

Comment for The Lancet Respiratory Medicine

Title:

Enhancing Preparedness for Tackling New and Re-Emerging Infectious Disease Epidemic Threats

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New and re-emerging infectious diseases with epidemic potential continue to cause much human and animal suffering worldwide. Many new and re-emerging infectious diseases are zoonoses (infections occurring between humans and animals). The major impact of rapid geographical spread of infectious diseases is usually borne by developing countries as highlighted by the 2014-2016 Ebola Virus (EboV) epidemic. Once the infectious disease takes hold locally, it can spread rapidly within the region, and the rest of the world is put at equal risk due to weak health systems, ease of international travel, global food systems, livestock and wildlife trade and the poor international capacity to identify and respond quickly and effectively to disease outbreaks. The EBOLA epidemic and the emergence this century of previously unknown zoonotic respiratory tract infections with epidemic potential, including for example coronaviruses (MERS, SARS), highly pathogenic avian influenza viruses (HPAI-H5N1) highlights an urgent need to change the current global status quo and enable local, regional and international human and animal health systems to be more proactive, coordinated and better prepared to prevent another epidemic.

All sub-Saharan African regions are highly biodiverse with approximately 80% of the population rural and highly dependent on livestock agriculture. Animal and human interactions are now more frequent. Movement of pathogens or potential pathogens between wild and domestic animals and people increases as the domestic populations expand, creating novel ecotones and ecosystemic perturbation (e.g. deforestation edge) explaining the rise in novel disease emergence such as EboV. As population rises food security demands, encourage intensification of livestock agriculture and this further enables evolution of novel zoonoses (HPAI, MERS-CoV) and their spill-over. The scale and overwhelming effects of the recent EBOLA epidemic in West Africa clearly demonstrates the inter-connectedness of poverty related and neglected diseases with the profound negative impact it had on other infectious diseases national programs. Several lessons were learnt from the EboV outbreak that could help guide development of more effective and appropriate health response capacities in Africa. The EboV epidemic aptly illustrated several failures of the current global status quo on outbreaks of infectious diseases with epidemic potential. The highly medicalized approach and ineffectiveness of the local and regional surveillance and alert mechanisms prevented or delayed appropriate socioecological management of the epidemic. Much of the spread and impact of EboV in West Africa was rooted in the emerging environmental, socioeconomic and socioanthropological changes taking place in this rapidly developing region of West Africa. An apparent inability of the affected countries and WHO to act quickly, communicate effectively and mobilise communities was a critical factor in its spread. The poorly coordinated response by the

international community despite donor funds being available exacerbated this. Better understanding of eco-epidemiological conditions ripe for the emergence and spread of disease, along with accurate case identification are key to effective outbreak control. Accurate, rapid field based diagnostic tests would have helped institute early interventions and screening for suspected cases. Absent were effective public health awareness and engagement, active disease surveillance, early diagnosis, rapid communication of data for health systems and communities to implement intervention or self-help measures are crucial components of controlling their spread. The early response to the EboV epidemic was faced by the slowness of various stakeholders to share public health data in real time. Patients, HCWs and relatives were ostracised from their communities due to stigma. Improved understanding of socio-cultural and political determinants of infectious disease transmission, and effective implementation of interventions is required. Behavioural factors also contributed to rapid outbreak spread and anthropological insights are essential to understand culturally acceptable way to address these needs in any future outbreak response. Foreign aid workers and research groups aroused local anxieties among communities due to ignorance of, or insensitivity to, cultural norms. Many healthcare workers (HCWs) lost their lives, thus risks for any outbreak need to be addressed to reduce healthcare worker morbidity and nosocomial transmission.

The lack of local capacity and preparedness in affected West African countries to conduct comprehensive, multidisciplinary and well-coordinated research was also evident during the EboV epidemic. Research studies to evaluate and determine optimal management protocols and trial new treatments and vaccines were slow to start, and were dominated by foreign groups, with scanty involvement of African scientists or local policy makers. There is an urgent need to develop trusting partnerships between Africa and western countries and other stakeholders to take forward the model of developing equitable south-north partnerships for building effective outbreak response capacities in all African regions. Newer treatments under development and those under compassionate-use regulations were available but their usage and evaluation to inform optimal evidence-based management, were retarded by absence of rapid ethical review processes for research in emergency situations. Thus an urgent need also exists for the establishment of a multidisciplinary consortium capable of provide accelerated evidence for the optimal clinical management of patients and for guiding the public health response to any severe infectious outbreak in Africa.

A more collaborative, inclusive and strategic 'ONE HEALTH' partnership between the human, environmental and animal health sectors is required to address emergent zoonotic threats effectively and improve current public health institutions' capabilities on disease preparedness, surveillance, and response. This will also enable issues around the growing threat of antimicrobial resistance (AMR) to be tackled. Whilst antibiotic resistant bacteria have spread globally due to increased travel and population movement, and migration, the problem of AMR in Africa remains largely undefined whilst access to appropriate antibiotics remains poor for the majority. The very recent WHO expert panel recommendations on AMR points out the lack of surveillance data and highlights the need for coordination between human and animal surveillance systems. Thus a multi-disciplinary consortium of human-animal-environmental 'ONE HEALTH' partners derived from existing human and animal health sectors in Africa is now essential for preventing another major epidemic in Africa. New opportunities now arise for this to be taken forward effectively as a pan-African 'ONE HEALTH' network. Post-Ebola African political commitment has dawned with the recent establishment of the African CDC. This coupled with the recent funding of four research and capacity development networks across Central, West, East and Southern funded by the European and Developing Countries Clinical Trials Partnership bring hope for a more consolidated and coordinated approach. This involves numerous sub-Saharan African capacity development, research and training collaborative networks with extensive experience from work on TB, HIV, malaria and viral hemorrhagic fevers. There are various strengths of this critical mass of pre-existing resources, knowledge and capabilities.

Based on a comprehensive 'inter-epidemic' work programme, they could develop a coherent, adequate and rapid interdisciplinary health response to emerging threats, a standardised methodological approach. This could involve identification and strengthening of suitable sites or regional networks, resolution of administrative, regulatory, disciplinary, ethical and cultural barriers, harmonise clinical case definitions and management guidelines, pre-approval of adaptable protocols, mechanisms to rapidly exchange high quality data and samples, etc.) that would ensure the readiness to immediately perform coordinated basic science research, define source of outbreak and transmission dynamics, and conduct large-scale multi-site clinical studies. Opportunities for establishing regional high quality laboratories and surveillance systems in Africa, span the full spectrum from baseline or current real time status information.

Replicating the mobile laboratory model in all Africa regions will also enable to take forward the important agenda of establishing effective Rapid Response Team for outbreaks with support of

national governments and public health services. Existing links with ongoing initiatives on emerging infections such as PREPARE (<http://www.prepare-europe.eu/>), ISARIC (<https://isaric.tghn.org/>), GLOPID-R (Global Research Collaboration for Infectious Diseases Preparedness, (<http://www.glopid-r.org/>), WHO collaborating centres and regional WHO offices, OIE (World Organisation for Animal Health) and CHATHAM House will ensure smoother and quicker implementation of findings into optimal health guidelines, standards and policy recommendations. Critically, links need to be developed between public health, veterinary, wildlife health and clinical laboratories. This is important to ensure the timeliness and quality of surveillance, research and response to zoonoses and the vexed issues of antimicrobial resistance in Africa. Benefits are not only accrued to public health but also food security and biodiversity conservation. Importantly, the future of health services in Africa will depend on empowering a whole generation of young African healthcare workers, scientists and technical staff to take leadership of emerging and re-emerging infections through high quality training and mentorship. The time is now ripe for Africa to take bold steps to develop its own capabilities and capacities to rapidly identify and respond quickly and effectively to potential outbreaks. The challenge is now for African governments, scientists, public health personnel to take leadership of developing a new vision and strategy for the emerging and re-emerging infectious diseases and AMR portfolio across the continent.

References

Mathis M, Briand S, Prentice T. Emerging and re-emerging infectious threats in the 21st century. *Wkly Epidemiol Rec.* 2015 May 15;90(20):238-44.

World Health Organization. Zoonoses. <http://www.who.int/zoonoses/diseases/en/> -accessed May 22nd, 2016

World Health Organization. Ebola virus disease outbreak <http://www.who.int/csr/disease/ebola/en/> -accessed May 23rd, 2016

Zumla A, Heymann D, Ippolito G. Be prepared: Europe needs Ebola outbreak consortium. *Nature.* 2015 Jul 2;523(7558):35

Ippolito G, Lanini S, Brouqui P, Di Caro A, Vairo F, Abdulla S, Fusco FM, Krishna S, Capobianchi MR, Kyobe-Bosa H, Lewis DJ, Puro V, Wolfel R, Avsic-Zupanc T, Dar O, Mwaba P, Bates M, Heymann D, Zumla A. Ebola: missed opportunities for Europe-Africa research. *Lancet Infect Dis.* 2015 Nov;15(11):1254-5.

Jacobsen KH, Aguirre AA, Bailey CL, Baranova AV, Crooks AT, Croitoru A, Delamater PL, Gupta J, Kehn-Hall K, Narayanan A, Pierobon M, Rowan KE, Schwebach JR, Seshaiyer P, Sklarew DM,

Stefanidis A, Agouris P. Lessons from the Ebola Outbreak: Action Items for Emerging Infectious Disease Preparedness and Response. *Ecohealth*. 2016 Mar;13(1):200-12.

Thiam S, Delamou A, Camara S, Carter J, Lama EK, Ndiaye B, Nyagero J, Nduba J, Ngom M. Challenges in controlling the Ebola outbreak in two prefectures in Guinea: why did communities continue to resist? *Pan Afr Med J*. 2015 Oct 11;22

World Health Organization. WHO publishes list of top emerging diseases likely to cause major epidemics.

<http://www.who.int/medicines/ebola-treatment/WHO-list-of-top-emerging-diseases/en/> - accessed June 1st, 2016.

WHO. GOARN: http://www.who.int/ihr/alert_and_response/outbreak-network/en/ -accessed May 28th, 2016.

ISARIC. International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) <https://isaric.tghn.org/> -accessed May 28th 2016

GLOPID-R. Global Research Collaboration for Infectious Disease Preparedness <http://www.glopid-r.org/> (accessed Aug 1, 2014).

Rüegg SR, McMahon BJ, Häsler B, Esposito R, Nielsen LR, Ifejika Speranza C, Ehlinger T, Peyre M, Aragrande M, Zinsstag J, Davies P, Mihalca AD, Buttigieg SC, Rushton J, Carmo LP, De Meneghi D, Canali M, Filippitzi ME, Goutard FL, Ilieski V, Milićević D, O'Shea H, Radeski M, Kock R, Staines A, Lindberg A. A Blueprint to Evaluate One Health. *Front Public Health*. 2017 Feb 16;5:20. doi: 10.3389/fpubh.2017.00020.

Zumla A, Alagaili AN, Cotten M, Azhar EI. Infectious diseases epidemic threats and mass gatherings: refocusing global attention on the continuing spread of the Middle East Respiratory syndrome coronavirus (MERS-CoV). *BMC Med*. 2016 Sep 7;14(1):132. doi: 10.1186/s12916-016-0686-3.

Zumla A, Goodfellow I, Kasolo F, Ntoumi F, Buchy P, Bates M, Azhar EI, Cotten M, Petersen E. Zika virus outbreak and the case for building effective and sustainable rapid diagnostics laboratory capacity globally. *Int J Infect Dis*. 2016 Apr;45:92-4. doi: 10.1016/j.ijid.2016.02.1007.

MERS: <http://www.who.int/csr/don/10-march-2017-mers-saudi-arabia/en/>

Nkengasong JN, Maiyegun O, Moeti M. Establishing the Africa Centres for Disease Control and Prevention: responding to Africa's health threats. *Lancet Glob Health*. 2017 Mar;5(3):e246-e247. doi: 10.1016/S2214-109X(17)30025-6.

Table/Figure

Needs : Global Preparedness for New and Re-Emerging Infectious Disease Epidemic Threats

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| <p>1. Establishment of a 'ONE animal-human-environmental HEALTH' consortium to tackle emerging and re-emerging infections with epidemic potential and antimicrobial resistance with aims of:</p> <ul style="list-style-type: none">i) Exploiting existing capabilities and capacities across human and animal health groups and develop cross cutting collaborations with synergy to have a multiplier effect.ii). Enhancing capacity to monitor local and regional Zoonotic and re-emerging diseases–trends, and for surveillance, predicting outbreaks and risk modelling,iii). Improved understanding of sociocultural and political determinants of infectious disease transmission, and effective implementation of interventions is required for vulnerable populations.iv). Engaging community leaders and defining social and cultural factors which influence patient acceptance of prevention and intervention measures.v). Developing local capacities for conduct of research:<ul style="list-style-type: none">a). Multidisciplinary human and animal interface/infections research: (operational, anthropological, social science, basic science, translational clinical, clinical trials, implementation research) in two situations: 1). In the emergency outbreak or epidemic situation. 2). In the inter-epidemic period.b). develop, evaluate, standardize and harmonize protocols for clinical management, laboratory, infection control and clinical trialsvi). Develop capacities for rapid ethical review processes for research in emergency situations. |
| <p>2. Development of:</p> <ul style="list-style-type: none">i). Effective public health surveillance and laboratory, ethics and research capacities for the rapid investigation of outbreaks at source.ii). Mobile laboratories for field use across all four Africa regions with state of the art diagnostics capabilities including rapid sequencing and biopsy with histological analysis and PCR.iii). Regional, robust 'ready to go (within 48-72 hours) outbreak rapid response teams, at each of the four African regions (Central, West, East and South) to assist when an outbreak occursiv). Capacities for providing accelerated evidence for the optimal clinical management of patients and for guiding the public health response to any severe infectious outbreak.v). 'State of the art' data management and communication systems and develop a common strategy for data collection, collation, analyses, integration, sharing and reporting at all four Africa regions. |
| <p>3: Empowerment by quality mentorship, of younger generation African scientists, clinicians, public health staff, healthcare workers, laboratory personnel, veterinarians, community workers, policy makers, and others to take leadership of this important portfolio of emerging infections. This will help sustain what is developed and will strengthen Africa's ability to deal with emerging infections. This should include educational and training courses on infection control and the field epidemiology</p> |

4. More effective political, policy maker and funder engagement - crucial for rapid action on surveillance alerts and clinical data on emerging diseases. To formally engage governments, policy makers and all stakeholders to develop a common plan, algorithms and protocols for a more coordinated response to outbreaks. Several African initiatives (African Union, SADAC, African CDC initiative, African Strategies for advancing Pathology Group, ASLM and others) need to work together for creation of local or regional surveillance and early outbreak response networks, and for increase awareness of AMR and the optimal 'one health approach' (animal and human health) to preventing zoonotic infections and AMR. Harnessing other global organisations/initiatives eg: Chatam House-UK and UK-Public Health England, WHO-AFRO, Africa-CDC, African country Ministries of Health, WHO-VIAG, WHO-GOARN, ISARIC, PREPARE, GloPiDSouth Africa, USAID-Africa Global Centre for Mass Gatherings Medicine, to ensure rapid dissemination of data/knowledge and more rapid action for future outbreaks.

5. Need for good participatory practice and developing more trusting equitable and trusting south-north, and south-south partnerships on emerging and re-emerging infections.