Palliative care for drug-resistant tuberculosis: when new drugs are not enough

The availability of new and repurposed drugs for the treatment of drug-resistant tuberculosis (DR-TB) provides hope in a field in which treatment options are severely limited and treatment success rates rarely exceed 50%. Despite the ongoing search for shorter, more tolerable, and more efficacious treatment regimens, DR-TB remains a death sentence for a considerable proportion of people affected. Additionally, these patients must bear debilitating side-effects of centuries-old medication, along with social isolation, stigma, loss of income, and psychological distress. Despite reports of reduced mortality among patients receiving bedaquiline, low treatment initiation rates and delayed access to new drugs means that, for the foreseeable future, a large proportion of patients with DR-TB will still be considered to have a terminal illness and will require integration of palliative care into the management of their condition.

In the traditional understanding, palliative care is only instituted in the terminal phase of an illness, once life-prolonging or curative treatment has ended, and the focus is on preparing the patient and family for death. However, the literature suggests that palliative care is potentially beneficial when introduced at the time of diagnosis of a serious or life-limiting illness.

To highlight the benefits of this integrated approach, we describe here the journey of a young person who, despite having had access to an optimised treatment regimen with new and repurposed second-line TB drugs, finally succumbed to pre-extensively drug-resistant (pre-XDR; resistant to rifampicin, isoniazid, and either a fluoroquinolone or an injectable agent) pulmonary TB at the age of 28 years.

Thulani (not his real name) lived for most of his life in Khayelitsha, an informal settlement near Cape Town, South Africa. Few health-care providers in Khayelitsha are trained in palliative care and the few existing palliative facilities in Cape Town are unable or disinclined to accept patients with DR-TB because of the high risk of transmission. Therefore, patients in whom second-line treatment fails are often discharged from medical services following withdrawal of curative therapy and are sent home with little or no ongoing care and support.

Thulani was 27 years old when he presented to his local clinic with TB symptoms in March, 2015. He had previously been successfully treated for drug-susceptible TB in 2011. Tests on his sputum samples revealed a diagnosis of multidrug-resistant TB (MDR-TB) and he commenced the standard 20-month treatment journey as an outpatient in April, 2015. He was unemployed and lived alone with no significant close contacts other than his uncle's new wife who visited him occasionally. He reported feeling stigmatised in his community as he was transgender and aware of perceptions that TB is linked to HIV infection, even though he had tested negative on multiple occasions.

After 3 months of daily painful intramuscular injections and at least 15 tablets every day, his monthly sputum cultures eventually converted to negative (no bacteria grown, indicating a favourable response to treatment). Because Thulani was feeling much better, he interrupted treatment for about 6 weeks before returning to clinic with recurrence of symptoms. He received one-on-one adherence counselling, with a strong focus on identifying challenges that made it difficult for him to continue treatment. Unfortunately, despite good adherence to treatment over the next few months, he began to lose weight and abscesses developed at the site of the intramuscular injections. Sputum cultures eventually reverted to positive. In December, 2015, after 8 months with no sputum culture conversion and ongoing clinical deterioration, MDR-TB treatment was considered to have failed and so the injectable agent was withdrawn and he commenced a strengthened regimen including bedaquiline, linezolid, and clofazimine. At that point, further analysis of the latest positive sputum culture indicated acquired resistance to the injectable agent in addition to MDR-TB (ie, pre-XDR-TB), thereby further confirming the necessity for the strengthened regimen that was offered.

After 6 months of daily attendance at his local clinic and adherence to the strengthened regimen (14 months of second-line treatment in total), the patient had not gained weight, his chest X-ray showed extensive bilateral disease (therefore not eligible for surgical intervention), and his sputum cultures remained positive, indicating pre-XDR-TB treatment failure. Until this point, the management of this patient was predominantly curative, with a focus on optimising adherence and strengthening the treatment regimen to offer him the best chance of cure. However, it must be noted that the clinical management also incorporated aspects of palliative care from early on in his treatment journey. Both the patient and his aunt, the only relative supporting him at that time, received verbal and written information from lay counsellors about his disease during sessions in the clinic and at home, and he was invited to join monthly peer support groups with other patients. Patient-centred care focused on symptom management, continuity of care, and one-on-one adherence counselling sessions.

By August, 2016, Thulani was thin, wasted, and struggling with shortness of breath, which limited his activities and kept him mostly housebound. His case was presented to the provincial DR-TB review committee

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(convened by the Department of Health to review individual cases and advise on clinical, medico-legal, and ethical issues) and the national TB clinical advisory committee for guidance; the expert recommendations were to withdraw treatment and manage palliatively. Over multiple counselling sessions, the clinicians and counsellors (with whom the patient had a therapeutic relationship) used Buckman's principles for breaking bad news to inform the patient of this decision and his likely prognosis. The team acknowledged the patient's denial of his situation as a phase in the grief cycle and respected the patient's autonomy and his request to continue any treatment that was still available to him, acknowledging the importance for him not to feel that all hope was lost.

For **Buckman's protocol** see *Oncologist* 2000; **5:** 302–11

The new care plan for Thulani focused on symptom assessment and management, contacting next-of-kin with whom Thulani reported some level of relationship, and practical end-of-life planning, alongside ongoing TB treatment. He was given a fan and his doctor prescribed oral morphine tablets for self-administration as required for his shortness of breath. Short-term admissions to the local sub-acute inpatient DR-TB facility enabled access to oxygen and nursing care as needed. This facility is the only sub-acute inpatient facility in Cape Town that caters specifically for patients with DR-TB in a community setting. Although not a hospice, it is currently run by a local non-governmental palliative care organisation and provides two beds for palliative management of patients in Khayelitsha. All other hospices in Cape Town are unable to accept patients with TB because of infection control concerns.

The patient support team arranged for collection and delivery of his TB medications and morphine tablets from the clinic each week, to either his home or the inpatient facility, and advised him on infection control precautions in his house in the event of visitors. An emergency action plan was put in place—the patient was provided with a bucket and towels in the event of haemoptysis, along with emergency contact numbers and a laminated letter containing relevant clinical details in case of emergency admission to hospital.

Thulani's emotional and clinical condition soon improved; his level of activity increased and the next four monthly sputum cultures reverted to negative. Ongoing counselling still focused on realistic expectations regarding the prognosis, but on request from the patient, the clinical team agreed to explore other possibilities to further improve his small chance of cure. In March, 2017, an application was approved to commence a salvage regimen that included privately procured drugs, delamanid and meropenem; the latter was administered through an intravenous port that was surgically inserted for easy administration of the drug but necessitated admission to hospital. The established palliative care pathway provided continuity of patient-centred care alongside the reintroduction of curative care and necessitated ongoing communication between staff in the hospital and the patient's local care facilities.

Over 4 months on the salvage regimen, Thulani continued to deteriorate with ongoing weight loss and increased doses and frequency of morphine needed to control his symptoms. His sputum cultures reverted to positive and the intravenous port had to be removed because of skin breakdown and poor healing at the wound site. Despite his own conviction that he was slowly improving, he agreed to be transferred back to the sub-acute inpatient facility in Khayelitsha; here he was afforded his own room to preserve his privacy and dignity and the end-of-life pathway was implemented. TB treatment was eventually withdrawn only when the patient felt too weak to swallow his tablets and he agreed to stop. Other medical interventions addressed management of pain, breathlessness, and secretions, and the entire multidisciplinary team provided emotional support as well as any information requested by the patient. During his short stay in this unit, the patient was encouraged and assisted to reconnect with estranged family members and friends who visited to provide him with companionship and spiritual support in his last days. In June, 2017, Thulani passed away peacefully, surrounded by some family members and other people he had known and trusted throughout his treatment journey.

This young person's story illustrates the complexity of the challenges associated with managing DR-TB. The concept of palliative care is often misunderstood by health-care workers and policy makers. Rather than being a strategy to be implemented after all else fails, palliative care encompasses holistic management of the patient right from the diagnosis of a life-limiting illness. Early management of treatment side-effects and assessment of physical, emotional, and spiritual pain constitute the basis of effective DR-TB care, after the initial diagnostic interventions and treatment decision making. The principles of basic palliative care can and should be incorporated into the clinical training of all individuals involved in the management of DR-TB.

Unfortunately, patients like Thulani are often referred to as having failed treatment. However, it is more likely that the patients themselves have been failed; failed by their bodies that no longer respond to treatment, failed by friends and family who ostracise and stigmatise them for having this disease, failed by the drugs that are toxic, arduous, and largely ineffective, and failed by a health-care system that requires patients to conform to its rules and restrictions rather than adapting to patients' specific needs. Integration of palliative care principles therefore remains essential to the management of individuals with DR-TB.

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