A Global Approach to Tackling Emerging Infectious Diseases

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THE PAST two decades have been marked by the accelerated emergence and re-emergence of infectious diseases worldwide, challenging the optimistic belief that humans had infectious diseases under control. In an enlightening session presented at IDWeek 2024, held in Los Angeles, California, from October 16th–19th, three experts offered a global approach to identifying and responding to emerging infectious diseases, providing multi-disciplinary perspectives that encompassed ecology, healthcare, and diagnostics.

AN ECOLOGICAL PERSPECTIVE ON DISEASE EMERGENCE

Current ongoing disease threats, such as influenza, Marburg virus, mpox, and Oropouche virus, serve as a reminder that the global issue of emerging diseases is here to stay, opened Marion Koopmans, Erasmus Medical Center, Rotterdam, the Netherlands.

In the era of the Anthropocene, where health is increasingly affected by the impact of humans on the planet, changes in demographics, climate, land use, and technology are key drivers of zoonotic disease emergence. The global footprint of human presence, including large scale deforestation, biodiversity loss, and animal farming with low biosecurity, increases the probability of a spillover event, where a species-specific pathogen is transmitted to a new host. This was recently observed with the highly pathogenic avian influenza A virus, which spilled over from wild birds to mammals. The transition from low pathogenic to highly pathogenic avian influenza A can be considered a man-made problem, said Koopmans, as the accumulation of mutations and genetic reassortment that drive changes in pathogenicity mainly occur on large density poultry farms.

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These spillovers can be linked to ecotones, "where normally distinct ecosystems converge, leading to novel interactions and risks," explained Koopmans. A 2010 study by Rimoin et al.[1] examined mpox spillover events in Democratic Republic of Congo, finding that the risk of mpox infection in humans was significantly higher in ecotones spanning deforested areas. This should have warned us of the current fast-expanding, multi-country mpox outbreak, stated Koopmans. She added that different mpox clades are derived from repeated zoonotic spillovers and require very different types of action, complicating control of disease spread.

Furthermore, the dissemination of a pathogen between humans is amplified by global travel and trade, as well as poor infrastructure in densely populated areas, continued Koopmans. This was seen with Ebola, which remained a localized outbreak until major urban slums in West Africa became hotspots for viral dispersal from 2014–2016.

Finally, changes in human demographics can also alter disease impact: an ageing population with increased comorbidities is at higher risk for severe illness from emerging diseases. This was observed during the COVID-19 pandemic, where SARS-CoV-2 disproportionately affected vulnerable populations.

Planetary Health, which addresses the impacts of human disruptions on life on Earth, and One Health, which aims to sustainably balance the health of people, animals, and ecosystems, both focus on understanding the root causes of disease emergence, integrating new solutions from a transdisciplinary perspective. This holistic approach to disease prevention will be crucial to get ahead of ongoing and future disease outbreaks, concluded Koopmans.

> **The transition from low pathogenic to highly pathogenic avian influenza can be considered a man-made problem**

A CLINICAL APPROACH TO EMERGING INFECTIOUS DISEASES

Peter Rabinowitz, University of Washington, USA, transitioned from an ecological to a clinical perspective on emerging infectious diseases, presenting a series of informative clinical cases related to environmental changes.

The first case was a 55-year-old male complaining of abundant tick bites, fever, and abdominal pain during a summer in Massachusetts. Despite no rash and negative Lyme disease test, a physical exam revealed splenomegaly, and complete blood count test showed anemia and thrombocytopenia. A diagnosis of babesiosis was made. Rabinowitz emphasized that global warming is having profound effects on vector-borne disease transmission. For instance, *Aedes aegypti*

mosquitos are extending their range, driving dengue spread. "The population at risk of dengue is going to continue to increase," warned Rabinowitz. As reflected in this case, temporal changes in tick-borne disease are also being observed.

The second case was of construction workers on a solar power installation site in the Southwest, who were seen in primary care complaining of fatigue, night sweats, weakness, difficulty breathing, fever, cough, joint/muscle pain, and weight loss. They noted that, around the construction site, recent drought had been followed by heavy rain. After serology, a diagnosis of coccidioidomycosis was made. Rabinowitz explained that an increase in droughts can alter potential vector breeding sites, leading to a heightened risk of coccidioidomycosis concentrated within a specific calendar period, related to periods of precipitation following droughts.

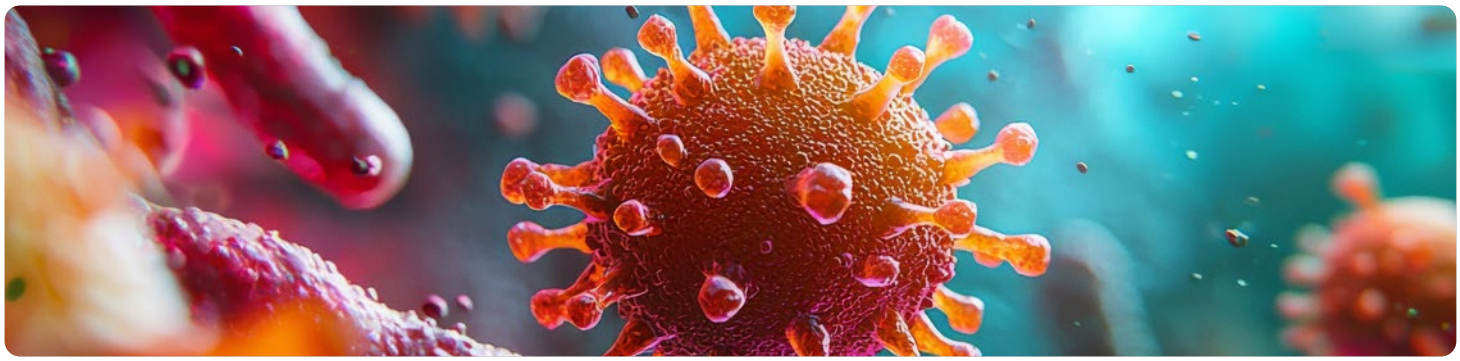
The third case was a 44-year old female returning from a recent trip to East Africa, where she was in contact with flooded areas. She complained of fever, nausea, and abdominal discomfort without diarrhea, and a physical exam revealed conjunctival reddening and abdominal tenderness. Blood tests showed elevated white count, low platelets, and elevated liver function tests. The patient was hospitalized for acute hepatitis, and a diagnosis of leptospirosis was made. An increase in floods, said Rabinowitz, heightens the prevalence of waterborne pathogens like *Leptospira* bacteria, as well as *Vibrio vulnificus*, a bacterium causing life-threatening septicemia and severe wound infections, and *Vibrio cholerae*, responsible for cholera. Floods also create a water habitat for breeding of vector-borne diseases.

"How can we be astute clinicians?" asked Rabinowitz. Taking medical history is crucial, including collecting data on animal contacts and environmental exposures that could point to vector-borne or zoonotic diseases. Specific weather events, like heat, drought, or flooding, should also be considered. He added that risk maps are available online to evaluate flood risks or arbovirus detection, and efforts should be made to integrate these into electronic health records. Furthermore, these environmental determinants should be combined with social determinants to assess patient vulnerability.

While performing a physical examination, it is important to remember the pathognomonic signs of different infectious diseases, such as reddening of the eye in leptospirosis. Rabinowitz added that key findings, like rashes, jaundice, or lymphadenopathy, should give hints to clinicians that a disease is "different from the usual".

With diagnostic tests, Rabinowitz emphasized the value of coming up with a pre-test probability to inform testing strategies and allow for a more judicious use of molecular tools. He also urged clinicians to be aware of the limitations of serology, such as cross-reactivity and time lag.

"An astute clinician is like Sherlock Holmes," concluded Rabinowitz. By having a wide differential and thinking broadly to develop



targeted diagnostic strategies, clinicians can be the first to detect an emerging infection. Keeping up to date with the patient is essential, as well as communicating with other healthcare providers and veterinarians. Finally, alerting public health authorities when new cases are detected will be crucial for effective infection prevention and control.

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NOVEL DIAGNOSTICS FOR EMERGING INFECTIOUS DISEASES

Paul Eder, National Institute of Allergy and Infectious Diseases (NIAID), Maryland, gave a comprehensive overview of current challenges and solutions in the development of diagnostics for emerging infectious diseases, with a focus on work conducted by the NIAID to tackle high-priority issues, including zoonotic viral infections, resistant fungal infections, nosocomial antimicrobial resistant (AR) bacterial infections, and community AR sexually transmitted infections.

Among the numerous NIAID clinical research networks, Eder drew attention to the Centers for Research on Emerging Infectious Diseases (CREID), a global network of multidisciplinary investigations into how and where viral pathogens emerge and cause disease outbreaks. Now active for 5 years, the CREID funds research programs across the globe, reaching over 30 countries and 47 research sites beyond the USA and across South America, Central Africa, and Southeast Asia. The studies focus on developing diagnostic solutions, such as monoclonal antibodies and novel antigens for antigen-detection tests, for emerging pathogens like Ebola, Marburg virus, and mpox.

NIAID is seeing the expansion of diagnostic product development programs to maximise public health readiness ahead of emerging infectious diseases. Eder presented three powerful, innovative *in vitro* diagnostic systems for identification and classification of emerging pathogens. First, the fully automated ESKAPE+ detection system (Clear Labs, San Francisco, California) uses next generation sequencing to identify AR bacteria directly from the blood, including *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter spp.* (ESKAPE pathogens). Second, a semi-automated bacterial and fungal detection system (Siemens Healthineers, Erlangen, Germany) can identify and sequence pathogen DNA directly from the blood, and identify its antimicrobial resistance marker from a large number of primer sets in under 6 hours. Finally, the most recently funded product, a single-cell RNA response profiling system (GE HealthCare, Chicago, Illinois) for antimicrobial susceptibility testing can identify small changes in growth of microbial RNA in the presence or absence of antibiotics, generating an antimicrobial susceptibility testing phenotype in less than 2 hours.

Eder emphasized key challenges to overcome in future diagnostic systems, including broader pathogen identification capabilities, and faster and better characterization of antimicrobial resistance. He added that faster, simpler, and more sensitive antigen detection tests are also needed for earlier intervention in community settings. As emerging infectious agents evolve, the development of diagnostic tools needs to co-evolve to keep pace, concluded Eder.

References

1. Rimoin AW et al. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. Proc Natl Acad Sci USA. 2010;107(37):16262-16267.