Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company’s public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Public Health and Clinical Laboratories: Partners in the Age of Emerging Infections

James L. Beebe, Ph.D., D(ABMM), Colorado Department of Public Health & Environment, Laboratory Services Division, Denver, Colorado

Abstract
Clinical and public health laboratories have experienced unprecedented challenges in the form of demands to comply with revised regulations and economic pressures to be more efficient while preparing to respond to everything from pandemic influenza to bioterrorism. These forces have been an impetus for laboratorians to communicate, cooperate, and collaborate as never before and to seek the common ground where knowledge and resources can be shared to weather the profound economic and political forces at work today. The appearance of newly emerging and reemergent infections caused by agents of foodborne illness, anthrax, smallpox, plague, influenza, and other diseases has fostered cooperative network enterprises between clinical and public health laboratories, allowing the early detection of outbreaks of common and unusual pathogens and the measurement of the effectiveness of public health measures.

Introduction
The pace of change in the laboratory community continues to accelerate. Both clinical and public health laboratories have experienced unprecedented challenges. Demands for compliance with revised regulations and economic pressures to be more efficient while preparing to respond to everything from pandemic influenza to bioterrorism. These forces have been an impetus for laboratorians to communicate, cooperate, and collaborate as never before and to seek the common ground where knowledge and resources can be shared to weather the profound economic and political forces at work today. In 1997, a Health and Human Services-commissioned report by the Lewin Group (1) identified the trends that were affecting public health and clinical laboratories. Those forces are still at work. Table 1 is a summary of some of the economic forces, including the rise of managed care organizations and their attendant accumulation of bargaining power with reference laboratories. In the face of ever-rising health care costs, hospitals are enduring relentless pressure to reduce laboratory costs, resulting in the formation of consortium laboratories among hospital groups, referrals of specimens to private reference laboratories, closings of smaller hospital laboratories, and reductions in laboratory staff.

Table 2 shows the forces at work for clinical laboratories, which are fighting battles on two fronts to maintain staff levels against further erosion. Management is asking for workforce reductions, while fewer qualified applicants are available for open positions. With the closing of many medical technology schools over the past two decades, graduating medical technologists, clinical laboratory scientists, and technicians number less than half of projected workforce needs. At the same time, the federal Health Insurance Portability and Accountability Act (HIPAA) has placed new demands for secure patient information handling, adding another burden on laboratory staff (1,2).

Table 3 lists the forces at work with public health laboratories. While engaged in traditional public health activities, these laboratories are experiencing multiple new pressures, including HIPAA
and CLIA regulatory compliance issues, the need to be prepared for analytic response to bioterrorism acts, loss of state funding with a parallel need to bill Medicaid for patient testing and provide testing on a fee-for-service basis. While a significant amount of funding support and technology transfer has accompanied the charge to state and local public health laboratories to develop capability for bioterrorism testing, state funding for traditional public health testing has withered (1).

In this setting, new, emerging infections continue to arise. Emerging infections have required public health laboratories to be able to test accurately for many new agents, either confirming clinical laboratory findings or testing specimens referred from clinical laboratories. The prospect of a continued emergence of newly recognized pathogens or reemergent agents is waxing strong.

In spite of all these issues, or because of them, public health and clinical laboratories are working together to surmount the challenges and provide quality in both patient care and public health laboratory testing. Several new initiatives have been launched to facilitate the collaboration of laboratorians, but while most public health laboratorians know what clinical laboratories do, the reverse is often not true. Table 4 illustrates the parallel, but different, roles each plays. Clinical laboratories are focused on patient care, while public health laboratories are focused on the health of the entire population. Clinical laboratory information is directed to physicians, and from them, ends at patient care. In contrast, public health laboratories gather information for public health experts and epidemiologists, who must determine the cause of illnesses and outbreaks affecting patients in many hospitals, detect new and unusual threats to the health of the community, and respond to these threats and prevent them. These roles are complementary, and as many laboratory professionals are discovering, mutually supportive.

Table 1. Market economic forces

| Nature of Changes                                                                 |
|----------------------------------------------------------------------------------|
| Managed care organizations and a few private laboratory companies dominate market |
| Cost reductions are the driving force                                             |
| Reimbursement rates for laboratory services are falling                         |
| Consolidation of reference laboratories                                          |
| Consolidation of hospital laboratories                                           |

Table 2. What is happening to clinical laboratories?

| Nature of Changes                                                                 |
|----------------------------------------------------------------------------------|
| Staff shortages, aging workforce, fewer choosing laboratory for career           |
| Downsizing, consolidation, partnerships                                          |
| Laboratory management focused on cost control                                   |
| Reimbursement driving changes in laboratory activity                             |
| Increasing regulatory demands from HIPAA, CLIA                                  |

Table 3. What is happening to public health laboratories?

| Nature of Changes                                                                 |
|----------------------------------------------------------------------------------|
| Fee-for-service testing on the rise, state support decreasing                    |
| Federal support for bioterrorism preparedness                                    |
| Medicaid-reimbursed laboratory testing                                          |
| Emerging infectious diseases                                                     |
| Regulatory demands increasing, such as HIPAA, CLIA                               |
| Select agent certification and security issues                                   |

Table 4. Comparison of clinical and public health laboratory roles

| Clinical                          | Public health                        |
|-----------------------------------|-------------------------------------|
| Health (sick) care                | Health of public                     |
| Provide information regarding a   | Provide information regarding        |
| PATIENT to PHYSICIAN              | POPULATION to public health          |
| Diagnostic, therapeutic, and      | PROFESSIONALS                        |
| disease management testing        | Some diagnostic testing, screening,  |
|                                  | epidemiologic typing, human and     |
|                                  | environmental testing                |
| Outcome: recovery from illness     | Outcome: health of population; detection and intervention; prevention |

The 1988 Institute of Medicine report, *The Future of Public Health* (3), defined for the first time the functions of public health as (i) assessment, (ii) policy development, and (iii) assurance. These
functions could be translated as follows. (i) What illness is afflicting the population and what is the cause? (ii) After knowing what is wrong and what the cause is, what laws or regulations must be enacted, and what testing must be conducted to ensure remediation and control of the problem? (iii) How can we be assured the problem remains under control? The public health laboratory has a role in all three of these elements. The public health laboratory should be able to respond to outbreaks, provide and manage analytic information, monitor the environment, advocate for high-quality testing, and provide reference testing services, training, and leadership in the overall effort to secure health for all (4).

In recent years, emerging infections have arrived unpredictably but frequently. Table 5 shows some challenges that have confronted medical and public health authorities and their support laboratories during the last 4 years. Recently, Cockerill and Smith (5) provided their perspective on the impact of emerging infectious diseases on clinical laboratories, promoting the adoption of advanced nucleic acid amplification methods. While this technical advance is certainly desirable, it may not be economically feasible for most clinical laboratories. The authors point out the recently developed capability of public health laboratories for testing for SARS, coronavirus, and variola as examples of agents that can be identified through cooperation between clinical and public health laboratories.

The need for cooperation and collaboration among laboratories has been long recognized by public health experts. In 1994, a CDC strategy document (6) outlined the need for the formation of networks to gather information to detect, report, and analyze information regarding infection. This document became the foundation for actions that led to the formation of networks that are cementing bonds between clinical and public health laboratories.

**PulseNet**

Clinical laboratories have traditionally referred isolates to public health laboratories for confirmation and serotyping, but beginning in 1998, these isolates were subjected to a new powerful method to type the strains. Public health laboratories began to use pulsed-field gel electrophoresis (PFGE) to type isolates of *Escherichia coli* O157:H7 and other foodborne-illness pathogens, subdividing these isolates into closely related groups or clones, and allowing epidemiologists to efficiently investigate cases of infections and determine the cause. Often, clusters of cases are seen immediately by public health laboratory scientists when a group of isolates with a unique pattern are observed. Epidemiologists can investigate smaller numbers of cases and spend less time collecting the information that points to a particular food product. This has occurred many times since the initiation of the PulseNet system. Outbreaks caused by *Salmonella* spp., *Shigella* spp., *E. coli* O157, and *Campylobacter* and *Listeria* spp. are detected, and the numbers of cases are limited when the incriminated food product is determined and recalled. Clinical laboratories are being encouraged to refer such pathogens quickly, rather than letting a group of isolates accumulate for convenient transport to a state laboratory, where outbreaks of foodborne illness can be identified rapidly, resulting in limitations on the extent of outbreaks (7).

PFGE patterns uploaded by public health laboratories to the CDC PulseNet database are examined by epidemiologists looking for the appearance of clusters that cross state borders. Numerous multi-state and national foodborne-illness outbreaks have been uncovered that could not have been detected by other means. PulseNet works because clinical laboratories are effective in cultivating agents of foodborne illness and referring these isolates quickly to public health laboratories that perform PFGE typing, conduct a statewide analysis, and then upload this information to the CDC database for nationwide analysis. This partnership has raised the level of detection of foodborne illness to unprecedented levels, virtually ensuring that no multistate outbreak of foodborne illness of any significant magnitude will go undetected. When three state laboratories determine a strain to be the same by PFGE typing, the recovery of a single isolate by each of three clinical microbiologists in three different states might be enough to detect a nationwide food problem.

**Emerging Infections Program**

The recovery and referral of isolates have done more than detect outbreaks of foodborne illnesses. By extremely accurate measurements of the number of infections in 10 states, the CDC’s Emerging Infections Program (EIP), a program for surveillance of invasive bacterial infections, has shown that vaccines, such as the pneumococcal vaccine, are highly effective and virtually eliminate illness in vaccinated groups (8).

**FoodNet**

An EIP program called FoodNet is an alliance of 10 state public health programs and clinical laboratories, which, year-to-year, has determined the overall rates of sporadic cases (not outbreaks) caused by a number of foodborne pathogens and the factors associated with infection. The isolation of agents such as *Salmonella*, *Shigella*, and *Listeria* spp. and *E. coli* O157, which are recovered by clinical laboratories and referred to state public health laboratories, is doubly important because it provides critical information in revealing outbreaks and allows measurement of the overall disease burden of sporadic cases. Sporadic cases are those in which an outbreak has not occurred but some part of the food system has failed. Over the
past 8 years, extremely accurate data have shown that the numbers of cases of illness due to some foodborne pathogens have declined (9,10). These data provide hard evidence that food safety measures are actually protecting people from foodborne illness.

The New Networks

Initiatives in several states have spawned a new model for progressive collaboration between clinical and public health laboratories. With support from the CDC, states, and other agencies, cooperative state-based networks, such as the Colorado Laboratory Forum, the Minnesota Laboratory System, the Nebraska Laboratory System, the Washington State Clinical Laboratory Initiative, the Michigan Laboratory System, and groups in 10 other states, have been set up. Table 6 shows a broad array of activities in which these new networks are engaged, including improving communication, providing education and training, enhancing the quality of laboratory data, responding to emergencies, and sharing information. As an example, the Colorado Laboratory Forum consists of laboratorians from clinical, public health, veterinary, agricultural, forensic, environmental, federal, military, food, and research agencies, with the following goals: to facilitate communications, improve analytic capabilities of all member laboratories, and facilitate education and training. The goal is to solidify these state groups into a National Laboratory System (11).

Response to Bioterrorism

Clinical laboratorians can capture the first evidence of biologic-agent use by culturing the agent and conducting presumptive identification tests. During the anthrax spore attacks of 2001, it was a clinical microbiologist who, shortly after taking training provided by public health laboratories, recognized and referred the isolate from the first case of anthrax (12).

Public health groups have provided training for clinical laboratorians to ensure that agents of anthrax, plague, and tularemia, rarely seen by any laboratory worker in the United States, are recognized and referred as soon as possible. The partnership is evident. Clinical microbiologists are at the front lines, handling, culturing, and testing primary specimens and providing the information needed to make the primary diagnosis. Public health microbiologists are in the best position to train clinical microbiologists about bioterrorism agents and then to rapidly confirm the identity of referred isolates.

Laboratory Response Network

Trained and equipped, public health laboratories are using leading-edge methods developed at the CDC, such as real-time PCR, luminex-type assays, and time-resolved fluorescence antigen immunoassays (13). These new methods have elevated identification accuracy to new heights while reducing the time needed for confirmation to a few hours rather than the many days conventional techniques typically require. Clinical laboratory microbiologists, by serving in the role of sentinels, have responded to the call, rapidly referring suspicious isolates to their partner public health laboratories, which can then either confirm the identity of or rule out a possible agent of bioterrorism.

Conclusion

Clinical and public health laboratories each have an indispensable function, and neither can be successful without the other. Many public health laboratory scientists have had to adopt a new leadership role for the state or city to which they are responsible, providing training; establishing safe and secure laboratory facilities for possessing, using, and maintaining select agents; channeling funding to clinical laboratories for bioterrorism preparedness and communications; and maintaining links between laboratories.

The end result of these collaborative efforts is difficult to ascertain, but collectively, factors such as the reduction in the size and frequency of outbreaks and sporadic cases of infection, proof that food safety practices are effective, and validation of the efficacy of new vaccines can result in a healthier population, the goal of both medical care and public health. A healthier population means a reduction in the overall cost of health care related to infections. The alliance of clinical and public health laboratories promises to be a key component in slowing the rise of health insurance costs and managed care expenses.

References

1. Lewin Group. 1997. Report for the Office of the Assistant Secretary for Planning and Evaluation, Office of Health Policy. Public Health Laboratories and health system change. The Lewin Group, Falls Church, VA.
2. Check, W. 1998. Managed care deeply affecting clinical microbiology. ASM News 64: 495-500.
3. Institute of Medicine, Committee on the Study of the Future of Public Health, Division of Health Care Services. 1988. The future of public health. National Academy Press, Washington, DC.
4. Witt-Kushner, J. et al. 2002. Core functions and capabilities of state public health laboratories. Morb. Mortal. Wkly. Rep. 51:1-8.
5. Cockerill, F.R., III and T.F. Smith. 2004. Response of the clinical microbiology laboratory to emerging (new) and reemerging infectious diseases. J. Clin Microbiol. 42:2359-2365.
6. Centers for Disease Control and Prevention. 1994. Addressing emerging infectious disease threats: a prevention strategy for the United States. Centers for Disease Control and Prevention, Atlanta, GA.
7. Swaminathan, B. et al. 2001. PulseNet: the molecular subtyping network for foodborne bacterial disease surveillance, United States. Emerg. Infect. Dis. 7:382-389.
8. Robinson, K.A. et al. 2001. Epidemiology of invasive Streptococcus pneumoniae infections in the United States, 1995-1998: opportunities for prevention in the conjugate vaccine era. JAMA 285:1729-1735.
9. Marcus R. et al. 2004. Dramatic decrease in the incidence of Salmonella serotype Enteritidis infections in 5 FoodNet sites: 1996-1999. Clin. Infect. Dis. (Suppl. 3): S135-S141.
10. Centers for Disease Control and Prevention. 2004. Preliminary FoodNet data on the incidence of infection with pathogens transmitted commonly through food-selected sites, United States, 2003. Morb. Mortal. Wkly. Rep. 53:338-343.
11. McDade, J. and J. Hughes. 1998. The US needs a national laboratory system. U.S. Medicine 34:9.
12. Jernigan, J.A. et al. 2001. Bioterrorism-related inhalational anthrax: the first 10 cases reported in the United States. Emerg. Infect. Dis. 7:933-944.
13. Heatherley, S.S. 2002. The Laboratory Response Network for bioterrorism. Clin. Lab. Sci. 15:177-179.