REFLECTIONS: NEUROLOGY AND THE HUMANITIES

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Reflections for October

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TOUGH CHOICES

Loveness Mwinga (not her real name) steps out of my sparsely furnished clinic at Chikankata Hospital and into the bright Zambian sunshine. She is tired, having walked for 4 hours to make it to her follow-up appointment with the Epilepsy Care Team and collect her 3-months' supply of phenobarbital. For all its potential side effects, the drug has been a lifesaver for Loveness. Before she began treatment, she experienced seizures almost weekly. Without warning, her convulsions would begin with falling backwards and then violent whole body spasms. She would awaken surrounded by cautious observers, urine and feces soaked, humiliated. The bush tea she was given to drink daily by the ng'anga (traditional healer), though costly, had done little to ease the problem. Loveness lived in fear of injury—a woman in the neighboring village had a seizure while drawing water from a nearby stream and drowned as onlookers, frightened that the angry spirits causing the seizure might leap onto them, debated whether it was safe to help her until it was too late to intervene.

When the seizures continued to occur regularly despite the traditional medicines, Loveness' husband relocated her to an older dwelling a few yards distant from the communal living area in her village. She took her meals alone. She prayed for the fits to leave her and not return. It was only after she had a seizure while preparing nsima (maize porridge, in this case cooked over an open fire) and was admitted to the hospital's burn unit that someone told her there was a medication that could stop the fits. Since beginning treatment, the seizures rarely occur. Her life has been transformed. She has been able to move back into the family home. The other villagers smile and laugh with her again. She and her husband are expecting another child after the harvest.

As part of her antenatal care, Loveness attended the Maternal and Child Health program's clinic. It is here that she was told that she is infected with HIV, and that there are important medications she can take that will protect her child from the disease and will also help keep her healthy. The midwives referred her to Muka Buumi (muka buumi means "mother/milk of life") Clinic for the antiretroviral treatment. Her husband, though not willing to come

for testing himself, allows her to come for the appointments. Loveness feels fortunate that there are some tablets that can help her seizures and other tablets that can also keep the slimming virus at bay. She now prays that both the medications she needs will be in stock when she travels to the clinic for her appointments.

What Loveness does not know and what I contemplate as she crosses the road from our Epilepsy Care Team office to queue outside of Muka Buumi is that the 2 medications she has come to collect, phenobarbital and Triomune (a fixed-dose combination tablet containing stavudine, lamivudine, and nevirapine), should not be prescribed together. Phenobarbital was formulated in 1904. In developed countries, it has been largely replaced by newer agents with fewer interactions and a better side effect profile. The enzyme induction properties of phenobarbital means that coadministration of phenobarbital and Triomune likely results in insufficient antiretroviral drug levels, suboptimal viral suppression, and opportunities for the HIV virus to develop resistance to one or more components of this critical HIV medication. Nevirapine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), is particularly affected by enzyme-inducing agents. And the single mutation that allows the HIV virus to develop resistance to nevirapine imparts resistance to the entire family of NNRTIs. The phenobarbital-Triomune combination has implications for Loveness' health, but the public health implications of this combination reach far beyond the borders of Zambia. Our global armamentarium of antiretroviral agents is limited even when cost is not the issue. As 2008 experiences with an extremely drug-resistant tuberculosis case in a US traveler has shown us, air travel has indeed made our world a smaller place. Public health crises in far-flung Africa are not so distant from US shores. We ignore these problems at our own peril.

But what to do for Loveness and her baby? The World Health Organization supports phenobarbital's use as the first-line treatment for epilepsy in resource-poor settings and at <\$5 per person per year for treatment, phenobarbital is the only anticonvulsant that the Zambian public health sector can afford to purchase. Triomune is substantially more

expensive at \sim \$198 per person per year, but the second-line antiretroviral agents that could be used with an enzyme-inducing agent are almost \$500/year and are simply not available at most of the HIV clinics in the region. Newer anticonvulsants that are not enzyme inducers are even more inaccessible at \sim \$1,800 per year.

Loveness is not unique. There are 4.6 million people who require antiretroviral treatment in Africa and although exact figures are not available, ~42.5 million people in the developing world have epilepsy. The overlap between these groups is not trivial. We see them almost daily in our Epilepsy Clinic.

I have only one medication to offer Loveness for her epilepsy. Muka Buumi has only Triomune to treat Loveness and protect her unborn child from the ravages of HIV/AIDS. Shall I protect the public good and withhold the epilepsy medication that has so transformed her life? If I do, how long before she is readmitted for seizure-related burns or injuries or abandoned by her family and village? Will she find the life as a perpetual "epileptic outcast" in her community worth living? Or shall we provide the treatments we have and await the time when Triomune will no longer be effective? I choose to care for the patient in front of me. As Loveness slips into Muka Buumi Clinic, I worry about the impact of my decision on her HIV care and I ruminate on the future hypothetical patients who may find themselves with a form of HIV that will not respond to available treatments.