

HIV/AIDS AND TUBERCULOSIS IN BOTSWANA.

An EPIDEMIOLOGIC SITUATIONN ANALYSIS
FROM THE 1980`s to 2000.

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FOREWORD

In March of 1995, I lost my first relative to HIV/AIDS. Since then, I have come to part with many of my beloved ones like many people in my country. We do hope and believe as a nation that one day this cup will come to pass but will do so with the devastation and impoverishment of a whole nation. It was not an easy task for me to embark on writing this paper, but I do believe that in order to defeat AIDS and TB, we have to de-stigmatise these diseases and be able to talk about them with ease and openness.

Botswana has long been marvelled at as the "African wonder". For amongst all the poverty, war and disease of the continent, she has maintained a stable economy, the longest democracy and effectively eradicated poverty and illiteracy. People elsewhere did not know about this little country, since there were neither war nor hunger. If they did, it was certainly to do with wildlife and Okavango, the jewel of Africa. In the past decade, our country has taken centerstage like all of Africa. She has not been spared, of all the misery and suffering that has become Africa. Today, we find ourselves on the world headlines. We are dying out in the thousands due to AIDS and TB. Our achievements are facing a clear and present danger.

GLOSSARY.

- **ANC:** Antenatal Care.
- **BNTP:** Botswana National Tuberculosis Program.
- **DOT:** Direct Observation Treatment.
- **EPTB:** Extra Pulmonary Tuberculosis.
- **GDP:** Gross Domestic Product.
- **IEC:** Information Education and Communication.
- **MDRTB:** Multi Drug Resistant Tuberculosis.
- **MoH:** Ministry of Health.
- **MTP2:** Medium Term Plan.
- **NoF:** Number of Female.
- **NoM:** Number of Male.
- **STD:** Sexually Transmitted Diseases
- **TB:** Tuberculosis.

ABSTRACT.

AIDS related diseases are a leading cause of death in Sub Saharan Africa, more so in Botswana. As of 2001, Botswana had the highest TB notification rate in the world, 600 per 100 000. The reason for this is the strong association between HIV infection and subsequent TB disease. HIV reduces the number of CD4 positive T cells in the body thus weakening cell mediated immunity which is crucial in combating intracellular microbes like Mycobacterium TB, which are resistant to other defence mechanisms. Extra Pulmonary TB is common in AIDS patients and is actually used in some countries as an AIDS defining condition. Although such TB might be a source of mortality in Botswana, it is very much under diagnosed.

Knowledge on Drug Resistant TB and EPTB, are based on research done in western countries. The question still remains as to the role of HIV on these special manifestations of TB, in a setting of sub Saharan Africa, a region with 3\4 of all HIV/AIDS cases in the world. It can be of great value to research on this, in order to improve the management of TB in AIDS patients and subsequent improvement in the quality of life in such patients.

INTRODUCTION.

As part of my medical degree here at UiTø, I have had two elective periods during which I travelled to Botswana. In the fall of 1999, I was attached to the SDMO (senior district medical officer) in Maun, Dr Chipandwe. During that period, I got an insight into how the health system functions in Botswana, the challenges faced by the staff and what to expect in the future, when I eventually join the team. During this period, I found myself drawn to the extent of HIV/AIDS spread and the fact that most of these patients suffered from T.B. Since I was in Maun, acquiring data on the situation on the whole of Botswana was not possible. I decided at that time, to embark on finding such data if it existed and writing a paper on it.

During the two years that have passed, these two diseases have become the leading cause of mortality and make up a significant percentage of the total hospital admissions. Factors contributing to such a rapid spread of HIV might seem obvious to many but a web of factors ranging from economic, culture, education have to be considered. Promiscuity alone cannot be taken as the only thing that resulted in this catastrophe. I find it hard to label my people as being such and would like to believe that there is more to that than meets the eye.

METHOD.

Much can be done in the laboratory when one talks of HIV/AIDS. Such research would involve experiments to do with viral RNA and DNA. I was interested in indulging such research, especially with my thoughts on TB in AIDS patients, and whether HIV contributes in anyway to any eventual Drug resistant that might be apparent in such patients. That would require time in the lab, to grow the microbes on media and do subsequent drug resistant testing. Eventually I would have to do DNA fingerprinting of the microbes that I found resistant, with clustering in mind. Botswana is not a rich country and such an experiment, done by a medical student, would be a luxury. I do hope that in the near future, I will be able to embark on such a research.

I then decided that approaching the issue from epidemiology point of view, would do for now. The Ministry of Health in Botswana does keep statistics on different diseases. Such is the duty of the Epidemiology unit headed by Dr. Moeti. Such statistics are reliable since all outpatients and inpatients are registered in Botswana. Botswana have reliable access to health services as 85% of the population lives approximately 15km away from a health post, clinic or hospital. I acquired data on Tuberculosis for the years 1999 and 2000, which also contains data dating as far back as 1976. I also secured a MTP2 for the period 1997-2002 for HIV/AIDS. [3].

CHAPTER 1

1.0 Botswana -The country.

Botswana is a landlocked country lying at the centre of Southern Africa, bordered by Namibia, South Africa, Zambia and Zimbabwe. Botswana is a former British Protectorate, which became independent in 1966. It has a population of 1.7 million and a total area of about 582 thousand square kilometres, making it a sparsely populated country. As of 1991, the population density was 2.3 persons per kilometre squared. Most parts of the country are semi arid, with an average rainfall of 4- 500 mm in the eastern parts and 250-300 mm in the western parts. Kalahari desert occupies approximately 87% of all land mass, rendering a large part of the country uninhabited. Most of the population lives along the eastern corridor, with ample arable land and better rainfall.

Gross national per capita for the period 1997 - 2001 averaged US\$ 3310, which is high by African standards. An estimated one third of the population might be living in poverty despite the high GDP [2].

1.1 Demographic and Population situation (1997- 2002).

Like other developing countries, Botswana has a young population structure. From the 1991 population census, approximately 29% of the population was below the age of 15. This represented an age dependency ratio of 83:100 [2] This has changed dramatically, ten years later due to HIV/ AIDS. Age group 15-49 years, made up forty five percent of the population according to census conducted in 1991. The figure increased to forty seven percent according to 2001 census. In Botswana, this age group is the most sexually active, considering the fact that 89% of all HIV/AIDS cases fell into this age group as of 2001. Most ANC visitors, for the first time, belong to this group. It is unfortunate, since this happens to be the most economically active part of the society i.e. most of the workforce is aged between 15 and 49 years, at both household and national level. The impact of HIV/AIDS will therefore change the dependency ratio as the number of orphans increase and the young “breadwinners” succumb to disease. (Table 1: Selected demographic indicators 1971-2001). [3].

Between 1971 and 1991, infant mortality rate per 1000 declined from 92 to 45 while under 5-mortality rate fell from 151 to 56 over the same period. Life expectancy increased from 55.5 to 61.7, during these 20 years [3]. In 2001, life expectancy had dropped to 44, and under 5 mortality rates had risen to 142. (Table1). HIV/AIDS has reversed the gains Botswana made in child health indicators in the past 20 years. Sexual activity in Botswana is high and starts early. On average, 23% of first ANC attendees in health facilities are teenagers. About 6 % of these are under the age of 15, annually [3]. This high level of teenage pregnancy shows a tendency towards unprotected sex within this age group

1.2 Health Services in Botswana

Health care in Botswana is based upon the **Primary Health Care (PHC)** concept. District Councils (local government) have the responsibility for PHC. This is organised as a network of clinics and smaller health posts. All are staffed with one or more nurses and family welfare educators or community health workers. About 85% of the population lives within 15km of a PHC facility. [2].

The central government provides hospital services. There are three levels, Primary hospitals, District hospitals and Referral hospitals. There are two referral hospitals, Princess Marina in the south and Nyangagwe in the north. Within the Ministry of Health, there are specialised units for certain programmes e.g. AIDS/STD Unit, Epidemiology Unit. These programmes are managed both at District and Central level. The Private sector has grown in the last 10 years, especially after the introduction of a government medical aid scheme for civil servants. There is one Private hospital, two mission hospitals and three mine hospitals.

CHAPTER 2.

2.1 HIV/AIDS Situation Analysis.

HIV/AIDS. (1986 - 2001).

HIV epidemic is well established in Botswana. Approximately 39% of the general population was infected according to UNAIDS and Sentinel Surveillance Survey conducted in 2001 [8]. Survey extrapolates figures pregnant women who are tested on their first ANC visit. It is common for most Botswana women to make at least one such visit during their pregnancy. An estimated 95% do so. The survey also collects data from STD patients, who are offered testing. Figures from reported AIDS cases, cases of HIV signs and symptoms are also used. Having said that, it is quite possible that this survey underestimates extent of the epidemic, but it does give an idea as to the actuality of the spread of HIV in Botswana. Compared to 1995, when only 13 % of the population was infected, figures from 2001 show a dramatic increase, one, which has put Botswana at the epicentre of this epidemic. Within the age group 15-45, 23% was infected in 1995. It was estimated that a total of 332 000 persons could be HIV positive by 2001 at the end of 1995. With current statistics indicating 39% that turned out to be an underestimate. HIV infection rates are increasing by 1.5 times every two years. 60 000 persons were infected as of 1992 compared to 180 000 by 1996 [3]. (Table 2: reported HIV cases in Botswana by age and gender 1986 – 1996 and Table 3: Estimated number of adults and children living with HIV/AIDS, end of 2001.)

The figures available as of today are a possible underestimate as to the extent of the epidemic. Reluctance to be tested, delays in reporting and under reporting, can contribute to such an underestimate. A cumulative total of 3260 AIDS cases were reported to AIDS/STD unit during the first four months of 1996. This was in contrast to 10 775 cases of related HIV signs and symptoms reported over the same period [3]. In the past decade, the most economically active have been the most affected in terms of reported HIV signs and symptoms. This group accounted for 89% of all signs and symptoms.

In 1995, 34%, range 28.7%- 39.6%, of all pregnant women visiting ANC clinics for the first time, were positive (Sentinel survey). Of these, 79% was aged between 15 and 29. In 2001, median prevalence in pregnant women tested in 22 districts (190 sites) was 36.6%, range 25.8% - 55.8%. HIV Seroprevalance amongst pregnant women presents a better picture as to the likely AIDS trends in Botswana since it is custom for Botswana women to make at least one antenatal care clinic attendance once they find out that they are pregnant. Hence surveillance data from this group is fairly representative for infection rates amongst pregnant women. (Table 5: seroprevalance among pregnant women from 1992 to 1995). Such seroprevalance surveys have been extended to men attending clinics for STD treatment. Gaborone and Francistown, the two largest towns have been designated as permanent monitoring sites. Other areas rotate on an annual basis. [3].

Results from the pregnant women group show a staggering rise in seropositivity. In Gaborone alone, the percentage increased from 14.9% to 39.1% in the period 1992-2001. Francistown had an increase of 23.7% to 44.9% in the same period, i.e. 4.5 out of 10 pregnant women were HIV positive in Francistown. Selibe Phikwe is the urban

area with the highest prevalence. In 2001, 55.6% of ANC visitors were HIV positive, compared to 27 % in 1994. [3]

Youth, aged between 15 and 29 show the highest infection rate, which made up 56% of reported HIV signs and symptoms during 1996. Female youth are more vulnerable, since they made up 69% of all reported cases. It has long been speculated that women are more prone to STD's due their anatomical build up. Such infections can go unnoticed for a long time in women and it is common to have multiple infections, at least in Botswana. Such lesions and ulcers make transmission of HIV easier if protection is not used. HIV is also proving a challenge to children aged 0-4 years. As of 1996, 1052 cases were reported, relating to signs and symptoms. By the end of 2001, 28 000 children were estimated to be living with HIV/AIDS, while 69 000 were orphans [3]. (Table 4: annually reported cases between 1987 and 1996).

At the beginning of this epidemic, urban areas were the most affected, with the rural areas having lower seroprevalence rates. But that gap has since narrowed and today, there is not much difference. Seroprevalence in Ghanzi for example, doubled from 9.5 to 18.9 between 1993 and 1995. In 2001, median HIV prevalence in non-urban areas, was 38.6%, range 26.4% - 50.9%.

Sexually Transmitted Diseases and HIV/AIDS.

STD's are still a major health problem in Botswana indicating unsafe sexual practices. 135 343 cases of STD cases were reported in 1993. Multiple STD infections are most common amongst women. An etiological survey conducted in Gaborone, found that 71% of women with STD had multiple infections [3]. The usual specific diagnosis treatment regime has now been replaced by a syndromes approach to the problem of STD.

STD's and HIV/AIDS are closely related. They are both transmitted in the same mode. Most STD causes lesions or ulcers, which facilitate HIV transmission by increasing infectiousness and susceptibility. A survey conducted in 1993, in urban areas, showed that 41% of men and women with genital ulcers were HIV positive. In 1995, the figure had increased to 50%. In rural areas, the figure was 35.4 % as of 1995.

In order to deal with HIV/AIDS, the problem of STD has to be dealt with. STD's increase the risk of contracting HIV. Measures for preventing STD's and HIV are the same. Changes in sexual behaviour, still remain a major weapon in combating both. Proper treatment of STD is undoubtedly very important. (Table 5: HIV seroprevalance among men with other STD's in Botswana 1992-1995)

Everyone in the sexually active group in Botswana is at risk of contracting HIV. At this stage and time in Botswana, there is no point in defining the population in terms of risks groups. The epidemic is now widespread in the whole population.

Epidemic Dynamics: Factors

There has been a lot of speculation as to why HIV/AIDS has reached such catastrophic proportions in Botswana. The population of Botswana is relatively small (1.7 million) and effects of this epidemic are more visible, more felt than perhaps in a larger population. The transit of HIV from the "risky" population to the rest of the population took only a few years. As in other developing countries, unprotected sex still remains the main mode of transmission. It is circumstances, cultural, socio-economic or biologic, which lead to such risky behaviour. (See discussion)

Labour Migration is a common phenomenon in the whole of Southern Africa. This leads to disruptions in family life. As early as 1880, 2600 Botswana men were working in South African mines. Migration peaked in the early 1930`s, when as much as 16% of all Botswana men migrated for work in South Africa. At that time as much as 43% of total income was from migrant work. This tendency has since then decreased. In 2001, only 12 000 Botswana men worked in South African mines [2] Disruptions of family life have encouraged a tendency towards multiple sexual partners. Mine workers also have a tendency towards lung diseases such as Silicosis and **Pulmonary Tuberculosis (PTB)**, shown by a nationwide study done in 1984, which showed that 71% of all male PTB patients were former mine workers. In 1996, this figure had reduced to 45%, as a subsequent reduction in migrant labour.

Trade has increased with the onset of democracy in South Africa. Movement of goods by road through Botswana, from South African ports has increased dramatically. These movements were earlier identified as a major factor in the spread of HIV/AIDS. Francistown had the highest prevalence by the early 90`s. This was due to its proximity to Zimbabwe and other northern countries, which had the highest prevalence at that time. That has since changed and the pool of infection is now widespread throughout the whole population.

Gender bias is a feature that is apparent with HIV/AIDS in Botswana. Since the early years of this epidemic, as much as 56% of infections in the age group 15-49 years were women. In the youth group (15-29 years), as much as 68% were women. [3]. This disparity cannot be explained solely on biological factors, such as multiple STD lesions being more common amongst women and the fact that most women have STD lesions without even knowing it. It has since been said that transmission is more efficient from men to women than converse. Considering the anatomical features of both sexes, that is most likely true but other factors contribute to such disparity.

In Botswana, women are subject to socio-economic, legal and cultural disadvantages that make them more vulnerable to HIV/AIDS. According to a Civil Registration Pilot Survey conducted between 1990 and 1994, 80% of all birth within that period were to single mothers, most of them youth [3]. Women are not empowered against prejudicial, cultural and traditional practices in sexual and reproductive matters as well as in relationships. In short, women have very little to say in matters of intimacy. In the Tswana culture, a man is the head of the family. In most cases, a woman cannot tell her husband to start using a condom should the need arise. Neither can she instruct

her husband to go visit a clinic and get treatment if she finds herself with STD. Conservative; traditional men are proving a challenge in the fight against HIV. - Gender equality is not something integral to Botswana culture and it will never be. Men are regarded as the head and women rather prefer a man who acts as such. Despite that, gender equality has to be promoted, especially in reproductive matters. Men on the other hand, need to be more responsible.

STD's as mentioned previously, play a major role in the dynamics of HIV/AIDS.

They are evidence of unprotected sex. In a **Knowledge Attitude Practice and Behaviour** study conducted in 1994, 32.5% of sexually active males in Francistown reported having had sores or discharge in that year, Manu 31.1%, Tutume 30.7% [8].

It is clear then that control of STD is also a key to control of HIV/AIDS.

Other factors such as rape and harassment are still a common problem. Prevalence of such deeds is still high. Teenage girls also indulge in sexual relations with older men. This explains the disproportionate rate of HIV infection between teenage boys and girls. Prisons have of late proved to be the latest HIV pools due to sodomy between inmates. A study conducted by Department of Prisons has shown that this behaviour is quite common.

Mobile Population. The tradition of shuttling between homesteads, lands and cattle posts across the seasons, and more recently urban areas, make Botswana one of the most mobile populations in the world. This constant mobility makes distinction between a rural and an urban area, in terms of disease patterns, ineffectual. Rapid economic growth has resulted in excellent road networks and vehicle purchase,

making all areas of the country accessible. This mobility can account in part, to the more uniform prevalence of HIV seen in the country today.

Botswana operates a decentralised public service. Workforce is constantly being located and relocated across districts where services are required. Because of the lack of skilled manpower, this transfer system results in separation of couples and disruption of family life. Urban rural ties are also still strong, resulting in regular contact during long weekends and holidays. The rapid spread of HIV is possible due to this unmitigated population mobility. Combining this with the fact that 60% of the population is 30 years old or younger, one can see the tremendous challenge Botswana faces in fighting HIV. [3]

Socio economic factors. A literacy survey conducted in 1993, showed a national literacy rate of 69.9%; 66.9% for men and 70.3% for women. [3]. This was the highest in Sub Saharan Africa at the time. This however does not empower people to have access to jobs in a highly competitive labour market. At the time, unemployment was 21%. Such unemployment is concentrated among secondary school leavers and has intensified poverty profile in Botswana. Poverty, it seems, makes people more vulnerable to HIV and TB, and less able to respond effectively to their consequences.

2.2 EPIDEMIOLOGY OF TB IN HIV PREVELANT COUNTRIES.

It is now known that individuals infected with both tuberculin bacilli and HIV have an increased risk of developing tuberculosis. HIV is now identified as the strongest risk factor for TB disease observed in the past 100 years, in individuals carrying the bacilli. Its impact is so great that it has disrupted the delicate balance between tubercle bacilli and its human host, which in the absence of man made intervention (i.e case finding, chemotherapy) , had existed. Recent data from developing countries shows that tools available for TB control in these countries, are failing to restrain the spread of TB, mainly due to the HIV epidemic. It is quite possible that HIV, compared to the disease process itself much less affects the rate of transmission .[14]

In the “pre HIV” era, TB was controlled with relative success, especially in developed countries. The source of infection (smear positive, CXR positive), was almost always exclusively diseased and could be quickly rendered non- infectious. As mentioned above, there existed a balance in the host. In such a setting, any reduction in sources of infection led to an improved epidemiological situation. Reliable diagnostic tools and efficient chemotherapy regimes also contributed.

HIV has been a setback in a setting of high prevalence since not only are the diseased individuals a source of infection, but also those who are HIV positive, with dormant bacilli. Diagnostic tools are also not that reliable in such a setting. Many cases are extra pulmonary and require other diagnostic procedures. Pulmonary cases have a tendency to be smear negative. HIV influences TB Incidence in several ways, including:

1. Progression of recent infection into disease because of the progressive immunodeficiency.
2. Re-infection.
3. Multiplication of TB bacilli in quiescent foci after remote TB infection.

Such an influence depends on the prevalence of HIV in the community and its trends, the prevalence of TB in the population aged between 15 – 45, breakdown rate from remote to active TB infection, level and trend of annual risk of TB infection and detection rate of new and relapse cases of TB and cure rate of smear positive cases. For a HIV negative individual, the lifetime risk of TB is 5-10 % compared to 50% in positive individuals. [14]

2.3 TUBERCULOSIS SITUATION ANALYSIS.

Tuberculosis was introduced in Botswana by the first decade of the past century, mainly by miners returning from South Africa. TB remains one of the major health problems in Botswana. From the early 1950's TB has been responsible for 20% of all hospital admissions. It has been the highest cause of mortality, with 20% of all deaths attributed to it [2]. It is the single most common cause of death amongst AIDS patients today.

Botswana has the highest TB notification rates in the world, 600 per 100 000 in 2001 [4]. By 1990, notification rates was 202/100 000. This was a decrease compared to earlier years mainly due to the introduction of a National Tuberculosis Program (NTP) and DOT program in the late 70's and early 80's (Table 10: TB Notification rates in Botswana 1976-1999). Since 1991, there has been a sharp increase in the notification rate, figures from 1998 being 506/100 000, showing an increase of about 10- 15% per annum. In total, case rates increased by 120% from 1989 to 1996. Such increases in notification rates are associated with HIV/AIDS. (Table 11: TB and HIV association: 1999.) [4]

Implementation of DOT and BNTP was a success story, marvelled at by the rest of the world. In 1989, the annual risk of TB infection had declined from 5.8% in 1956 to 0.1 % in 1989. Notification rates also declined during this period. By 1999, the total registered TB cases were 8647 compared to 2938 in 1989. This shows a three times increase, in ten years. As of 2001, TB notification rate had risen to approximately 600 per 100 000. Botswana does report all diagnosed cases, cases not confirmed by

positive sputum test and all confirmed Extra Pulmonary TB cases. This gives a much higher number compared to other countries, which only report positive sputum cases e.g. South Africa and Zimbabwe. [4]

Botswana faces a TB epidemic, with 10 000 new cases registered in 2001. The notification rate rises on average by 30/100 000 per year. There is a tendency for rural areas to have higher rates, e.g. southern district 1383 per 100 000, kgalagadi 1263 per 100 000 (1999). Urban areas had a lower prevalence, Gaborone 517/100 000, Francistown 669/100 000 and Saline Pike 721/ 100 000. It is worth noting that rural areas have a relatively low sputum examination rate compared to urban areas, hence possible over diagnosis. [4]

Treatment of TB has been complicated by the onset of HIV/AIDS. In addition to new cases of TB, there has now been a surge of **recurrence** cases that is patients who completed their treatment but came back due to recurring signs and symptoms. In 1999 about 6% of all TB patients fell into this category. About 1% of these had failed to respond to their first treatments. These are possible Multi Drug Resistance patients. As of 1999, 2% of all TB patients were those that had not completed their first treatment well and came back with recurring signs and symptoms (**after default**). These patients are clearly a risk for developing drug resistant TB strains. (Table 12: TB notification according to patient type). Most of the reported TB cases in Botswana have been pulmonary. In 1998, only 11% were extra pulmonary and by 1999 that figure increased to 13.8%. The figure today is much higher due to HIV/AIDS. It is obvious that the figure could be much higher since EPTB is under diagnosed in Botswana. [4]

In Botswana, TB is diagnosed by both sputum smear and chest radiograph. In 1999, 36.1% of all TB cases were found to be sputum positive. The WHO expects at least 66% sputum positives of all PTB cases. This shows poor practices in collection of sputum smears amongst possible TB patients. In 1999 41.6% of PTB cases were put on treatment without sputum testing, another poor practice. This was an improvement from 1998 when as much as 45% of cases were treated without sputum smears.

When one looks at the **age distribution of TB disease**, one sees a trend very much like the one for HIV/AIDS (Table 14: TB male/female ratio according to different age groups). The most affected age group, between 20 and 49 years, is also the most sexually active and economically active. There is also a significant increase in the 0-4 years, which is a result of children born with HIV/AIDS. It is hoped that this trend will reverse as the government has introduced a rigorous program to curb transmission from mother to child by providing antiviral treatment to HIV positive pregnant mothers and their infants after birth for a period of 6 months, without charge. This program has now been extended to include the rest of the population. Such mothers are also advised not to breastfeed and are provided free milk formula. TB occurred almost equally amongst male and female as of 1998. The male/ female ratio stands close to 2:1 (Table 14: TB male female ratio, according to different age groups). [4]

Chapter 3.

TB resurgence is closely parallel to the HIV/AIDS epidemic. Botswana has seen the highest increase in TB cases since it is the most burdened by AIDS. Infection associated with TB and HIV is special in that TB is readily transmitted regardless of HIV status.

3.1 Pathogenesis

TB is a bacterial disease caused by *Mycobacterium TB*, occasionally *M. Bovis*, *M. Africanum*. These organisms are also known as tubercle bacilli, because they cause lesions called tubercles. They are also described as Acid fast Bacilli, due to their staining red with certain dyes under the microscope. They keep the dye on washing with acid and alcohol, hence the name acid fast.

TB is most commonly transmitted from a person suffering from infectious pulmonary through infected droplet nuclei. These nuclei are created when a diseased individual coughs or sneezes. Tiny droplets dry rapidly and the very smallest of them may then remain suspended in the air for several hours. This explains why poor ventilation promotes TB spread especially in poorly ventilated conditions. Only particles less than 10 micrometers can reach the alveoli, while larger ones settle in the upper respiratory tract, to be removed by mucocilliary system. In an immune competent individual, TB can be well contained over a lifetime. Only 10% of immune competent persons carrying the bacilli develop TB during the course of their life, with the rest having a positive tuberculin test (not always), as the only evidence of infection. Exposure leads to a primary infection, which begins with multiplication of the bacilli in the lung to form the GHONS FOCUS. Lymphatics then drain the bacilli

to the hilar lymph nodes, resulting in lymphadenopathy. The Ghons focus and these lymph nodes constitute the Primary complex. Within 4-6 weeks, a delayed hypersensitivity and cellular immunity reaction develops, mediated by the CD4 positive T cells, a target for HIV. This immune reaction, contains the infection in a dormant state forming a caseous granuloma. This can be for life, and any event that disturbs this containment, eg immunodeficiency, stress etc, results in disseminated TB. [13]

HIV results in dysfunction and depletion of CD4 positive T cells with subsequent disturbances in the functioning of monocytes and macrophages. Acid Fast bacilli excite a transient immune mediated response upon entering lung tissue. This response sensitises CD4 positive T cells to produce cytokines, which in turn attract macrophages to the site. Interferon gamma induces the macrophages to change morphology, and a sub cellular apparatus for protein synthesis develops resulting in a voluminous cytoplasm. At this stage, these cells are known as Epithelioid cells (Langhans cells in TB.). Fusion of such cells does occur, giving rise to multi nucleate histiocytic giant cells. These cells play a role in phagocytosis, secretion and cell-mediated immunity. In TB, they form an enclosure around AFB, together with lymphocytes and fibroblasts. This type of response is called a Granulomatous Inflammation. Such cell mediated immunity (Type 4 reaction) results in evolution of a tubercle (follicle) with central caseation. The formation of such a follicle or tubercle takes approximately 3 weeks. Caseation is a result of ischemia, bacterial activity and the type 4 reactions. The giant cells, lymphocytes contain the bacilli as such in healthy individuals for a lifetime in 90% of the population.

HIV binds CD4 positive cells, via receptor gp120. HIV has two main effects on these cells. It alters the cells genetic material, by inducing transcription of its viral RNA into DNA, which is subsequently introduced into the cells nucleus. This leads to abnormal cell function and cell death, releasing more virus particles.

Depletion of CD4 positive T cells can manifest itself over a long period of time (latent), manifested by B cell stimulation with subsequent Antibody formation and lymph node enlargement. With time, this results in total failure in immune mechanisms, especially cell mediated immunity, in which CD4 T cells play a central role. HIV patients are thus more susceptible to TB and other infections in which such immunity plays a central role.

3.2 TB in an HIV Patient.

TB in HIV patients is characterized by a rapid **development** into active disease after exposure.

- Incidence of Extra Pulmonary TB (EPTB) is highest amongst HIV patients. About 60-70% of such cases are HIV related [1]. In Botswana, EPTB is very much under diagnosed, despite it being the most likely cause of death in AIDS patients [3]. The most common sites for EPTB are the lymph nodes (lymphadenitis), blood and bone marrow (disseminated). The later usually results in positive blood cultures (26-56%). The CD4 count in disseminated cases usually is 190-198 mm³. Genitourinary involvement is also a feature of EPTB with Renal and testicular involvements usually found upon autopsy. Meningitis, Hydrocephalus and CSF pleocytosis are also common. [11]

- Chest radiographs of such patients are usually atypical. Findings include, **hilar adenopathy, diffuse infiltrates very much like those of Pulmonary Pneumocytosis, lower lobe involvement which is not typical of TB in HIV negative patients, pleural effusions and cavitations.**
- CD4 counts usually match with the clinical picture at hand. A count of about 250-500 mm³ usually results in pulmonary disease. A count of less than 100 mm³ usually results in military disease.

3.3 Recurrence of TB in AIDS Patients.

Although it is obvious that patients infected with HIV/AIDS and TB, have an accelerated progress to overt development of active TB, pathogenesis of this complex is still very much unclear. TB in an AIDS patient can either be a primary or a secondary exogenous infection. In some cases, it is a reactivation of dormant bacteria.

A cohort study conducted amongst 326 South African miners, looked at HIV-1 infection and TB recurrence, after cure. The purpose of the study was to determine if relapse or re infection or relapse contributed more to TB in AIDS patients [6]. Patients were examined 3 and 6 months after cure. DNA fingerprinting (AFB) of the initial and subsequent episodes, compared to determine the source of recurrence. Similar DNA sequences would indicate relapse whereas different indicated re infection. Kaplan Meir curves from this study showed that HIV-1 positive individuals were most likely to have recurrences, due to reinfection compared to HIV negative individuals. No significant difference was found for Relapse between HIV negative and positive

patients. 62%(13\21) of recurrences in HIV-1 positive individuals were attributable to reinfection compared to only 6%(1\18) in those who were HIV negative (p=0.0003). This study was conducted in mine workers (possible clustering), and working in the mine was identified as a risk factor for TB. Increasing years of employment and residual cavitation were significant risk factors for relapse and HIV a major factor in reinfection. [6]

This study shows the importance of long-term chemotherapeutic secondary prophylaxis in HIV-1 positive patients, in countries with a high prevalence of both HIV and TB. In such settings, lifelong chemoprophylaxis for cured patients who are known to be HIV positive can be useful.

CHAPTER 4. Multi Drug Resistant TB and HIV Infection.

Resistance to drugs by disease causing microorganisms is defined as temporary or permanent capacity of such organisms and their progeny to remain viable or to multiply in presence of concentration of drug that would normally destroy or inhibit the growth of other cells.

In microbiology resistance and susceptibility are relative terms. All populations of microorganisms contain a certain proportion of resistant mutants. The numbers are small in wild strains never exposed to drugs. In populations exposed to standard drugs for TB, the proportion is ca. 1 in 1 million, 1 in 100 million for Rifampin. Three kinds

of drug resistance to T.B medications are defined in Epidemiology. These are as follows:

- **Primary Drug Resistance:**

This kind of resistance is found in previously untreated patients. That is to say that an individual who is already carrying such traits of AFB infected them.

- **Acquired Drug Resistance:**

In this kind of resistance to TB medication, the patient initially has drug susceptible bacilli, which in the course of time become resistant. This is due to inadequate, inappropriate application of treatment or non-compliance.

- **Initial Drug Resistance:**

Mitchison (1968) defined this as drug resistance in a patient who denies history of previous treatment.

4.1 Origin of Drug resistance to TB medication.

The development of resistance occurs only by random mutations occurring in chromosomes. The average mutation rate leading to expression of antibiotic resistance is 2-3 per million bacterial replications for Isoniazid and Streptomycin and 2-3 per billion bacterial replications for Rifampicin and Ethambutol. It will therefore take more than a trillion replicating bacilli to give an organism resistant to Rifampicin and Isoniazid at the same time. Since there are about 100 million to

1 billion replicating bacilli in a lung cavity with active TB, it is less likely that drug resistant bacilli are found in untreated patients i.e Primary Resistance. Drug resistance is a consequence of selection when therapy is applied.

Resistance to Isoniazid or Rifampicin, is a single step mutation, compared to that of Penicillin, which is a multiple step mutation(Rist, 1964). The proportion of resistant cells in a given bacillary population is always greater than the rate of mutation. Some of the mutants do back mutate to sensitivity, while others perish. (David, 1970). [15]

World Figures for Resistance.

	Isoniazid	Rifampicin	Streptomycin	MDRTB.
Primary Resistance	1-17%	0-3%	24%	0-11%
Secondary Resistance.	4-54%	1-14%	0-9%	0-48%

MDRTB is defined as resistance to both Isoniazid and Rifampicin. This is highest among AIDS patients. In Europe, 25-40 % of such cases were AIDS patients.

4.2 Cellular Mechanisms

There are three mechanisms with which microorganisms are able to withstand drug action.

Barclay and Associates (1954), found that Isoniazid and PAS(Para amino salicylic acid) labelled with radioactive Carbon 14, are less taken up by resistant strains compared to parent strains. Youatt(1969) also came to the same conclusion of differences in cell permeability, being the main difference between resistant strains and parent strains. The same findings were found for Kanamycin and Streptomycin by Nichida (1959). **[15]**

The other two mechanisms have not been much researched upon as interference in uptake or penetration of drug. Destruction of the drug is one possible way bacilli can acquire resistance. Development of insusceptible metabolic pathways that prove to be impossible for the drugs to dismantle is also a way with which the bacilli can withstand action of these drugs.

4.3 Acquired Drug Resistance.

Primary drug resistance due to infection with bacilli generated from another person still poses a major problem. This is much true in developing countries that have high prevalence of both HIV/AIDS and TB for example Botswana. In such a setting, there is an increased chance for exogenous infection(in HIV positive individuals) and also increased resistant cases in the community.

Acquired resistance is increased when there is a history of previous treatment for TB. The risk is greater if the treatment fails or there is a relapse with the individual still on medication. Inadequate treatment is common in developing countries. Weak drug regimes and inappropriate duration of treatment are unfortunately common in such countries. Other factors include, treatment while living in a high tuberculosis incidence area, birth or residence in such an area, particularly Asia and Africa and a young age.

Biological determinants include, initial bacterial population, local factors inside the host favourable for multiplication of such bacteria e.g. AIDS patients, presence of drug in insufficient concentrations and patients drug inactivation status. Treatment with single drugs, inadequate dosage, insufficient duration and adding a single drug to a failing regime, contribute. The level of primary resistance in population is an indicator of the quality of TB control efforts in the past. Poorly managed chemotherapy programs are one of the main reasons for the emergence of resistance.

The increasing trend of private medical practices globally, has resulted in inadequate drug regimes and interrupted treatments due to economic constraints, inadequate training and little supervision. Breakdown in social services especially in developing countries and increasing poverty provide ideal conditions for selection and propagation of resistant organisms. In the rich countries e.g. Norway, MDRTB is low, but there are important important sub populations of such countries in which this type of TB is becoming a cause of concern. e.g immigrants, the poor.

The pandemic of HIV has had an important impact on the emergence of MDRTB. HIV shortens the cycle of transmission of TB, this has shortened the lag of appearance of primary MDRTB in some communities from 13-18yrs to 7-12yrs.[13]

DISCUSSION.

The impact of HIV/AIDS and TB in Botswana is already discernable. It is felt at sectoral, community, household and personal levels. All in all, the macroeconomic consequences result which have a direct impact on the well being of the nation as a whole. It is now over a decade since the epidemic took a strong foothold in Botswana and an assessment as to its consequences is necessary in order to develop countermeasures, which are effective and actually work. Macroeconomic and social impacts are a function of the stage of the epidemic at which an effective plan is implemented. The longer the wait, the more disastrous the impacts. Both government and the private sector are already experiencing an increase in labour costs due to high morbidity and mortality. Extra costs are also incurred in the training of new personnel due to the labour turnover. Quality of workforce has deteriorated in a country where low productivity had been an issue before the epidemic. Expenditure on health services has increased as such services are provided free in Botswana. Implementation of mitigation programs has also been increased with the thought that prevention is better than cure.

HIV has increased the incidence of TB. Co infection is high, with data from Francistown in 1990 showing a co infection rate of 67%. HIV is progressively eroding gains made by the TB control Program implemented in the early 80's. Notification rates are on the rise. An example is an increase from 2939 cases in 1990 to 5390 in 1995. The infection rate increased from 226 to 369 during this period. This coincided with the advent of HIV epidemic and as HIV, TB does show clustering around the sexually active group. (15-49yrs). [3]

The extent of the epidemic is vast in a country with such a small population. It is the task of the health authorities to break the transmission chain in hope of saving at least one generation. This can be achieved in many ways, some of which are:

- Strengthening epidemiological surveillance activities.
- Prevention of sexual transmission of HIV
- Prevention of HIV transmission through blood and blood products.
- Prevention of perinatal transmission.
- Strengthening diagnostic management and infection control.
- Setting up systems for monitoring and evaluation.

An STD/AIDS unit was established in 1992. This unit is further divided into four subunits, namely; Counselling and home based care, IEC, Surveillance and STD subunit. The unit as whole functions under adopted guidelines of the National AIDS control program. The following year, a national AIDS policy was prepared and adopted under the Presidents directive. This indicated anxiety on the government side, which has proven to be well founded. The policy provides a guide and framework for a national multi sectoral response to the epidemic.

There is an urgent need to tackle factors mentioned earlier as being central to the spread of HIV, and subsequent TB. Poverty alleviation by supporting income generating opportunities is necessary. Short and long term incentives for job creation need to be supported. Gender equality, though being a sensitive issue, needs to be encouraged via incorporation of the rights and protection of the girl child in all government policies. Laws and policies that disadvantage women

need to be eradicated. Sharing with women in decision-making empowers them and they can learn to have a say in matters of their own sexuality. It is high time that cultural norms are reviewed in order to identify those that enable the spread of HIV. Employment creation in the rural areas can reduce the migration to urban areas with subsequent shuttling between the two, can help in reducing tendencies towards multiple sex partners and encouraging a solid family life.

Laws dealing with rape, defilement and sexual harassment have to be reviewed and tougher sentences passed to offenders, since such offenders often practise unsafe sex. A youth sexual and reproductive health policy has been in place long before the onset of the epidemic. It needs to be revisited and modified in order to promote open dialogue among the youth about sexual matters and most importantly safe sex.

Since it is apparent that HIV positive individuals are more vulnerable to TB than immune competent individuals, it might be useful to endorse a policy of life long prophylaxis with anti TB medication. However this would require diligence on the part of the patient and the policy enforcer due to the danger of drug resistance surfacing if there is non-compliance. The study conducted on South African mine workers showed a tendency towards recurrences in HIV positive individuals mainly due to reinfection, than relapse. Primary Prophylaxis can thus be of use in such individuals.

STD's in Botswana have to be dealt with effectively. Not only are they evidence of unsafe sexual practices, they also provide easy access for the virus via lesions

and sores. The syndrome approach of treatment adopted by the government, though effective at times in treating STD's as early as possible, does pose a danger of resistance to antibiotics used in the future. In this approach, treatment is started on the basis of symptoms presented by the patient, instead of awaiting a confirmation of the diagnosis by other means. In Botswana, methods of prevention, including condoms, have always been provided to the public free of charge. The use of condoms is now being advocated more aggressively by campaigns and adverts on radio and television. A more effective method of abstinence, especially for the youth, has to be promoted, parallel to the condom campaign.

Treatment of MDRTB requires prompt recognition of the disease, rapid accurate drug susceptibility tests, and early administration of an individualised re treatment plan.

Table number.....TITLE.

1. Selected Demographic indicators, 1971-2001.
2. Reported HIV cases by age and gender, '86-'96.
3. Estimated number of adults and children living with HIV/AIDS, 2001.
4. Annual reported AIDS cases in Botswana, '87-'96
5. Seroprevalance amongst pregnant women, 1992-1995
6. HIV Seroprevalence amongst men with other STD`s in Botswana.1992-1995
7. AIDS Cases by age .1997-1998.
8. AIDS Cases, Male: Female Ratio, 1997
9. AIDS Cases, Male: Female Ratio, 1998
10. TB Notification rates in Botswana, 1976-1999.
11. TB and HIV Association
12. TB Notification in different age groups, 1999
13. TB Notification according to patient type.
14. TB Male: Female ratio in different age groups.

TABLE 1: Selected demographic indicators: 1971-2001

INDICATORS	1971	1981	1991	2001
Population (million)	596,944	941,027	1,326,796	1700 000
Total Fertility rate	7.1	6.2	5.2	4.4
Population Growth	1.8 %	4.7%	3.5%	1.6
Crude birth rate	45.5	47.2	39.3	34
Crude death rate	13.7	13.9	11.5	17
Infant mortality	92	71	45	74
Under 5 mortality	151	109	56	142
Life expectancy				
All	55.5	56.5	61.7	44
Males	52.5	52.3	59.4	
Females	58.6	59.7	65.9	
Pop. 5-15(%)	29.9	28.8	28.6	
Pop.15-49 (%)	39.4	40.8	45.5	
Rural population	91.4 %	81.8 %	54.3%	
Urban population	9.0%	18.2%	45.7%	
Gender ratio (males/100 females)	84.0	89.0	92.0	
Dependency ratio (per 100)				
Age less than 15	101	99	83	
Age more than 65	12	11	10	
Total	113	110	93	
Population density	1.0 per km ²	1.6 per km ²	2.3 per km ²	

Source: Botswana Population census 1971, 1981 and 1991

Table 2: Reported HIV cases in Botswana by age and gender 1986- 1996.

AGE	FEMALE	MALE	TOTAL
0 - 4	502	550	1052
5 - 14	50	28	78
15 - 29	3344	1566	4910
30 - 49	1625	2121	3742
50 +	92	193	285
No age child	91	91	182
No age adult	269	253	522
Total	5973	4802	10 775

Source: AIDS/STD Unit, MoH aids Update, 1996.

Table 3: Estimated number of Adults and children living with HIV/AIDS, end of 2001.

Adults (15-49)	300 000 adult rate (%) 38.8.
Women (15-49)	170 000
Children (0-15)	28 000

Total Adults and children 330 000.

Source: Epidemiological Fact Sheet on HIV/AIDS, 2002 Update. UNAIDS, WHO.

Table 5: Seroprevalence amongst pregnant women. 1992- 1995.

AREA	1992	1992	1993	1993	1994	1994	1995	1995
	N	%	N	%	N	%	N	%
Gabs, urban	841	14.9	801	19.2	1205	27.8	1307	28.7
F/Tow n urban	796	23.7	803	34.2	799	29.7	626	39.6
S/Phik we,urb.					307	27.0		
Serowe ,Palap.			267	19.9			262	29.9
Southe rn rural					508	16.0		
Chobe/ kasane			71	18.3			103	37.9
Tutum					303	23.1		
Kwene ng.			306	13.7				
Gantsi rural			126	9.5			95	18.9
Ngami/ Maun.			299	12.7	227	19.4		
Lobats e urban			258	17.8			231	38.9

Source: AIDS/STD Unit, MoH. Sentinel Surveillance in Botswana Reports 1992, 1993, 1994 and 1995.

Table 6: HIV Seroprevalence amongst Men with other STD's in Botswana.

SITE	1992		1993		1994		1995	
	N	%	N	%	N	%	N	%
Gabs	385	21.8	265	30.2	391	38.1	309	34.9
Ftown			305	48.5	247	53.8	217	50.7
Maun					93	26.9		
Sphik.					269	43.6		
Lob.			185	16.2			85	50.6
Chobe			39	43.6			59	35.6
Ghan.			132	15.2			61	11.5
Maha.	168	23.2						
Serow.							154	48.7

Source: AIDS/STD Unit, MoH, HIV Sentinel Survey Botswana. Reports 1992,1993,1994 and 1995.

Table 7: AIDS cases by age (1997-1998).

Age	1997	1998	Total	%
All	2245	2811	5056	100.0
0-4	363	81	444	8.8
5-9	17	36	53	1.0
10-14	1	10	11	0.2
15-19	21	104	125	2.5
20-24	220	521	741	14.7
25-29	366	809	1175	23.2
30-34	381	502	883	17.5
35-39	338	342	680	13.4
40-44	198	197	395	7.8
45-49	134	108	242	4.8
50-54	84	67	152	3.0
55-60+	121	34	155	3.1

Source: UNAIDS, Epidemiological Fact Sheet, 2002 Update.

Table 8: AIDS Cases Male: Female ratio (1997)

Age group	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-60+
NoM	196	11	1	1	46	152	200	187	136	91	59	62
NoF	167	6	0	20	174	214	181	151	62	43	26	59
Ratio												

Table 9: AIDS Cases Male: Female ratio (1998)

Age group	0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-60+
NoM	31	12	4	65	304	538	258	184	97	56	34	20
NoF	50	24	6	39	217	271	244	158	100	52	33	14
Ratio												

Table 8 &9 Source: UNAIDS, Epidemiological Fact Sheet, 2002 Update

Table 10: TB Notification Rate, 1976-1999.

YEAR	TB Notification Rate/ 100 000
1976	380
1981	290
1984	295
1989	200
1992	300
1993	330
1996	450
1998	500
1999	525

Source: Epidemiology and Disease Control Unit, MoH, 1999.

Table 11: TB and HIV Association.

STUDY	TB CASES	HIV tested	HIV positive	%TB\HIV
F\town, 1990	400	400	268	67.0%
Steen, Mazonde, 1992	214	214	45	21.0%
Maganu, Rumisha 5 districts, 1995	1333	310	228	73.5%
BOTUSA, whole country, 1997	551	240	117	48.7%

Source: Epidemiology and Disease Control Unit, MoH, 1999.

Table 12: TB Cases according to Age, 1999.

Age Group	Notified Numbers.
0-4	500
5-9	250
10-19	480
20-29	2100
30-39	2600
40-49	1500
50-59	550
59+	499

Source: Epidemiology and Disease Control Unit, MoH, 1999.

Table 13: TB Notification According to Different Patient type.

Patient Type	% Of the total notification cases
New Cases	91%
Default	2%
Failure (possible MDRTB)	1%
Relapse.	6%

Source: Epidemiology and Disease control unit, 1999.

Table 14: TB Male: Female Ratio according to different age groups.1999

Age	0-4	5-9	10-19	20-29	30-39	40-49	50-59	60+
NoM	334	120	164	895	1479	892	480	427
NoF	312	126	315	1186	996	412	172	170
M/F	1.07:1	0.95:1	0.52:1	0.75:1	1.5:1	2.2:1	2.8:1	2.5:1

Source: Epidemiology and Disease Control Unit., 1999.

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