Buddha Basnyat—tackling typhoid and other infections in Nepal

Buddha Basnyat comes from a military family and grew up in Kathmandu, Nepal. "My father suggested military service might not be the best career for me, and I think he was right!", Basnyat told *The Lancet Infectious Diseases*. But his inspiration for medicine came from an unusual source: the books of the Scottish physician-turned novelist, AJ Cronin. He explained: "In one book, *The Citadel*, the hero is a general practitioner based in Wales, UK, dealing with tuberculosis, typhoid, and other diseases consigned to the past in high-income countries, but that are seen every day in Nepal". Cronin's influence meant Basnyat was as much interested in the humanitarian side of medicine as the scientific side. As Nepal had no medical schools in the 1970s, he attended the Government Medical College in Patiala, in neighbouring India, and then returned to Kathmandu for an internship supervised by missionary doctor John Dickinson at Shanta Bhawan Hospital. "John was a great mentor who schooled me in tuberculosis and typhoid, and also another common condition in Nepal I knew nothing about—altitude sickness", explains Basnyat. Dickinson saw Basnyat's potential, and helped secure a Masters course for him in respiratory physiology at Foothills Hospital, University of Calgary, Alberta, Canada. Despite the initial culture shock, it was a tremendous experience where Basnyat would learn critical thinking and also basic science research including driving ventilation with carbon dioxide to study upper airway receptors.

He returned to Kathmandu in 1984 with his respiratory physiology degree, and with the desire to be US board-certified in medicine. Luck struck again, as Basnyat met Phoenix-based physician Brendan Thompson, a tourist in Kathmandu. "Despite hardly knowing me, Brendan worked relentlessly to get me an internal medicine residency place at the Good Samaritan Hospital in Phoenix, Arizona, in 1986", he explained. There, Basnyat learnt all he could on internal medicine using the *Harrison's Textbook on Internal Medicine* as his guide—a book in which today Basnyat himself has a chapter on altitude sickness! He was joined in Phoenix by his wife Geeta and their two young children, but Basnyat wanted to eventually return to Kathmandu and, after saving money to build a house they moved back in 1989. He then taught physiology at the Institute of Medicine in Kathmandu, saw patients in a travel medicine clinic he set up, volunteered at Patan Hospital, and led treks in the Himalayas for a California-based company.

In 2001, Basnyat did a landmark study showing that 250 mg of acetazolamide was a sufficient dose to prevent acute mountain sickness, compared with 750mg dose recommended by experts but that caused extensive side effects. The study, a randomised controlled trial (RCT) among Mount Everest trekkers, inspired his love for conducting RCTs. And with UK doctor David Hillebrandt, he helped establish an International Diploma in Mountain Medicine.

Basnyat has just retired from his role as director of the Oxford University Clinical Research Unit-Nepal (OUCRU-NP), hosted by Patan Hospital and the Patan Academy of Health Sciences in Kathmandu, Nepal, although he will continue as chairman of OUCRU-Nepal. The concept of OUCRU-Nepal came about after Basnyat wrote a letter to the editor of *NEJM* about a review article on typhoid fever in 2002. Some of the authors of the review, including current director of the Wellcome Trust Jeremy Farrar, then based at the Oxford Unit in Vietnam, and Guy Thwaites decided to visit Basnyat at Patan Hospital. "They saw how rampant typhoid was in Nepal, and wanted to help. And that is how OUCRU-Nepal came into existence".

Backed with OUCRU funding and support, Basnyat and his Nepal team began to carry out multiple therapy-changing RCTs in typhoid fever, some published in this journal. One seminal study clearly showed the danger of using fluroquinolones (originally the drugs of choice) in the treatment of typhoid fever in South Asia. The findings helped WHO make changes to typhoid treatment guidelines.

Later, with the help of Andrew Pollard from the Oxford Vaccine Group, Basnyat and his team (notably Mila Shakya) were able to conduct the typhoid conjugate vaccine trial, with interim results in *NEJM* in 2019 and final results in *The Lancet Global Health* in 2021. The vaccine efficacy was about 80%. The Nepali Government, after initial resistance, rolled out the vaccine in April 2022 with the support of GAVI. Some 8 million children have now been vaccinated. Basnyat has also been active in COVID-19 research; Nepal joined the RECOVERY trial for COVID-19 treatment in hospitalised patients which is the largest trial of its kind in the world. After the UK, Nepal is the next largest contributor of participants.

Basnyat hopes his successor as OUCRU-Nepal director, Abhilasha Karkey, will be able to expand into trials in other diseases such as typhus, tuberculosis, and dengue. He laments that South Asian countries are not part of the latest tuberculosis vaccine trial despite South Asia being the biggest hub for tuberculosis. Now that his own work has slowed down, he will have more time to visit his family and friends in Nepal and abroad including his son and daughter, both in the medical profession in the USA. Basnyat laughs: "I even dust off and re-read the old AJ Cronin novels from time to time just for nostalgia!"

Tony Kirby