Principles for Outbreak Investigation: COVID-19 and Future Infectious Diseases

Testimony of:

Connie Savor Price, M.D.
Chief Medical Officer
Denver Health
Professor of Medicine
Division of Infectious Diseases
University of Colorado School of Medicine

United States House of Representatives
Committee on Science, Space, and Technology
Subcommittee on Investigations & Oversight
Wednesday, July 14, 2021
Washington, D.C.

Chairman Foster, Ranking Member Norman, and Members of the Investigations and Oversight Subcommittee:

My name is Connie Savor Price. I am a practicing infectious diseases physician and healthcare epidemiologist with experience and expertise in outbreak management. I have served as a consultant to public health authorities on control of emerging infections, including Middle East Respiratory Syndrome (MERS) for the Kingdom of Saudi Arabia and Severe Acute Respiratory Syndrome (SARS) for the Ontario Ministry of Health. I am the Executive Director for HHS Region 8 Ebola and Special Pathogens Treatment Center and our Regional Disaster Health Response System. I am a Professor of Medicine in the Division of Infectious Diseases at the University of Colorado School of Medicine. I am honored to be here today to talk with you about the principles for investigating infectious disease outbreaks in the context of public interest in the origins of COVID-19. I was asked to address the following questions:

What level of data transparency and international collaboration is expected and necessary for a complete investigation into the origins of an infectious disease?

When a threat to the public's health occurs, epidemiologists and/or other relevant experts (e.g. hospital infection prevention specialists) investigate the problem so they can identify sources and risk factors, implement prevention and control measures, and communicate with stakeholders. Whether the event occurs in the hospital setting or in a community, there is a well-described, systematic process for performing a complete investigation into the origins of an infectious disease outbreak [1-5]. The process requires significant collaboration among public health officials, laboratory personnel, clinicians, and other stakeholders in areas affected by the outbreak. The detailed review begins with the initial cases (known or suspected) but should also include a time period preceding the current problem to determine whether earlier cases existed, and if so, the occurrence rates between

the period of the current problem and a comparator period. A high level of data transparency is required, including full and complete access to patient medical records and other pertinent clinical information (e.g., radiology, laboratory, and other studies); to infected patients and their contacts (for interviews); and to laboratory specimens and/or microbiologic isolates (for molecular epidemiology (e.g. genomic sequencing) to support the clinical investigation. As an example, in May 2013, I was invited by the Saudi Ministry of Health to join an international team to investigate a cluster of novel coronavirus infections in the eastern region of the Kingdom. This infection would later become known as Middle Eastern Respiratory Syndrome (MERS). The outcome of our findings was published in the New England Journal of Medicine within weeks of the conclusion of our investigation [6]. As described in the methods section of the manuscript, our team was allowed access to medical records so that we could review clinical and demographic information and determine potential contacts and exposures. In collaboration with Saudi epidemiologists, case patients and contacts were interviewed. Clinical specimens from a sampling of patients were accessed from storage and sequenced to provide additional information on transmission, evolution, and origin, which was later further described in a more extensive subsequent genomic analysis [7]. Although our investigation focused on transmission in the healthcare settings, our investigation yielded important information that would inform subsequent investigations into community origins.

What data collection and preservation standards are in place at hospitals to ensure they can track emerging infectious diseases?

In the United States, the CMS requires that a healthcare facility maintains an infection prevention and control program in order to prevent, recognize, and control, to the extent possible, the onset and spread of infection within the facility, including surveillance and investigation to prevent the spread of infection. It also requires that the hospital complies with

the reportable diseases requirements of the local health authority. To comply with this regulation, accrediting agencies, such as the Joint Commission, survey hospital infection prevention infrastructure and written plans for detecting and controlling infections, including new emerging infections. Public health authorities may also monitor data received from hospitals to look for concerning trends.

As part of standard work, once a trend of concern is identified by the hospital infection control program, case ascertainment and maintaining an epidemiologic description of the outbreak will inform initial hypotheses for explaining the potential cause, source, and mode of spread of the outbreak's causative agent(s). A related step to confirming diagnoses is the need to proactively save specimens (e.g., microbiologic strains already isolated) for longer than conventional holding periods and not discard them so that they are available for further analysis if new questions arise later in an investigation.

What is the relationship between hospitals and national and international health authorities when it comes to investigating the emergence and spread of infectious diseases?

In the United States, the CDC provides some surveillance data and clinical guidance on management of emerging infectious diseases. They also routinely provide consultation and laboratory assistance to healthcare facilities and health departments that are working to solve outbreaks or investigate infection control breaches and other adverse events, but only upon request. Hospitals will reach out to their local/state public health, or vise-versa, if a concerning reportable or a trend is identified. The health department, in turn, may extend a formal invitation to CDC for help leading an on-site team. Public health will help gather additional information from interviews, case/chart reviews, observations and possibly environmental sampling. The team analyzes this information and helps develop control measures. In the case of a multistate outbreak, the CDC coordinates the investigation, working closely public health

partners, who in turn work with their labs and healthcare facilities. The World Health Organization (WHO) will investigate outbreaks if invited by the government, but is more often looked to as an important and exclusive source for global disease surveillance information.

What data must be shared by hospitals, labs, and governments in order to complete a comprehensive investigation of a zoonotic spillover episode?

These are well described by our CDC [8].

The initial steps in an investigation require that one confirming or verifying the diagnosis through:

- Reviewing full medical records of suspected cases and selected non-cases during the time period of initial emergence and for some time period prior to initial emergence. Record coded patient identifiers, age, sex, race/ethnicity, date of illness onset or diagnosis, symptoms, signs, laboratory findings, or other relevant data.
- Verifying the results of laboratory testing
- Saving specimens (e.g., microbiologic strains already isolated) so that they are available for further analysis
- Access to affected persons for clinical examination by health-care personnel when possible
- Interviewing the affected persons and their contacts

Any existing routine surveillance that exists should be reviewed, such as public health agency surveillance data; medical system billing/coding data from other hospitals, laboratories, or ambulatory care settings; institutional setting records (e.g., school and workplace attendance records); and other special surveys.

The outbreak should be characterized in terms of time, place, and person:

- Time of onset of illness (symptoms, signs, or laboratory test positivity) among affected persons; period of likely exposure to the causal agent(s) or risk factor(s); time when treatments were administered or control measures were implemented; and time of potentially related events or unusual exposures.
- Place of residence and occupation; venues for recreational activity; activity sites (e.g., rooms or units in which persons were hospitalized; rooms visited during a convention or meeting; or seating or activity locations on transportation conveyances, such as planes or cruise ships).
- Person /demographic characteristics (e.g., age, sex, and race/ethnicity), occupation, and diagnoses; and features shared by affected persons.

To support the comprehensive clinical investigation, laboratory samples should be accessible for sequencing or other molecular epidemiologic investigations.

These data should inform next steps, i.e., environmental sampling, obtaining specimens from suspect animals (e.g. bats, suspected intermediary host).

Thank you for the opportunity to testify before you today on data and access that investigators need in order to trace an outbreak to a discrete origin. Upholding the principles for transparency, scientific integrity, and objectivity is critical to understanding the origins of any outbreak, especially COVID-19.

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Connie Savor Price, MD is the Chief Medical Officer (CMO) at Denver Health and a Professor of Medicine in the Division of Infectious Diseases at the University of Colorado School of Medicine. Prior to becoming the CMO, she served as the Chief of Infectious Diseases and the Medical Director of Infection Control and Prevention at Denver Health for 13 years. Dr. Price is board-certified in internal medicine, infectious diseases, and medical microbiology. Her research and clinical interest focuses in healthcare epidemiology and methods to prevent and rapidly detect emerging and antimicrobial resistant infections. Dr. Price has a track record of successful federal funding as a Principal Investigator from the National Institutes of Health, the Department of Defense, and the Agency for Healthcare Research and Quality. She has published >75 manuscripts and delivered >175 lectures on the prevention of healthcare associated infectious diseases and related topics. She is active in the Infectious Diseases Society of America, served in an elected position on the Board of Directors of the Society of Healthcare Epidemiology of America, and as past chair of the American Society for Microbioloty section on Healthcare Epidemiology. Dr. Price was the physician representative on the inaugural Colorado Healthcare Associated Infections advisory committee for public reporting of healthcare associated infections for Colorado. She has recognized expertise in outbreak management and has served as a consultant to public health authorities around the world on control of emerging infections, specifically MERS and SARS, as well as Ebola preparedness.