

rural conference

"TB in the World of HIV"

Port St Johns 19 - 21 May 2005



Report and Recommendations

TABLE OF CONTENTS

Introduction	3
Attendance	4
The Objectives of TB Conference	5
Interaction Of Hiv And Tb	5
Report Of Tb Programs Of Qaukeni And Nyandeni Districts	7
Report Of Hiv Program In Qaukeni	8
Better Diagnosis Of Tb Needed	10
Diagnosing Tb In Children	12
New Diagnostic Tools	12
Making Our Laboratory More Efficient	13
Treatment Of Tb	14
Tb Treatments And Antiretrovirals	15
Need To Integrate Tb And Hiv Services	16
Adherence To Treatment	16
The National Tb Control Program And Government Commitment	17
Interruption Of Drug Supply	17
Community Health Workers And Dots	17
Community Involvement And Health Promotion	17
Monitoring Our Tb Program	18
Operational Research	18
Conclusions	19

Introduction

Port St Johns, a small coastal town in the middle of the rural Eastern Cape, is situated in the former homeland of Transkei, now the Nyandeni local service area. In May 2005 a workshop was held in Port St Johns to discuss the TB and HIV epidemics in two districts of the Eastern Cape (Nyandeni and Qaukeni) and to plan a strategy to tackle the problem.

As in most provinces of South Africa, the Eastern Cape has been affected by both the TB and HIV epidemics. HIV sero-prevalence at ante natal units is 24% and TB incidence is 675 per 100000 people.

In 2003 the international NGO MSF – Doctors Without Borders started a comprehensive HIV program in partnership with the Nelson Mandela Foundation and the Eastern Cape Department of Health (ECDOH). This program now provides care for more than 5 000 people living with HIV at the twelve government clinics of Lusikisiki, in the Qaukeni local service area. It offers education, nutritional support, diagnosis, treatment and prevention of opportunistic infections. By the end of April 2004 it was also providing antiretrovirals to 700 adults and 43 children and monitoring them. Both Qaukeni and Nyandeni have been identified by the DOH as priority areas for TB care.

The National government of South Africa adopted the March 2000 Amsterdam “Stop TB” declaration and a strategic plan for 2001-2005 was put in place. This covered diagnosis and treatment, multi-drug resistance, sputum collection, prophylaxis, side effects of drugs, record keeping, notification and the protection of health workers. Despite strong investment from the government in ongoing support and training, and DOTS implementation, the cure rate for detected smear positive cases had not exceeded 65% by 2002 in many parts of South Africa, including the Eastern Cape.

For the last 2 years the numbers of persons accepting voluntary counselling and HIV testing (VCT) has increased exponentially in the Qaukeni district. This has shown that a large proportion of patients are co-infected with both TB and HIV. TB is the most common opportunistic infection in persons infected with HIV and is by far the major cause of hospitalisation and mortality amongst HIV infected patients. Thus one cannot tackle the one epidemic without tackling the other. Provincial policy is to offer comprehensive one stop services for co-infected patients. A major constraint in our districts is the scarcity of health professionals, which motivates further for an integrated TB/HIV programme.

More people are dying unnecessarily from TB these days in the Eastern Cape as TB may present differently in HIV infected individuals with more sputum smear negative pulmonary TB and an increase in extra-pulmonary TB. This requires a change in the current clinical practice with greater emphasis on those who have negative sputum smears by following this up with sputum cultures and by treating empirically while waiting for cultures or with the use of algorithms using clinical signs, chest X-ray and other criteria based on the response to broad spectrum antibiotics.

Please direct comments to: Dr Hermann Reuter, phone: 039 - 253 1611, fax: 039 – 253 1373, or email: msf.lus@mweb.co.za

Attendance

The conference brought together a number of role-players to listen to expert presentations in order to improve our understanding of TB and HIV and then to discuss and formulate new approaches to the challenges.

Represented from provincial department of health were:

Dr Bevan Monwabisi Goqwana – MEC for Health in the Eastern Cape
Ms Nomalanga Makwedini – Director of HIV/AIDS in the Eastern Cape
Ms Carol Sheard – Program Manager of TB in the Eastern Cape
Ms Dideka Seth – Program Manager for TB – HIV Integration in the Eastern Cape
Ms Liziwe Lunyawo – Program Manager for HIV – VCT in the Eastern Cape

District health managers included:

Ms Ndiniza – TB Program Manager for Qaukeni District
Ms Mofokeng – HIV Program Manager for Qaukeni District
Ms Mabandla – TB Program Manager for Nyandeni District

Experts in the field of TB, HIV and primary health care included:

Prof Gary Maartens – Advisor to National TB program, UCT, Groote Schuur Hospital
Prof Helmuth Reuter – Ukwanda Center for Rural Health, University of Stellenbosch
Dr Ben Marais – TB Paediatrician, University of Stellenbosch, Tygerberg Hospital
Dr Theunis Koetzee - Rural AIDS & Development Action Research, ProTest site, Limpopo
Dr Neil Martinson – HIV Perinatal Research Unit, Wits, Chris-Hani Baragwanath Hospital
Dr James Nuttall – HIV Paediatrician, UCT, Red Cross Children's Hospital
Ms Karen Shean – Brooklyn Chest TB Hospital
Dr David Coetzee – Public Health and Family Medicine, UCT
Dr Menzeleleli Msauli – Family Medicine, Unitra/Walter Sisulu University
Dr Pamela Mda – Regional Training Centre, Umtata General Hospital
Dr Xola Kanta – General Practitioner, Lusikisiki
Dr Don O'Mahony – Eastern Cape chair of Academy of Family Practice / Primary Care
Dr Martha Bedelu – MSF Lusikisiki
Dr Chrysanthus Foncha – MSF Lusikisiki
Dr Peter Saranchuk – MSF Khayelitsha
Dr Eric Goemaere – MSF South Africa

Health workers from Qaukeni and Nyandeni included:

Sixty clinic and hospital nurses, private and DOH doctors, pharmacists and laboratory managers

The community was represented by:

TB service users, HIV support group members, community health care workers, treatment activists from the Treatment Action Campaign and other community organisations.

During the opening ceremony which was held by candle light due to a power failure the aims and objectives of the conference were outlined and messages of support were presented from the Rural Doctors Association of SA (RUDASA) and the Treatment Action Campaign (TAC).

The Objectives of TB conference

1. Improve TB care and integrate TB and HIV services
2. Empower and motivate health care workers to deal with TB and HIV
3. Understand the best way to diagnose TB
4. Improve communication and referral to hospital
5. Encourage community health workers to respond to both the TB and HIV epidemics in an integrated way
6. Get support from the provincial TB control program in solving key problems e.g. drug supply

Outcomes we aimed to achieve included:

Objective 1: Improve TB care and integrate TB and HIV services

- Have a more patient-centred care
- Ensure good quality sputum collection for all suspects
- Evaluate diagnostic algorithms for smear negative TB
- Ensure health workers concentrate on all aspect of care of HIV/TB co-infected patient
- Reinforce importance of Co-trimoxazole prophylaxis
- Understand concurrent TB treatment and ARVs
- Plan how TB and ARV registers can be linked
- Implement a TB prevention policy for HIV patients
- Strengthen guidelines on management of TB in children
- Ensure good patient follow-up and recording
- Offer VCT to all TB patients and ensure all HIV patients are regularly screened for TB
- Emphasise patient empowerment with regard to TB similar to that of HIV program
- Plan a review of the TB program using “District Rapid Assessment Tools”

Objective 2: Empower and motivate health care workers to deal with TB and HIV

- Understand the seriousness of the impact of HIV on TB
- Solve common problems
- Stimulate teamwork from TB managers, nurses and communities
- Understand how ARV rollout can be used to strengthen the TB program

Objective 3: Improve communication and referral between clinic and hospital

- Evaluate and develop guidelines on which patients need to be send for CXR
- Understand tests that can be done to diagnose extra-pulmonary TB at hospital level
- Strategise on ways of keeping patients on streptomycin injections in low care wards
- Strengthen channels of communication.

Objective 4: Encourage community health worker to respond to TB in the same way as they respond to HIV

- Demonstrate and standardise tasks that can be done by community health workers
- Establish the role of TB support groups and self-appointed treatment assistants with CHW
- Show how TB and HIV CHW networks can be integrated
- Increase community awareness of TB.

Objective 5: Get support from the provincial TB control program in solving key problems

- Strategise on how to overcome human resource shortage
- Establish how to ensure drug supply continuity
- Improve laboratory support at provincial level (TB cultures and sensitivity)
- Establish what should be done for re-treatment cases of TB

Interaction of HIV and TB

In areas of high HIV-prevalence, the HIV epidemic undoubtedly contributes to the increased TB burden. Untreated HIV infection leads to progressive immune deficiency and increased susceptibility to infections such as tuberculosis. HIV is the strongest factor capable of promoting progression of mycobacterium tuberculosis infection to active tuberculosis both in people with recently acquired (exogenous re-

infection) and with latent mycobacterium tuberculosis infections (endogenous reactivation). The lifetime risk for active TB in an HIV-negative person is 5 to 10% while the *annual* risk in HIV-infected persons is 5 to 15%.

TB in HIV disease is associated with decreased survival. TB specific mortality is four-fold higher among HIV-infected patients than amongst the uninfected (17.8 and 4.4 deaths per 100 per year for HIV-infected and uninfected patients respectively). In Southern Africa, tuberculosis is the leading cause of mortality in HIV infected persons.

Table 1 and 2 show the increase of people with TB over the last few years. This increase occurred in spite of all efforts by the department of health to control TB.

Table 1: TB Cases in South Africa¹

	EC	FS	GP	KZN	LP	MP	NC	NW	WC	ZA
1996	-	-	-	-	-	-	-	-	-	109328
1997	-	-	-	-	-	-	-	-	-	125913
1998	31763	10857	19024	28637	5500	3985	10814	2877	28820	142277
1999	30990	8885	17450	34481	5825	5226	9043	4698	31566	148164
2000	28963	9414	24861	28039	4735	5339	12191	3896	33848	151286
2001	36520	13024	27622	39586	10619	6925	14277	4435	35687	188695
2002	48 130	14 221	30 515	52 016	10 098	6 536	17 612	5 642	39 650	224420

Source: Department of Health's National TB Control Program 2003 Fact Sheet and Health Systems Trust

Table 2: Incidence of TB, all types (per 100 000)

	EC	FS	GP	KZN	LP	MP	NC	NW	WC	ZA
1999	565	327	224	386	109	174	537	254	757	360
2000	425	341	320	317	86	178	448	345	810	349
2001	523	462	347	436	187	224	504	396	840	426
2002	675	497	376	565	173	207	635	481	919	497

Source: Health Systems Trust

As can be seen in Table 3 extra-pulmonary TB has increased significantly between 1996 and 2003, with most of this increase being attributed to the HIV epidemic.

Table 3: TB Cases by Type in South Africa

	PTB Cases	All TB cases	% PTB	% EPTB
1996	92380	109328	84	16
1997	104141	125913	83	17
1998	115537	142277	81	19
1999	118686	148164	80	20
2000	120075	151286	79	21
2001	144910	188695	77	23

Source: Health Systems Trust

¹Province abbreviations – EC: Eastern Cape; FS: Free State; GP: Gauteng; KZN: KwaZulu-Natal; LP: Limpopo; MP: Mpumalanga; NC: Northern Cape; NW: t; WC: Western Cape; ZA: South Africa

Report of TB Programs of Qaukeni and Nyandeni Districts

Qaukeni is made up of three local service areas: Lusikisiki, Flaggstaff, Bizana with a total population of 661 894. There are four hospitals and 39 clinics. Telephones were recently installed in seven clinics and most clinics rely on rain water collected from the roof.

Nyandeni is made up of two local service areas: Libode and Port St Johns with a total population of 461 600. There are four hospitals and 42 clinics. Most clinics have no electricity and only 11 have telephones. There are severe staff shortages, with only 50% of nursing posts filled and Qaukeni has no district pharmacist and no information manager.

TB indicators presented at conference

Indicator	Qaukeni	Nyandeni
All cases	1023	1279
Bacteriological coverage	42%	61%
Total PTB	844	
New smear +	336	60%
Smear conversion (Q4 2004)	75%	(New) 18,2% (76,4% not available) (retreat) 30,4% (62,7% not available)
Treatment completion (Q1 2004)	87%	11,2%
Cure rate	46%	12,2%
Interruption rate	18%	
Mortality rate	5%	3,8%

It was acknowledged that possible inaccuracies and incompleteness of data is due to shortage of staff and a backlog of entering data into the electronic system.

TB/HIV Integration in Qaukeni

27 of the 44 facilities (61%) in Qaukeni reported on these indicators.

Total number of TB patients: 1566
Number offered VCT: 528 (34%)
Number tested for HIV: 249 (47%)
Number tested HIV positive: 197 (79%)
Number on cotrimoxazole: 109 (55%)
HIV infected people screened for TB: 136
HIV infected with smear positive for AFB: 71

It was acknowledged that this might not be a true reflection as no reliable tool is used at clinics to document cotrimoxazole usage.

Challenges noted by TB program managers

The area is rural and underdeveloped. It is difficult to recruit and retain staff. As the TB program has to compete with other programs for human resources it is difficult to achieve target outcomes. However we strive to improve the management of TB and hope that this conference contributes to this aim.

There is a shortage of staff at both the department of health and National Health Laboratory Services. There is inadequate transport of specimens and communication of results back to the hospital and clinics. This makes case finding and monitoring difficult.

In spite of attempts to treat TB as a priority program there is an erratic drug supply to clinics caused by a combination of factors including shortage of nurses and pharmacists, inadequate ordering training and supervision, management problems at Umtata Central Medical Stores and the lack of communication and transport facilities.

High rates of treatment interruption rates, due to geographical distances to clinics and underdevelopment of rural areas results in poor treatment outcomes.

Data capturing is inadequate, especially as regards to entry into electronic register mainly due to shortages of staff.

Report of HIV program in Qaukeni

In 2003 MSF together with department of health implemented a comprehensive HIV program at the twelve rural clinics of Lusikisiki. VCT and MTCT programs were set up and, nurses trained in the management of opportunistic infections (OIs). Clinic held records were introduced and registers for monitoring purposes. In October 2003 the clinics began too to provide antiretrovirals.

The catchment population for the clinics of Lusikisiki is 156 853, and the HIV prevalence was 24% in the last antenatal survey. There is a severe shortage of health care workers with only 50% of nursing posts at clinics filled. This has remained constant over the last three years. However the workload has increased from 16 465 consultations in April 2004 to 27 275 consultations in April 2005. At Village clinic each professional nurse saw 78 patients per working day.

Implementing VCT

The following graph shows the number of people tested for HIV at clinics in Lusikisiki each month. It shows that on average 41% of people test positive for HIV.

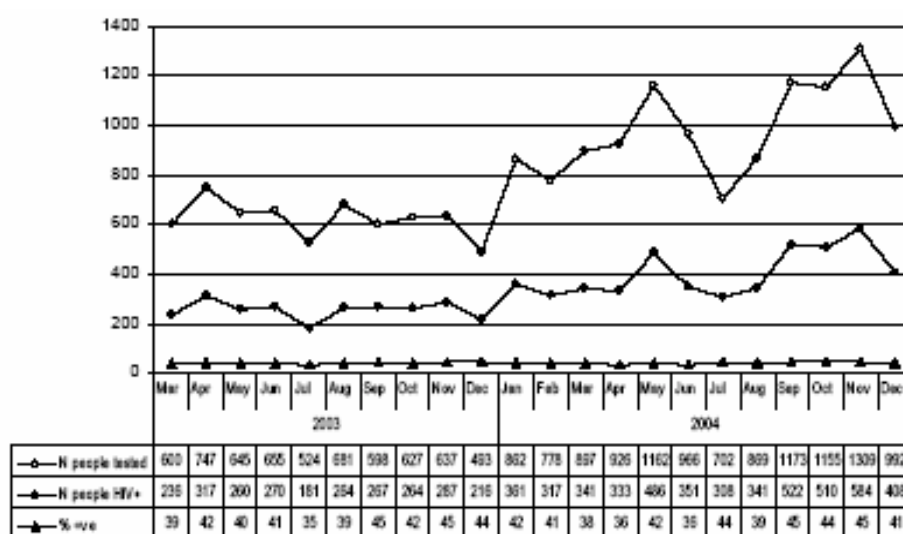


Figure 2. Monthly uptake of VCT and prevalence of HIV infection in all clinics and referral hospital since March 2003 until December 2004.

In 2003 about 600 people tested each month. There is a steady increase in 2004 and this may be as a result of ARVs being available, giving people an incentive to know their HIV status. But it also reflects that when counsellors were given more responsibility in the VCT program the number of people testing increased. In June and July 2004 counsellors attended training courses and as a result there was a marked decrease in the number of tests conducted.

Programme for the Prevention of Mother-to-Child Transmission prevention (PMTCT)

The table shows the number of women accepting VCT and the number that tested positive at a busy clinic of Lusikisiki. On average the acceptance rate of VCT was 69 % at the clinic with 28,5 % testing positive. Acceptance rate is up from 23 % in the previous year. The smaller clinics generally have a higher acceptance rate. Overall HIV prevalence amongst pregnant women on average is 31 %.

	New Pregnant	VCT offered	VCT done		VCT delayed		HIV +ve	
JAN	353	142	133	38 %	9	62 %	27	20 %
FEB	249	237	233	94 %	4	6 %	73	31 %
MAR	210	187	155	74 %	32	26 %	49	32 %

PMTCT is available at 38 of the 40 clinics in Qaukeni district. The national protocol is followed and a single dose of nevirapine is provided to the mother. However in Lusikisiki all HIV-infected women who have a CD4 cell count less than 200 are provided with triple-therapy. In October 2004 the district

pharmaceutical therapeutics committee agreed to conduct operational research on a more effective regimen for mothers with CD4 cell counts greater than 200, including AZT and single dose nevirapine. This was not implemented as the national department of health indicated that this would soon become the standard protocol. In June 2005 Qaukeni will start PCR testing for children born to HIV-infected mothers. Outcomes for children of mothers who used the nevirapine only protocol will be compared with outcomes for children of mothers who followed the AZT and nevirapine protocol.

Decentralising ARVs to clinic level

It was decided that every effort should be made to provide ARVs at the clinic rather than in the hospital in order to make ARVs more accessible to a rural population and to support good adherence. The graph below shows the monthly enrolment of patients on ARVs in Lusikisiki. By the end of April 2005 700 adults and 43 children were receiving ARVs.

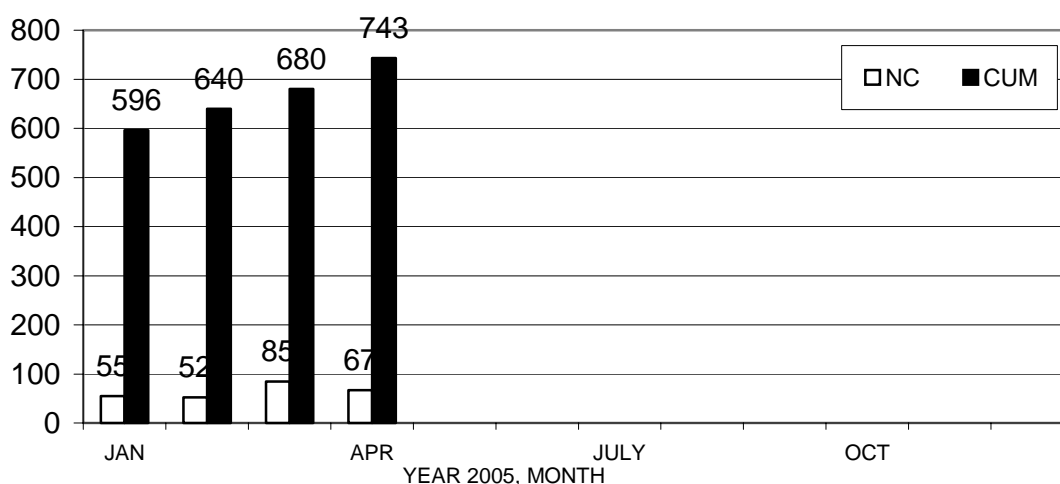
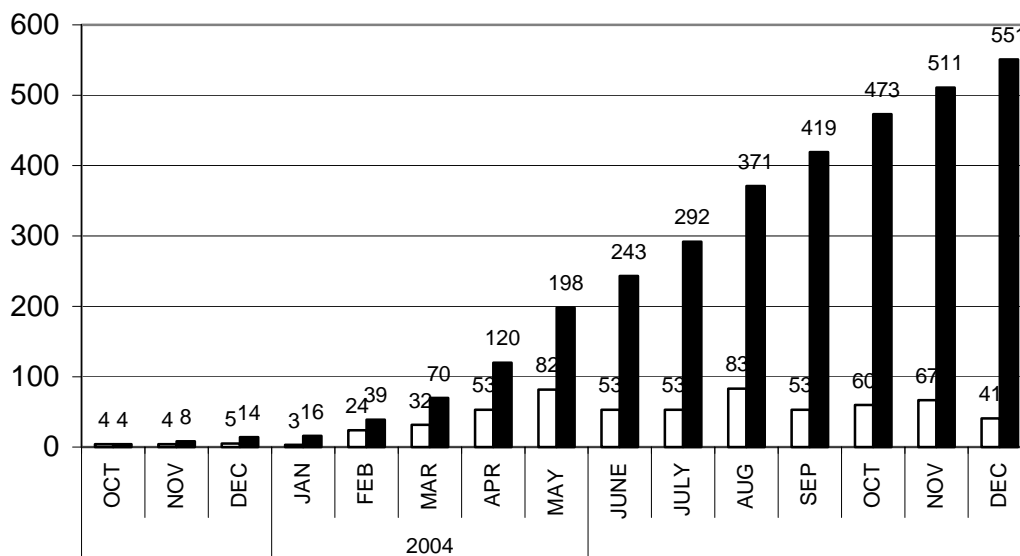


Figure 1. Number of patients enrolled on ART in Lusikisiki per month in 2003, 2004 and 2005 in both hospital and 12 referral clinics: cumulative (CUM) and new cases (NC).

The program has achieved good outcomes. After the first six months patients on ART had a median weight gain of 9kg (51kg to 60kg). The median CD4 cell count increased from 80 to 258 and 91% of patients had an undetectable viral load. There has been a high level of community involvement through the Treatment Action Campaign and adherence committees, based at all clinics have provided adherence

support. This may account for the high level of undetectable viral loads. There are thirteen ARV treatment points and there is no waiting list for ARVs.

With support from the Columbia University and the Regional Training Centre, hospitals and selected clinic in Flagstaff and Bizana started providing ARVs making this service accessible in the whole district.

Better Diagnosis of TB Needed

It is generally accepted today that it is more difficult to diagnose active TB in persons who are co-infected with TB as there is a greater rate of sputum smear negative TB. An MRC report on World TB Day, 24 March in 2000 reported in Kwa-Zulu Natal showed that 64,4% of TB patients were also infected with HIV. This year on World TB Day the MRC estimates 83,4% of TB patients to be co-infected with HIV in Kwa-Zulu Natal as reported by Anso Thom and Kerry Cullinan in Health-e on 24 March 2005. There is also an increase in cases of extra-pulmonary tuberculosis as seen in Table 2.

Because the diagnosis of active TB is more difficult in people with HIV, the diagnosis is often delayed and there is an increased risk of mortality. The delay in diagnosis also means that more people can be infected by the individual before he/she starts TB treatment.

We need better tests in order to diagnose TB more quickly and accurately. However there are no rapid test currently available. This should lower the mortality from TB. It is currently the number one killer of HIV-infected people in South Africa, with mortality nearly tripling in the past five years, see Table 4.

Table 4: TB Mortality in South Africa (% of all deaths)

	EC	FS	GP	KZN	LP	MP	NC	NW	WC	ZA
1997	4103 (9.2)	2008 (8.0)	2834 (4.3)	5880 (8.6)	1193 (5.4)	1198 (6.1)	669 (8.0)	1922 (7.8)	1703 (5.2)	21510 (6.9)
1998	-	-	-	-	-	-	-	-	-	28487 (7.7)
1999	6162 (11.6)	3014 (9.6)	4850 (6.5)	9114 (10.8)	1802 (6.3)	2166 (8.5)	819 (9.0)	3225 (10.1)	2533 (6.7)	33685 (8.9)
2000	-	-	-	-	-	-	-	-	-	42102 (10.2)
2001	8539 (13.1)	4185 (11.4)	7299 (8.5)	15176 (14.6)	2663 (7.7)	3500 (11.2)	1122 (10.8)	4540 (11.5)	3378 (8.3)	50402 (11.2)
2002	-	-	-	-	-	-	-	-	-	59951 (12.0)

Source: Stats SA

Routine work-up

Sputum smear examination (AFB) remains the cornerstone of TB diagnosis. When a person presents with a cough greater than two weeks, especially if associated with night sweats and loss of appetite and weight, that person should be investigated for TB with two good quality sputum samples. These samples should be sent to the laboratory as soon as possible. The results should be sent back to the clinic just as quickly. Unfortunately, this process is currently too slow in rural areas. Ways of improving the transport of specimens from clinics and the communication of results from the laboratory back to the clinics need to be sought urgently.

If both smears are negative, then the doctor or nurse should reassess the patient. If the patient still has symptoms of active TB, then another sputum sample should always be sent for TB culture.

Smear negative TB is more common in people living with HIV. In rural areas where turn around times are long and distances to clinics are great it is reasonable to take a specimen for sputum culture at the first visit over and above the two specimens for direct smear (AFBs) in people known to be HIV positive.

If TB is suspected in a person who has had previous TB treatment or who has been in contact with an MDR-TB patient a sputum specimen should be sent for smear, culture and sensitivity on the first visit (irrespective of HIV diagnosis) to test for the possibility of MDR-TB.

Smear-negative diagnosis

Because an HIV-positive person has a weakened immune system, that person's body will not form as many cavities in the lungs in response to active infection with TB. The person's sputum therefore will not contain as many acid-fast bacilli (AFBs). Brindle, Nunn et al² documented that HIV infected

² Brindle RJ, Nunn PP, Githui W, et al. Quantitative bacillary response to treatment in HIV-associated pulmonary tuberculosis. Am Rev Respir Dis 1993; 147:958-961

individuals had ten times less bacilli in their sputum. This is called paucibacillary TB. With increasing prevalence of HIV and TB co-infection it is estimated that paucibacillary TB now makes up 75% of TB in South Africa. Although less infectious than smear positive TB it still is infectious and usually stays longer undiagnosed. One study by Frieden³ showed that smear negative TB accounted for 15-20 % of transmission but other experts believe it is higher in countries with high HIV prevalence. A diagnosis of TB will be more likely to occur on a sputum culture which requires fewer AFB to reveal the presence of TB. Toman⁴ points out that sputum microscopy is likely to be positive when there are at least 10000 organisms per millilitre of sputum . In contrast, culture can detect far lower numbers of TB bacilli, with about 100 organisms per millilitre giving a positive culture according to van Deun⁵. An analysis of 109 consecutive patients diagnosed with TB in Khayelitsha showed that only 18 people were diagnosed with a positive smear. Another 37 patients were diagnosed with a positive culture and another 38 patients were diagnosed on clinical diagnosis as reported by MSF and UCT⁶. In fourteen published studies the proportion of smear negative PTB among HIV positive TB patients ranges from 24 - 61%⁷ with a weighted average of 28% of TB patients being diagnosed as smear negative. Considering increased rates of extrapulmonary TB amongst co-infected patients it means that if we rely on smear only we can miss 40 – 80% of TB diagnosis in people with HIV.

Unfortunately, a culture for TB takes 4 weeks (excluding time taken to get results back to the clinic and the patient). Waiting such a long time for a result can result in death from TB. We can use other investigations to be more confident about a diagnosis of pulmonary TB while waiting for the culture result. These include chest x-ray (CXR) and C-reactive protein (CRP).

In the absence of CXR facilities and laboratories to do a CRP blood test (as in many rural areas), there are other criteria that can help to suggest a diagnosis of TB while waiting for culture results. These include a lack of response to a course of a broad-spectrum antibiotic and a deteriorating level of function in the presence of TB symptoms.

Smear-negative Algorithm

All of the above criteria can be used to create a ‘Smear-negative Algorithm’ which can allow for empiric treatment with TB medication while waiting for the culture result, with a high degree of confidence that the diagnosis is active TB. The purpose of such an algorithm is to prevent death from TB when smears are negative by starting empiric TB treatment, without unnecessarily overloading the local TB program. Such a Smear-negative Algorithm will differ for urban and rural areas, depending on the availability of the different investigations.

A Smear-negative Algorithm in rural areas of the Eastern Cape will concentrate on clinical symptoms, deteriorating level of function, and ‘lack of response to antibiotic’ criteria. An algorithm in an urban area will in addition make use of CXR and CRP.

If a person improves on empiric TB treatment, this also increases the confidence of a diagnosis of smear-negative TB. Of course, before such a Smear-negative Algorithm can be put into place, there are certain basics that must be present in the TB program in the area. Problem with the supply of TB medication must be overcome, good community support must be available to limit the number of people who interrupt TB treatment, and there must be efficient reporting of sputum results by the laboratory back to the clinic.

Extra-pulmonary TB

TB can occur in most organs in the body. Often these people will have a negative smear and other diagnostic tools can be used to make a bacteriological or clinical diagnosis.

Pleura of the lung, pericardium of the heart – this will require a CXR or needle tap to diagnose. Lymphadenitis (inflammation of the lymph nodes) or skin (cold abscess or scrofula) – this will require a needle aspiration to diagnose

³ Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. *Lancet* 2003; 362 (9387) : 887 - 99

⁴ Toman K. *Toman's tuberculosis. Case detection, treatment and monitoring*, 2nd Edition. Geneva: WHO, 2004: 35-43

⁵ van Deun A. *Toman's tuberculosis. Case detection, treatment and monitoring*, 2nd Edition. Geneva: WHO, 2004: 35-43

⁶ MSF, Infectious Disease Epidemiology Unit, School of Public Health and Family Medicine, University of Cape Town. Report on the Integration of TB and HIV services in Site B Khayelitsha, February 2005: 9-10

⁷ Aerts D, Jobim R . The epidemiological profile of tuberculosis in southern Brazil in times of AIDS. *Int J Tuberc Lung Dis* 2004; 8 (6): 785-91

Bruchfeld J, Aderaye G, Palme IB, et al. Evaluation of outpatients with suspected pulmonary tuberculosis in high HIV prevalence setting in Ethiopia: clinical, diagnostic and epidemiological characteristics. *Scand J Infect Dis* 2002; 34 (5): 331-7

Meninges – this will require a lumbar puncture
Abdomin – this will require a sonar and/or needle tap
Bone and joints – this will require X-rays

Conclusion

TB is a curable disease if diagnosed early. But TB is harder to diagnose early in HIV positive people who make up the majority of people being diagnosed with active TB in areas where there is a high prevalence of HIV. Sputum culture should be available to diagnose TB when smears are negative, and a Smear negative Algorithm should be in place to allow early initiation of empiric TB treatment while waiting for the culture result. By integrating TB and HIV care we can prevent many unnecessary deaths from TB in HIV positive people.

Operational research should be conducted to Lusikisiki to determine to what level nurses can make a clinical diagnosis of smear negative TB at clinic level.

Diagnosing TB in Children

Although a child with HIV is more likely to get TB, most childhood TB is still in HIV negative children, due to the lower HIV prevalence amongst children when compared with adults. Nurses in the two districts report that there are few children being treated for TB, however paediatricians warn that this probably reflects substantial under diagnosing of TB in children in the districts.

Even though the TB program prioritises bacteriologically proven TB, it is rarely possible to make such a diagnosis in children. The diagnosis is usually made on clinical or empirical grounds based on the following criteria:

- o Presence of an adult contact
- o Presence of symptoms and signs
- o Reaction to tuberculin skin testing – (the Mantoux is preferred)
- o Monitoring of the weight over time – (over 1 - 3 month period, during this time the child should be dewormed and provided with food and iron supplements)
- o CXR findings – (this often plays a key role)

These criteria can be used in validated clinical algorithms.

Gastric aspirate and sputum induction improve the chance of a bacteriological diagnosis but are only feasible in hospitals or larger clinics. In older children, especially those older than ten years sputum can be collected for microscopy and possibly for culture.

At the moment tuberculin skin tests are not available at clinics in the two districts although a provincial spokesperson has stated that the Tine test should be available at clinics. A future alternative would be T-cell based serological blood tests (e.g. T-spot, Quantiferon gold) which can confirm previous exposure to TB like the tuberculin skin tests do however they are more sensitive especially in children with a weakened immune system.

It was emphasised to provide TB prophylactic treatment to high-risk children, i.e. children less than three years or those with a weakened immune system irrespective of age who have an adult TB contact.

New Diagnostic Tools

The fact that a large number of adults with TB are now smear negative, and that most TB in children is based on a clinical diagnosis, the conference expressed an urgent need for better diagnostic tools. Although no clear alternative could be identified yet, there are numerous promising tests that should be studied in operational research projects. Furthermore as this is a priority area, we should advocate that it be put on the political agenda and that funding should be made available for piloting new ideas.

The present range of new tests includes:

Faster TB culture

TB culture is more sensitive than smear, however it can take up to six 4 weeks to culture the organism. There are new fluid culture media that show a colour change faster than the presently used technique. This presents an improvement on the present gold standard.

Sputum induction

Ultra sonic nebulisers can be used with hypertonic saline solution to induce coughing. This stimulates cough and helps to draw out deeper sputum from the lungs. This improves the yields on smears and cultures and can be used for adults and children. However this needs a dedicated person to operate it and care has to be taken to sterilise the machine between each patient.

Phage Assay

This technique makes use of bacteriophages, viruses that infect bacteria. Sputum is placed on a culture medium. Phages are added. These phages infect TB bacilli. A virucidal is then added to kill all phages that did not invade the TB bacilli. The virucidal is neutralised. The culture is then incubated overnight and the phages that survived inside the TB bacilli grow. This test is very specific and its sensitivity is between that of a smear and of a culture. The benefits are that it is as cheap as a culture but provides a result much quicker. This technique is very promising as resistance can be determined within two days.

Nucleic acid amplification tests (NAA)

These tests are not feasible in rural areas as they require sophisticated laboratory and highly trained staff and they are still very expensive.

Antigen testing and other modalities

Antigen detection is promising but the problem is that they can not distinguish between latent infection and active disease.

The immune response and the production of γ -IFN still requires further development in order to identify markers such as suppression of Th1 immune response to differentiate active TB.

Testing the ADA is a good marker for ascites and pleural fluid in combination with the differential White Blood Cell count, but is poor for cerebro-spinal fluid.

Making our laboratory more efficient

The correct procedure for taking specimens was stressed.

- a. Collection of sputum should be supervised by a community health worker or nurse
- b. The procedure should be explained and conducted in a private but well-ventilated space
- c. The mouth should be rinsed with water, 2 to 3 deep breaths should be taken and then a deep cough to produce sputum
- d. The health worker should examine the sputum to ensure that it is purulent or mucoid sputum rather than saliva
- e. The sputum jar should be closed tightly
- f. Ensure that the jar is correctly labelled
- g. Store the jar in a fridge if it is not sent to laboratory on the same day

A high workload was reported at the laboratory. There is one technologist who examines the sputa under the microscope, prepares all cultures and urines for analysis. The AFB technique involves decontamination for 30 minutes, concentrating specimens for 30 minutes, and then smears are made and stained with kinyoun and left to air dry for 20 minutes. Each smear is examined under a light microscope and only reported negative after 15 – 20 minutes of looking at 100 fields. Positive smears are reported faster depending on the number of bacilli present. All positive smears are counter checked by a second person and ten percent of negative smears are checked for quality control purposes.

In St Elizabeth laboratory 40 slides are done on average per day by a single person who also does other microbiology work. WHO recommends that one technologist should examine a maximum of 16 slides per day.

It was recommended that the NHLS should either employ more technologists or invest in a fluorescent microscope which is more sensitive and faster. The sensitivity of a fluorescence microscope compared to that of ZN staining improves by 15 – 18 % (Githui⁸, Kivihya-Ndugga⁹). About fifteen times as many fields can be scanned with this microscope in the same period. Although a fluorescence microscope is

⁸ Githui W, Kitui F, Juma ES, Obwana DO, Mwai J Kwamanga D. A comparative study on the reliability of the fluorescence microscopy and Ziehl-Neelsen method in the diagnosis of pulmonary tuberculosis. East Afr Med J 1993; 70 (5) : 263 - 6

⁹ Kivihya-Ndugga LE, van Cleeff MR, Githui WA, et al. A comprehensive comparison of Ziehl-Neelsen and fluorescence microscopy for the diagnosis of tuberculosis in a resource-poor urban setting. Int J Tuberc Lung Dis 2003; 7 (12) : 1163 – 71.

about 4-5 times more expensive than a light microscope Colebunders¹⁰ recommends it for laboratories processing more than thirty smears per day.

The NHLS will endeavour to communicate all positive sputum results to clinics by telephone, and the DOH will try to install telephone lines in all clinics. Extensions for fax machines should also be provided. The goal is to have sputum collection at least weekly but ultimately aiming for twice weekly. Smear results should be back within a week and culture results back within one month.

Treatment of TB

The conference discussed a number of important concepts:

- The importance of correct dosing (especially with Rifampicin containing FDCs)
- The increased risk of drug resistance in re-treatment patient
- The need for longer treatment duration and step-up in drugs for re-treatment patients

A number of problems areas were identified that require urgent attention:

The importance of pyridoxine treatment in HIV-co-infected TB patients to prevent peripheral neuropathy and other INH-related neurological disease and of cotrimoxazole in preventing opportunistic infections (OIs) was noted. The disruption in the supply of cotrimoxazole, pyridoxine and sometimes even of the antituberculous drugs is a source of grave concern and should be corrected immediately.

It was decided that the continuous supply all TB drugs, pyridoxine and cotrimoxazole should be a priority in the district. Although pyridoxine is regarded as level 1C in the Eastern Cape (i.e. only clinics visited by a doctor should get it), it is inexpensive with few side-effects, and therefore it should be distributed to all clinics.

There are a number of problems associated with the use of streptomycin in re-treatment patients including:

The need for patients to travel long distances to clinics every week day

The high cost of hospitalisation and the lack of beds

Difficulties in administering parental drug in patients who are often very thin, may be dehydrated and who dislike painful injections

Higher risk of abscess formation in immuno-compromised patient

It was decided that the National TB Control Programme should, as a matter of urgency, consider an alternative anti-tuberculous drug in place of streptomycin for re-treatment patients. This should include the following recommendations:

Until another drug has been identified, clear guidelines about the use of streptomycin (SM) should be produced.

At this stage the only clear guidelines on contraindication to the use of SM are the following:

Adults >65 years

Pregnant women

Other contraindications could include:

Anticoagulation therapy (e.g. patient with DVT)

Renal failure

Dehydration

Deafness from previous exposure to aminoglycosides

Guidelines regarding hospitalisation are required e.g. what needs to be done in a person who cannot be hospitalised and who cannot come to the clinic on a daily basis

Indications for hospitalisation are not clear

For some patients 3-times weekly SM may be a better option than 5-times weekly

For those who do not have access to 3-time weekly treatment hospital beds should be allocated

¹⁰ Colebunders R, Bastian I. A review of the diagnosis and treatment of smear-negative pulmonary tuberculosis. Int J Tuberc Lung Dis 2000; 4 (2): 97 - 107

For those who cannot be admitted and who cannot receive SM in the community, SM should be omitted from re-treatment regimen

Policies about TB patients in provincial hospitals need to be revised.

In the meantime managers in Lusikisiki should refer long term TB patients from St Elizabeth (provincial hospital, Qaukeni) to Holy Cross (district hospital, Qaukeni) or Bambisana (district hospital, Nyandeni) rather than letting them depend on clinics where there are no district nurses who can provide injections at home.

The absence of monitoring of cotrimoxazole and pyridoxine was noted. It was decided that it should be monitored in the same way as the rest of the TB programme.

The problems associated with using pre-treatment weight to establish dosages was found to be a problem, especially in co-infected patients who often gain weight very rapidly. The National TB Control Programme should reconsider the policy on calculating drug dosage on pre-treatment weight, especially in HIV-positive patients who often gain more than 20% of pre-treatment weight when treated for TB and HIV.

The problems associated with with the need to take multiple drugs for long periods of time for pulmonary and extrapulmonary TB were noted. The advantages of fixed dose combinations are important and they should be used whenever possible. It was decide that we should advocate for a global effort to develop more efficient drugs that would decrease duration and complexity of treatment.

TB Treatments and Antiretrovirals

Antiretrovirals can be given at the same time as TB medication. Often when TB is diagnosed, the patient accepts VCT and is found to be HIV infected. This alerts the clinician and the patient to the need for a CD4 cell count and the possibility of providing antiretrovirals.

However a number of important issues need to be considered including: the interaction between antiretrovirals and TB medications, the shared toxicity of these drugs, and the occurrence of paradoxical worsening of TB in some patients when starting antiretrovirals.

Interaction of TB drugs and ARVs:

Ritonavir induces liver enzymes to metabolise some medicines faster. This can cause lower levels of Nevirapine and most protease inhibitors. This means that for patients on first-line ARV regimens, Efavirenz should be used rather than Nevirapine. For patients on second-line ARV regimens, Ritonavir 300mg should be added to each dose of Lopinavir/Ritonavir.

Toxicity	Anti-tuberculous therapy	Antiretroviral therapy
Peripheral neuropathy	Isoniazid	Stavudine Zalcitabine Didanosine
Rash	Rifampicin Isoniazid Pyrazinamide	Non-nucleoside RTI i.e. Nevirapine and Efavirenz
Nausea	Pyrazinamide	Didanosine Zidovudine Protease inhibitors
Hepatitis	Rifampicin Isoniazid Pyrazinamide	Non-nucleoside RTI Nucleoside RTI Protease inhibitors

Shared toxicity

The table above indicates the shared toxicity between TB medication and ART.

The health care provider should be aware of these side-effects and monitor patients closely and manage them according to the protocol.

The Protocol for when to start ARVs in a person on TB treatment is as follows:

- CD4 > 200 defer ARVs until TB is cured
- CD4 50-200 defer ARVs until 2 months of TB Rx completed
- CD4 < 50 or severe disease (e.g. KS) start ARVs after 2 weeks

Need to integrate TB and HIV services

If services are well integrated the patient can be monitored for adherence, possible side-effects and treatment outcomes during the same clinic visit and preferably by the same health care worker.

Adherence to Treatment

Good adherence to TB treatment is needed to achieve cure and to prevent the development of MDR-TB. Although South Africa achieves a low rate of treatment completion and a cure rate of only 54%, we still have a low MDR-TB rate of 1% in patients with TB for the first time and 3% in patients with recurrent TB. Many people attribute this to the use of fixed-dose combination tablets (FDCs) in South Africa for many years. This should serve as lesson for the ARV program in South Africa. At present South Africa is one of the few countries in Africa not using anti-retroviral FDCs.

In South Africa adherence to ARVs appears to be better than to TB medication. In Khayelitsha Site B (the country's biggest ARV clinic with 4 800 TB consultations each month) adherence to ARVs after 36 months is greater than 95%, whereas only 76% of TB patients complete their TB treatment. Interestingly of the co-infected over 90% complete their TB treatment.

In Lusikisiki early data from the ARV program show that of the first 61 patients, none were lost to follow-up after 6 months, whereas in last quarterly TB review only 82% of 1023 patients completed treatment.

The conference examined the different approaches to adherence followed in the two programs. The TB program traditionally relies on directly observed treatment. The ARV program has a patient centred approach of empowering the ARV users so that they can take responsibility for their own health, with the use of material supports such as pill boxes and pill diaries. Even the terminology used points to the need for a new human rights approach in the TB program. We talk of people living with HIV, as opposed to TB suspects or TB cases. We talk of adherence not compliance, and treatment interrupters rather than defaulters. But the real difference lies in the level of patient preparation for treatment. This is done through continuous education and counselling of service users in individual counselling sessions and in support groups. Similar material supports should be used for TB medications.

It was recommended that TB adherence support groups should be started. If a person knows about their disease, they are more likely to be adherent. We must empower them! Patients should be referred to a group once sputum has been taken. Even if the sputum is negative, the person will learn about TB. The TB support group should be separate from the HIV one in order to ensure that TB is not spread amongst HIV infected persons and to ensure confidentiality, but this should be assessed per clinic.

The National TB Control Program and Government Commitment

The National TB Control program is based on the WHO DOTS strategy with its five pillars:

- Government commitment to sustained TB control activities
- Definite diagnosis based on smears
- Standardised short-course of TB drugs which should be directly observed
- A regular, uninterrupted supply of essential anti-TB drugs
- Standardised recording and reporting to evaluate performance

The first pillar is government commitment. Concern was expressed that the serious crisis of shortages of staff can lead to a possible deterioration of all health programs which are struggling with the added burden of the HIV epidemic. The department of health must look at short term and long-term goals to solve the human resource crisis, especially in rural areas. These should include better living conditions for health care workers at rural clinics and a financial incentive for health care workers who do further training in HIV and TB care.

Interruption of Drug Supply

The conference noted that there were many obstacles to a regular and uninterrupted drug supply. They related to poor infrastructure, large distances in rural areas and underdevelopment under Apartheid, with poor education opportunities. However the conference felt that if there is government commitment, these structural obstacles can be addressed by affirmative action and removing the disparities between rich and poor and urban and rural.

A lack of staffing at the Umtata Central Medical Stores was identified as a major stumbling block to an uninterrupted drug supply. The district hopes that with the recognition and training of pharmacist assistants some of the present problems of interrupted drug supply to clinics can be overcome. The districts are committed to ensure that one professional nurse per clinic be accountable for drug ordering and receiving.

Community health workers and DOTs

The representative of the community health workers of O.R.Thambo municipality which includes Nyandeni and Qaukeni, reported that community health workers had not received stipends this year, and that they have never received the R1 000 proposed by the minister of health. The Director for HIV/AIDS pointed out that the Eastern Cape, with its 900 health care facilities had more facilities than any other province. The budget allocation was not sufficient to sustain the provincial program to pay stipends to five community health workers per facility. It was explained that the strategy of paying the stipends via the municipal budgets had not worked effectively, and that the province was in the process of finalising agreements with CBOs to manage the community health care workers. The conference participants noted that due to shortages of nurses and increasing number of sick people in the community, these community health care workers were taking on more responsibility. These tasks included HIV counselling, sputum collection, adherence training and home visits, home-based care, keeping of registers, and conducting support groups. This high level of responsibility would not be sustainable unless payment was done monthly.

The conference also recommended that a more skilled level of therapeutic adherence counsellor should be introduced. This professional category of worker should be permanently employed to help with the ARV roll-out and the TB program.

Community Involvement and Health Promotion

The district health system encourages community participation in health services. Health care workers often see health promotion as the nurses telling patients what to do: e.g. if you cough for two weeks come to the clinic, if you have TB take medicines for six months. Although this is not wrong, this form of education is only a very small aspect of health promotion.

The conference discussed that promoting health is not about blaming poor people for poor health. Instead it should make poor people aware of ways to fight for the better distribution of resources. This can

happen through changes in laws that favour the rich, and it can happen through active participation by the poor in the health services' decision-making structure.

The Ottawa Charter of Health Promotion

The Ottawa Charter of Health Promotion was taken as basis for discussion. It outlines that health promotion means:

* Building healthy public policy

Health promotion puts health on the agenda of policy-makers in all sectors and at all levels, making them aware of the health consequences of their decisions and their responsibilities for health. This includes better housing, food security, jobs, a good land policy and agricultural support for small farmers, clean water, availability of condoms and more clinics with well trained nurses.

* Strengthen community action

Health promotion works through concrete and effective community action in setting priorities, making decisions, planning strategies and implementing them to achieve better health. At the heart of this process is the empowerment of communities, their ownership and control of their own endeavours and destinies. This requires full and continuous access to information, learning opportunities, as well as funding support.

* Develop personal skills

Health promotion enhances life skills through providing information and education for health and increases the options available to people to exercise more control over their own health and over their environments, and to make choices conducive to health.

* Re-orient health services

The role of the health sector must move increasingly in the direction of health promotion and beyond the responsibility for only providing clinical and curative services. A change of attitude and organization of health services, which refocuses on the total needs of the individual as a whole person, is required.

A high level of community participation was apparent at the workshop when more than 100 support group members from different clinics of Port St John, lead by TAC activists, staged a march in support of the conference, highlighting the fact that clinic nurses should request TB culture tests for all people living with HIV who are suspected of having TB as the smear test was not sensitive enough. This illustrated how communities can participate in policy decision making once they have been empowered through progressive health promotion and education.

The conference noted that in rural areas there was a system of chiefs. The chiefs listened to everyone's opinion before taking a decision. In a similar way the South African democracy might not have a strong political opposition party, however it was useful to have an active civil society participating in policy formulation.

Monitoring our TB Program

The District Rapid Analysis Tool for TB presently used to evaluate and supervise clinics has been updated to integrate TB and HIV. It is recommended that it include an evaluation of the diagnosis of smear negative TB.

Operational Research

Important areas of research need to be discussed with academic institutions at the Universities of the Transkei (Walter Sisulu), Stellenbosch and Cape Town and other partners. These include:

Operational research to identify the degree to which trained nurses can place sputum smear negative patients, who have clinical signs and symptoms and who have not responded to a course of antibiotics, on TB treatment.

The feasibility of using ultrasonic nebulisers at rural hospitals and large clinics.

The feasibility of doing TB phage testing at rural laboratories.

The feasibility of using counsellors with appropriate training, to do HIV testing.

Conclusions

The conference managed to define the scope of the TB/HIV problem in the rural part of the Eastern Cape. It identified problems that prevent accurate data collection and hamper service delivery. The severe shortage of medical staff in rural areas and underdeveloped infrastructure requires urgent attention.

In order to prevent numerous premature deaths due to the concurrent HIV and TB epidemics the widespread provision of antiretrovirals is required. They reduce the chances of an HIV infected person developing TB by between 60 and 80% and also prevent many other HIV related opportunistic infections. Yet many challenges lie ahead to reduce the prevalence of both HIV and TB and to treat people with TB more effectively.

It highlighted the diagnostic dilemma, with special emphasis on smear negative TB and TB in children. The conference delegates committed to work hard to implement the present protocols as effectively as possible. It was recommended that Qaukeni undertakes operational research towards developing better diagnostic tools and protocols. Support for this was requested from the department of health and the scientific community.

The need for further integration of TB and HIV services was emphasised. Lessons learned in both programs can be shared. The TB programs use of standardised FDC regimens holds benefits that should be incorporated in the ARV program. The HIV program on the other hand can share the value of patient centred approach to adherence with high level of peer-education and empowerment.



"We cannot win the battle against AIDS if we do not also fight TB."
Nelson Mandela said in a news conference at the 15th International AIDS Conference, Bangkok, July 15, 2004