Multi-Drug resistant TB treatment at AngloGold Ashanti

In recent months, media articles have raised the issue of multi-drug resistant (MDRTB) and Extensively Drug Resistant Tuberculosis (XDRTB) in Southern Africa and internationally. This follows both a drive to highlight an international awareness campaign and the detection of an XDRTB strain in KwaZulu-Natal, which is a new mutant virulent strain that had not previously been identified.

MDRTB refers to Multi Drug Resistant TB where the TB organism demonstrates resistance to at least Isoniazid (H) and Rifampicin (R), two of the most effective first line anti-TB drugs available. XDRTB stands for Extensively (or Extremely) Drug Resistant TB, where the TB organism demonstrates resistance to one of the second line injectable drugs (Kanamycin (Km), Amikacin (Am), or Capreomycin (Cm)) and to the Fluoroquinolones.

A global perspective

According to the World Health Organization (WHO), 8.9 million new cases of TB were reported in 2005, with 80% of these in 22 highest-burden countries. South Africa is placed at fifth highest in burden of disease and seventh highest in disease incidence. Further, of the 1.7 million TB related deaths in 2004, 98% were in the developing world. MDRTB is present in 102 of 109 countries which report TB statistics to the WHO.

The WHO estimates suggest that 424,203 MDRTB cases were detected in 2004, representing 4.3% of all new and previously treated TB cases. More than half of these were in China and India, while the highest estimated prevalence was in countries of the former Soviet Union and certain provinces of China. This represents a 55% increase over the estimates for 2000.

The first global survey of TB culture and drug sensitivity testing showed that 10% of global MDRTB bacterial isolates fulfilled the criteria for XDRTB. Of MDRTB isolates detected in Africa, less than 1% were XDRTB. This may not be a true reflection of the situation and might reflect the lack of cultures (TB bacterial samples) being tested in Africa (owing to lack of infrastructure and the high cost of testing).

TB in South Africa

Not only is South Africa experiencing a high burden of TB cases, this is negatively influenced by the high rates of HIV infection in the country. The South African mining industry has seen a steady rise in the incidence of TB over the past 20 years, fuelled by the HIV epidemic and, to a lesser extent, by the prevalence of silicosis.

Identifying the outbreak of XDRTB in KwaZulu-Natal has been facilitated by the application of DNA technology. The organism – named the KZN strain – demonstrated particular virulence, causing 52 deaths in 53 patients in the initial case finding report whilst demonstrating resistance to all available treatment. Further investigation identified the strain in patients in 28 hospitals in KwaZulu-Natal, but not necessarily in the severely resistant form. The KZN strain has not been identified among AngloGold Ashanti employees.

TB in AngloGold Ashanti

Currently the TB incidence within AngloGold Ashanti's South African operations is estimated at a rate of 3,000 per 100,000 individuals. AngloGold Ashanti Health's TB Control Programme is

robust, incorporating and exceeding the criteria stipulated by the South African National TB Control Programme Guidelines, and the Department of Mineral and Energy Guidelines for the Control of TB in the Mines.

Recent TB case finding reports indicate that between 85% and 90% of the current TB cohort (employees with TB) are also infected with HIV. Despite the TB Control Programme (with outcomes which exceed the WHO objectives of 85% successful treatment outcomes for new TB cases), the incidence of TB remains high.

MDRTB-infected patients were first identified at AngloGold Ashanti in 1987. Following a noted increase in the number of patients presenting with MDRTB in 2003, a combined research project was initiated at AngloGold Ashanti's request with the Department of Biomedical Tuberculosis Research at the University of Stellenbosch using DNA fingerprinting technology to evaluate the epidemiology and identify the possible causes. Within the cohort of MDRTB, the health service currently has three patients who meet the criteria for XDRTB, where the disease is not responding to the available medication. These patients obviously pose a threat to other patients, health care workers and visitors.

Two of the six classes of second line alternative drugs used for the treatment of MDRTB were previously not available in South Africa. The health service has since remedied this situation via the intervention of the Medicines Control Council (MCC), in the event that any cases of the virulent strain of XDRTB (as identified in KwaZulu-Natal) manifest within AngloGold Ashanti.

A particular area of concern is that, with increased exposure, health care workers naturally have a higher incidence of TB than lay people and consequently a higher incidence of MDRTB. Since 1999, four health care workers in service are known to have contracted MDRTB; one has recovered and three have died.

The MDRTB risk to health care workers has prompted even greater infection control effort in our health facilities including; provision of special respiratory protective equipment for staff, ward ventilation control measures, installation of UV lights and a six monthly medical surveillance programme.

AngloGold Ashanti's response to MDRTB and XDRTB

The average incidence of MDRTB in the West Vaal hospital in the Vaal River operations over the last four years (2002 to 2006) is 5.3% of all TB cases. The WHO defines an MDRTB 'hot spot' as an area with rates of 7% and above. States in the former Soviet Union and Eastern Europe, for example, have MDRTB rates of 10 to 14% and higher.

Mortality as a result of MDRTB is much higher than that associated with normal TB. Strongly influencing that mortality rate is the presence of HIV infection in the patient.

Of the total cohort of 140 patients being followed:

- 20% were cured
- 1.4% were treatment failures (XDRTB)
- 32% died, although not necessarily from the MDRTB
- 7.1% were transferred out to other appropriate facilities
- 7.9% left employment voluntarily
- 23.6% were still on treatment
- 7.9% of patients who had laboratory evidence resistance but without clinical evidence of disease are being followed up (with negative subsequent laboratory tests)

The drug cost for treating normal TB is approximately R4 per day and R155 per day for MDRTB.

In response to the presence of and increase in MDRTB patients, AngloGold Ashanti Health has set up an Isolation MDRTB ward at the West Vaal Hospital where patients with confirmed MDRTB are treated. This is the only facility of its kind outside of the state facilities in South Africa.

A comprehensive strategy has been developed in the face of rising MDRTB and the detection of a few XDRTB cases. Elements of the strategy include:

- Transmission and environmental controls to limit the spread of the disease, including early identification and limiting the spread in the clinical environment;
- Patient-centred controls, which include the promotion of cough education and etiquette, identifying and fast tracking coughing patients through clinic and hospital waiting areas and contact tracing;
- Staff-centred controls, including ensuring that staff wear personal protective equipment (PPE) in all designated high risk areas;
- More efficient treatment follow-up, particularly for treatment defaulters;
- Monitoring and surveillance of statistics; and
- Information, education and communication.

All of the above are normal elements of well run 'drug sensitive' TB control programmes and strict application will do much to reduce the incidence of MDRTB and XDRTB

Despite having a sophisticated TB laboratory on site (that makes use of up to date and current best practice microscopy and culture technology) it may still take from two to eight weeks to confirm the diagnosis of normal TB or MDRTB. This prolongs the potential infectious period before isolation of patients in the MDRTB ward can be justified. The possibility of transmission of normal sensitive TB or MDRTB strains in the setting of a high HIV prevalence in the population is therefore a significant reality.

Rapid identification of MDRTB strains using DNA technology such as that used at the University of Stellenbosch has the potential to confirm diagnosis within 48 hours on a single sputum sample. At present this is however still a research tool and as such is expensive and available in only a few specialised laboratories. It requires development into a form that can be performed at any laboratory.

The health service is currently investigating the introduction of rapid techniques to identify resistance to Rifampicin (Rifampicin resistance is a surrogate marker of MDRTB as nearly all cases of Rifampicin resistance are associated with Isoniazid resistance, which fulfills the diagnostic criteria for MDRTB), with plans to have this diagnostic regimen up and running for routine use at the West Vaal Hospital TB Laboratory in the first quarter of 2007. This could result in the current delay in identification of possible MDRTB patients being shortened to 48 hours, making it possible to institute appropriate isolation infection control measures for the suspects much earlier, thus preventing spread of the condition.

According to Dr Alistair Calver, senior specialist physician at AHS, "The biggest challenge to achieving higher successful outcome percentages is the fact that our mortality rates from other AIDS-defining conditions within our TB cohort is high. This reflects a need to get more of our HIV infected employees onto our Wellness Program and Anti-Retroviral Therapy (ART) at an earlier stage before they become ill."