In Pursuit of Tuberculosis Elimination: Then and Now

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Outline of Talk

- Background - CDC TB Program in the 1970s and 1980s
- The National Plans
- 20 Years of Progress
- Remaining Obstacles
- Random Thoughts about the Way Forward
- Summary/Conclusions

DOT, Directly observed therapy
Program Themes in 1973

- Close the remaining TB sanitoriums (ensuring the availability of outpatient treatment facilities was not emphasized)
- Eliminate low yield TB skin testing programs (e.g., testing of school children)
- Keep treating patients as they appear (use of rifampin was OK, use of DOT if necessary), do contact investigations and occasional selected screening and give preventive therapy, and
- TB will soon cease to be a public health problem!!

DOT, Directly observed therapy
Wade Hampton Frost

“...the biological balance is against the survival of the tubercule bacillus”...”the eventual eradication of tuberculosis requires only that the present balance against it be maintained.”

1970’s TRANSLATION:

We can just keep doing what we are doing and TB will go away on its own.

Reported TB Cases United States, 1953 – 1985
James O. Mason, M.D., Dr. P.H.

CDC Director, 1983-1989
A Strategic Plan for the Elimination of Tuberculosis in the United States
1989 Strategic Plan - The Three Strategies

- More effective use of existing prevention and control methods
- The development and evaluation of new technologies for treatment, diagnosis, and prevention
- The rapid assessment and transfer of new technologies into clinical and public health practice

1989 Strategic Plan - Things We Realized

- We were not using existing tools and knowledge optimally
- We needed new tools (new technology) to achieve TB elimination
- Having new technology doesn’t mean it gets used (there is a science of technology transfer or “diffusion of innovations” as Rogers calls it)
- Achieving these goals would take a long time
- We would need a lot of help (partners) to make this dream a reality

1989 Strategic Plan - Examples of Things We Did Not Anticipate

- The emergence of MDR TB (despite a warning from MS in the mid-1970s)
- The quadrupling of 1st generation immigrants (from ~10 M in 1970 to ~40 M now) and where they would come from (despite a warning in the mid-1970s)
- The movement of the HIV epidemic
- The time and resources necessary to develop new technologies (we were very naïve)
- The time and resources required to translate new technologies into practice

MDR TB, Multi-drug resistant tuberculosis
Some Benefits of the Strategic Plan for National TB Control Efforts

- Garnered agency management’s support for the program
- Helped justify the creation of ACET
- Provided a rationale for an increase in TB program funds (initially redirection of HIV/AIDS $$)
- Provided a template for the National Action Plan to Combat Multidrug Resistant Tuberculosis

ACET, Advisory Council for the Elimination of Tuberculosis
Reported TB Cases United States, 1953 – 1991
National Action Plan to Combat Multidrug-Resistant Tuberculosis

Meeting the Challenge of Multidrug-Resistant Tuberculosis: Summary of a Conference

Management of Persons Exposed to Multidrug-Resistant Tuberculosis
Benefits of the Plans to Global TB Control Efforts

- Created initial incredulity and criticism
- Involvement of key opinion leaders (e.g., Barry Bloom) in the process helped direct attention to the global TB problem
- The epidemiologic events and the plans placed TB back into scientific and public discussion and this peaked the interest of economists (e.g., Chris Murray) which led to World Bank involvement
- WHO began to look to the U.S. (not just Europe) for help in expanding its TB program
Overview of Progress

- There has been a tremendous increase in awareness of TB as a national and global problem
- A marked increase in the number of people working in the field
- Increased numbers of scientific publications; science base expanded; *and new tools are coming on-line.*
- Marked increase in the amount of money being spent to address the problem
- Mobilization and organization to address the problem
- Impact of all this is reflected in health outcomes domestically and globally
TB Case Count and Rate* Among U.S.- and Foreign-born Persons, by Year, United States, 1993–2010

* Per 100,000 population.
Data are updated as of Feb 26, 2011 and are provisional.
Examples of Progress in Funding

- More than 20-fold increase in CDC TB program budget ($5 M in 1989)
- Increase in NIH TB funding (only $300,000 when plan was developed)
- Increase in funding for WHO TB program
- Increase in funding for TB for USAID
- Global Fund to Fight AIDS, TB, and Malaria ($20 B)
- PEPFAR ($32 B)
- Continued leveraging of HIV/AIDS $$
- Global Drug Facility

PEPFAR, President’s Emergency Plan for AIDS Relief
Examples of Progress in Organization and Advocacy

- Establishment of ACET
- Mobilization of national advocacy organizations
- World Health Assembly/WHO declaration of TB as a global health emergency
- World Bank support
- Stop TB Partnership with all its components
- IOM reports - from 2000 and continuing today
- Millennium Development Goals
- Center for Global Health Policy
- Global Fund to Fight AIDS, TB, and Malaria

ACET, Advisory Council for the Elimination of Tuberculosis
Examples of Progress in Diagnostics

- Foundation for Innovative Diagnostics
- Tuberculosis Clinical Diagnostics Research Consortium
- Liquid culture, drug susceptibility testing (DST) and speciation
- Interferon Gamma Release Assays (2005)
- Manual line-probe assays NAAT with DST
- LED microscopy with same day diagnosis
- Automated NAAT for detection and DST
Ongoing Work with Biomarkers

- Prediction of durable cure
- Indication of latent infection and its eradication/prediction of reactivation risk
- Prediction of vaccine efficacy
Examples of Progress in Drug Development and Treatment

DOTS

Drugs in development

- Rifamycins, e.g. rifapentine
- Fluoroquinolones, e.g. gatifloxacin, monofloxacin
- Nitroimidazoles, e.g., PA-824, OPC-67683
- Diarylquinoline, e.g. TMC-207
- Oxazolidinones, e.g., linezolid, PNU-100480
- Ethylenediamines, e.g., SQ-109

ART, Anti-retroviral therapy;
Examples of Progress in Drug Development and Treatment (2)

TB Trials Consortium
TB Alliance
Critical Path to TB Regimens
Global Drug Facility
Green-Light Committee
ART and PT in HIV-infected patients
3 mo. SCPT with INH and rifapentine

ART, Anti-retroviral therapy; PT, Preventive therapy; SCPT, short course PT
Work in Progress on Vaccines

- Approximately 10 candidates in the pipeline
- Live mycobacterial vaccines
- Vaccines that boost BCG prime
- Killed whole bacterial vaccines as adjunct

BCG, Bacille Calmette-Guérin
Examples of Progress in Epidemiology

- In the U.S., improvements in individual case reporting
- In the U.S., genotyping of isolates and more extensive drug susceptibility testing
- Domestically, characterization of the TB problem in the foreign-born
- TB Epidemiologic Studies Consortium
- Improved global reporting of cases and DR
- Modeling of global problem and impact of interventions

DR, Drug Resistance
Examples of Progress in Case-finding

- Transmission (Social) Network Analysis in Contact Investigations
- Standardized symptom algorithm in HIV-endemic regions
- Active community case-finding strategies in high HIV prevalence areas
Examples of Remaining Obstacles

- “Obstacles are those frightful things you see when you take your eyes off your goal.” Henry Ford
- Optimal strategies for HIV and TB program collaboration
- Optimal strategies for TB control in refugee and immigrant health programs
- Global recession amplifies need to sustain and leverage advocacy and resources more effectively and efficiently
- Challenges to early detection
- More sensitive, specific and rapid tests for disease and infection
Examples of Remaining Obstacles (2)

- Non-adherence with therapy and PT
- MDR and XDR TB
- Need for a better vaccine
- Need for better treatment regimens
- Need for better preventive therapy (PT) in HIV-infected persons; prove value of new 12 dose regimen in the field
- Need for better biomarkers
- Challenge of moving from discovery to translation and implementation; getting the funding balance right
- Resistance to the adoption of innovations
Random Thoughts/Considerations for the Future (1)

- Should there be a process for regularly updating the national plan? If so, who should do it and how often?
- How does the national plan relate to or link to global plans and strategies?
- Should a revised plan make more clear who is accountable for implementation and outcomes?
- What is the national plan for reducing TB in the foreign-born? In the U.S.-born?
- What is the national process for adoption and diffusion of innovations?
Random Thoughts/Considerations
For the Future (2)

- Are there TB innovations that should be adopted in the U.S. now?
  - E.g., for contact investigations, case finding, PT, diagnosis

- What role could “non-TB innovations” play in TB elimination?
  - E.g., smart phones, social networking sites, text messaging

- How can TB control activities (esp. case-finding and prevention) be better integrated into other non-HIV programs (e.g., chronic disease)? How can TB control better leverage the resources of other programs? What to do about neglected tropical disease programs, in particular, reducing TB by reducing helminth infections in Africa?
Random Thoughts/Considerations for the Future (3)

- What to do about the “LTBI problem”?
- Are there really 2 billion people currently infected? Or is there a subset currently infected and at risk of disease?
- All LTBI is not the same. How much of the increased risk in some groups is related to recent infection (or re-infection) and how much is related to host factors?
- Begin by using PT in the HIV-infected. In high HIV-prevalence settings, early, active case-finding coupled with SCPT might accelerate a reduction in TB prevalence.

LTBI, latent tuberculosis infection
Tuberculosis Case-rates, by Time since Entry into the U.S.
Random Thoughts/Considerations for the Future (4)

- Tackle the issue of LTBI in the foreign-born in the U.S.
- Should we launch a major effort to find biomarkers for increased risk of disease (i.e., to address TB in the foreign-born in the U.S. and address the global TB problem)?
- What role should TB advocates play in addressing socio-economic determinants of infection and disease?
- As we redouble our efforts to use existing tools, it may be critical that we set our sights on finding what Clayton Christensen calls “disruptive technologies” as a means of completely eliminating TB?
A confluence of events, including the 1989 plan, has moved the world from complacency about TB to action. There has been a dramatic increase in awareness, advocacy, organization, funding, and scientific knowledge. The most important outcomes have been lives saved and disease averted. Although many obstacles remain, there is no reason to believe they cannot eventually be overcome. As Stephen Kaggwa, a Ugandan immigrant said, “Try and fail but don’t fail to try.”
And before I go, let’s exonerated Wade Hampton Frost

“…an effective program must…”
Isolate cases to protect the community,
Provide medical care for cases at public expense,
Institute more vigorous efforts to find cases earlier, and
Improve the economic circumstances of vulnerable populations, i.e., the poor, who do not yet have TB but who are “most imminently endangered”.

Frost WH. American Journal of Public Health 1937;27:759-766
So, Dr. Frost was right. He was misinterpreted. TB will go away, but only if we sustain our efforts.