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NEWS AND VIEWS

PulseNet China

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The Chinese pathogen molecular typing surveillance network, PulseNet China, applies well-recognized and standardized molecular technologies to all bacterial pathogens, to develop future laboratory-based surveillance systems for all bacterial infectious diseases. Working with this system, the bacterial disease outbreaks with potential national or global spreading can be detected early and prevented.

Laboratory-based surveillance is an essential and fundamental component of any infectious diseases control and prevention system, assumed as crucial capability for the early detection and containment of disease outbreaks in order to prevent local or global spread.[1] Molecular typing of bacterial isolates has become an essential component of epidemiological investigations of infectious diseases caused by pathogens. The method used by PulseNet laboratory is pulsed-field gel electrophoresis (PFGE), which is an ideal means to analyze the restriction fragments patterns of chromosomal DNA of almost all bacterial species. The restriction enzymes selected usually have rare or few restriction sites on bacterial chromosomal DNA, resulting in larger fragments, which can only be separated by PFGE methodology. This usage results in a unique fingerprint image that can be documented digitally and analyzed easily by computer. Since each isolate has only a single PFGE pattern, the unique PFGE patterns of isolates from various sources are able to compared. If the two isolates share the same PFGE pattern, they are considered identical, or from a same source. However, further epidemiological study would be required to confirm the laboratory findings. This is the principle, in theory, for PulseNet surveillance.[2,3]

The essence of PulseNet is that all participating laboratories use the identical method, with identical reagents, and follow identical protocols for same bacterial species, in order to achieve valid information sharing globally. Further more, all persons who performed those experiments must be trained using identical teaching materials to reduce the artifactual differences in data generated by different persons.

In 1995, the US CDC established PulseNet for the first time on. Consequently, the PulseNet network is now being established in Canada, Europe, the Asia Pacific region and Latin America. These independent networks cooperate together in a PulseNet international family allowing public health officials, their laboratories and scientists to share molecular and epidemiological information in real time and to enable the rapid recognition and investigation of multinational bacterial disease outbreaks, such as the *Vibrio cholera* outbreak that occurred in Haiti in 2010.[4,5]

PulseNet China was established by the National Institute for Communicable Diseases Control and Prevention (ICDC), China Center for Disease Control and Prevention (China CDC) in September 2004, and has been devoting efforts to set up a Chinese pathogen molecular typing surveillance network system ever since then. PulseNet China was modeled after PulseNet US, but differs substantially. Mainly, PulseNet US only applies to food-born pathogens, such as *Salmonella*, *Shigella*, *Vibrio* and so on. PulseNet China relates to all bacterial pathogens, such as *Yersinia pestis*, *leptospira* species, *Streptococcus suis* and many other pathogens. More importantly, we are attempting to use PulseNet China as model to develop future laboratory-based surveillance systems for all bacterial infectious diseases of China.[6] PulseNet China is also a component of PulseNet Asia Pacific and PulseNet International as well. PulseNet China has been recognized as the most important recent advance in China's food safety system.[7]

Currently, PulseNet China consists of one central laboratory connected to 31 provincial central laboratories, which are under the leadership of the Administrative Steering Committee, supported by the Technical Committee[8] and operated by ICDC, China CDC. The procedural mechanisms of PulseNet China are shown in the flow diagram (Figure 1).[9] Outlined there are the mechanisms for data transmission, cluster searching and comparison, reporting and feedback, training and technical support, inspection and supervision, outbreak investigations and biosafety.

Currently, standardized PFGE methods have been established for most food-borne bacterial pathogens as well as most of bacterial pathogens having significant public health significance in China. The PulseNet China platform has already had an impact; its use of these standardized methods and interrogation of some of the national molecular typing databases has enabled the rapid detection of an emergence of the molecular locus sequence typing 4821 complex of group C serotype of *Nesseria meningitidis* in 2005,[10] as well as the emerging of sequence type 7 of *Streptococcus suis* in 1996, which caused two larger outbreak of human infection in 1998 and 2005,[11] and the emerging of the Xv serotype of *Shigella flexneri* in recent year in China. PulseNet China, using the national PFGE databases, has also participated in several worldwide investigations of food-borne illness.

Collectively due to these efforts, PulseNet China has made much needed contributions to outbreak investigations. In the domestic
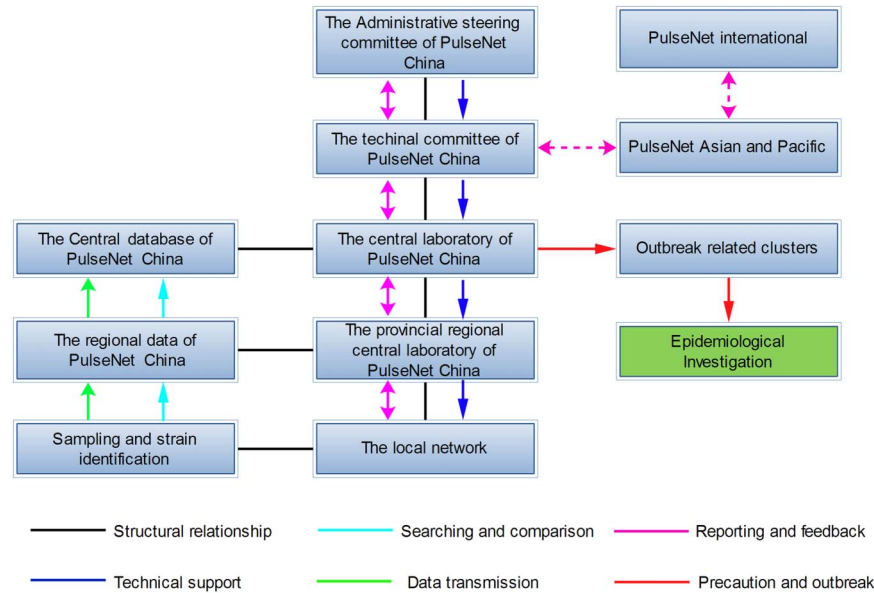
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Figure 1 Mechanisms of PulseNet China operation.

areas, the PulseNet China's central laboratory participated in the cholera outbreak investigations in Mengcheng City, Anhui Province, and in Huai'an City, Jiangsu Province back in August 2010. During retrospective investigations, indistinguishable pulse types were found by comparing PFGE profiles of isolated strains, providing critical evidence for the source of the cholera infections. When cholera cases were found in Beijing, Shanghai, Tianjin, Zhejiang and Jiangsu in June and July in 2011, PFGE strain comparisons were carried out in the same way.

As a component of PulseNet International, PulseNet China also participated in the collaborative investigation, *Salmonella typhimurium* Infections Associated with Exposure to Clinical and Teaching Microbiology Laboratories in USA, PulseNet China conducted an investigation on whether this strain has caused infections in China, and compared the ATCC14028 patterns to *S. typhimurium* collected by the ICDC, China CDC, as well as network labs in PulseNet China. In the outbreak of *Escherichia coli* O104:H4 that occurred in Germany in June 2011, PulseNet China obtained the PFGE collection of the O104:H4 outbreak-related strain from PulseNet International to search for a possible identical strain in China.

In the future, PulseNet China will (i) strengthen local, provincial and national pathogen surveillance infrastructures and implement prevention and control programs; further expand the laboratory network, reinforce typing capability in the province regional central laboratories as well as other bacterial surveillance units as CAIQ, agriculture, military and other key agencies/organizations; (ii) establish highly efficient mechanisms for pathogen molecular typing surveillance in member of PulseNet China, including improved communication among laboratories and implement timely data sharing between laboratories and epidemiologist. Improve procedures for obtaining isolates or specimens from clinical laboratories, improve procedures for timely molecular typing, reporting, biosafety and establish criteria needed for outbreak investigations, as well as provide treatment and facilitate other assistance towards containing bacterial infectious diseases and improving prevention; (iii) further expand the categories of pathogens for molecular typing, such as zoonotic and emerging pathogens. Enlarge the amount of information available for considering the identification of strains; (iv) carry out standardization of new molecular typing methods for bacteria; enforce quality assurance and quality control within the network laboratories; (v) conduct training for personnel and capacity building, including training workshop for the second generation of molecular typing techniques, such as MLVA, and BioNumerics software; and (vi) focus on the construction of an efficacious data exchange systems for network laboratories.

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