1 INTRODUCTION

Women of advanced maternal age (AMA), namely pregnant women aged 35 years and older at the time of conception, are at an increased risk of having a baby with a chromosome abnormality, mainly Down syndrome (Mueller and Young, 2001). A small proportion of pregnant women of AMA in South Africa have access to testing for chromosome abnormalities during pregnancy. Where the options of counselling and testing are available, a woman offered AMA counselling is faced with difficult choices regarding her pregnancy. These relate to her risk for having an infant with a chromosome abnormality and how this may be addressed (Harper, 2001). Alone, this situation may present dilemmas and anxiety for women, however the HIV/AIDS pandemic being experienced in South Africa is complicating their predicament.

HIV/AIDS is not a genetic condition. However, the impact that it has on the genetic counselling process of women of advanced maternal age has become increasingly observed. In the Antenatal Genetic Counselling Clinics held at three academic hospitals in Johannesburg, South Africa, the percentage of pregnant women who are HIV positive is increasing (Doherty and Colvin, 2004). For a pregnant, HIV positive woman to make fully informed decisions regarding her pregnancy and her reproductive choices, she requires a clear understanding of the impact her HIV status has on her own future health, and that of her unborn baby.

This present study was undertaken to investigate the HIV status of women of AMA presenting for genetic counselling and to further ascertain the maternal perception of the impact of HIV infection on the health of the fetus, and to the future health of the women

themselves. The women's considerations on termination of pregnancy based on the HIV transmission risk to the fetus, as opposed to the risk consequent on AMA status, was also explored. The number of HIV positive women who requested amniocentesis was documented and compared to the number of HIV negative women who requested amniocentesis. The problems facing the HIV positive women with regard to the availability and effectiveness of antiretroviral prophylaxis prior to amniocentesis was also documented.

1.1 The Human Immunodeficiency Virus and AIDS

The human immunodeficiency virus (HIV) is a retrovirus that is transmitted through sexual contact and via the intravenous transfusion of contaminated blood and blood products. It can also be transmitted vertically from mother to child during pregnancy, birth and through breast milk. In developing countries, HIV is most commonly transmitted by heterosexual contact and by mother to child vertical transmission (Fauci and Lane, 2001). The risk of mother to child transmission (MTCT) depends on several factors, including maternal viral load and CD4 count, mode of parturition and availability of antiretroviral treatment during pregnancy and delivery (Fauci and Lane, 2001). The type and regimen of antiretroviral therapy (ART) also influences the transmission rate (Cooper et al., 2002).

HIV infection is characterised by immunodeficiency resulting from the progressive decline and deterioration of the CD4+ T-cells (Fauci and Lane, 2001). CD4 antigens are surface antigens of T lymphocytes, which act as primary receptors for HIV. When the level of these cells falls below 200 cells per microlitre, the risk of developing

opportunistic infections and cancer becomes high. The median duration from primary HIV infection to clinically apparent disease or AIDS is ten years (Fauci and Lane, 2001). Prognosis for patients is influenced by the type of AIDS-defining illness (ADI), with median survival time from onset of ADI being 11½ months (Post et al., 2001). The eight most common ADIs are extrapulmonary tuberculosis (TB), herpes simplex virus (HSV), Kaposi's sarcoma, oesophageal candidiasis, pneumonia (Pneumocystis carinii), cryptoccocal meningitis, encephalopathy and wasting. Survival of infected individuals ranges from greater than 24 months where the ADI is TB or HSV to just one month where there is wasting (Post et al., 2001). HIV positive children are vulnerable to infectious diseases including pneumonia, pulmonary tuberculosis and gastroenteritis, with older children also being susceptible to chronic cardiac disease and wasting syndrome (Meyers et al., 2000; Langston et al., 2001; Chakraborty et al., 2002; Ansari et al., 2003). A study conducted in Malawi (Taha et al., 2000) found that by two years of age, 35% of HIV infected children had died and by three years of age 89% of children had died, with only 1% remaining symptom free. Survival time was shortest when AIDS related conditions such as splenomegaly, oral thrush and developmental delay were present. All of these data relate to situations in which ART was not available.

1.1.1 The Epidemiology of HIV Infection

Over 70% of the world's estimated 36 million HIV infected individuals live in sub-Saharan Africa (Badri et al., 2002). In South Africa it has been difficult to accurately estimate the number of adults who are infected with HIV. Prevalence has been based on data extrapolated from antenatal surveys, and according to these the HIV rate has risen from 1% in 1990 to 25% in 2000 (Dabis and Ekpini, 2002; Doherty and Colvin, 2004).

These figures may be an accurate reflection of the prevalence in pregnant women, with the population incidence estimates ranging between 10.4 and 14.2% (Doherty and Colvin, 2004). The data suggest that one in four women attending antenatal clinics are HIV positive. According to Dabis and Ekpini (2002), the mother to child transmission rate in Africa ranges from 25 to 45%, with transmission dependent on maternal viral load and length of breast feeding. Worldwide approximately 600 000 infants are infected with HIV via their mothers per year (McIntyre and Gray, 2002). It was estimated that there were
330 000 deaths of children under 5 years in sub-Saharan Africa in 1999 due to HIV infection. HIV infection accounted for 7.7% of all under 5 year old deaths in sub-Saharan Africa in 1999 compared with 2% in 1990 (Walker et al., 2002).

In Africa there is a more rapid progression from HIV to AIDS, compared to industrialised countries, due to poor baseline health, poor nutrition and ill equipped health services (Dabis and Ekpini, 2002). The median age of survival without medical intervention for HIV positive women in Southern Africa is nine years. Children born to mothers with HIV/AIDS have additional risks other than becoming HIV infected; children, whose mothers have died from HIV/AIDS, have a three to four times increased risk of mortality due to lack of parental support and care, compared to children whose mothers are living. At the end of 2001 an estimated 12.1 million children in Africa had lost their mother or both parents to AIDS, and this figure, it is thought, may more than double within the next ten years. By 2010, 9% of children in Africa younger than 15 years will be orphans (Dabis and Ekpini, 2002). Of South Africa's approximately 885000 orphans in 2002, 38% were estimated to have been orphaned as a consequence of parental AIDS (Doherty and Colvin, 2004). Without provision of ART, these figures are expected to rise sharply over the next 10 years (Doherty and Colvin, 2004).

1.1.2 Vertical HIV Transmission from Mother to Child

Mother to child transmission of HIV can occur during pregnancy, delivery and via breast milk (Dabis and Ekpini, 2002). The higher the maternal viral load, the greater the risk of intrauterine and intrapartum transmission. The longer the infant is breastfed the greater the chance of transmission; the risk of transmission due to breast feeding ranges between 10 and 20% (Dabis and Ekpini, 2002). Breast feeding increases the risk of transmission as the virus is present in the breast milk, but as safe alternatives to feed the infant are not always available, breast feeding may remain the only available mode of infant nutrition. The main problems with formula feeding are a lack of clean drinking water, no means to sterilise water and bottles required for formula feeding, and the long term cost and availability of formula. If formula feeding is a viable option, the best prevention in developing countries seems to be antiretroviral perinatal prophylaxis and changing infant feeding from breast to bottle (McIntyre and Gray, 2002).

The World Health Organisation (WHO, 2004) has suggested the following strategies to reduce mother to child transmission:

- prevention of new infections in adults (parents of the future)
- prevention of unwanted pregnancies
- prevention of transmission from mothers to their infants
- provision of care and support to HIV-infected women, their infants and family

1.1.3 Prevention of Vertical Transmission of HIV

Provision of antiretroviral treatment to pregnant women peripartum and to the neonate to reduce the transmission risk to the baby should be the minimum health care provided (Dabis and Ekpini, 2002). Ideally pregnant women should be on a multi-drug regimen to lower viral load, thereby reducing the risk of mother to child HIV transmission at any stage of the pregnancy. In developed countries the risk of MTCT was shown to be reduced from approximately 30% to less than 5% due to the introduction of particular prevention strategies (Yeung and Gibb, 2001).

1.1.3.1 Combination therapy

In resource rich settings, the use of highly active antiretroviral therapy (HAART) has been demonstrated to be effective in reducing the risk of mother to child transmission. This therapy, however, needs to be tailored to the individual, and aspects such as adherence, drug interactions and toxicities require careful and continuous medical supervision (Ahdieh, 2001). The HAART regimen usually involves a combination of three or more drugs, which includes at least one protease inhibitor (PI) and/or a non-nucleoside reverse transcriptase inhibitor (NNRTI). PIs inhibit the splicing of viral proteins resulting in the production of non-infectious virus. NNRTIs, such as nevirapine, inhibit viral reverse transcriptase by disturbing the catalytic site (Taylor and Low-Beer, 2001). It has been shown that combination regimens are more effective in suppressing viral replication, and a lower viral load reduces the risk of transmission from mother to child (Taylor and Low-Beer, 2001). The risk of transmission can be reduced to 1.2% where HAART is administered (Cooper et al., 2002).

1.1.3.2 Single dose regimens

In resource constrained settings, inadequate finances and infrastructure may limit the practicality of implementing combination therapy programs. However the use of single dose regimens may be a consideration. In the Ugandan HIVNET 012 trial (Guay et al., 1999), a 200mg dose of nevirapine was given orally to pregnant woman at the onset of labour, and a 2mg/kg dose was given to the neonate within 72 hours of birth. The trial showed a 47% reduction in the three-month transmission rate from mother to child, with only 13.1% of infants becoming HIV positive. The advantages of this treatment program are its viability and relative cost-effectiveness; and because it is a once off treatment at birth, is easily adhered to. However, problems with this treatment may arise if HIV resistance to nevirapine occurs after the single dose.

In a later Ugandan study (Eshleman et al., 2001) 21 of 111 (19%) individuals showed viral resistance after a single dose of nevirapine, with the resistance occurring especially in cases of high viral load and low CD4 counts and possibly in particular HIV subtypes. However, following nevirapine resistance in these 21 patients, none showed detectable resistance to the drug after 12 to 24 months. But levels of nevirapine resistant HIV may not be demonstrable if they are low (Eshleman et al., 2001). In another study (Cunningham et al., 2002) new nevirapine resistance mutations in the HI virus were seen in 14/95 (15%) of pregnant women receiving a single dose of nevirapine, and the development of these mutations was not related to viral load or CD4 count. It is thought that within an individual's viral population, there are virus "species" that have resistance to nevirapine. When other viruses sensitive to the drug are suppressed, the population of the resistant virus type increases and resistance to the drug becomes evident. Some time after the single dose, other populations of the virus in the individual multiply and the apparent resistance to the drug diminishes. Assays used to detect mutant virus were not able to detect levels if lower than 20% to 25% of all "circulating virus" (Cunningham et

al., 2002). Resistance to a single dose of nevirapine drug therapy is important to elucidate as it may have consequences for future pregnancies (McIntyre and Gray, 2002).

1.2 Advanced Maternal Age and Chromosome Abnormalities

It has been well documented that advancing maternal age is associated with an increased risk of having an infant with a chromosome abnormality (Mueller and Young, 2001). Chromosome disorders contribute significantly to the burden of congenital disorders. The most common forms of live born babies with chromosome disorders are due to trisomies (Mueller and Young, 2001). Chromosomal trisomies are usually due to non-disjunction, where there is a failure of separation of the homologous chromosome pairs during the formation of the gametes. This error is strongly associated with increasing maternal age, and although the cause is uncertain, it is thought to be due to the ageing of the oocyte. If an ovum containing two of a chromosome pair is fertilised by a normal sperm, the resultant zygote will contain three copies of this chromosome and the fetus will have a trisomy (Mueller and Young, 2001). The extra genetic material results in over expression of certain genes, the principal result of which is intellectual disability (Cohen et al., 2002).

1.2.1 Down Syndrome

The most common genetic cause of intellectual disability is Down syndrome (Cohen et al., 2002). All individuals with Down syndrome have intellectual disability with IQs that range from 25 to 75 (Mueller and Young, 2001). A small group of children with Down syndrome assessed in a rural setting in South Africa all had a general intelligence quotient (IQ) of less than 40 (Christianson et al., 2002), while those tested in an urban South African environment had a mean IQ of 54 (Neser et al., 1989). A child with Down syndrome tends to have speech and language difficulties (Neser et al., 1989; Cohen et al., 2002) and may understand more than he or she can express through speech, thus resulting in an underestimation of the child's abilities. It has been shown that developmental functioning is improved by early and continuous intellectual stimulation (Neser et al., 1989).

Other clinical features of Down syndrome include: hypotonia, brachycephaly, epicanthic folds, upslanting palpebral fissures, protruding tongue, small and lowset ears, single palmer crease, and sandal gap (gap between the first and second toe). About 40 to 50% of babies born with Down syndrome have cardiac abnormalities that commonly include atrial septal defect, ventricular septal defect, patent ductus arteriosus or tetralogy of fallot. Individuals may develop hypothyroidism requiring life long medication. The life expectancy of individuals with Down syndrome in industrialised countries is 50 to 60 years, and most adults will develop Alzheimer's disease in later life (Mueller and Young, 2001, Cohen et al., 2002).

After Down syndrome, the most common live born babies with trisomies have Trisomy 18 and Trisomy 13, with birth incidences of 1 in 6500 and 1 in 12500 respectively (Rimoin et al., 2002). These are both conditions that have a poor prognosis, with long term survival rare. Most (90%) have cardiac anomalies, and all are severely

intellectually delayed. Other possible chromosome abnormalities that occur include numerical or structural abnormalities (Mueller and Young, 2001).

1.2.1.1 Down Syndrome in South Africa

In South Africa there are relatively high numbers of AMA women and the birth prevalence of Down syndrome is as high as 2.10 per 1000 (1/476) births in rural areas (Venter et al., 1995). However, Down syndrome is not well recognised in some communities of South Africa and few women have heard of Down syndrome (Christianson, 1996). Under-recording of the birth prevalence of Down syndrome in the South African setting is possibly due to the lack of neonatal diagnosis by doctors, mothers' inability to detect the features of Down syndrome in their babies, and the death of up to two thirds of these children by the age of two years (Christianson, 1996; Christianson et al., 2002). A high mortality in infancy and early childhood due to congenital heart defects, malnutrition and infection (Christianson, 1996) means that 65% of infants and children with Down syndrome die before two years of age (Christianson et al., 2002).

Unpublished data (Schön, 2004) indicate that only about a third of AMA women in Johannesburg are aware of Down syndrome. Women who are unaware of the risks associated with advancing maternal age therefore do not seek and thus have no access to genetic counselling, prenatal diagnosis or selective termination of pregnancy. Women in the community who are educated about Down syndrome and the risks associated with AMA can use family planning to reduce unwanted pregnancies, and those AMA women who decide to have children, have the further choice of genetic counselling, prenatal diagnosis and the option of selective termination of pregnancy.

1.2.2 Genetic Counselling

Genetic counselling is an educational process that deals with the risk of genetic disorders in a family (Harper, 2001). It aims to assist people in understanding the medical facts and recurrence risks while supporting them to make the best possible adjustment to the disorder or risk of disorder appropriate to their circumstances (Baker et al., 1998). Genetic counselling endeavours to empower people to make decisions which will help them to live and reproduce as normally as possible by providing optimum patient care in preventing or managing possible genetic disorders (Biesecker, 2001; Christianson and Modell, 2004).

1.2.2.1 Genetic Counselling for AMA

Ideally, genetic counselling should be offered to all pregnant women of advanced maternal age. In a genetic counselling session with an AMA woman, her risks, as a consequence of her age, for having a child with a chromosomal abnormality are explained and discussed. With advancing maternal age, the risks of having a baby with chromosome abnormalities increase exponentially from 1 in 526 for a 20 year old woman, to 1 in 192 for a 35 year old and up to 1 in 8 for a woman of 49 years (Table 1-1 and Figure 1-1).

Table 1-1 Risks of chromosome abnormalities in infants of mothers of advancing age

(Palomaki and Haddow, 1987)

THE RISK OF CHROMOSOME ABNORMALITIES COMPARED WITH MATERNAL AGE		
Maternal Age	Liveborns with Trisomy 21	All Chromosome Abnormalities At Delivery
20	1/1734	1/526
25	1/1250	1/476
30	1/965	1/385
35	1/386	1/192
40	1/110	1/66
45	1/31	1/21
46	1/24	1/16
47	1/19	1/13
48	1/15	1/10
49	1/11	1/8

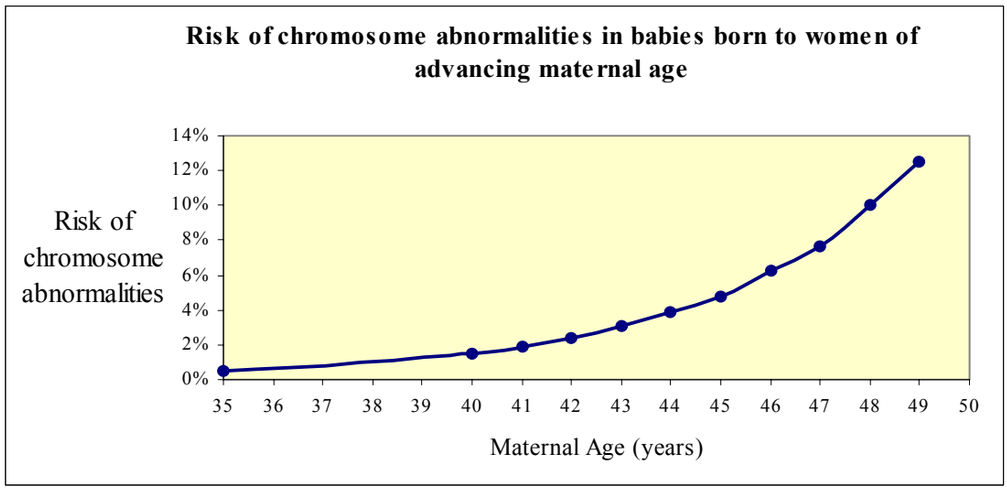

Figure 1-1 Exponentially increasing risk of chromosome abnormalities in the offspring of women of advancing age at time of conception (adapted from Palomaki and Haddow, 1987)

In different countries the definition of "advanced maternal age" varies. In Sweden it may refer to women who conceived over the age of 37 years (Sjögren and Uddenberg, 1989), while in the United States it is recommended that all pregnant women 35 years or older be offered fetal karyotype analysis by CVS or amniocentesis (Harris and Verp, 2001).

In South Africa, AMA encompasses pregnant women over the age of 35 years, as recommended in the Policy Guidelines (Department of Health, 2001). However, although 17.2% of pregnant women in South Africa are AMA (United Nations, 2003), the vast majority of these women do not have access to genetic counselling or amniocentesis for chromosome analysis. For the minority who are seen antenatally at hospitals where these services are available, for example the three academic hospitals Johannesburg General, Coronation and Chris Hani Baragwanath, most are not asked their age or offered genetic counselling, even though 70% present at primary health care clinics before 20 weeks gestation to have their pregnancy confirmed (Christianson and Modell, 2004; Schön, unpublished data, 2004).

1.2.3 Prenatal Diagnosis

After full genetic counselling regarding the risk of chromosome abnormalities and the implications of having a child with a chromosomal abnormality, particularly Down syndrome, the option of prenatal testing is explained. This includes explaining the procedure and risks of chorionic villus sampling (CVS) or amniocentesis, and the options available if an abnormality is detected. The woman's considerations regarding this information are also explored. The session should provide an environment wherein the woman being counselled is fully educated regarding her circumstances, and is able to discuss and explore her feelings. All decisions made are solely hers, to be made according to her social circumstances, cultural and religious beliefs (Baumiller et al., 1996). Should an abnormality be detected, a selective termination of pregnancy is offered. This would be discussed during a subsequent counselling session. A woman who remains unsure about testing may be given the opportunity to consider testing and discuss the options with her partner, returning to the clinic should she wish to undergo

testing – provided she is 11 to 14 weeks gestation (for CVS) or less that 24 weeks pregnant (for amniocentesis). This is a consideration, as the majority of women referred for genetic counselling do not present with their partners. A woman may opt for testing although she is against termination of pregnancy, using the procedure to forewarn her of an abnormal baby and allow her to prepare for this.

1.2.3.1 Testing: Chorionic Villus Sampling and Amniocentesis

The options for prenatal testing depend on the gestation of the pregnancy and the hospital at which the woman is seen. CVS is only available at Chris Hani Baragwanath Hospital, while amniocentesis is performed at all three academic hospitals in Johannesburg.

In a CVS, fetal tissue from the placenta is optained trans-abdominally under local anaesthetic (Maxwell et al., 1986). During amniocentesis a small volume, about 20ml, of amniotic fluid is obtained trans-abdominally from the uterus (Stranc et al., 1997). The amniocentesis is ideally performed between 16 and 20 weeks gestation, although in our clinics amniocenteses are offered up to the end of the 23rd week of pregnancy.

Both techniques are invasive and carry risks including vaginal bleeding and infection, as well as the risk of abortion (Harris and Verp, 2001). The risk of abortion varies depending on the skill of the operator, but where the doctor performing the test is suitably experienced, the risk of miscarriage due to CVS is given as 1-3% (Papp and Papp, 2003; Brambati et al. 1998; Stranc et al., 1997) and the risk after amniocentesis is given as 0.5-1% (Papp and Papp, 2003; Stranc et al., 1997; Tabor et al., 1986). It is

explained to the patient that the risk of miscarriage due to invasive testing exists and a miscarriage can occur even when the fetus does not have a chromosome abnormality.

1.2.3.2 Chromosomal Analysis

The CVS and amniotic fluid samples are analysed in the cytogenetic or serogenetic laboratories at the NHLS (National Health Laboratory Service), Braamfontein, Johannesburg. Preliminary results are available within two days for late gestation amniocentesis (22 to 24 weeks gestation).

Where the pregnancy is less than 21 weeks gestation only chromosome karyotyping is done. The fetal cells obtained from the amniotic fluid or the CVS are cultured and thereafter the chromosomes of a number of fetal cells are studied. This process takes three to four weeks and is capable of identifying large structural chromosome aberrations or numerical abnormalities of any of the 23 pairs of chromosomes (see Figure 1-2).

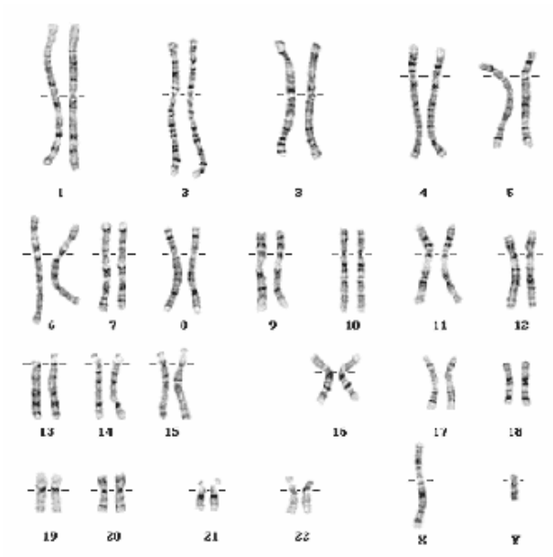

Figure 1-2 Example of a chromosome karyotype for a normal male (46, XY) showing 23 pairs of chromosomes arranged in descending size with the sex chromosomes X and Y listed last.

If the pregnancy is further advanced (21+ weeks) a karyotype, as well as polymerase chain reaction (PCR) analysis, are carried out because rapid analysis of the sample is preferable. The cells cultured from amniocenteses done at later gestations may be slow growing (Mukhona, personal communication, 2005) and it could therefore take longer for a result to be available. Amniocenteses performed close to the time of fetal viability require a prompt result should termination of pregnancy for abnormalities be requested. Quantitative fluorescence PCR (QF-PCR) assays are able to rapidly and accurately detect numerical disorders of specific chromosomes, viz chromosomes 21, 18, 13, X and Y (Bili et al., 2002; Pertl et al., 1999). These are the chromosomes most often associated with viable chromosome abnormalities (Mueller and Young, 2001). Fluorescent labelled primers are used to amplify short tandem repeats (STRs) which are specific to these five chromosomes. Once DNA is extracted and amplified, the PCR products are electrophoresed on an automated fluorescent DNA sequencer, which allows analysis of the intensity of the fluorescence and peak dimensions produced. The majority of samples are informative with two markers per autosome. In normal samples, two peaks of the same size, or one large peak, are observed; in trisomies there may be three peaks, two peaks in a 2:1 ratio or, rarely, one large peak. The advantage of this analysis is a rapid result – within 48 to 72 hours numerical anomalies of these chromosomes can be detected. The disadvantage of this technique is that it may not detect cases of mosaicism and not all chromosomes are studied (Bili et al., 2002; Pertl et al., 1999).

1.2.3.3 Results of Testing

If the chromosome results are normal the patient is informed telephonically. During the counselling session she is made aware that a normal chromosome result does not mean that there cannot be other abnormalities in the fetus. Where a fetal chromosome abnormality is detected, the AMA woman is invited for further genetic counselling and full discussion of the implications of the abnormal result. The options available to her, including selective termination of pregnancy, are discussed.

1.2.4 Termination of Pregnancy Act

The termination of pregnancy act (South Africa. Government Gazette, 1996: 4) sets the guidelines for when an abortion can be legally performed in South Africa. Termination on request for social reasons may be performed up to 12 weeks of pregnancy; from 13 weeks to 20 weeks a termination is legal under the following conditions: if continued pregnancy poses a risk to the mother's physical or mental health, if there is a substantial risk of severe physical or mental abnormality in the fetus, if the pregnancy is due to rape or incest, or if the woman's social or economic circumstances would be significantly affected by the continuation of pregnancy. After 20 weeks gestation, with no gestational age limitation set, terminations may be done if two medical practitioners, or one practitioner and a midwife, are of the opinion that the fetus is severely malformed or the pregnancy poses a risk to the woman's life or a risk of fetal injury.

1.3 The Impact of HIV on Genetic Counselling

1.3.1 Comparison of Risks

Counselling a woman about the risks of having a baby with a chromosomal disorder because of her advanced age involves the discussion of risks, which are relatively small when compared with the risk of HIV transmission from infected mothers to their babies, where HAART is not available. As noted in section 1.2.2.1, the risk of having a baby with a chromosomal abnormality increases exponentially as a woman gets older. The risks of chromosome abnormalities in the babies of women of advanced maternal age are significant, but to deal with these risks while ignoring the risk of HIV transmission is incompatible with appropriate, logical and ethical patient care, when the risk of transmission of HIV from a pregnant woman to her baby is as high as 30% without any antiretroviral treatment, and 13.1% with nevirapine treatment (given prior to birth and a dose given to the neonate shortly after birth).

A genetic condition with a risk of transmission as high as 13.1% and as poor a prognosis as HIV in infants, would warrant counselling regarding the option of selective termination of pregnancy.

1.3.2 HIV and Amniocentesis

Few studies examining the risk of transmission of HIV from a pregnant woman to her fetus due to amniocentesis have been conducted, but there have been studies showing a strong association between third trimester amniocentesis and vertical transmission of HIV. An observed four-fold increase in transmission due to third trimester

amniocentesis was documented by Tess et al., (1998) and another study (Shapiro et al., 1999) showed that amniocenteses without antiretroviral cover resulted in an increase in transmission rate from HIV positive women to their fetuses. Use of HAART therapy appears to reduce the risk of MTCT during amniocentesis. The viral load in the amniotic fluid was undetectable in women using HAART therapy, even when it was detectable in maternal blood (Maiques et al., 2003). It is thought that the use of nevirapine also reduces transmission risk at the time of amniocentesis although whether, and by how much, this risk is reduced remains unknown. It is therefore inferred from these studies that second trimester amniocentesis carries at least a similar, inherent risk of vertical transmission from mother to fetus, but the exact risk is not known. Studies to evaluate the issue in the second trimester have not been done, and would be unethical in a situation where ART is available.

As HIV has been shown to be present in amniotic fluid of infected women (Mundy et al., 1987) it would be considered unethical to offer an HIV positive woman a second trimester amniocentesis for chromosome analysis without making her aware of the potential risks involved. The risk of transmission is affected by maternal viral load, and women who have advanced HIV disease are at a higher risk of infecting their fetuses. It could be suggested that an amniocentesis be treated as a needle stick injury to the fetus, and the fetus should be protected by maternal ART prior to and after the procedure.

1.3.3 Decision Making

Counselling a patient about her risks of having a baby with a chromosome abnormality because of her age raises anxiety levels and may be particularly stress provoking in many of these women. To raise additionally in such an environment the concern about

HIV infection, and its impact on the woman's, and her unborn baby's health, totally alters the structure, evolution and outcome of the counselling session. The counsellee is faced with an often overwhelming volume of negative information, and placed in a position in which it may be exceedingly difficult to fully consider her options. She may need time to internalise the information, and her interpretation of the information needs to be explored, with any issues of social isolation, stigmatisation and low self-worth being dealt with (Biesecker, 2001) before she is in a position to make a decision.

1.4 Aims

The aims of this project were the following:

- Determination and comparison of the percentage of AMA women seen at Genetic Counselling Clinics at Johannesburg General, Coronation and Chris Hani-Baragwanath Hospitals over two six-month periods in 2003 and 2004, who had been tested for HIV, and the percentage of these who tested HIV positive
- Comparison of the uptake of amniocentesis between HIV negative and positive AMA women
- Investigation of the HIV positive women's perceptions of the impact of HIV on the future health of themselves and their fetus; exploration of the HIV positive AMA women's choices regarding amniocentesis
- Documentation of the women's knowledge and awareness of option of termination of pregnancy based on HIV transmission risk
- Exploration of how these choices were affected by the requirement of ART during the amniocentesis to minimise the transmission of the virus from mother to fetus.