

## OPINIONS

### Turning the tide on tuberculosis: a combined effort

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#### **The many sponsors of tuberculosis drugs must work together to find new effective treatments, says *Mel Spigelman*.**

Tuberculosis (TB) — often defeated, never vanquished. This ancient microbial killer, fuelled most recently by the increased disease susceptibility in the HIV/AIDS population, has resurfaced as a major global health threat. Approximately one third of the world's population harbour the causative organism and almost 9 million new cases of active disease — and over one and half million deaths — occur each year.



New tuberculosis treatments are needed desperately

Improving the situation, especially in the poorer nations of the world, will require a coordinated approach to TB therapy that involves the different stakeholders in TB drug research and development.

#### **A disease of the poor**

The TB burden is especially onerous in those impoverished countries least able to cope. TB is primarily a disease of the poor, found much more frequently in populations of the lowest socioeconomic strata. Transmission of the disease occurs much more readily in conditions of overcrowding and poor ventilation and has been associated with other health risks of poverty such as poor nutrition.

The relationship between TB and poverty not only increases susceptibility for contracting the disease, but also influences the ability of those afflicted to cope with the disease, and the way most societies deal with TB.

In large part because most TB patients have extremely limited resources, there has historically been minimal effort to discover new tools to diagnose, prevent or treat the disease. The newest class of drugs approved for TB use is over 40 years old, the only vaccine is decades older and the most common diagnostic test has been in use for a century.

#### **The right mix**

What will it take to bring modern drug treatments to the field of TB? Until now, much emphasis

has been placed on either incentivising pharmaceutical companies to devote requisite attention and resources to discovering and developing new TB drugs or to establishing nonprofit organisations — such as the Global Alliance for TB Drug Development — specifically dedicated to developing new therapies for TB.

But if TB drug therapy is to make the quantum leaps necessary to markedly alleviate the disease burden, especially within a reasonable period of time, there will need to be a concerted effort to coordinate and combine the progress made by individual contributors to this cause.

TB therapy is somewhat unique in that active disease requires combination drug therapy — commonly using four drugs to treat what is known as drug-sensitive disease, and up to seven drugs to tackle drug-resistant TB.

Combination therapy of active TB infection is necessary to avoid the drug resistance that almost invariably arises when the disease is treated with a single drug. It also increases the efficacy in curing patients, as the multiple drugs work through different mechanisms of action.

What TB therapy needs, however, is not simply one or even two new drugs, but most likely multiple new drugs that can — and must — be tested and then given together.

### **Working together to beat TB**

Because of the pharmaceutical industry's competitive and secretive nature — driven largely by the potentially enormous profits to be derived from successful new products — there has been very little precedent in combining new drugs from different sponsors during clinical testing or earlier stage research.

TB, however, presents not only the need, but also the potential for combining forces at these stages of the research and development cycle. As there are not very great, if any, profits to be made from TB drugs, pharmaceutical companies may be more willing to cooperate with each other.

Developing a new treatment regimen for TB is a long and arduous process. It takes at least seven years to perform the clinical trials necessary to prove that a new TB treatment is superior to the standard therapy.

Such lengthy programs should only be undertaken with those combinations of drugs capable of making the most progress — combinations that should be designed independent of whether the individual component drugs are 'owned' by one, or by multiple, sponsors.

The challenge and opportunity presenting itself to those organisations involved in new TB drug research and development is to work together in novel partnerships to achieve these goals. Only through this paradigm shift in thinking and acting can the rapid progress necessary to turn the TB tide be realised.

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