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Prevent TB to End TB: The Implementation of Latent TB Treatment

Tuberculosis (TB), a predominantly preventive respiratory disease, is the biggest infectious disease killer (causing more deaths than malaria or HIV) in the world, especially in TB hubs like Nepal and India in South Asia. Almost one fourth of the human population resides in South Asia.

In Nepal alone 47 people die of TB every day. There is no effective vaccine against TB although Gates and other foundations are conducting clinical vaccine trials, which may well cost over a billion dollars. Importantly the development of these new vaccine will, in all likelihood, take many years, assuming the vaccine is found to be effective in the first place.

In the meantime, many people will continue to die due to TB in countries like Nepal. The problem is that latent TB treatment (as opposed to full blown TB treatment) is spectacularly underutilized in these countries to control TB.

TB preventive therapy (TPT) using 3HP is a two drug Isoniazid and Rifapentine) regimen given once a week for three months for effective latent TB treatment with game-changing results as clearly shown by Richard Chaisson from Johns Hopkins University and his colleagues in the New England Journal publication.

This TPT regimen using 3HP could clearly work as a "vaccine" and potentially save millions of lives as we wait for the new vaccine to come to fruition. The full cost of the 3 HP drugs per patient is about 10 USD.

There is a strong overlooked parallel with HIV infection. Like TB, there is no vaccine for HIV. But strong activists for HIV did such a great job over decades in finding funds and encouraging patients to take preventive drugs to halt HIV progression to AIDS that most people with HIV infection (especially in the Western world) have no fear of progression to AIDS. Unfortunately, there are no effective activists for TB, a predominantly poor person's disease.

My personal interest in the treatment of latent TB as a means to effectively control TB incidence was triggered when I read about Dr George Comstock, an American clinical epidemiologist, from Johns Hopkins University. Dr Comstock worked in Bethel, Alaska in the late 1950s and early 1960s amongst the native population where TB was rampant, almost exactly (and amazingly) as it is right now in low income countries like Nepal.

To his immense satisfaction Dr Comstock found that when latent TB was properly treated in the native population (in addition to treating full-blown disease), the TB rates in Bethel came down drastically. The US has applied Dr Comstock's strategy and helped control the spread of TB in the US.

Why can't low income countries like Nepal apply this well-known strategy to help eliminate TB as so cogently argued some years ago in the NYT (view here).

The 3 HP regimen, a modern variation with much fewer side effects than the regimen Dr Comstock used, is clearly available today and can be deployed in poor countries like Nepal and save millions of lives as we wait for the vaccine.

Although highly recommended by the WHO and other such institutions for implementation in countries like Nepal, the 3 HP regimen is not deployed chiefly due to shortage of funds.

There is no time to waste as TB continues to kill mercilessly as we wait for a vaccine.

I am a Nepali doctor, certified by the American board of internal medicine, and I trained in Phoenix Arizona. I have been working on "biblical" diseases like TB and typhoid fever (another life-threatening, rampant bacterial disease) for decades. Recently we trialed a new typhoid fever vaccine and published the findings in the NEJM in 2019 (view here). The Nepali government administered this vaccine to 8 million children in April 2022. I was one of the two Principal Investigators for that game- changing trial and the implementation of its findings.

The implementation of 3 HP will be carried out by the Britain Nepal Medical Trust (BNMT) which has been working on Tuberculosis control in close collaboration with the Nepali government since 1967 (View BNMT website). I am the Vice Chair in the BNMT. Dr Maxine Caws, PhD who is the Principal Investigator in the BNMT from the Liverpool School of Tropical Medicine in the UK with a wealth of experience in tuberculosis control, will play a major role together with Mr Raghu Dhital who is the CEO of BNMT in carrying out this 3 HP project.

The short CVs of Dr Max Caws, PhD and myself are included at the end.

In conclusion, trying to control TB in Nepal and the surrounding region is a very ambitious task, more so than typhoid fever control. The cost for Nepal alone for 3 HP implementation in all the districts may be around 30 million USD. We can start with 4 districts in Nepal with lower costs (about one and half million USD. Latent TB although not making the patient sick is a time bomb. At some point many with latent Tb will develop active TB and spreading the disease to another group of people to start the cycle again. This cycle can easily be broken as those who are treated for latent TB will not (> 90%) suffer from active, transmittable TB.

Please kindly read the British Medical Journal (BMJ) editorial entitled "Prevent TB to End TB" that we recently wrote that clarifies what I have written above.

In addition, please kindly watch the five minute YouTube video.

We are also teaming up with Rotary Clubs to get this project rolling in other districts in Nepal as mentioned in the video. Dr Scott Leckman, a very active Rotarian, from Utah, is playing a very active role.

For a fuller article on Tuberculosis in South Asia, please read this article from 2018 that we wrote.

ABOUT THE AUTHOR

Buddha Basnyat is a medical doctor practicing medicine in Kathmandu, Nepal. His research interests are infectious disease (specifically typhoid, TB) and high altitude illness.

He has published widely in both these fields in well-known medical journals (The Lancet, BMJ, NEJM) and written chapters in the latest standard medical textbooks (Harrison's Textbook of Internal Medicine, Oxford Textbook of Medicine and Manson's Tropical Diseases).

In addition, he is the Principal Investigator (PI) for the largest just-completed, international randomized placebo controlled drug trial in typhoid fever (ACT- South Asia trial).

In 2022, largely based on the efficacy results of the new typhoid conjugate vaccine study (published in the NEJM in 2019), in which he was the PI, the Nepali government with the help of GAVI (Vaccine Alliance) administered the typhoid conjugate vaccine to 8 million Nepali children and included this vaccine in the annual vaccination schedule of Nepal.

He is also the PI from Nepal for the Oxford University's Recovery trial, which was the largest Covid 19 treatment trial of hospitalized patients in the world, where Nepal has made a strong contribution. The Recovery Trial has now transitioned to studying hospitalized influenza patients as one of the disease areas with no clear-cut drugs for treatment.

He is the Chair of The Oxford University Clinical Research Unit-Nepal, the Medical Director for the Travel and Mountain Medicine Center, and The Himalayan Rescue Association (dealing with high altitude medical problems in the Himalayas).

In all these institutions his primary interest is to encourage young people to do clinical and implementation research and practice evidence-based medicine.

He is a Fellow of the American College of Physicians, Fellow of the Royal College of Physicians (Edinburgh) and a Trustee of the Royal Society of Tropical Medicine and Hygiene. He is also on the Board of the Nick Simon's Institute in Nepal.

He is the Honorary Consul for Canada in Nepal, since 2013.

View Google Scholar page for Buddha Basnyat for article citations

ABOUT DR MAX CAWS

Dr Max Caws, PhD leads a research program in Kathmandu, Nepal at the BNMT as a Senior Researcher in Tuberculosis at the Liverpool School of Tropical Medicine, UK with a portfolio of funding including the EU, Nick Simons Foundation, and the Wellcome Trust.

She is Principal Investigator for the IMPACT TB consortium project (funded by Horizon2020 and Nick Simons Foundation; www.impacttbproject.org), to scale-up and generate evidence to inform policy decisions on active case finding within the national TB program of Viet Nam and Nepal.

She is also Principal Investigator for the Epidemic Intelligence consortium project on COVID-19 sequencing. Other research interests span the full spectrum of the challenges in TB elimination, from phylogenetic evolution and virulence of the bacilli to clinical treatment trials and socioeconomic aspects.

She was previously based at Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam for eleven years where she was Head of the Tuberculosis Research Group and a University Research Lecturer at Oxford University, UK.

She has published over 100 articles in international peer-reviewed journals, including high impact articles in Nature Genetics, Science Advances and Lancet Infectious Diseases.

She serves on grant review panels, DSMB and National Advisory Boards for TB.