NACCHO
National Association of County & City Health Officials
The National Connection for Local Public Health

09-04

STATEMENT OF POLICY

Tuberculosis Control and Elimination Research Priorities

Policy

The National Association of County and City Health Officials (NACCHO) endorses a long-term international research strategy as a critical element for reduction of tuberculosis (TB) morbidity and mortality in the United States and recommends that national and global entities, such as the United States federal government, National Institutes of Health, Centers for Disease Control and Prevention (CDC), international counterparts to CDC, World Health Organization (WHO), and other agencies, non-governmental organizations, and foundations, such as the Global Fund to Fight AIDS, TB, and Malaria, provide policy and financial support for such a strategy.

Local health departments (LHDs) are an essential component of local, national, and global TB control. LHDs conduct TB screening, investigate suspected cases, provide treatment to patients diagnosed with TB to reduce disease transmission, and lead efforts to manage infectious individuals who do not comply with treatment as assigned by their medical provider. Without local infrastructure in place, research components, however useful, will not be able to become operational. Therefore, if funding is not sufficient to support all needed programmatic and research activities, then funding should be prioritized to support and maintain or expand program and infrastructure to control TB.

TB incidence in the United States is being driven largely by importation from countries with high incidence of disease and prevalence of infection.[1] Particularly alarming is the increasing incidence of Multi-drug Resistant TB (MDR TB) and Extensively Drug-resistant TB (XDR TB) in this population.[2] For this reason, NACCHO encourages coordinated worldwide research efforts to mitigate, control, and eventually eliminate TB and supports funding, workforce development, and expertise for the following initiatives:

- Translational and operational research projects that evaluate cost effectiveness and enumerate "best practices" of TB programs in order to transfer knowledge and skills needed to incorporate current and emerging technologies into practice and are replicable in a wide range of field settings
- Development and deployment of safe and more effective TB vaccines that do the following:
  - Prevent infection in infants;
  - Prevent progression of latent infections to active disease, directed primarily to adults;
  - Are priced in a tiered fashion so they are affordable in the poorest settings;
  - Can be manufactured in developing countries given appropriate technology;
  - Can be systematically deployed and administered in the field using strategies similar to those that eradicated smallpox; and
  - Assist in the treatment of active disease (i.e., immunotherapeutic vaccines)
- Development and delivery of new and effective antibiotics

- Development and delivery of new, easily accessible, and dependable diagnostic tests for TB infection and disease and for rapid antibiotic drug sensitivity testing
- Epidemiological studies that clarify the following:
    - Patterns of drug resistance;
    - The role of visa and/or visa status in the transmission/spread of TB across international borders;
    - The role of labor migration in global transmission/spread of TB;
    - The basic science of TB interacting within human hosts that triggers progression of TB infection to disease;
    - The role of genomics in the virulence and transmissibility of TB;
    - Characterization of the development of TB disease in especially high risk populations; and
    - The implications of the worldwide rise in the incidence of diabetes as an accelerant in the progression of TB infection to disease in the developing and developed world
- Clinical studies and post-licensure surveillance to fully assess the safety and efficacy of new pharmaceuticals, vaccines, and the use and interpretation of new diagnostics

Justification

Effective vaccines for many vaccine preventable diseases, such as smallpox, polio, measles, mumps, rubella, and *Haemophilus influenzae*, have been a cornerstone for reductions in morbidity and mortality in large populations.[3] The need for vaccines in TB prevention and control is even more essential given the long course of therapy, rapidly emerging resistance of many strains to current antibiotic therapy, the high cost of curative care and the high burden of disease worldwide. The only currently available vaccine is the *Bacillus Calmette-Guérin* vaccine, which provides nominal and variable effectiveness and is administered primarily to children.[4]

Adequate antibiotic treatment to cure TB is a key strategy for reducing communicability of TB and ultimate reduction of morbidity and mortality associated with the disease.[5] Availability and distribution of appropriate antibiotics that assure a high probability of cure is needed to reduce spread of disease and decrease the probability that organisms develop resistance. Indeed, rising rates of MDR TB and XDR TB demand that greater efforts and financial incentives by the U.S. federal government and other member nations of WHO be deployed to encourage pharmaceutical companies to invest in safe and more effective antibiotics that reduce the duration of therapy while maintaining low relapse rates.

For over one hundred years, the only available test for TB infection was the Tuberculin Skin Test utilizing the Mantoux method of delivering the Purified Protein Derivative. Recent advances have added serological interferon-gamma release assays, such as Quantiferon and Elispot, as options with improved characteristics (increased sensitivity and specificity) comparable to the TST.[6] Use of these tests should be expanded domestically. These tests, however, remain out of reach for most international applications due to high expense and technical constraints.

Research is needed to more fully improve the inherent reliability characteristics of the abovementioned tests as well as reduce their complexity so that they can be more easily deployed in the developing world. Improving these tests and exploring promising new methods, such as identification of volatile organic compounds for breath detection of TB, will necessarily benefit availability and use in the U.S. as more rapid first-line diagnostic tools for both infection and disease.

Traditional bacteriological confirmation of TB that includes drug susceptibility testing (DST) requires a minimum of four to six weeks to determine adequate antibiotic coverage.[7] In countries with high incidence and

prevalence of drug resistant disease, access to DST early in the course of therapy is critical to reduce the chances of inadequate antibiotic coverage and the subsequent emergence of avoidable acquired drug resistance. While some advances in rapid DST, such as line assays and/or Beacon testing, are promising, many of these technologies are still too expensive and technically complex to have wide-scale application in the U.S. and in areas of the world where drug resistance is most prevalent.[8] Improvements in these technologies will have similar direct beneficial applications in the U.S. and in reduction of importation of drug resistant strains from countries of high prevalence of drug resistance.

Much of the empirical basic science and epidemiology of TB infection and disease is based on studies conducted decades ago. Field applications, such as concentric circle case finding for infection, are based upon old models of smear and culture counts that have been aided and greatly improved by newer genomic studies of transmissibility. Better understanding of the cellular and immunologic mechanisms of infection and disease progression, particularly in high risk individuals, is expected to lead to potential improvements over older, outdated case finding techniques and uncover cellular mechanisms that could be applied to the design and development of new treatments.

Performance measures derived from well-crafted empirical studies demonstrating the best application of epidemiological techniques, using current and emerging diagnostic testing, and integration of program elements of HIV and TB programs need to be developed. These important applied research questions, addressed in conjunction with the development of improved bio-technological tools, are needed to provide optimal return on investment in technology.

Such concurrent integration of translational and operational research with current and developing technology will require greater international governmental cooperation as well as better coordination among global agencies that are having an increasing influence upon efforts to control and eliminate TB in the world.

Record of Action
Approved by NACCHO Board of Directors
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