Tuberculosis (TB) is one of medicine’s oldest plagues, and HIV infection is its newest. Together, TB and HIV infection have a synergy that clearly threatens much of the hope for conquering either plague.

The science of TB and its control has been one of the greatest achievements in medicine. Robert Koch discovered the tubercle bacillus in 1882, and he succeeded in fulfilling his postulates through remarkable achievements of culture, staining, and experimental studies in animals [1]. Successful therapy began with the discovery of streptomycin in 1943 [2], and the genome of Mycobacterium tuberculosis was sequenced in 1998. TB has been a curable disease for 40 years, and a cure can now be achieved for as little as $16/patient. There are also highly effective methods to achieve TB control. Nevertheless, it has been estimated that (1) ~30% of the global population is infected, (2) a new infection occurs every second, and (3) ~1.7 million deaths due to TB occur every year [3, 4].

The science of HIV/AIDS has a similarly remarkable story of achievement, with the putative agent discovered in 1983, zidovudine receiving approval as the first effective antiretroviral agent in 1987, and extraordinary achievements in treatment being made since the introduction of highly active antiretroviral therapy in 1996. Despite such progress, and similar to what has been noted for TB, current estimates indicate that 39.5 million people are living with HIV infection, 4.3 million new infections and 2.9 million deaths occurred last year (in 2006), and only ~5% of infected individuals received treatment [5].

The intersection of these 2 diseases is a synergy from hell:

- Both diseases are concentrated in areas of poverty where there are minimal resources for diagnosis, treatment, and infection control.
- Both diseases represent major public health failures, despite the great achievements in treatment that have been made.
- The diseases are linked by biology: depending on geographic area, the ~40 million people living with HIV infection are 6–50 times more likely to develop active TB than are people living without HIV infection [4]. These coepidemics are a particularly noxious combination, because each epidemic accelerates the other.

The emergence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) is an especially worrisome development that represents the consequences of both TB/HIV coinfection and lapses in public health.

- The MDR-TB outbreak that occurred in New York City in the early 1990s is an example of such consequences. The outbreak was clonal and was closely associated with HIV infection, many cases were nosocomial, and most cases were lethal [6].
- The MDR-TB epidemic in Tomsk Oblast in Russia accompanies what is probably the most explosive epidemic of HIV infection in the world [7].
- The recently reported outbreak of XDR-TB in KwaZulu Natal in South Africa showed that 39% of 475 culture-positive cases were MDR-TB and
that 6% were XDR-TB. Of 53 patients with XDR-TB, all who underwent testing were found to have HIV infection, and the median duration of survival after specimen collection was 16 days [8]. The emergence of MDR-TB and XDR-TB has been described as a reflection of weakness in TB management, with an urgent need existing for effective disease control and health care infrastructure, including the use of culture, sensitivity testing, and strict supervision of therapy [9]. It is also a reflection of the convergence of the TB and HIV infection epidemics and the likely transmission of MDR-TB and XDR-TB to an enlarging pool of HIV-infected and immunocompromised individuals.

An additional need is new drugs—there have not been any since 1965 [10]. The highest priorities appear to be (1) drugs that could be substituted for rifampin, because of the multitude of drugs that interact with rifampin, especially antiretroviral drugs; (2) drugs to simplify the complexity and shorten the duration of treatment; and (3) drugs effective against drug-resistant strains.

Despite the grimness of this summary, we have reasons to be optimistic:

- TB is a treatable and preventable disease, and substantial success in these areas has been achieved when efforts have been applied adequately, such as in the control of MDR-TB in New York City [6] and Latvia [11]. The point to emphasize is that the methods for successful prevention and treatment are at hand and established.
- TB has an extraordinary and, in many ways, unique resource—The Global Alliance for TB Drug Development (TB Alliance)—as discussed in the article by Spigelman [12] in this supplement. The TB Alliance is a think tank that establishes priorities for drug development and identifies the agents that are most likely to accomplish specific goals. By comparison, pharmaceutical approaches for most other diseases are largely driven by what the market will bear.
- The resources of the Global Fund to Fight AIDS, Tuberculosis and Malaria and the US President’s Emergency Plan for AIDS Relief have quite dramatically increased the resources and expertise available to deal with both TB and HIV infection in the areas of greatest need, as is noted in the supplement article by Nunn, Reid, and De Cock [13].

There is one additional issue that is important to emphasize: experts in TB and experts in HIV infection live in different worlds, obtain grants from different sources, write for different journals, and go to different meetings. This great divide applies to clinical care, research, and training; it is lessened by the overlap between the 2 diseases, but not as much as it should be. The conference on which this supplement is based, as well as the supplement itself, represent an important milestone in joining these 2 disciplines, sharing data, and launching collaborations.

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**References**