excluded Poliomyelitis. The following *epidemic and pandemic diseases* were analysed: Avian Influenza A(H5N1), A(H7N9), A(H7N6), A (H7N4) A(H10N8), A(H3N2), A(H5N6), A(H9N2), Chikungunya, Cholera, Crimean-Congo haemorrhagic fever, Ebola virus disease, Lassa fever, Marburg virus disease, Meningitis, MERS-CoV, Monkeypox, Nodding syndrome, Nipah virus infection, Plague, Rift Valley fever, Shigellosis, Typhoid fever, Viral haemorrhagic fever, West Nile fever, Yellow fever, Zika virus disease.
If a disease caused more than 1 epidemic event by year in a country, it was only counted once for the year it occurred in that country.
Includes cases imported or locally transmitted.

Challenges

Epidemics – bigger, faster, severer

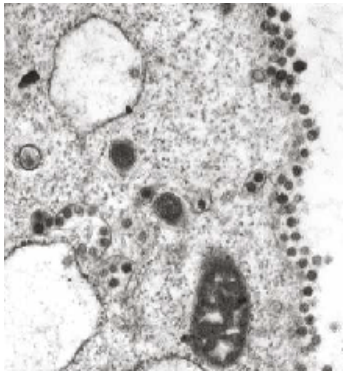
- **Urban** outbreaks (scale change)
- Interconnected world - traffic ↑
- Vulnerable population ↑ (aging, NCD, fragile, conflict, …)

Genesis: Virtual network of SARS clinicians

1) **Clinical information for case definition, public health purposes**

2) **Virtual network of SARS clinician**

   - New disease
   - International spread
   - No vaccine, no medicine, IPC?



50+ clinicians in 14 countries, telephone conference twice a week

face-to-face meeting, 14 June 2003

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REVIEW ARTICLE

CURRENT CONCEPTS

Avian Influenza A (H5N1) Infection in Humans

The Writing Committee of the World Health Organization (WHO) Consultation on Human Influenz

consisted of the
el, M.D., National
Infectious Diseas-
f Health, Bethesda,
Phil., Hospital for
Chi Minh City, Viet-
M.B., B.S., Depart-
Institute of Medi-
har; Frederick G.
eur), University of
Randy Hyer, M.D.,

AN UNPRECEDENTED EPIZOOTIC AV
that is highly pathogenic has crossed the
human fatalities and poses an increasing
scribes the features of human infection with infl
mendations for prevention and clinical manage
World Health Organization (WHO) Meeting on
Human Influenza A/H5, which was held in Hano
many critical questions remain, modifications of

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REVIEW ARTICLE

CURRENT CONCEPTS

Update on Avian Influenza A (H5N1) Virus Infection in Humans

Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza A (H5N1) Virus*

THE UNPRECEDENTED EPIZOOTIC OF AVIAN INFLUENZA A (H5N1) VIRUSES among birds continues to cause human disease with high mortality and to pose the threat of a pandemic. This review updates a 2005 report[1] and incorporates information recently published or presented at the Second World Health Organization (WHO) Consultation on Clinical Aspects of Human Infection with Avian Influenza A (H5N1) Virus.[2]

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Norms and standards

Review

WHO Rapid Advice Guidelines for pharmacological management of sporadic human infection with avian influenza A (H5N1) virus

Holger J Schünemann, Suzanne R Hill, Meetali Kakad, Richard Bellamy, Timothy M Uyeki, Frederick G Hayden, Yazdan Yazdanpanah, John Beigel, Tawee Chotpitayasunondh, Chris Del Mar, Jeremy Farrar, Tran Tinh Hien, Bülent Özbay, Norio Sugaya, Keiji Fukuda, Nikki Shindo, Lauren Stockman, Gunn E Vist, Alice Croisier, Azim Nagjdaliyev, Cathy Roth, Gail Thomson, Howard Zucker, Andrew D Oxman, for the WHO Rapid Advice Guideline Panel on Avian Influenza

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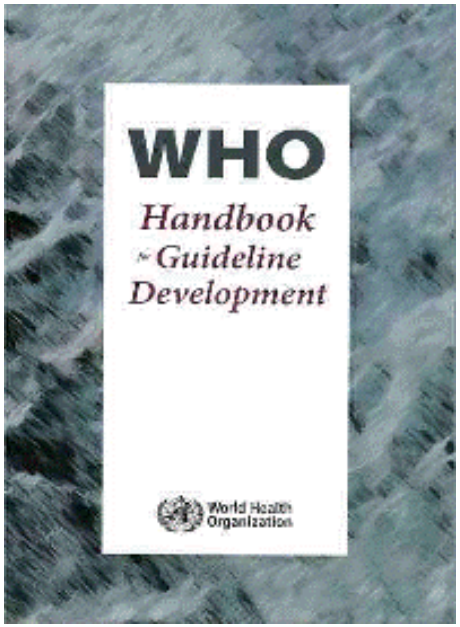
WHO Guidelines - Process

In accord with WHO standard for guideline development; requires substantial evidence review and assessment.

- Commissioning of systematic reviews and GRADE assessments
- Followed by panel review with good regional representation



GRADE

http://www.who.int/kms/guidelines_review_committee/en/index.html

http://www.gradeworkinggroup.org/index.htm

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And needs for research

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Missed opportunities

- Though rich in information, due to lack of systematic and standardized data collection, absence of ready-to-go protocols, the clinical community hasn't made as much progress as epidemiology and laboratory communities.

- If we know care & cure, PHEIC response would be different.

  Data suggest drastic improvement of CFR just by timely and appropriate patient care

    VHF – 80~90% to 20% (Marburg 1976)

    H5N1 – 60% to 30% (WHO pooled analysis)

Protocols
CRFs

ISARIC/WHO Severe Acute Respiratory Infection
Biological Sampling Study Version 2.5.2
By ISARIC Working Group 3

Choose historical version

TIER1 Single sample point
TIER2 Serial sampling light
TIER3A Sampling contacts
TIER3B Healthcare workers
TIER3C Pharmacology

Highlight tiers

Click to choose tiers above, select text (CMD-A), copy (CMD-C) then paste (CMD-V) each page into a new word processor document.
You are using Firefox - unfortunately the formatting works best using Chrome, Internet Explorer or Safari.

Create direct link to current settings.

Case record forms for use in the first 50 cases:
WHO New Outbreak Case Record Form
WHO New Outbreak Follow Up Form
WHO Data dictionary

Case record forms for use in subsequent cases:
ISARIC Core Case Record Form
ISARIC Supplementary Data Form
ISARIC Core Follow Up Form

Click here to log in to online data entry system

Intro | Summary | Protocol | Adult Info | Adult Consent | Consultee Info | Consultee Consent | Young Assent | Child Assent | Cartoon

ISARIC/WHO Severe Acute Respiratory Infection Biological Sampling Study
SUMMARY 17th May 2013. Version 2.5.2

ISARIC World Health Organization

Tiers included in this protocol are:

Tier 1 (Single biological sample) - Clinical samples will be collected on enrolment day (Day 1; ideally at initial presentation to a health care facility). Clinical information will be collected at enrolment and discharge.

Tier 2 (Serial biological sampling) - Clinical samples and data will be collected on enrolment day (Day 1; ideally at initial presentation to a health care facility), and then alternate days for the first 2 weeks, then weekly until resolution of illness or discharge from hospital, and again at 3 and 6 months after enrollment.

Table 2. Sampling pattern - In Patient Recruitment

		Serial samples.															
	Recruitment	Week 1						Week 2								Further samples	Convalescent samples
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15		3 months after recruitment
>40kg	R		S						S								C
20 to 40kg	R		S						S								C
10 to 20kg	R		S						S								C
4 to 10kg	R		S						S								C
>4kg	R		S						S								C
Sample priority	1		2						3								4

R = recruitment samples. S = serial samples including pathogen samples; P = research pathogen samples only; C = convalescent samples (see Table 3). In the event that local resource limitations require sampling frequency to decrease, samples will be prioritised as shown (1=highest priority).

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Protocols
CRFs

ISARIC/WHO Severe Acute Respiratory Infection
Biological Sampling Study Version 2.5.2
By ISARIC Working Group 3

Choose historical version

TIER1 Single sample point
TIER2 Serial sampling heavy
TIER3A Sampling contacts
TIER3B Healthcare workers
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Table 2. Sampling pattern - In Patient Recruitment

		Serial samples. Continue until resolution of acute illness*															
	Recruitment	Week 1						Week 2								Further samples	Convalescent samples
Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Weekly until max 100 days	3 months and 6 months after recruitment
>40kg	R	P	S	P	S	P	S	P	S	P	S	P	S	P	S	S	C
20 to 40kg	R	P	S	P	S	P	S	P	S	P	S	P	S	P	S	S	C
10 to 20kg	R	P	S	P	S	P	S	P	S	P	S	P	S	P	S	S	C
4 to 10kg	R	P	S	P	S	P	P	P	S	P	P	P	S	P	P	S	C
>4kg	R	P	S	P	S	P	P	P	S	P	P	P	S	P	P	S	C
Sample priority	1	11	2	11	5	11	7	11	3	11	8	11	10	11	9	6	4

R = recruitment samples. S = serial samples including pathogen samples; P = research pathogen samples only; C = convalescent samples (see Table 3). *Resolution of acute illness is defined in section 3.7. In the event that local resource

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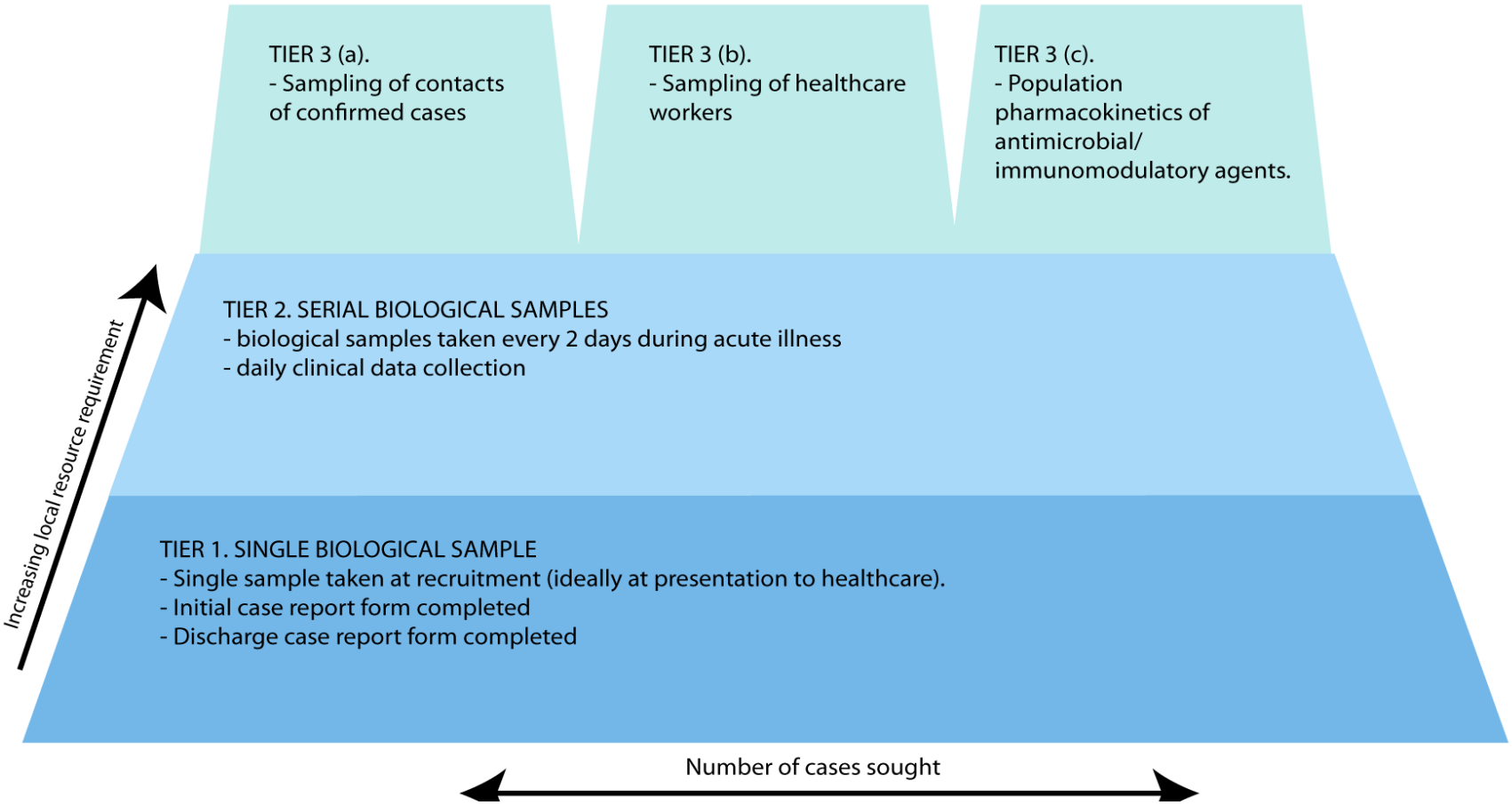
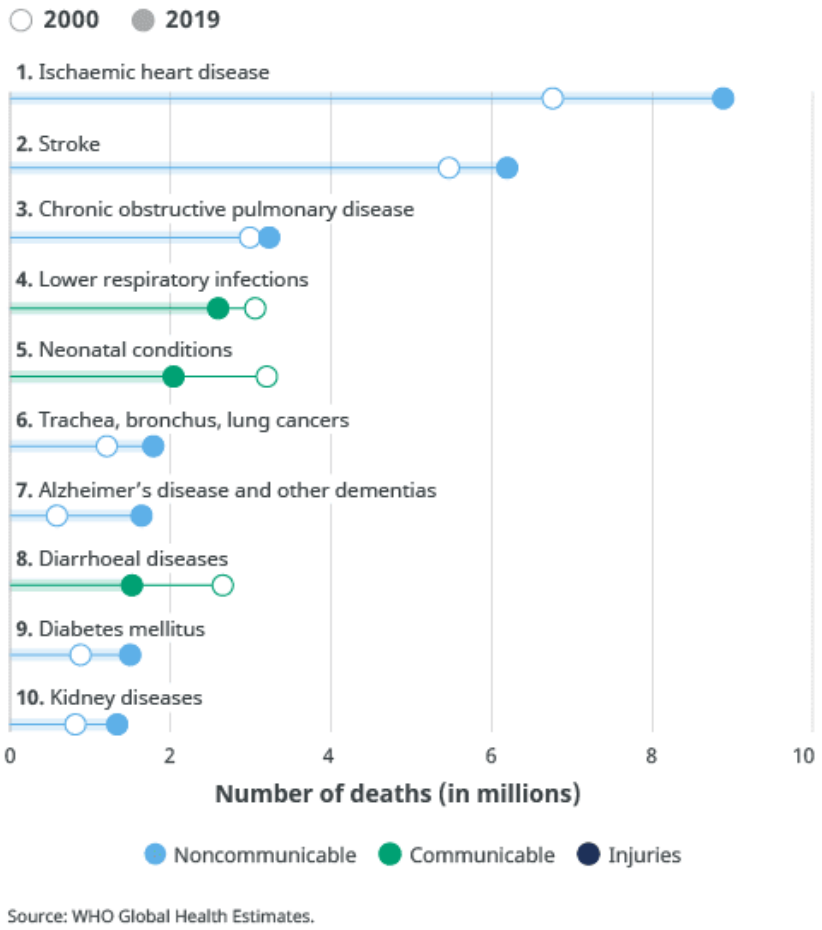
Globally accessible and applicable



10 Leading causes of death globally 2020



Source: WHO Global Health Estimates.

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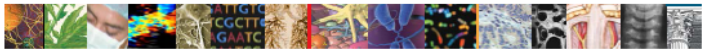
Ebola in West Africa (2014)

Monrovia, Liberia, 2014

EDCARN Peer-reviewed Publications



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Lamontagne F, et al. NEJM, Oct 2014; 371(17):1565-6.

Perspective

OCTOBER 23, 2014

Doing Today's Work Superbly Well — Treating Ebola with Current Tools

François Lamontagne, M.D., Christophe Clément, M.D., Thomas Fletcher, M.R.C.P., Shevin T. Jacob, M.D., M.P.H., William A. Fischer II, M.D., and Robert A. Fowler, M.D.C.M., M.S.(Epi)

Perspective Piece

Brett-Major DM, et al. AJTMH, Feb 2015; 92(2): 233-7.

Being Ready to Treat Ebola Virus Disease Patients

David M. Brett-Major,* Shevin T. Jacob, Frederique A. Jacquerioz, George F. Risi, William A. Fischer II, Yasuyuki Kato, Catherine F. Houlihan, Ian Crozier, Henry Kyobe Bosa, James V. Lawler, Takuya Adachi, Sara K. Hurley, Louise E. Berry, John C. Carlson, Thomas. C. Button, Susan L. McClellan, Barbara J. Shea, Gary G. Kuniyoshi, Mauricio Ferri, Srinivas G. Murthy, Nicola Petrosillo, Francois Lamontagne, David T. Porembka, John Schieffelin, Lewis Rubinson, Tim O'Dempsey, Suzanne M. Donovan, Daniel G. Bausch, Robert A. Fowler, and Thomas E. Fletcher

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ORIGINAL ARTICLE

Bah EI, et al. NEJM, Jan 2015; 372(1): 40-7.

Clinical Presentation of Patients with Ebola Virus Disease in Conakry, Guinea

Elhadj Ibrahima Bah, M.D., Marie-Claire Lamah, M.D., Tom Fletcher, M.R.C.P., Shevin T. Jacob, M.D., M.P.H., David M. Brett-Major, M.D., M.P.H., Amadou Alpha Sall, Ph.D., Nahoko Shindo, M.D., Ph.D., William A. Fischer II, M.D., Francois Lamontagne, M.D., Sow Mamadou Saliou, M.D., Daniel G. Bausch, M.D., M.P.H.&T.M., Barry Moumié, M.D., Tim Jagatic, M.D., Armand Sprecher, M.D., James V. Lawler, M.D., M.P.H., Thierry Mayet, M.D., Frederique A. Jacquerioz, M.D., María F. Méndez Baggi, M.D., Constanza Vallenas, M.D., Christophe Clement, M.D., Simon Mardel, M.D., Ousmane Faye, Ph.D., Oumar Faye, Ph.D., Baré Soropogui, Pharm.D., Nfaly Magassouba, D.V.M., Ph.D., Lamine Koivogui, Pharm.D., Ph.D., Ruxandra Pinto, Ph.D., and Robert A. Fowler, M.D.C.M.

ORIGINAL ARTICLE

Schieffelin JS, et al. NEJM, Nov 2014; 371: 2092-2100.

Clinical Illness and Outcomes in Patients with Ebola in Sierra Leone

J.S. Schieffelin, J.G. Shaffer, A. Goba, M. Gbakie, S.K. Gire, A. Colubri, R.S.G. Sealfon, L. Kanneh, A. Moigboi,* M. Momoh, M. Fullah,* L.M. Moses, B.L. Brown, K.G. Andersen, S. Winnicki, S.F. Schaffner, D.J. Park, N.L. Yozwiak, P.-P. Jiang, D. Kargbo, S. Jalloh, M. Fonnie,* V. Sinnah,* I. French, A. Kovoma,* F.K. Kamara, V. Tucker, E. Konuwa, J. Sellu, I. Mustapha, M. Foday, M. Yillah, F. Kanneh, S. Saffa,* J.L.B. Massally, M.L. Boisen, L.M. Branco, M.A. Vandi, D.S. Grant, C. Happi, S.M. Gevao, T.E. Fletcher, R.A. Fowler, D.G. Bausch, P.C. Sabeti, S.H. Khan,* and R.F. Garry, for the KGH Lassa Fever Program, the Viral Hemorrhagic Fever Consortium, and the WHO Clinical Response Team†

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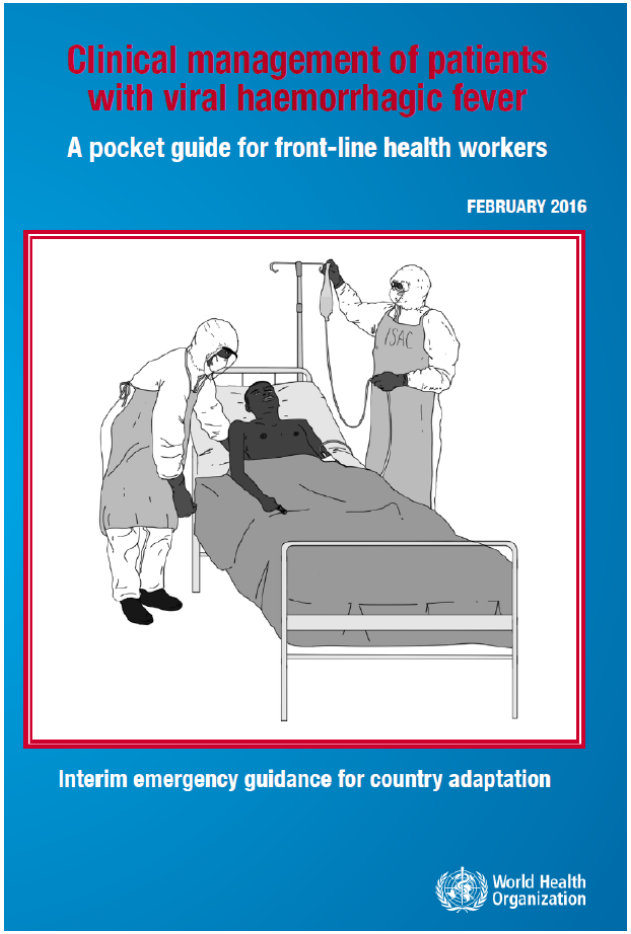
Updated WHO pocket manual
2nd generic version, Feb 2016



- Based on Sierra Leone version but removes SL specific sections
- More details included on:
  - Pregnancy and newborn
  - Breast feeding
  - Paediatric care
  - PPE
  - Discharge
- Culmination of best evidence and consensus gathered iteratively from multiple stakeholders (Mar 2014 to Feb 2016)
- **Supportive but aggressive** approach to clinical management

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Case Management: the Paradigm Shift

Ebola Hemorrhagic Fever → **Ebola Virus Disease**

~~**Isolation unit**~~ → **Ebola Treatment Unit**

- **safe burials; dead body transport; IPC**
- **trace → isolate → palliate**

- **trace → isolate → treat**
- **Spontaneous reporting → barrier nursing → early treatment, PEP, etc.**

Quality of ETU clinical care can affect the strength of the public health response

- Rumors surrounding type of care in ETUs resulted in community avoidance or violence for certain ETUs
- Increased community trust in ETUs resulting from survivor testimonies

“ Research is in our DNA”

Descartes - Je ponse donc je sui,
cogito, ergo sum
We think so we exist,
We think to become smarter,
We get smarter to strive for peace, health and happiness.
A way to become smarter, we call it ‘Research’

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You are more likely to encounter the first case of pandemic than quarantine officers at the border

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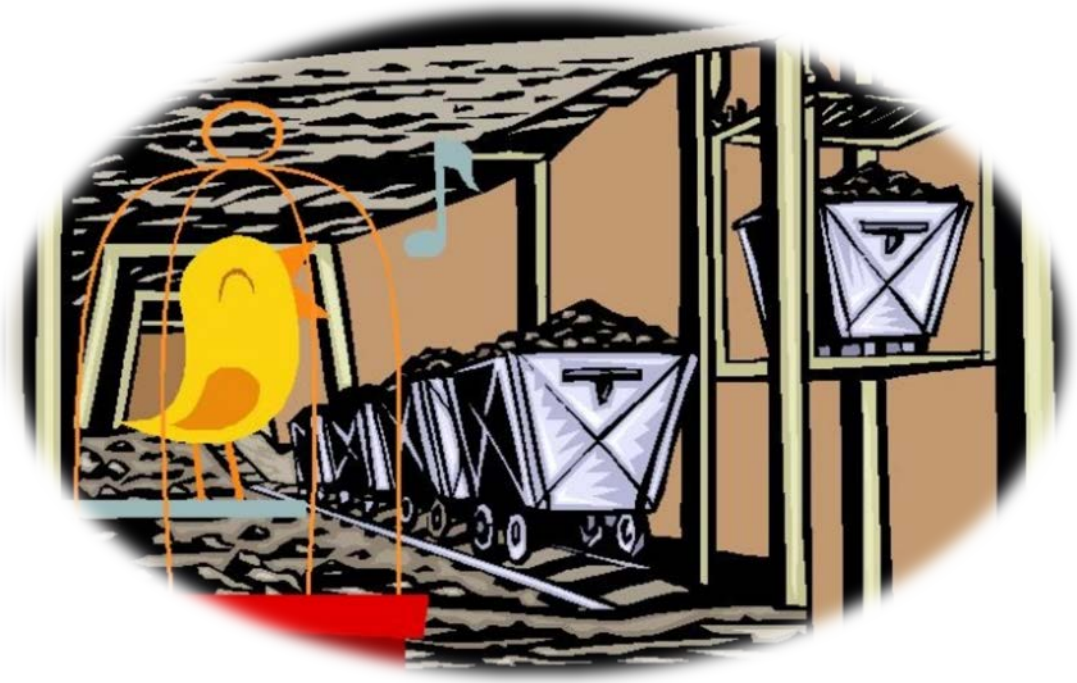
Infection control is everyone's business



THANK YOU

Photo: WHO/Lorenzo Pezzoli

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