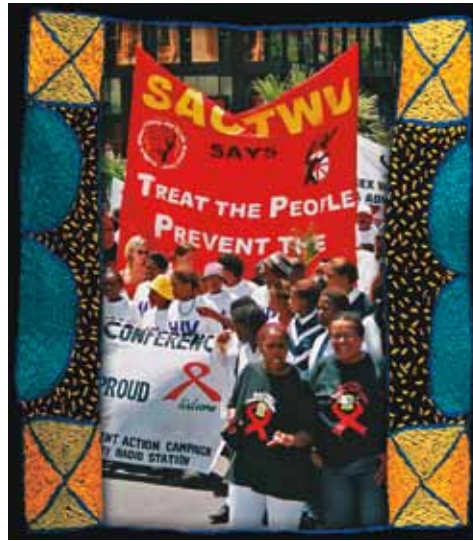


SOUTHERN AFRICAN
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OF HIV MEDICINE



SEPTEMBER 2011



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Cover: The cover photo was taken by Faizel Slamang in February 2003 at a march organised by the Treatment Action Campaign at Parliament in Cape Town, demanding a public sector HIV treatment plan (go to pp. 30 and 32 for more photos). The caption on the banner – 'Treat the People, Prevent the Infections' – was prescient in the light of the growing evidence of the role of antiretroviral drugs in preventing the sexual transmission of HIV. In this issue (p. 9) Nathan Geffen discusses the findings of the landmark HIV Prevention Trials Network (HPTN) 052 Trial, demonstrating that early initiation of antiretroviral therapy can help to prevent the sexual transmission of HIV-1 in serodiscordant couples.

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THE SOUTH AFRICAN
MEDICAL ASSOCIATION

FROM THE EDITOR

NEW DIRECTIONS AT THE JOURNAL

As some readers of the *South African Journal of HIV Medicine* will know, Professor Linda-Gail Bekker has elected to step down as editor, and I am moving into this position beginning with the September issue. Under Linda-Gail's leadership the journal has grown considerably, and we are indebted to her for her contribution over the past years. On a personal note Linda-Gail has been immensely helpful during the handover of the editorship, and I am happy to report that she will continue to provide guidance while serving on the journal's editorial board.

We are looking forward to continuing the journal's emphasis on presenting research and clinical experiences from across the region, and keeping readers updated around local and international developments. To this end we will seek to expand several sections over the coming issues, including:

- feedback reports from local and international conferences
- editorial reviews intended to share viewpoints and promote discussion on important topics, and
- programmatic reports that share local experiences in implementing HIV treatment and prevention services on the ground.

These new sections will be in addition to the ongoing emphasis on research articles and case reports that are established strengths of the journal. We are also aiming to increase the number of articles published in each edition, so please keep your submissions coming. In addition I want to continue Linda-Gail's 'open door' policy regarding suggestions for future content. If you have ideas, thoughts or feedback, please e-mail me directly (landon.myer@uct.ac.za).

This issue of the journal features a number of important contributions. An opinion piece from Nathan Geffen discusses the implications of the recently announced findings of HPTN 052, demonstrating

that antiretroviral therapy is an effective form of HIV prevention in serodiscordant partnerships. There was a time when HIV prevention and treatment were distinct spheres (in both service delivery and our thinking about the epidemic), and these boundaries are rapidly falling away. Next, Coceka Mnyani and colleagues discuss the risks associated with invasive obstetric procedures in HIV-infected women, a valuable follow-up to the previous issue's emphasis on PMTCT. In an original scientific article, Greg Jonsson and colleagues report on a survey of HIV-related knowledge among psychiatric patients in Soweto. A case report on HIV and primary lymphoma of the breast (Barnardt) reminds us of the unusual complications that can accompany advanced HIV disease, while another case report demonstrates the value of simple microscopy in diagnosing a deep fungal infection in an HIV-infected child (Crous). Finally, in a report back from a local meeting Kevin Rebe discusses the findings of a recent conference on the health of men who have sex with men.

This issue also features a special article on the teaching (and understanding) of clinical immunology in the context of HIV/AIDS. Clive Gray and colleagues developed an innovative approach to 'lure clinicians into learning immunology' – no easy task. This work has won several awards, and is well worth checking out: www.immunopaedia.org.

I hope that this breadth and depth is a flavour of things to come! Happy reading.

LANDON MYER

Editor

Associate Professor, School of Public Health and Family Medicine, University of Cape Town

MESSAGE FROM THE EXECUTIVE

The National Strategic Plan for 2011 – 2016 is being written as you read this issue of the *Journal*. Through its members, the Society has contributed a lot to the draft that it is hoped will be out in the next few weeks. The previous Plan was constructed in extremely difficult political circumstances (the then Minister of Health and senior Department of Health officials were still part of the old Mbeki era of HIV denial), and involved long meetings arguing over the most ridiculous points of science. This Plan is a completely different beast – broadly consulted in multiple meetings with every corner of society, with the DoH leading from the front. The writing team is reviewing a huge number of submissions, and integrating the suggestions into a strategic plan.

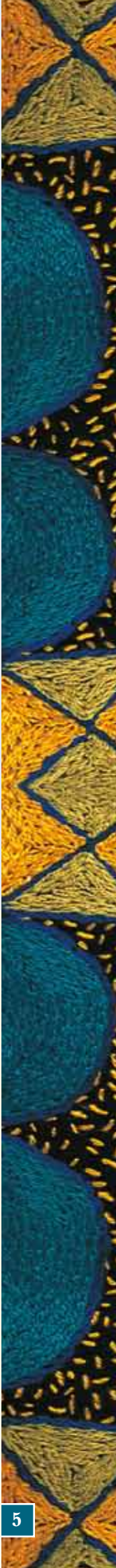
The plan suggests that there will be more firm targets on everything from monitoring the number of people on ART to human rights abuses

to drug stock-outs, and some dramatic 'game changers'. Keep your eye on this space – we'll be profiling the Plan through the Society.

The Executive's term of office is up, as the board has taken over, in terms of the new Companies Act. They have kindly remained as an advisory board, but elections for a new set of directors for the Society will take place in November. I encourage people to consider standing, even though the current Exco is a hard act to follow. Finally, welcome to Landon as the new, energetic editor of the *Journal* – we can't wait to see how you build on the LGB legacy.

FRANCOIS VENTER

President



REVIEW

IMMUNOLOGY FOR CLINICIANS: A 'TROJAN HORSE' APPROACH*

Clive M Gray, Shayne Loubser, Carina Kriel, Monica Mercer

National Institute for Communicable Diseases, National Health Laboratory Services, Johannesburg, South Africa

Heather Brookes

University of Johannesburg, Johannesburg

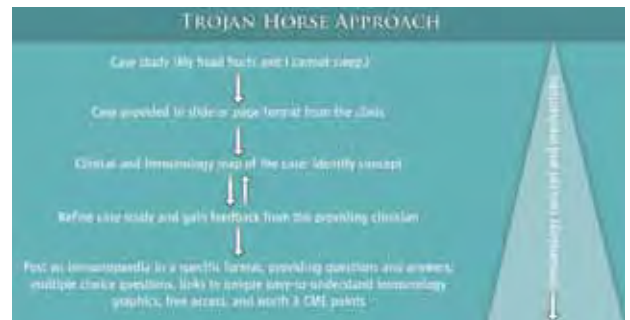
A South African website imparts basic immunology information to clinicians and other health care workers.

To determine how a program for learning immunology could be most useful for clinicians in South Africa, we consulted with the country's 20 leading HIV specialist pediatricians. They told us that immunology and its underlying concepts were perceived to be complex and arcane and that there was a need for immunology to be better integrated into "real-life" clinical practice. Most saw immunology as predominantly a laboratory science with little application to clinical practice; this highlighted a gap between clinical management of patients and theoretical understanding of the etiology and immunopathogenesis of disease. We speculated that one of the possible reasons for this perception and knowledge gap is that immunology is not an independent discipline within the South African medical curriculum. Instead, it is diffusely integrated into disciplines such as pathology or internal medicine and is not specifically provided for during post-degree training.

We initially developed the project Immunopaedia (www.immunopaedia.org) to help bridge the knowledge gap between laboratory research and pediatric HIV clinical science. The rationale for Immunopaedia was based on the paradox between the void in knowledge of immunology among HIV infectious disease clinicians and the need to understand and treat the HIV epidemic in South Africa. South Africa has one of the fastest-growing HIV epidemics with over 5.5 million people living with HIV, many of whom are young children and women (1). The 2008 national population-based surveys estimated HIV prevalence at 16.9% (2). Provision of treatment and care for such a large population makes it hard for HIV clinicians to stay informed about the latest developments in infectious disease. Immunopaedia was thus created to provide an easy-to-understand summary of the effects of HIV infection on the immune system, which could facilitate improvement in clinical practice. Immunopaedia has since progressed to include more general immunology knowledge that is relevant to other disease conditions. We use a clinical case-based perspective to target interns in multiple clinical specialities. Immunopaedia is an alternative to more advanced online immunology studies that target the basic-science student (3). Information and educational materials are available through open access, and the site can be used as an adjunct to more formal courses or as a stand-alone learning tool.

*SPORE Science Prize for Online Resources in Education) Series Winner (www.sciencemag.org/special/spore/). Corresponding author: C Gray (cgray@nicd.ac.za).

From *Science* Vol. 329, 24 September 2010, pp. 1613-1614. Reprinted with permission from the American Association for the Advancement of Science.



Trojan Horse approach. Immunopaedia uses a case study to lure clinicians into learning immunology. Shown are the steps followed for each case before posting on the Web site. The case is used to underpin an immunology concept.

Our main method is what we have termed the "Trojan Horse" approach. Derived from the Greek *Iliad*, "Trojan Horse" has come to mean any ploy or scheme used to insinuate a rival into a securely protected stronghold. We use clinical case studies as our Trojan Horse to tempt clinicians, most of whom consider immunology to have little application to clinical needs, to engage with immunological concepts relevant to diagnosis and treatment (see the figure, above). We explain the key immunological points related to the cases by means of a series of graphics.

The Web site consists of three key components: Clinical Cases, Immunology Learning, and Treatment and Diagnostics. At present, 34 clinical cases are available on the site. In addition to HIV, clinical cases span topics such as hypersensitivity, tuberculosis (TB) immunopathology, primary and secondary immunodeficiencies, drug responses, gastrointestinal disorders, autoimmunity, and malignancies. Each of our cases is used to examine an immunological concept that leads to greater understanding of the human immune system. For example, a case of a 14-year-old boy presenting with severe hip pain allowed us to discuss ankylosing spondylitis and to explore the concept of mimicry and the "arthritogenic peptide" hypothesis. The case of repeated apnea and infections in a premature infant allowed us to highlight "physiological immunodeficiency" caused by impaired humoral and cellular responses in premature infants, a situation that leaves such infants vulnerable to both viral and bacterial pathogens. Another presenting case was an 8-month-old boy with recurrent infections. We explored the most likely hypothesis, that the mother had a primary HIV-1 infection during pregnancy in the third trimester and that the child was infected perinatally before maternal seroconversion. These are real-life cases, and in the last-mentioned case, as often in real life, the underlying immunological problem may not be clear.

Each case discussion provides, in consecutive windows, patient presentation, history, differential diagnosis, examination, investigations,

discussion, treatment, and a final outcome. Related case studies are cross-referenced. Users then evaluate their knowledge and understanding of the concepts in the case study by means of questions accompanied by explanations. To earn the full quota of continuing medical education (CME) points, the user can complete five multiple choice questions for each case study that are freely available but require log-in information. Integral to our approach with each case study is the use of clear graphics to explain the immunological basis and mechanisms underlying the condition. The graphics can be downloaded freely as a PDF and used for offline reference or for further teaching tools.

The second key component, Immunology Learning, is divided into three main areas: "Immunology" (dealing with the basics), "Childhood Diseases and Vaccinations" (dealing with hypersensitivity reactions and immune reconstitution, for example), and "Infections" (dealing with a range of infections from rickettsia to Guillain-Barré syndrome).

The third key component, Treatment and Diagnostics, covers information related to TB and antiretroviral (ARV) drugs, modes of drug action, the HIV life cycle, and specific guidelines for treatment. The "Diagnostic Tools" section provides laboratory assay information, such as enzyme-linked immunosorbent assays (ELISAs), polymerase chain reactions (PCRs), and flow cytometry.

Immunopaedia provides links to other Web sites that focus on medical and general aspects of HIV, pediatrics, and treatment guidelines. The design of the Web site is such that the user can easily find a source of information in the form of a case study, a graphic, or a scientific article on specific immunological conditions. In addition, breaking scientific news on clinical immunology is posted on the home page and is updated daily. Registered users are sent a monthly newsletter that coincides with a monthly clinical case study posting.

For the clinical case component, medical practitioners submit case studies from their clinics. Our team of clinical and immunology experts reviews and modifies these case studies for presentation on the Web



Workshop participants evaluate case study material. Participants of workshops come from tertiary teaching hospitals within South Africa and include interns specialising in paediatrics, pathology, and internal medicine.

site (see the first figure). The rationale behind this approach is that case studies from, or closely related to, real situations are effective learning tools (4). The case-study approach is a form of experiential learning; it integrates practice, knowledge, and skills that further equip clinicians in their professional work (5). As the user reads through the case study on the site, dividing the case study into stages in separate windows, the user is challenged to think about and predict a possible diagnosis based on the clinical evidence he or she has just read. This process is similar to the way a clinician might operate on the job, and the approach fosters lateral and critical thinking, as well as self-guided learning (6).

Immunopaedia also includes a workshop component as a follow-up to the online material (see the second figure). We use the workshops to evaluate our new case-study material before posting it on the Web site, and our teaching team travels to medical schools within South Africa to hold 3-hour sessions for medical interns who are specializing in pediatrics, pathology, or internal medicine. The aim of the workshops is to create greater awareness and increased use of Immunopaedia as a learning site for clinical immunology.

The monthly average number of unique users was 320 in 2007; 1518 in 2008; 2326 in 2009; and 1723 in 2010 (through June). Since the site first went live, we have received a total of 87,550 visitors, of which 11,520 have spent more than 5 minutes on the site. Each user who completes a case study earns three CME points, and in total, we have awarded 699 CME points over 3 years. We currently have 892 registered users.

Future directions for Immunopaedia involve the expansion of our user base to include point-of-care clinicians for the ARV drug roll-out in South Africa. We will use clinical case studies to highlight common diagnostic decision points as a mechanism to educate clinicians on laboratory tools and interpretation of results. Immunopaedia is an immediate source of information for professionals and represents an effective means for learning and dissemination of immunology information. Our aim is to integrate immunology into clinical options for patient management.

ABOUT THE AUTHORS

Clive Gray, founder of Immunopaedia, has a PhD in immunology and conducts research on HIV/AIDS in South Africa. He received the Elizabeth Glaser Pediatric AIDS Foundation International Leadership Award, which has allowed the development of Immunopaedia. Shayne Loubser writes the immunology materials and produces the computer-generated graphics for each case study. Carina Kriel is the curator and coordinator of the Web site and oversees all administrative aspects. Monica Mercer (not pictured) holds an MD and is a clinical materials writer and leads the development of educational materials. Heather Brookes (not pictured) has a PhD in language, literacy, and culture and is a consultant for Internet learning. From left to right: Shayne Loubser, Clive Gray, and Carina Kriel.



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OPINION

WHEN TO START ANTIRETROVIRAL THERAPY IN ADULTS: THE RESULTS OF HPTN 052 MOVE US CLOSER TO A 'TEST-AND-TREAT' POLICY

Nathan Geffen, MSc

Centre for Social Science Research, University of Cape Town

When is the best time to initiate antiretroviral therapy (ART) in adults? This is a vital question in HIV treatment and prevention services. More specifically, is the 350 cells/ μ l CD4 count threshold recommended by current World Health Organization (WHO) guidelines sufficient, or should we move to a 'test-and-treat' approach in which anyone who tests HIV-positive is offered ART, irrespective of their CD4 count? The recently announced results of the HPTN 052 trial take us closer, but not all the way, to a test-and-treat approach.

There are several important questions in determining ART initiation criteria, including what is best for treating the HIV-positive individual, what is best for HIV and tuberculosis (TB) prevention at the population level, and the costs of the different options for initiating ART. While there is not yet enough evidence to confidently change policy to recommend universal ART for all HIV-positive individuals, there are certainly enough data to support the implementation and evaluation of 'test-and-treat' pilot programmes.

WHAT IS BEST FOR TREATING THE HIV-POSITIVE INDIVIDUAL?

Clinical trials have shown definitively that a CD4 threshold of 350 cells/ μ l for initiating ART results in lower morbidity and mortality than 200 cells/ μ l.^{1,2} However, observational data on whether patients with HIV will benefit from initiating at a higher CD4 count are less clear.

Researchers from the North American NA-ACCORD cohort (including over 17 500 patients) found a nearly two times increased risk of death in patients who deferred ART to below 500 cells/ μ l.³ This study is cited in US treatment guidelines that provide for early treatment. However, the study's statistical methods have been criticised.^{4,5} Other evidence comes from the HIV-CAUSAL collaboration, which includes nearly 21 000 patients in Europe and America, including the NA-ACCORD patients. In this study no mortality benefit was observed for patients who started ART with a CD4 count above 500 cells/ μ l compared with those who started at 350 cells/ μ l. However, AIDS-defining illnesses were significantly more likely among patients who started treatment at lower CD4 counts.⁶

These studies do not offer conclusive evidence that initiating ART early (>500 cells/ μ l) will benefit patients. Both NA-ACCORD and HIV-CAUSAL are observational studies and subject to methodological limitations. The long-term side-effects of ART and the possible effect of treatment fatigue on adherence might mitigate against early initiation. Furthermore, participants in these studies were less likely to use sub-optimal drugs, such as stavudine, that are prevalent in many resource-limited settings.

It is hoped that two ongoing clinical trials will answer once and for all whether early treatment is beneficial. The Strategic Timing of Antiret-

roviral Treatment (START) trial is recruiting 4 000 volunteers. Patients with CD4 counts >500 cells/ μ l are randomised to either initiate immediately or defer to 350 cells/ μ l.⁷ This international trial currently only has one site in sub-Saharan Africa, the Desmond Tutu HIV Centre at the University of Cape Town (UCT). START is due to complete in 2015, and clinicians in Cape Town should encourage their patients with high CD4 counts to consider enrolling at the UCT site.

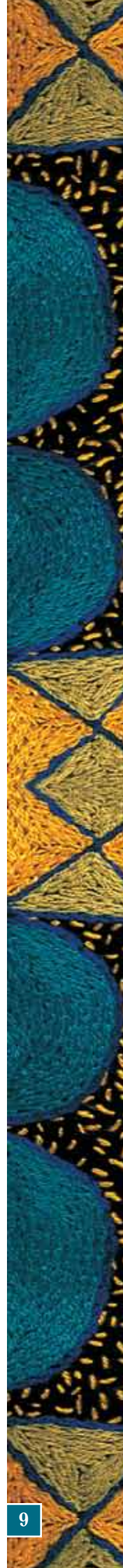
In addition, the ANRS 12136 trial in Côte d'Ivoire is due to complete in 2013. The trial objective is to compare the benefits and risks of initiating ART according to the WHO guidelines versus the benefits and risks of initiating ART immediately among HIV-positive adults with CD4 counts >350 cells/ μ l.⁸

WHAT IS BEST FOR HIV AND TB PREVENTION AT THE POPULATION LEVEL?

Several observational studies show that there is a strong correlation between reduced HIV incidence and either increased ART coverage or lower viral loads in the community. In San Francisco, new HIV diagnoses decreased along with mean community viral load from 2004 to 2008.⁹ In Taiwan, there was a more than 50% decrease in HIV infections ascertained by community surveillance after the introduction of free ART.¹⁰ In British Columbia from 1996 to 2009, the number of people receiving ART increased from 837 to 5 413, while the number of new HIV diagnoses fell over 50% from 702 to 338 per year.¹¹

Because of the possibility of confounding factors, these observational studies alone do not prove a causal effect, although they are strongly suggestive. This research was also conducted in populations where a large proportion of HIV-positive individuals are men who have sex with men (MSM), and the generalisability of the findings to heterosexual populations may be questioned. However, the recently terminated HPTN 052 study indeed demonstrates that ART reduces the risk of HIV transmission in serodiscordant predominantly heterosexual couples.

HPTN 052 was an international study that began enrolling in 2005. A total of 1 763 HIV-positive people in serodiscordant relationships and with CD4 counts from 350 to 550 cells/ μ l were randomised to either receive ART immediately (immediate group) or when their CD4 count fell below 250 cells/ μ l (delayed group). A total of 39 HIV infections



occurred, and genetic analysis demonstrated that most transmission was between partners enrolled in the trial. Only one HIV transmission took place from HIV-positive to HIV-negative partner in the immediate group versus 27 in the delayed group (hazard ratio (HR) 0.04; 95% confidence interval (CI) 0.01 – 0.27; $p < 0.001$).¹² The study was due to complete in April 2015, but the Data Safety Monitoring Board terminated it in May 2011 because of the highly significant results.

An additional important finding from HPTN 052 is that patients in the immediate initiation arm had fewer treatment endpoints, defined as first serious HIV-related clinical event or death (HR 0.59; 95% CI 0.40 – 0.88; $p = 0.01$). The difference was driven by the fact that three participants in the immediate arm versus 17 in the delayed arm developed extrapulmonary TB ($p = 0.002$). However, given the wide CI and the fact that the treatment initiation threshold was 250 cells/ μ l (not 350 cells/ μ l), this is not conclusive evidence of the benefit of early treatment to the patient.

Existing research suggests that a test-and-treat approach is likely to reduce HIV incidence. It is of course not a panacea: test-and-treat will seldom identify patients with primary HIV infection and therefore will not eliminate transmissions during primary HIV infection. Infections due to virological failure should also be expected, and there is the inevitable decline in efficacy when moving from trial conditions to programmes serving entire populations. Nevertheless, combined with scaled-up male medical circumcisions and condom distribution, we now have a formidable arsenal for reducing sexually transmitted HIV infections.

A further public health benefit of test-and-treat is the effect on the TB epidemic. Observational data also show a correlation between ART scale-up and reduced TB incidence. For example, one study in Masi-phumelele township in Cape Town found that pre-ART adult TB notifications increased by an average of 212 cases per 100 000 people per year, while post-HAART, adult cases decreased by 116 per 100 000 per year.^{13,14}

WHAT DOES THIS MEAN FOR GUIDELINES?

While 'test-and-treat' policies might still be a few years away, it is perplexing that the South African treatment guidelines still use an ART initiation threshold of 200 cells/ μ l except for pregnant women and people with TB (in which case 350 cells/ μ l is the initiation threshold). This is not a minor issue. A study by Médecins Sans Frontières of a Lesotho cohort found that the 639 patients who initiated above 200 cells/ μ l were 68% less likely to die and 39% less likely to be lost to follow-up than patients who initiated below 200 cells/ μ l. Only 56 patients were pregnant and 66 had TB, and thus would have been started on treatment according to the South African guidelines.¹⁵ By failing to update our guidelines to the WHO standard, i.e. offering ART to all patients at first CD4 count below 350 cells/ μ l, we are probably losing lives.*

WHAT ABOUT COSTS?

Costing and operational issues are major concerns in implementing a 'test-and-treat' strategy on a large scale. One analysis presented at the International AIDS Conference in 2010 estimates the cost of using ART for prevention in South Africa. This analysis concluded that expanding ART to all CD4 levels, beyond the recommended WHO threshold of 350 cells/ μ l, would add \$700 million to the cost of the programme, but that this would prevent 681 000 new infections over time, and consequently allow the cost of the programme to break even by 2022.¹⁶

*This policy was changed after this article was accepted. Now all HIV-positive patients with CD4 counts < 350 cells/ μ l are eligible for ART. – Editor

Another analysis by the Health Economics and Epidemiology Research Office (HERO) has examined the cost of ART using the WHO guidelines compared with a CD4 initiation of 200 cells/ μ l (South Africa's old guidelines). The cost of first-line tenofovir-based regimens is estimated to be R4 320 per patient for the first 6 months of treatment followed by R6 126 per patient per year.¹⁷ The ASSA2008 model estimates that there are 5.6 million people with HIV and 1.2 million on treatment.¹⁸ If hypothetically it were possible to initiate 1 million people on ART with CD4 counts > 350 cells/ μ l who pass through the HCT programme over the next year as part of a test-and-treat programme at an average of R7 000 per patient for the first year, the additional cost of ART would be R7 billion – a substantial burden on the state's finances. However there are also potential cost savings due to reduced HIV infections and possibly reduced opportunistic infections. The potential of reducing the cost of treatment by lowering ART prices, task-shifting, and the potential for the private sector to absorb a greater part of the cost of treatment than it currently does should also be considered.

The HERO study suggests that if task-shifting were implemented and optimal reference prices were paid for ART regimens, the WHO 350 cells/ μ l initiation threshold including tenofovir-based regimens would cost less to implement than using the old 200 cells/ μ l threshold with stavudine (without task-shifting and optimal reference prices). Analyses like this demonstrate that it is not necessarily guideline improvements that stand in the way of making programmes more affordable, but rather sub-optimal drug prices and programme design and staffing plans. In this light, it is possible that 'test-and-treat' approaches could be made highly cost-effective, and analyses of the costs and benefits of such an approach are clearly needed.

CONCLUSION

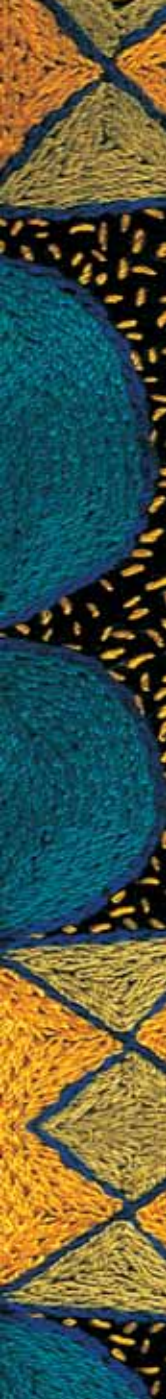
While we do not yet have sufficient data to change guidelines to adopt test-and-treat, there are sufficient data to support preliminary programmes to research this approach. The HPTN 052 results suggest that 'test-and-treat' may present an opportunity to reduce HIV incidence in South Africa. Nationally, we need to consider piloting in some health facilities the offer of ART to HIV-positive people in serodiscordant relationships, heterosexual or homosexual, irrespective of CD4 count. Such an operational research cohort would help us estimate the cost of a test-and-treat approach and identify its practical challenges and opportunities.

Declaration of conflict of interests: The author is on the Community Advisory Board for the START study.

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OPINION

HOW CAN WE REDUCE THE RISK OF MOTHER-TO-CHILD TRANSMISSION OF HIV DURING INVASIVE OBSTETRIC PROCEDURES?

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Antenatal invasive obstetric procedures may be diagnostic or therapeutic, and are performed at different stages of pregnancy for various indications. The most common indication for an invasive procedure during pregnancy is for fetal karyotyping when a chromosomal abnormality or a genetic defect is suspected, either from the couple's history or from ultrasound assessment of the fetus. Other less common but equally important indications may be diagnostic (fetoscopy, fetal tissue sampling, estimation of fetal haemoglobin) or therapeutic (aspiration of various fetal cavities, fetal blood transfusion and embryo reductions). In a high HIV prevalence setting like South Africa, a significant proportion of pregnant women in need of invasive procedures will be HIV-infected.

There are no published data on the number of invasive procedures done in South Africa, but unpublished data from national laboratories suggest that the services are under-utilised.¹ In 2008, 6 out of 7 national laboratories received 529 amniocentesis specimens done for advanced maternal age – this in a background of 1 049 300 live births.^{1,2}

In a high HIV prevalence setting like South Africa, where the estimated prevalence in antenatal clinic attendees was 29.4% in 2009, a significant proportion of pregnant women in need of invasive procedures will be HIV-infected.³ HIV clinicians need to be aware of the risk of mother-to-child transmission of HIV (MTCT) associated with invasive procedures, and should also be aware of strategies available to minimise the risk. This information needs to be given to clients during the counselling session before the procedure, and HIV clinicians may also be asked to advise obstetric colleagues on optimal management in cases where a HIV-infected woman requires a prenatal invasive procedure.

TIMING OF INVASIVE PROCEDURES IN PREGNANCY

Below is a list of commonly performed antenatal invasive obstetric procedures and the gestational age at which each procedure can, or should, be performed.

- Amniocentesis: from 16 weeks
- Chorionic villus sampling: from 11 to 14 weeks
- Cordocentesis: from 20 weeks
- Fetoscopy: usually in the 2nd and 3rd trimesters
- Fetal tissue sampling (biopsies of organs, muscle, etc.): usually in the 2nd and 3rd trimesters
- Aspiration of various fetal cavities, shunt insertion: any gestational age – usually from 16 weeks
- Embryo reductions: from 11 weeks.

Several complications may occur with invasive procedures, and as part of pre-procedure counselling the woman/couple should be made aware of the risk of procedure-related complications. These include injury to maternal bowel, fetal injury, failure to obtain a sample, chorio-amnionitis, and most significantly fetal loss.⁴ The Royal College of Obstetricians and Gynaecologists guideline on amniocentesis and chorionic villus sampling advises that patients should be informed of an additional 1% risk of fetal loss following an amniocentesis, and a slightly higher risk following chorionic villus sampling.⁵ A 2003 Cochrane Review advises that, for second-trimester testing, amniocentesis is the safer procedure – safer than early amniocentesis or transcervical chorionic villus sampling.⁶ For testing before 15 weeks of pregnancy, transabdominal chorionic villus sampling is the safer procedure.⁶ There is no literature to suggest that the risk of procedure-related complications is higher in HIV-infected women.

RISK OF MTCT WITH ANTENATAL INVASIVE PROCEDURES

There is limited literature on invasive obstetric procedures in the context of maternal HIV infection. Few studies have been published on the topic, most with a small number of patients. Important risk factors for MTCT such as maternal HIV viral load and CD4⁺ cell count are not always controlled for, and it may be difficult to infer causality in the reported cases of transmission after an invasive procedure. Without any maternal antiretroviral therapy initiated before an invasive procedure the risk of MTCT with invasive obstetric procedures is high, with rates of over 30% reported in some studies.⁷ In one study evaluating the effect of various factors on the risk on MTCT, third-trimester amniocentesis without any antiretroviral cover was associated with a fourfold increase in the risk of MTCT.⁸

With the use of combination antiretroviral therapy before antenatal invasive procedures, the risk of MTCT is reported to be similar to that of a HIV-infected pregnant woman who has not had an invasive procedure.⁹⁻¹¹ In studies reporting no MTCT with combination antiretroviral therapy, a significant number of women were initiated on therapy before conception, and the majority were virally suppressed at the time of the procedure.⁹ Despite the decrease in HIV transmission with antiretroviral cover, procedures that require more technical skills – such as chorionic villus sampling and cordocentesis – should still be avoided in the HIV-infected woman, as the risk of transmission to the fetus may be considerably increased.

Guidelines on the techniques of performing invasive procedures should be adhered to, and where possible the transplacental route should be avoided owing to the higher risk of transmission.¹²

RECOMMENDATIONS ON ANTIRETROVIRAL PROPHYLAXIS PRIOR TO INVASIVE PROCEDURES

There is now general consensus that any HIV-infected pregnant woman who needs to undergo an invasive obstetric procedure should have combination antiretroviral therapy initiated before the procedure, regardless of maternal CD4⁺ cell count.^{12,13} Ideally, antiretroviral therapy should be initiated at least 4 – 6 weeks prior to the procedure to achieve a significant level of maternal HIV viral suppression.¹⁴ If the gestational age precludes waiting for the period of 4 – 6 weeks, the clinician can still go ahead with the procedure as continuation of combination antiretroviral therapy after the procedure should provide post-exposure prophylaxis. There is, however, no evidence on the role of post-procedure combination antiretroviral therapy as post-exposure prophylaxis, but an analogy between needling procedures and needle-stick injuries has been made.

There are no data available to suggest a viral load at which HIV transmission is unlikely to occur with an antenatal invasive procedure, and data from general MTCT studies cannot be extrapolated to cases with invasive procedures. However, both the Royal College of Obstetricians and Gynaecologists and the British HIV Association recommend an undetectable maternal viral load at the time of the invasive procedure.^{12,13} If resources allow and there is sufficient time to

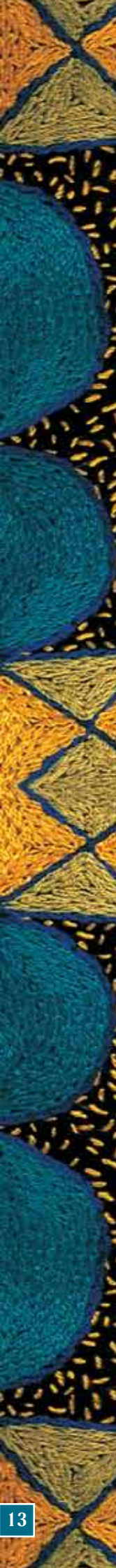
wait before the invasive procedure, the maternal viral load should be determined as part of pre-procedure counselling.

In a high HIV prevalence setting like South Africa, it is advisable that a repeat HIV test be offered immediately before the invasive procedure if a woman has initially tested HIV-negative early in pregnancy.

Although there are no well-established approaches for managing HIV-infected women undergoing invasive procedures, international guidelines and literature published on the topic do offer guidance for the clinician. Local guidelines that are in line with international best practices, but also account for the nature of HIV/AIDS and obstetric practice in South Africa, are required to guide local clinicians.

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ORIGINAL ARTICLE

KNOWLEDGE, ATTITUDES AND PERSONAL BELIEFS ABOUT HIV AND AIDS AMONG MENTALLY ILL PATIENTS IN SOWETO, JOHANNESBURG

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Aim. The aim of the study was to determine knowledge, attitudes and personal beliefs regarding HIV and AIDS in a group of mentally ill patients attending outpatient clinics in Soweto, Johannesburg.

Method. All patients attending four randomly chosen clinics in Soweto were invited to complete a self-administered questionnaire after obtaining informed written consent. The 63-item questionnaire, developed from others specifically for this study, included questions on socio-demographic and clinical characteristics; knowledge on how HIV is acquired and spread; attitudes and beliefs regarding HIV and AIDS; and condom usage. The statements in the knowledge sections were used to calculate a composite score, which if greater than or equal to 75% was defined as 'adequate knowledge'.

Results. A total of 1 151 patients with mental illness participated in the study. The mean age was 41.9 years (standard deviation 11.6) and the majority were males (50%); single (55%), and had achieved only a secondary level of education (53.3%). Overall, most of the study population did not believe in the myths surrounding the spread and acquisition of HIV and AIDS. There were however, significant associations between a low level of education and the belief that HIV is acquired from mosquito bites (odds ratio (OR) 1.61; 95% CI 1.19 - 2.18; $p=0.002$) and through masturbation or body rubbing (OR 1.76; 95% CI 1.34 - 2.33; $p=0.000$). Although more than 90% of the patients were aware of the facts regarding the spread of HIV, approximately 40% did not believe that one could acquire HIV through a single sexual encounter. The composite scoring for knowledge showed that less than half the patients had adequate knowledge of HIV/AIDS. This was significantly associated with gender and level of education: females were 1.6 times ($p<0.0004$) and patients with Grade 8 or higher education 1.5 times more knowledgeable ($p=0.002$).

Conclusion. Among mentally ill patients there is both a lack of knowledge about most aspects of HIV and AIDS and a belief in some of the myths associated with the acquisition and spread of the disease, especially among older, less educated patients. It is imperative that a targeted strategy be developed for this vulnerable group, taking into cognisance their inherent lower level of education and the cognitive impairment associated with mental illness, to educate them on all aspects of HIV and AIDS and to improve access to services.

The prevalence of HIV in developed countries is higher among patients with mental illness than among those without.¹ In the USA it is estimated to be 13 - 76 times that of the general population.² In southern Africa the prevalence ranges from 0% to 59% (0 - 22.9% before 1996 and 2.6 - 59% after 1996, suggesting an upward trend).³ The prevalence also varies according to where the study was performed, the highest being in Zimbabwe.⁴ Collins *et al.* more recently reported that in South Africa, despite the supposition that people with mental illness may engage in high-risk sexual behaviours more than the general population, the prevalence largely matches that of the general population.⁵ They suggest that as there is little injection drug use, the high prevalence of HIV in the general population is probably due to acquisition of the virus shortly after sexual initiation.⁵ Nonetheless, there is sufficient evidence that mental illness increases the individual's vulnerability to HIV infection.^{6,7} HIV risk among people with mental illness has been associated with lack of condom use, multiple sexual partners and injection drug use.^{8,9} The social exclusion that often accompanies life with mental illness may also increase vulnerability to infection. It may lead to exchange of sex for money or goods and an increase in coercive sexual encounters. In addition, cognitive deficits

associated with certain mental disorders may impair judgement and the ability to negotiate safe sexual encounters.¹⁰

In the general population, education and providing information about HIV and AIDS is one of the important ways of reducing risky sexual behaviour and the spread of the disease.¹¹ Yet studies have shown that levels of knowledge about HIV and AIDS are sub-optimal among patients with mental illness, and that levels differ among inpatients and outpatients and are influenced by psychiatric diagnosis.¹² Patients with mental illness tend to engage in risky sexual behaviour because of these lower levels of knowledge, which places them at risk of contracting or transmitting HIV.^{13,14} Melo *et al.* found in their study that high HIV and AIDS knowledge scores were associated with a past history of sexually transmitted infections, previous HIV testing and consistent condom use and that low knowledge scores were associated with mental illness.¹¹ Similarly, a study in a psychiatric hospital in Rio de Janeiro also showed knowledge to be lower in patients with mental illness compared with the general population.¹⁵ The authors used a 17-item AIDS knowledge test and found the average correct score to be only 61.2%. Chandra *et al.*, who assessed HIV knowledge among a group of Indian patients with

mental illness at baseline and 5 days later after an HIV risk reduction programme, showed that brief HIV-focused educational intervention can improve knowledge.¹⁶ However, different methodologies employed in the various studies make it difficult to ascertain accurate knowledge among psychiatric patients.

In spite of evidence showing poor knowledge of HIV and AIDS among mentally ill patients and the risks thereof, very few mental health services routinely assess knowledge of HIV transmission and risk behaviour,^{1,13} let alone attempt to educate this vulnerable group of individuals. HIV risk reduction interventions targeting South Africans with psychiatric illness remain few and far between. Collins examined the attitudes of 46 mental health care providers in four provinces of South Africa and reported that 'personal, contextual and political factors in the clinic and the hospital create barriers to integrating prevention activities. In particular, providers face at least three challenges to intervening in the epidemic among their patients: their own views of psychiatric illness, the transitions occurring in the mental health care system, and shifting social attitudes toward sexuality.'¹⁷ Although barriers exist in implementing such education programmes, the Mental Health Care Act No. 17 of 2002 requires the integration of all prevention and promotion programmes into psychiatric services.¹⁸ This is supported by research that shows it to be implementable.^{1,19}

Hodgson stated that: 'HIV for many South Africans defies precise classification: it does not fit the profile of a 'normal' disease. It affects the developed and the developing world in different ways and has a long period of apparent inactivity, and any of a large number of symptoms can present as the immune system weakens. This is further complicated by the association of HIV with sex, death, taboo and youth. It is therefore not surprising that people depend upon cultural models of illness, constructed from existing mythical frameworks and illness narratives, to provide meaning and to guide behaviour.'²⁰ Some prevalent cultural norms and beliefs include negative attitudes towards condoms ('flesh-to-flesh' sex is equated with masculinity and is necessary for male health); engaging in dry sex (the vagina is expected to be small and dry); the importance of fertility (which may hinder the practice of safer sex); polygamy (males are biologically programmed to need sex with more than one woman); misconceptions regarding the virus (that it can be contracted by sharing food, or mosquito bites; that sex with a virgin can cure the disease); that circumcised men cannot contract HIV; that alcohol kills HIV in the blood; and that you cannot contract HIV if you have one unprotected sexual encounter.²¹

The assessment of knowledge deficits will help in determining which patients need knowledge interventions as opposed to which need skills development or motivational behaviour change,¹¹ hence the need for this study, the aim of which was to determine baseline knowledge about prevention and acquisition of HIV among mentally ill patients in Soweto. It was hoped that the information obtained from this study would assist in developing protocols, guidelines and focused interventions to improve the level of knowledge and reduce the risk of spread of HIV among people with mental illness.

METHOD

The study design was cross-sectional in nature and undertaken to determine the knowledge, attitudes and personal beliefs among patients attending specialist psychiatric clinics in Soweto, Gauteng, from April 2009 to June 2009. There are 8 specialist psychiatry clinics in Soweto, of which 4 were randomly selected from a hat containing the names of all the clinics. Patients (18 years and older) from these four randomly chosen psychiatric clinics were approached to participate in the study in the waiting room while they were waiting to see the

psychiatrist. Informed consent was obtained after the contents of the form had been explained to the patients. Although the questionnaire was self-administered, a trained facilitator assisted patients where translation or explanation of the questions was necessary. The study was approved by the Human Research Ethics Committee of the University of the Witwatersrand.

There is no specific questionnaire that is validated to assess knowledge, attitude and personal beliefs in mentally ill patients in South Africa. For the purpose of this study, questions from other validated questionnaires for the general population were used to construct our 63-item questionnaire.²² We included questions on knowledge, attitudes and beliefs that were commonly recurring. Although not performed on mentally ill patients, the questions were general and appeared appropriate to be used in our study on mentally ill patients. The final questionnaire comprised of nine sub-sections; however the sub-sections analysed in this report were those on socio-demographic and clinical characteristics; knowledge on the acquisition and spread of HIV and AIDS; attitudes and beliefs regarding HIV and AIDS; and condom usage. The questions were rephrased where they might have been confusing, were not positively or negatively worded so as to prevent a set response bias, and attempted to take into consideration the cultural beliefs and norms of the participants so as not to appear offensive. The questions were in English and not translated into any of the official African languages. Reliability was ensured by having one facilitator and one interviewer, who was a nurse mental health practitioner with 30 years' experience.

Knowledge scores for the various categories were coded as 1 for a correct response and 0 for an incorrect or unknown response. A composite score was derived for each of the categories. A patient who achieved a composite score greater than or equal to 75% was defined as having 'adequate knowledge'. Nachega *et al.* used a similar technique in their study to determine average knowledge scores.²³ Kuder Richardson (KR20) reliability coefficients were calculated for the questions pertaining to knowledge of HIV and AIDS (0.6591), prevention of acquiring HIV (0.0464), mental illness and HIV association (0.5832), and all questions (0.7428).²⁴ Descriptive statistics, frequency distribution tables and chi-square tests for categorical data were produced using Stata (Stata Statistical Software, Release 10).²⁵

RESULTS

A total of 1 151 patients (50% males, 43.1% females, 6.9% unknown) with mental illness completed the self-administered questionnaire. Typical diagnoses seen at the community clinics comprise mood disorders (both unipolar and bipolar disorders), psychotic disorders, anxiety disorders, personality disorders and disorders due to general medical conditions. The numbers of patients approached and those refusing to participate in the study were unfortunately not recorded. Approximately 79% of patients were in the age group 25 - 54 years. Patients between the ages of 15 and 24 years and those over 55 years accounted for 6.1% and 15.4%, respectively. The mean age of the entire study population was 41.9 years (standard deviation 11.6), while that for males was 39.5 years and that for females 44.1 years. Female patients were significantly older ($p < 0.001$, two-sample Wilcoxon rank-sum test). Marital status was as follows: single (55.2%), married or living together (21.6%), divorced or separated (13.1%), and widowed (8.1%). Most of the patients had some formal education: Grades 1 - 7 in 38.8%, Grades 8 - 12 in 55.3%, and tertiary education in 3.2%. Only 80 patients (7%) were employed and 918 (79.7%) were receiving a grant (disability or pension); 499 patients (43.4%) had a positive family history of mental illness. More than half the patients (54.6%) were unaware of the details of their own current psychiatric illness.

Common psychiatric diagnoses included depression (8.2%), bipolar disorder (17.3) and schizophrenia (18.9%).

Ninety-three per cent of the study population was aware that AIDS is caused by the human immunodeficiency virus (HIV). Although only 2.26% responded that HIV and AIDS was a result of being bewitched, the majority (87%) were unsure, as they did not complete this question. Overall, most of the study population did not believe in the myths surrounding the spread and acquisition of HIV and AIDS. However, a significantly large number believed that sharing utensils (86.7%), masturbation or body rubbing (65.4%), and a bite from a mosquito that has bitten someone with HIV (72.3%) leads to the spread of HIV (Table I). Although more than 90% of the patients were aware of facts relating to the spread of HIV, approximately 40% did not believe that one could acquire HIV through a single sexual encounter.

There were significant associations between having a Grade 8 or higher level of education and the belief that HIV is acquired from mosquito bites (odds ratio (OR) 1.61; 95% confidence interval (CI) 1.19 - 2.18; $p=0.002$) or through masturbation or body rubbing (OR 1.76; 95% CI 1.34 - 2.33; $p=0.000$), and that there is no hope for people with HIV

and mental illness (OR 4.133; 95% CI 2.00 - 8.50; $p=0.000$). Similarly, there were significant associations between advancing age and the belief that HIV is acquired through masturbation or body rubbing (OR 1.12; 95% CI 0.85 - 1.46; $p=0.001$) and that there is no hope for people with HIV and mental illness (OR 0.961; 95% CI=0.93 - 0.98; $p=0.002$).

With regard to attitudes towards condom use, only half of the patients believed that the condom completely protects one from contracting HIV. Despite more than 90% of the patients reporting that they did not experience difficulty in obtaining condoms at clinics and believed that condoms did not decrease the full enjoyment of sex, only 70% of the patients reported that they used condoms with every partner they had sexual intercourse with (Table II). The majority of the patients reported that they engaged in safe sex practices.

Ten per cent ($N=197$) of the patients reported risky sexual behaviour, the reasons cited being lack of information about safe sex ($N=112$), lack of skills in dealing with provocative situations ($N=77$), because they were in hospital ($N=1$), no social support ($N=2$), actively using drugs and alcohol ($N=3$), and exchange sex, i.e. for cigarettes, a place to live or drugs ($N=2$).

TABLE I. MYTHS AND FACTS RELATING TO SPREAD OF HIV AND PROTECTION AGAINST ACQUIRING HIV (% OF QUESTIONS ANSWERED AS 'YES', 'NO' OR 'UNKNOWN')

	Yes	No	Unknown
Myths relating to spread of HIV			
Living in the same house as someone who has HIV	8.6	88.6	2.8
Sharing utensils	86.7	10.9	2.3
Sharing cigarettes, food or drinks	7.7	89.0	2.6
Hugging someone who has HIV	7.3	89.4	2.4
Kissing	25.1	72.8	1.9
Masturbation or body rubbing	65.4	31.5	2.5
Coughing	17.9	78.9	2.9
Mosquito that has bitten someone with HIV	72.3	24.5	2.6
Myths relating to protection against acquiring HIV			
A shower after sex reduces the risk of getting HIV	17.7	80.2	2
Oral sex is safe when partners don't swallow	80.5	16.1	2.9
Additional protective measures from traditional healers	24.2	71.8	3.9
Facts relating to spread of HIV			
In one sexual contact	57.0	40.2	2.8
Having sex with multiple partners	92.2	5.7	1.7
During anal sex	92.3	5.2	2.4
Having sex without a condom	82.3	5.1	1.9
Through broken skin, e.g. cuts or grazes	94.6	3.4	1.9
Through injection drug use	89.9	6.6	2.5
An HIV-infected pregnant woman infecting her baby	92.7	5.1	2

TABLE II. FREQUENCY DISTRIBUTION OF ATTITUDE TOWARDS CONDOMS AND SAFE SEX PRACTICES (% OF QUESTIONS ANSWERED AS 'YES', 'NO' OR 'UNKNOWN')

	Yes	No	Unknown
Attitude toward condoms			
Do you use condoms with every partner you have sex with intercourse with?	70.2	14.6	14.9
Condoms decrease my full enjoyment of sex so it is not necessary to use it	5.8	91.2	2.9
Have you ever had problems obtaining male/female condoms?	5.9	91.7	2.4
Safe sex practices			
I should have as many sexual partners as possible as it will prove that I am a real man	1.5	95.7	2.9
Are you faithful to a single partner?	76.7	8.3	14.9
Have you had more than one partner with whom you have had unprotected sex?	6.4	78.9	14.6

Using the composite scoring for knowledge described in the methodology, the results showed that 49% of the patients had adequate knowledge of HIV/AIDS and that 42% had adequate knowledge pertaining to the prevention of acquiring HIV (Table III). The patients' limited knowledge of HIV and AIDS was largely obtained from radio and television (12.7%), friends and relatives (6.2%), health care workers (5.5%), public speeches (0.4%), newspapers or magazines (0.5%), church (0.9%) and school (1.7%). However, a large majority of patients did not respond to this question.

Adequate knowledge about HIV and AIDS was significantly associated with gender, females being 1.6 times more knowledgeable than males ($p < 0.0004$), and a higher level of education, patients with grade 8 or higher of education being 1.5 times more knowledgeable than those with less education ($p = 0.002$). After controlling for age, gender and educational level, the results from multivariate logistic regression analysis showed similar associations to the unadjusted ORs.

DISCUSSION

Various studies have shown that a large proportion of patients with mental illness engage in behaviours that place them at high risk of contracting HIV, e.g. promiscuity, intravenous drug use with shared needles, and unprotected sex.^{2,14,26} Although clinical factors such as poor reality perception, affective instability and impulsiveness play a major role in such behaviours, lack of knowledge and/or inaccurate information about HIV infection is also a significant variable.²⁶

Published studies in developed countries conclude that knowledge about HIV and AIDS is poorer in mentally ill patients than the general population.²⁷⁻²⁹ Yet other studies, in a variety of psychiatric patient groups, reported higher proportions of correct responses to AIDS knowledge questionnaires, ranging from 63% to 80%³⁰⁻³² (comparable to that of the general US population).³³ Chuang and Atkinson at the Calgary Community Mental Health Clinic utilised a 10-item instrument to assess knowledge about HIV and AIDS.³⁰ Chandra *et al.* in India reported a low 34% accuracy in responses to questions on HIV and AIDS.¹⁶ We utilised a 63-item questionnaire and found that approximately 50% of the mentally ill patients surveyed had adequate knowledge of HIV and AIDS. While this level of knowledge is not the lowest reported among mentally ill patients, it is significantly lower than that of the general population, and specifically the Soweto population. Nachega *et al.* in their cross-sectional study of 105 HIV-infected adults attending an HIV clinic in Soweto reported that 89% had good knowledge about the cause of HIV infection and 83% knew about modes of transmission.²³ Similarly, the 2003 South African Demographic and Health Survey (SADHS), conducted on the general population, showed that 93 - 95% had heard of AIDS, 71 - 85% agreed that condoms reduce the risk of HIV infection, and 78% agreed with the statement that a healthy-looking person could be carrying HIV.³⁴ These studies support a better level of knowledge than that of mentally ill patients.

The most likely reason for low levels of knowledge is the very few education programmes specifically designed for patients with mental illness and conducted in mental health clinics, where the targeted group would be most accessible. Kloos *et al.* found that only a little more than half of their enrolled patients reported receiving HIV-related education, which was limited to brief one-time group overviews of HIV/AIDS.³⁵ Further, they report that education in groups is difficult because needs and levels of functioning vary widely within the different sub-groups of mental illness.³⁵ Other factors that influence levels of knowledge include age, gender and level of education. These individual factors are more significantly associated with improved knowledge rather than treatment setting factors and condom distribution.¹¹ Our study found that female patients and patients with higher level of education (Grade 8 and higher) were relatively more knowledgeable about HIV and AIDS. This is in contrast to Chandra *et al.*'s finding¹⁶ that men demonstrated better knowledge, and the Katz study,³⁶ which reported no gender difference in knowledge, either for total knowledge scores or for scores on individual items. It is likely that the bias towards females in this study may be because in general females tend to be better utilisers of health facilities (including antenatal clinics), where they access education and improve knowledge, while men are notoriously known to shy away from and avoid health facilities.^{37,38} With regard to education, several studies have also reported that higher levels of education lower the risk of being HIV-positive and that educated individuals are more responsive to the HIV/AIDS information campaigns and condom use.^{11,39,40} Koen *et al.* reported that negative symptoms associated with mental illness also impact on acquisition of knowledge.⁴¹

The participants in our study obtained their limited knowledge of HIV and AIDS mainly from radio and television, friends and relatives, and to a much lesser extent from health care workers. This is similar to Nigerian studies, which also found that the main source of information on HIV was electronic media (radio and television).^{22,42} Health care providers/institutions are significantly lacking as a source of information despite having the opportunity and having most contact with mentally ill patients. Education of the mentally ill must utilise all available modalities. The Vision Project, although not directed at patients with mental illness, showed that individuals with high programme exposure were one and a half times more likely than those with no exposure to have discussed AIDS with their partner and over twice as likely to know that condom use can reduce the risk of HIV infection.⁴³ Similar outcomes were reported in India by Chandra *et al.*, whose patients received an HIV educational programme and were then re-assessed for their knowledge 1 and 5 days later. The results indicated a poor level of baseline knowledge, which improved after education; knowledge gains were sustained at 5 days.¹⁶ There is strong evidence to support the recommendation that mental health practitioners should develop specific training programmes aimed at increasing knowledge among the mentally ill. These programmes must take into cognisance the lower level of education and cognitive impairment among mentally

TABLE III. KNOWLEDGE OF HIV/AIDS AND PREVENTION OF ACQUIRING HIV

	N	%
Adequate knowledge of HIV/AIDS		
No	592	51.4
Yes	559	48.6
Adequate knowledge pertaining to prevention of acquiring HIV		
No	665	57.8
Yes	486	42.2

OR = 1.55 (95% CI 1.21 - 1.99); chi-square test: $p < 0.0004$.

ill patients and should be incorporated not only in health facilities but also in the print media and the radio.

While education is important, misinformation, myths and urban legends have been found to be associated with higher rates of HIV risk behaviours (impulsivity, increased sexual activity, poor skills at negotiating safe sex and drug abuse) among mentally ill patients.¹⁹ Approximately 1 in 10 patients in our study engaged in risky sexual behaviour, largely because of lack of information or misinformation. One in 5 of our participants believed that a shower after sex prevented one from contracting HIV. This was similar to figures in studies by Koen *et al.*⁴¹ and Chandra *et al.*¹⁶ Katz *et al.* reported that 42% of their subjects were unaware that they could be infected by injection drug use.³⁶ Otto-Salaj *et al.* reported that 48% of their subjects believed that careful cleansing after sex would provide protection from the virus,³² and Kalichman *et al.* that 37% of their patients believed that showering after sex would prevent HIV infection.¹⁹ In the study by Chuang and Atkinson, a significant number of subjects believed that one could acquire AIDS by donating blood and 25% did not think that having only one unsafe sexual contact would make them vulnerable to HIV infection.³⁰ In our study, a much higher proportion (40%) of respondents believed that one could not acquire HIV after just one sexual contact. The majority also believed that sharing utensils (86.7%) and masturbation or body rubbing (65.4%) leads to the acquisition of HIV. More than two-thirds of the respondents held the belief that HIV can be acquired from the bite of a mosquito. In a Nigerian study, only 23.5% of patients held this belief,⁴² while only 57% in the SADHS rejected the statement that HIV cannot be transmitted by mosquito bites.³⁴ Our study also found significant associations between the frequency of some of these beliefs and a Grade 8 or lower level of education and advancing age.

Only half of our patients believed that condoms completely protect one from contracting HIV, and 90% believed that condoms do not decrease the full enjoyment of sex. Despite this, 14.6% of the participants did not use condoms with every partner they had sexual intercourse with and would not insist that either they or their partners wear condoms. This compares favourably with the SADHS study, in which 76% of men knew that using condoms and having sex with one uninfected partner prevents HIV, while only 68% of women knew this.³⁴

Bonhert *et al.* reported that while misinformation and myths may be associated with negative attitudes towards condoms and a greater number of sex partners, holding these beliefs was not an impediment to HIV testing or increased risk behaviour.⁴⁴

While the majority of our patients were aware that AIDS was caused by HIV, 1 out of 10 patients believed that it was caused by bewitchment. In comparison, in the SADHS 76% of women surveyed agreed that HIV could not be transmitted by witchcraft.³⁴ Witchcraft or invisible forces have long been thought of in Africa as causing untimely death or illness. In the South African context this is often seen as malicious individuals using spiritual entities or 'muti' to effect harm on another person. Jealousy is thought to be the main reason why a malicious lover, neighbour or relative would want to harm a particular individual. Of equal concern is the fact that 24% of our patients responded that they used additional protective measures from traditional healers to guard themselves against the acquisition of HIV. In a study among inmates (not reported as having mental illness) of Quthiing Prison in Lesotho, 2.1% of respondents interviewed thought that HIV was caused by bewitchment and 23% believed that traditional protective measures against witchcraft may prevent the transmission of HIV/AIDS.²²

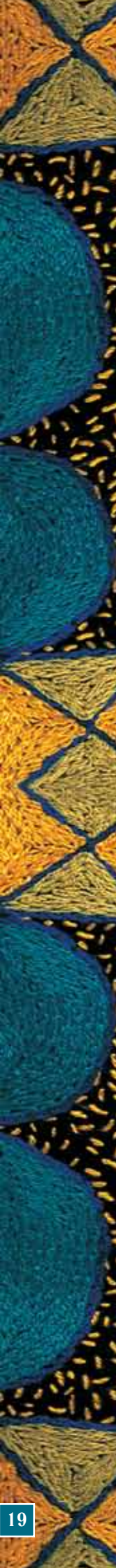
Efforts to combat HIV/AIDS in prevention campaigns need to include tackling cultural beliefs and not just provide information on cause and transmission. Understanding these cultural beliefs is important, as they influence decision making concerning choice of therapy. In these cases, hospitals or clinics are only approached for help as a last resort when traditional therapies have failed. It is then often too late for biomedical treatments to be effective. We also need to extend this information to what symptoms suggest infection and how to respond to those symptoms.⁴⁵ It is these gaps in our prevention programmes that continue to facilitate infection, as misinformation about AIDS leads to high-risk behaviours.³⁶

A few limitations to this study are worth noting. Although diagnosis was not correlated with clinical records and no measure of level of severity of psychiatric illness at the time of the interview was made, reliability was ensured by having one facilitator and one interviewer who was a nurse mental health practitioner with 30 years' experience. Our sample was also predominantly urban and hence may not be generalisable to other study populations. The self-report nature, although facilitated, might have caused bias that might have led to over- or under-estimation of certain variables. Similarly, a minimum level of literacy was required that may have biased the sample towards higher functioning and more literate respondents. Our questionnaire has not been validated in mentally ill patients or in a developing country and may have been too lengthy. Further work is required to explore and improve the psychometric properties of this questionnaire, and to develop preventive programmes and means to assess whether such programmes work in terms of retained knowledge and behavioural change. Sexual risk behaviour was not analysed in this research study, but is the basis of a future report.

CONCLUSION

Given the relatively high prevalence of both mental illness and HIV/AIDS in our general population, there is a proportion of patients with mental illness who lack knowledge about HIV and AIDS. Comprehensive basic information and medical facts concerning the acquisition, prevention and further transmission of HIV are needed. Promotion of HIV testing and counselling of psychiatric patients and their families is needed and should further enable this group to receive appropriate psychological support. The uninfected segment of the mentally ill population should have adequate knowledge about how to protect themselves against this devastating disease. Knowledge of HIV status, with appropriate counselling, may mean that these individuals can change risk behaviour to protect their quality of life and that of their families. Prevention activities should include peer programmes, leadership seminars, and development and distribution of adaptable programmes that target high-risk groups such as patients with severe mental illness.

Innovative ways of targeting messages and delivering focused prevention education packages to patients with psychiatric illness are needed in developing countries. We need to dispel myths about condoms and improve distribution of condoms (especially female condoms) in our clinics and psychiatric institutions. Although most mental health clinics in our area do not provide any sexual health orientation, it is vital that this situation is improved upon and that policies are developed towards implementing prevention packages among mentally ill patients, as prevention programmes based on research on group-specific needs are most likely to be successful.³⁶ Clinicians need to address basic HIV knowledge and risk reduction interventions with all patients they see on a daily basis.



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CASE REPORT

PRIMARY BREAST LYMPHOMA AND HIV/AIDS

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Primary extranodal lymphoma of the breast is rare and accounts for 0.04 - 0.53% of all malignant tumours, less than 1% of non-Hodgkin's lymphomas (NHLs) and 1.7% of extranodal NHLs.¹ Extranodal lymphoma arises from tissue other than lymph nodes and sites that normally contain no lymphoid tissue. This case describes the clinical and treatment dilemma posed by extranodal presentation in an AIDS-NHL patient.

CASE REPORT

A 40-year-old woman presented with a history of a painful left axillary mass that had progressively increased in size. She reported symptoms of night sweats and weight loss. Physical examination revealed a 17×13 cm left axillary nodal mass. Her left breast had the clinical appearance of mastitis. Abnormal laboratory studies revealed elevated serum uric acid (0.50 mmol/l, normal 0.15 - 0.35 mmol/l) and lactate dehydrogenase (1 009 U/l, normal 100 - 190 U/l) levels. An enzyme-linked immunosorbent assay was positive and the initial CD4+ count was 435 cells/μl. Microscopic examination of the lymph node mass confirmed a diffuse large B-cell lymphoma (DLBCL). Bone marrow aspiration and biopsy demonstrated no evidence of infiltration by lymphoma. Cerebrospinal fluid (CSF) examination was negative for lymphoma infiltration. Both the CSF cryptococcus Indian ink and latex tests were negative, but a positive *Varicella zoster* polymerase chain reaction (PCR) test was reported.

A mammogram was not feasible owing to painful ulceration of the breast mass. A computed tomography (CT) scan of the thorax and abdomen revealed a 5 cm lymphoid nodal mass in the left axilla and a 3.4 cm left supraclavicular lymph node. A gallium scan was consistent with uptake in an area overlying the left breast, anterior chest wall and markedly enlarged left axillary lymph nodes. Normal gallium biodistribution was seen in the rest of the body (Fig. 1). The case was considered to be a stage IIb_E AIDS-NHL.

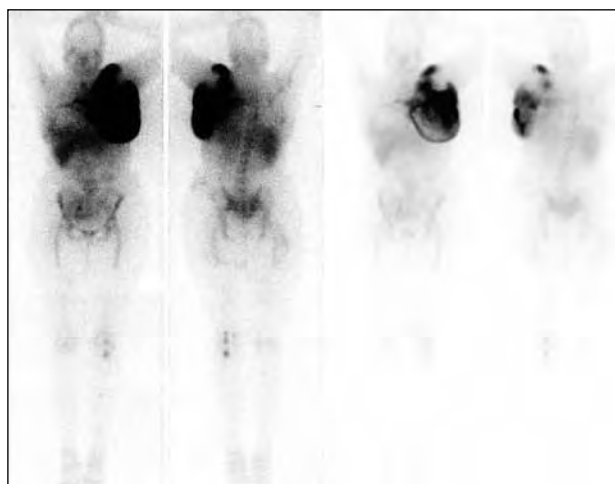


Fig. 1. Gallium-67 scans of lymphoma situated in the left breast and axillary lymph nodes and extending into the left anterior chest wall.

CHEMOTHERAPY

The standard CHOP regimen consisting of cyclophosphamide 750 mg/m², doxorubicin 50 mg/m² and vincristine 1.4 mg/m² on day 1 and prednisone 60 mg/day on days 1 - 5 every 3 weeks was started. She completed 3 cycles without significant toxicity but then presented with clinical progression. The left axillary lymph node and breast mass had the appearance of breast cancer with erythema, oedema and nipple retraction. A solid mass was palpable within the breast with associated skin ulceration and multiple cutaneous nodules over the left infra-clavicular region (Fig. 2).



Fig. 2. Clinical manifestation of an extranodal diffuse large B-cell lymphoma (DLBCL) of the left breast in an HIV-positive patient. Multiple cutaneous nodules, ulcerative skin lesions, erythema and enlarged axillary lymph nodes are present.

However, an infection with varicella zoster virus (VZV) was clinically apparent along dermatome T11 and 5 weeks later she reported

progressive bilateral lower limb pareses with associated weakening in bladder control. Magnetic resonance imaging (MRI) of the vertebral column showed degenerative changes with no focal spinal cord lesions. The patient defaulted and returned 8 weeks later reporting that the mass was more painful and larger with newly developed nodular cutaneous lesions of the left breast region. She was given a 4th cycle of CHOP and started concomitant antiretroviral therapy (lamivudine, stavudine and efavirenz). Four weeks later there was no visible change in the axillary and breast mass. The chemotherapeutic regimen was changed to second-line CMV (cyclophosphamide 750 mg/m², methotrexate 60 mg/m² and vincristine 1.2 mg/m²). A follow-up review revealed overt clinical progression, as there was an increase in both the size of the breast mass and the number of cutaneous lesions. A clinical oncology consult offered palliative radiotherapy, as she appeared resistant to first- and second-line chemotherapy.

The clinical dilemma was as follows: was this (i) a systemic NHL with extranodal involvement of the left breast; (ii) an overlooked primary breast lymphoma (PBL); or (iii) a misdiagnosed primary breast carcinoma? Before commencement of radiotherapy histological examination therefore again confirmed positivity for CD45 and CD20 lymphoma cells compatible with a DLBCL.

RADIO THERAPY

Palliative external beam radiotherapy (EBRT) with cobalt-60, consisting of 2 Gy × 18 fractions (36 Gy), was completed. The clinical target volume was determined by CT scan (Fig. 3). This included the left axillary nodal mass, the immediate lymphatic drainage, the left breast, the remaining left anterior chest wall and the left supra-clavicular region. Treatment was delivered using 8 MV photons with a 1 cm daily bolus.

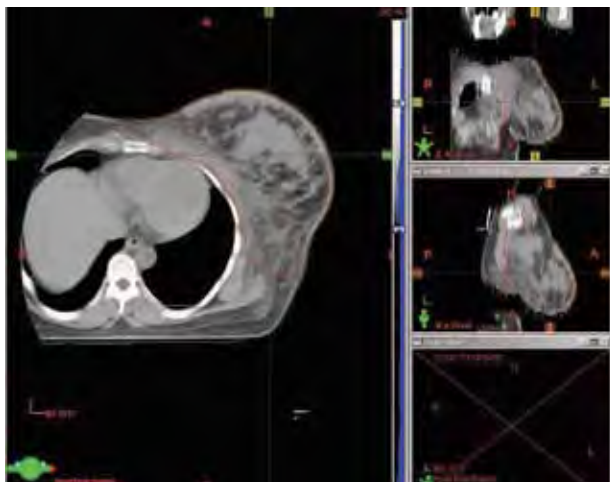


Fig. 3. SOMA vision – virtual simulator picture for the patient with breast lymphoma. The clinical target volume (CTV) is outlined in red.

Before initiation of EBRT the patient started allopurinol 600 mg/d to prevent tumour lysis syndrome. Her CD4+ count was 312 cells/μl, and trimetoprim-sulfamethoxazole as *Pneumocystis jiroveci* prophylaxis was added mid-course when the CD4+ count decreased to 56 cells/μl.

DISCUSSION

NHL is the second most common AIDS-associated malignancy and the AIDS-defining diagnosis in an estimated 1.6 - 8% of HIV patients.² PBL is rare, comprising 0.4 - 0.5% of all breast malignancies reported.³ Secondary breast lymphoma represents approximately 0.07%.⁴ When primary and secondary lymphoma cases are considered the most common sub-type is DLBCL (45 - 79%).⁵ Systemic AIDS-NHL treatment should include therapy for opportunistic infections (OIs) and the underlying HIV and involves modifications of conventional therapy.

There appears to be a survival advantage for patients receiving CHOP-ART therapy, suggesting that a decrease in OIs was responsible for reduction in morbidity.⁶ Based on a 15 - 20% central nervous system involvement at presentation, CNS prophylaxis is considered standard practice in AIDS-NHL. Series with chemotherapy reported a 50% complete response and a median survival of 18 months. An improved response rate does not significantly add to survival owing to relapse and death from AIDS progression.⁷

Neurological manifestations of VZV have been described. Encephalitis due to VZV infection results from small-vessel vasculitis, presenting weeks after the original infection. An urgent MRI scan or myelography is required to exclude extrinsic cord compression due to bacterial abscess, tuberculous abscess or lymphoma. If these are excluded, CSF should be sent for VZV PCR.⁸

The clinical and radiological features of PBL and carcinoma are similar, as both are diseases of middle age with a median onset in the 6th decade. Symptoms include pain, fever, sweating and weight loss. Contralateral involvement can be synchronous or metachronous up to 10 years after the primary lesion. Pathology remains the only way to differentiate between these malignancies, as treatment differs radically. Wiseman and Liao devised criteria to categorise breast lymphoma into primary and secondary forms.⁹ There is no standard treatment for PBL, and for small localised tumours adequate excision followed by radiotherapy may be effective. For widespread tumours with axillary involvement the addition of chemotherapy, surgery and radiotherapy may be required. The literature suggests that the Ann Arbor stage and histological sub-type are significant factors for survival.^{10,11} Reported 5-year survival rates vary from 9% to 85%. PBLs have a better outcome than primary breast carcinomas.¹²

Our patient presented with apparent systemic AIDS-NHL with extranodal involvement of her breast, but review of her clinical presentation and staging allows for reclassification as a PBL. Unfortunately she was lost to follow-up and attempts to contact her have failed. Close surveillance should be stressed, as contralateral involvement can appear up to 10 years after the primary lesion. The era of AIDS-related malignancies represents a challenge. There should be a heightened clinical suspicion for extranodal lymphoma in AIDS-NHL patients.

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CASE REPORT

MICROSCOPY 'AIDS' IN DIAGNOSING A FEBRILE INFANT

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A 5-month-old South African girl presented to a casualty department with a short history of fever. General examination did not reveal organomegaly or neck stiffness. In keeping with local guidelines, malaria was excluded on antigen testing and microscopy (thick and thin smear with Giemsa stain).¹ *Rickettsia typhi*, *R. conorii* and *Coxiella burnetii* were also excluded on the basis of serological testing.

The full blood count revealed pancytopenia with a haemoglobin (Hb) level of 7.9 g/dl (normal 10 - 15 g/dl), a white cell count (WCC) of $1.17 \times 10^9 / l$ (normal $5.50 - 18.00 \times 10^9 / l$) with an absolute lymphocyte count of $0.80 \times 10^9 / l$, and a platelet count of $47 \times 10^9 / l$ (normal $140 - 350 \times 10^9 / l$). Biochemical values were suggestive of renal dysfunction, with a serum urea level of 9.6 mmol/l (normal 1.4 - 5.0 mmol/l) and a creatinine level of 180 $\mu\text{mol/l}$ (normal 14 - 34 $\mu\text{mol/l}$), as well as a markedly elevated C-reactive protein level of 243.1 mg/l (normal 0.1 - 7.5 mg/l).

On investigation of the patient's immune status, it was established that she was HIV-1-positive as confirmed by HIV-1 DNA Amplicor assay version 1.5 (Roche Diagnostics, Mannheim, Germany), with an HIV-1 viral load of 2 738 930 RNA copies/ml by Abbott m2000 Real Time HIV-1 Assay (Abbott Diagnostics, Johannesburg) and a CD4+ lymphocyte percentage of 28%.

Initial standard paediatric blood cultures did not yield any growth after 7 days of incubation. A follow-up full blood count, performed 2 days after the initial investigations and assayed on the ADVIA 2120 (Bayer HealthCare, Diagnostic Division, Isando, Gauteng), differed markedly from the previous results, showing a WCC of $13.83 \times 10^9 / l$ with an absolute lymphocyte count of $10.99 \times 10^9 / l$. On microscopic examination of the peripheral blood smear (Fig. 1, a) these counts could not be verified and the leucocytes appeared markedly reduced. In addition, fungal elements could be demonstrated (Fig. 1, a and b).

Subsequent blood cultures, performed in paediatric bacterial blood culture bottles, confirmed the aetiological agent to be *Candida albicans*. Fungal morphology clearly showed the presence of oval yeast forms, slightly smaller than a lymphocyte nucleus (Fig. 1, a), with blastoconidia and pseudohyphae (Fig. 1, b). The fungus was identified by demonstrating formation of a germ tube on 4-hour incubation in horse serum.² Subsequent antifungal susceptibility, performed on the Vitek 2 system (BioMerieux, Randburg, Gauteng), demonstrated sensitivity to all antifungal agents tested (amphotericin B, fluconazole and voriconazole).

DISCUSSION

HIV-1 infection has been established as a risk factor for fungaemia in both children³ and adults.⁴⁻⁵ The routine use of fungal blood cultures

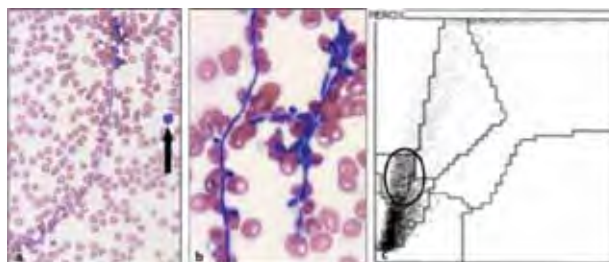


Fig. 1. Peripheral blood smear from a 5-year-old HIV-1-positive girl, showing marked fungaemia: a – size of fungal element in relation to lymphocyte (arrow); b – closer view of fungal elements, showing oval yeast forms with blastoconidia and pseudohyphae; c – peroxidase channel on ADVIA 2120 analyser. The encircled area depicts the region where lymphocytes are typically noted based on both size and peroxidase negativity. In this instance, these events are produced by yeast cells rather than lymphocytes.

remains controversial, being advocated by some authors⁶ and discouraged by others.⁷

Microscopic examination of the peripheral blood smear revealed a significant leucopenia, despite contradicting automated counts. WCCs as well as differential leucocyte counts have been described to be influenced by high fungal loads of *Candida* spp.⁸ The ADVIA 2120 uses both a lobularity and a peroxidase channel for leucocyte identification and quantification.⁸⁻⁹ In this case a comparison error had been flagged, indicating the probability of falsely elevated counts. This error, however, does not reflect on the laboratory report issued to the clinician, and is an analytical issue that needs to be addressed by the technologist and pathologist in the laboratory setting. Owing to their small size as well as their peroxidase-negative properties, the yeast cells had been identified as lymphocytes by the automated analyser (Fig. 1, c).

Considering the increased prevalence of fungal infections among HIV-1-positive patients,³⁻⁵ full blood count evaluation is best accompanied by morphological evaluation to detect any discrepancies between automated counts and actual observation.⁸⁻⁹ In most laboratory settings, morphology is evaluated once the clinician requests a differential count. Clinicians should further request differential counts once any full blood count parameters show significant abnormalities, or when there is a clinical suspicion of disease affecting the haematological system, including bleeding tendencies, infection, hepatomegaly, splenomegaly, lymphadenopathy, etc.¹⁰

In this clinical case, the rapid change in results over a 2-day period should have prompted the clinician to suspect an analytical issue with the samples in question.

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CONFERENCE REPORT

TOP2BTM SYMPOSIUM ON HEALTH CARE FOR MEN WHO HAVE SEX WITH MEN (MSM)

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Men who have sex with men (MSM) are at high risk of HIV acquisition and transmission, and country-specific HIV prevalence rates are always higher in MSM than among heterosexual men. South African data confirm this, with reported HIV prevalences of 10.4 - 33.9% across various studies. Donors and government health planners have recognised the need for targeted programmes that address the high burden of HIV transmission and disease in stigmatised populations such as MSM, as well as other 'most at risk populations' (MARPS) such as commercial sex workers, drug users and displaced refugees. Specific programmes targeting MSM and other MARPS have been included in the South African government's current National Strategic Plan for health care and will feature in the new plan under development.

Until recently, African MSM have been under-researched and under-resourced, and this has contributed to their stigmatisation. Fortunately this deficiency has been recognised locally and a number of innovative programmes have been developed to address this. The Top2btm symposium on prevention, treatment and care of MSM sought to bring together these programmes to share experiences. The symposium was held in Cape Town, organised by the Anova Health Institute with support from USAID and PEPFAR. The conference attracted 188 delegates from across Africa as well as Europe and North America, including local MSM community representatives, a variety of NGOs, government leaders and health care workers as well as prominent MSM researchers.

Dr Yogan Pillay, South Africa's Deputy Director General of Strategic Planning in the Department of Health, opened the conference on behalf of the Minister of Health. He affirmed government's commitment to implementing targeted HIV and sexually transmitted infection (STI) prevention and treatment programmes for MARPs, including MSM. He highlighted the importance of MSM-targeted HIV testing programmes, considering pre-exposure prophylaxis (PrEP), promoting post-exposure prophylaxis (PEP), encouraging MSM-related research and embracing the concept of antiretroviral treatment as prevention. Consideration is being given to providing state-funded ART to everyone at a CD4 count of 350 cells/ μ l or less; this would be especially beneficial to MSM, since the risk of HIV transmission is much higher during unprotected penile-anal sex than during unprotected penile-vaginal sex, and lowering the

viral load of positive MSM is likely to provide a large reduction in HIV transmission.

The conference incorporated four main themes:

1. Understanding the epidemiology of African (and South African) MSM
2. Prevention interventions to address HIV among MSM in Africa
3. Health care services for HIV-positive MSM
4. Research to improve understanding of African MSM.

THE EPIDEMIOLOGY OF MSM IN AFRICA

The conference proceedings were underpinned by several key concepts in thinking about MSM and HIV/AIDS. First, it is important to recognise that 'MSM' is a medicalised term describing the behaviour of sex between men; it does not describe a particular identity or population group. MSM are extremely diverse and probably have many differences from each other and only one main commonality, having sex with other men. MSM vary in the way they conduct their lives and in the sex that they have (for example, not all MSM engage in anal sex). They may identify as heterosexual, homosexual or bisexual. They may possess a masculine or feminine identity and they may identify with 'gay' or mainstream culture.

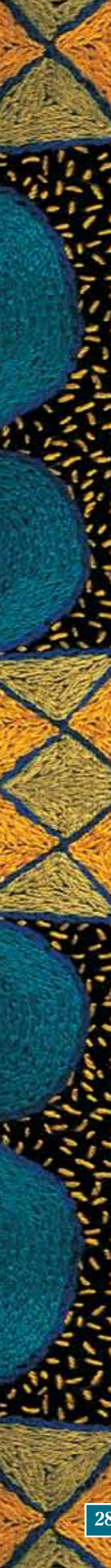
Related to this, it is common throughout Africa to find MSM who identify as heterosexual and are even married, appear masculine but sometimes have sex with men in addition to women. These MSM are particularly difficult to reach with traditional health programmes, as they are in many ways invisible in mainstream society.

Second, MSM experience a range of barriers to accessing health care, not least stigma and prejudice from health care providers themselves. MSM often receive counselling that is inappropriate to the lives they lead. For example, HIV prevention messages aimed solely at heterosexuals may ignore the risks of HIV transmission associated with anal sex. MSM are concerned about the double stigma they may experience in health centres relating to their sexual orientation and their HIV status, and are often reluctant to seek care.

With this background, the keynote address entitled 'Time to act: Responding to the HIV pandemic among MSM' was delivered by Professor Chris Beyrer of Johns Hopkins Bloomberg School of Public

ABOUT ANOVA HEALTH INSTITUTE & HEALTH4MEN

Health4Men is a special interest programme of the Anova Health Institute, which receives support from USAID / PEPFAR. This programme targets men who have sex with men (MSM) for HIV and STI prevention and treatment. The programme has a strong community focus aimed at improving social support and decreasing stigma experienced by township-based MSM. Health4Men seeks to improve access to health care services and provides education and training for MSM as well as for health care providers who deliver care to MSM clients. Educational programming includes regular training activities and academic symposia. The most recent of these was the Top2btm symposium held in Cape Town in May 2011.



Health (USA). Systematic reviews of HIV in low- and middle-income countries from which data are available consistently show that MSM are at higher risk of HIV compared with the local heterosexual population. Aggregate HIV prevalences among African MSM are reported to range from 8.8% in Sudan to 32.9% in Zambia. Many of these studies were performed using respondent-driven or 'snowball' sampling and therefore may not be generalisable; however, they do highlight the concentrated MSM HIV epidemic in countries where there is also a heterosexual epidemic. In addition, pooled data from studies in Malawi, Botswana and Namibia demonstrate health provider stigma: 5.1% of MSM sampled report being denied health care services because of their sexual orientation, and 22.3% reported 'any discriminatory event' based on sexuality. Provider stigma is just one of the challenges currently facing MSM.

For HIV transmission to occur, transfer of an HIV-containing fluid needs to gain entry into a new individual. The anal mucosal lining is thin, does not self-lubricate and is more liable to mucosal tears than vaginal mucosa. Biologically, unprotected anal sex, particularly receptive anal sex, carries a high risk of transmitting HIV (estimated to be approximately 1.4% with each episode, which is roughly 18 times higher than for vaginal sex). Condoms and other HIV-risk reducing interventions are therefore extremely important for MSM.

Individual-level HIV risks include unprotected anal sex, high numbers of sex partners, and injecting and non-injecting drug use. Structural level risks for MSM relate to stigma, discrimination and human rights concerns. A study in Namibia, Malawi and Botswana showed self-reporting of human rights abuse to be high; for example, 5.1% of MSM studied had been denied health services based on their sexuality and 23% reported any form of discrimination. This and similar studies show the difficulty faced by MSM trying to access healthcare in stigmatised and even criminalised environments.

HIV PREVENTION INTERVENTIONS FOR MSM

A number of presentations addressed HIV prevention for MSM. In sub-Saharan Africa the incidence of HIV is declining among heterosexual people but continues to rise in MSM, illustrating the need for innovative prevention programmes. Professor Linda-Gail Bekker from UCT called for a time of 'highly active HIV prevention'. In particular, the role of ART as prevention is gaining ground, and this was visible during discussion at the conference. Evidence cited included the Pre-Exposure Prophylaxis Initiative (iPrEx) and the recently released results of the HPTN 052 trial.

iPrEx recruited 2 499 HIV negative high-risk MSM and randomised them to receive either Truvada or placebo daily in addition to risk reduction counselling, monthly HIV testing, condom and lube provision and treatment of STIs. Most recruitment occurred in South America, but 90 MSM (4%) were recruited at a Cape Town site. Results showed a 44% reduction in HIV infections in the treatment arm and there was a significant dose-response relationship with better adherence associated with increased protection. Guideline documents for the use of PrEP are available and should be included as an option in the 'prevention package' for MSM.

The HPTN 052 trial recruited 1 763 discordant couples (only 3% MSM) and randomised them to either early (CD4 count 350 - 550 cells/ μ l) or late (CD4 <250) ART initiation for the positive partner. The trial found that earlier treatment decreased HIV transmission by 96% over the duration of follow-up. The study was stopped early by its monitoring board, and we await full publication. Early indications are good that ART did provide significant protection in heterosexual discordant couples, but the study was underpowered for MSM.

Other prevention strategies discussed by speakers for inclusion on the prevention 'menu' for MSM include:

Biomedical. In addition to PrEP, biomedical prevention options for MSM include post-exposure prophylaxis (PEP), innovative marketing and distribution of condoms (including the female condom for anal sex) and sexual lubricants, STI screening and treatment. Rectal microbicides are desirable but are not yet fully developed or proven to be effective. Medical male circumcision has not been shown to confer protection for MSM, except perhaps if they are exclusively the penetrative partner in anal sex or have concurrent sexual relationships with women, where the infective risk is from penile-vaginal sex. Programmes targeting MSM who use substances, particularly alcohol and crystal methamphetamine, are required, as are needle exchange programmes.

Behavioural. Counselling programmes to modify high-risk behaviour were emphasised. 'Serosorting' and 'seropositioning' (choosing sexual partners on the basis of their HIV status, or deciding on insertive or receptive anal intercourse depending on partner status) were discussed and may be of value but could be construed as 'sero-guessing' in areas where MSM do not know their status or misinform potential sex partners.

Structural. Advocacy is needed to decrease stigma and discrimination from general society and from health care providers. Dr Patrick Sullivan emphasised the role of using technology, specifically Internet-based and mobile phone-based platforms in prevention. Related to this, Health4Men announced a new mobi site where MSM in South Africa can access HIV information and ask questions from their cellphones (<http://h4m.mobi>).

HEALTH CARE SERVICES FOR HIV-POSITIVE MSM

Professor James McIntyre detailed the history of the Anova Health Institute's Health4Men project that led to the establishment of holistic sexual health and HIV prevention and treatment services for MSM in South Africa. Two MSM-targeted clinics operate in Cape Town (the Ivan Toms Centre for Men's Health) and Soweto (the Simon Nkoli Centre for Men's Health), with a satellite clinic in Pretoria. These clinics are supported by USAID/PEPFAR and the Department of Health and are at the forefront of health provision for MSM in Africa.

The Ivan Toms Centre for Men's Health in Cape Town has been operating for more than 2 years. The clinic offers a primary-care level, holistic package of HIV and STI prevention and treatment services, including the provision of government-funded ART for HIV-positive MSM who qualify for treatment according to national guidelines. The clinic includes an extensive mental health component in collaboration with the Department of Psychiatry at Groote Schuur Hospital. Approximately 3 000 clients have utilised the clinic's services so far. About half of these clients are HIV-positive and approximately 500 are currently receiving ARVs. The clinic addresses a large non-HIV STI burden, with syphilis and human papillomavirus infection being particularly common. For example, approximately 15% of individuals screened at the clinic are positive for syphilis infection.

This clinic is unique in not marketing itself as a 'gay clinic' or an 'HIV clinic'. The client cohort includes both negative and positive people, some of whom receive ART, and some remain in wellness programmes prior to initiating treatment. This model has advantages in terms of enabling health-seeking behaviour of MSM, as individuals are not identifiable as HIV-positive because of the clinic they attend. Many attend for other STIs, or for counselling or other services.

MSM treatment challenges were addressed in a number of sessions at the conference. The importance of training of health care workers to decrease homophobia in the health sector was stressed. Homophobia from the health sector acts as a structural barrier to health care access for MSM. Already organisations in South Africa, including the Anova Health Institute and the Desmond Tutu HIV Foundation, are conducting training programmes for health care providers to address this.

The conference discussions emphasised that there are some considerations that must be borne in mind when providing ART to MSM. Some groups of MSM are very body conscious, and adherence to drugs causing lipo-atrophy may be low. Similarly, MSM who develop erectile dysfunction may default protease inhibitors if these are perceived as contributing to the problem. Mental health and drug use, and how these may influence adherence, also need to be considered when initiating ART in HIV-positive MSM.

MENTAL HEALTH

The need to incorporate mental health services into the package of care for MSM was highlighted by Dr Kevin Stoloff from the Department of Psychiatry at Groote Schuur Hospital. His presentation, based on literature review and clinical experience at the Ivan Toms Centre for Men's Health, stressed that high levels of anxiety, depression, personality disorders, internalised homophobia, substance abuse and other mental health challenges make adherence support vital for MSM. These same mental health challenges may precipitate or enhance risk taking among MSM.

DRUG USE

Drug use is common, and some communities in South Africa are experiencing an explosive increase in crystal methamphetamine use. It is recognised that a large percentage of incident HIV infections in the developed world are related to crystal methamphetamine use, and the same may be true of some groups of South African MSM. Crystal methamphetamine use lowers inhibitions, increases risky sexual behaviours and may increase biological susceptibility to HIV infection. The drug can also be injected, which raises concerns about needle sharing and transmission of other blood-borne viruses such as hepatitis B and C. Crystal methamphetamine and other recreational drugs can have unanticipated drug-drug interactions and side-effects for HIV-positive individuals taking antiretroviral medications, making treatment of such people difficult from medication choice and adherence perspectives.

ANAL INTRA-EPITHELIAL NEOPLASIA

An under-recognised health care problem for MSM is anal intra-epithelial neoplasia (AIN) and anal cancer. A presentation on this issue highlighted the complete absence of screening and treatment services in South Africa. AIN is a precursor to anal cancer and parallels cervical intra-epithelial neoplasia in women. AIN is HPV-associated and may lead to cancers that involve peri-anal and anal skin. Screening for and early detection and management of AIN may prevent anal cancers. Many experts now advocate for the inclusion of AIN screening in routine care of MSM. Not doing so represents a missed opportunity to prevent serious malignancies.

TRANSGENDER ISSUES

Dr Anita Radix from the Callen-Lorde clinic in New York provided valuable insights into the health care needs of transgender people (TG). TG face individual and structural barriers to health care access that are sometimes different from those experienced by MSM. There is a dearth

of services for TG in Africa and many health care providers lack the skills to manage complex psychological and medical issues, including management of complex drug-drug interactions between hormones and ART. Health care worker sensitisation and education programmes are required.

4. RESEARCH

Professor Carolyn Williamson, a medical virologist at the University of Cape Town, discussed HIV subtypes that circulate in Cape Town. The predominant HIV subtype in MSM in developed nations is subtype B, contrasting with heterosexual epidemics where subtype C predominates, as in South Africa. Phylogenetic studies performed with 147 HIV samples from mixed urban and rural South African MSM showed approximately 80% to be subtype C, 13% to be subtype B and the balance to consist of various other subtypes. This may have consequences for future vaccine research for MSM in Africa, as a vaccine directed primarily against subtype B virus may be less effective in a subtype C or recombinant subtype epidemic.

CLINICAL SKILLS FOR HEALTH SERVICE PROVIDERS

Two workshops were included in the symposium, both aimed at improving the clinical skills of health providers who service MSM. The first workshop addressed discussing sex and taking a sexual history in a clinical setting. Participants received guidance in this arena and learned skills were reinforced by role-play activities with concrete examples of sexual histories taken from MSM who had recently attended the Ivan Toms Clinic. The second workshop addressed the use of post-exposure prophylaxis. Workshop attendees received background information and practical advice about the administration of PEP and for including this HIV transmission reducing intervention into the scope of services provided at their clinics. Key learning points from each of these workshops are presented in Boxes 1 and 2.

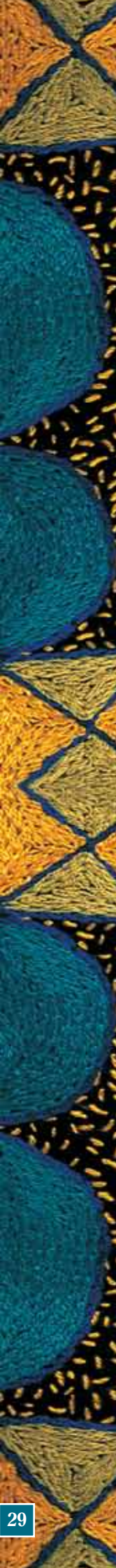
SUMMARY

In summary, the Top2Btm conference offered a full and broad-ranging programme with topics covering issues in epidemiology, prevention, treatment and research relating to MSM in Africa.

Throughout the conference the diversity of MSM communities in South Africa was stressed, as was the need for innovative and tailored programmes to address the health needs of these often hidden communities. Clinics such as the Ivan Toms Centre for Men's Health in Cape Town have developed expertise and a model for disseminating the knowledge and skills required to achieve the aim of targeted health care for MARPS, including MSM, in the country's National Strategic Plan for Healthcare.

Box 1. Taking a sexual history in a clinical setting

- Do not assume heterosexuality among men attending HIV clinics.
- Ensure privacy and confidentiality of information.
- Ensure staff training to enable them to confidently address a broad range of sexualities and sexual problems.
- Explain the context of the sexual history in terms of identifying health risks and individualising an HIV risk reduction plan.
- Build rapport with patients by asking generalised questions.
- Thereafter, ask all clients if they have sex with women, men or both.
- Use local colloquial language that is accessible to clients.
- Do not moralise about clients' sexual activities. The aim is to normalise all consensual sex while identifying areas where HIV transmission risk can be reduced.



Box 2. Post exposure prophylaxis (PEP)

- PEP is an effective strategy of using ARVs to reduce HIV transmission.
- Evidence for PEP efficacy among MSM is limited, as conducting randomised placebo controlled trials would be unethical.
- PEP is indicated for HIV-negative individuals who have been exposed to HI virus-containing body fluids (semen and blood).
- PEP should be initiated within 72 hours of exposure.
- Owing to the high HIV transmission risk associated with anal sex, possible HIV exposure during this sex act should be managed with triple-therapy PEP.
- Clients on PEP require counselling and support to minimise medication side-effects and psychological stress.
- Advocacy is required to increase PEP in Department of Health facilities, especially outside normal clinic hours.

Both prevention and treatment of HIV among MSM were addressed at the symposium. Antiretroviral medications are finding a new role as prevention and not just treatment. Intervention such as PEP, PrEP and earlier treatment initiation should feature in MSM-targeted health programmes.

Successful ART for MSM requires special consideration of medication choice and appropriate counselling that is not heteronormative. MSM-specific diseases such as anal dysplasia and cancer should be included as part of the package of services for MSM. Despite South Africa's progressive constitution, MSM still experience high levels of structural homophobia which negatively affects risk-taking and health-seeking behaviours, and advocacy is required to decrease this.

South Africa has produced a substantial body of MSM research and has contributed significantly to the global body of knowledge regarding African MSM. Organisations currently active in this field should continue their efforts. Symposia such as Top2Btm provide an opportunity for information sharing, identification of new opportunities to improve the health of MSM, and discussion aimed at furthering a research agenda for MSM throughout Africa.

All presentation slides delivered at the Top2Btm symposium are available on the Anova Health Institute Website (www.anovahealth.co.za) by following the link http://www.anovahealth.co.za/resources/entry/top2btm_msm_symposium/. For more information, please contact Health4Men on (021) 447-2844.



BOOK REVIEW

A Clinical Atlas of Skin Conditions in HIV/AIDS: An Illustrated Management Guide for Health Care Professionals. By Ncoza Dlova and Anisa Mosam. 2nd ed. Pretoria: HPMG, 2009. Pp. 100. ISBN 1-875098-40-2.

Written by two dermatologists from the University of KwaZulu-Natal's Nelson R Mandela School of Medicine, the much-needed 2nd edition of the *Atlas of Skin Conditions in HIV/AIDS* is now available. Immunocompromise in HIV cases results in a large variety of skin findings that significantly differ in quality and extent from those in immunocompetent people.

Acknowledging the fact that dermatological problems are often a challenge to clinicians, this is an important area demanding an easy-to-use atlas to identify the most common diseases. As HIV treatment increasingly becomes a condition to be treated at a general primary health care level, this becomes even more pertinent.

To meet the needs of the clinician, the atlas is put together in a way that makes it a pleasure to use quick reference for clinical findings. The book's chapters are structured by type of skin eruption rather than nosological disease entity, which adds to the ease with which a specific clinical presentation can be found. These groups of skin conditions are 'Blisters', 'Papulosquamous conditions', 'Papules and nodules', 'Ulcers', 'Nails', 'Oral lesions', 'Miscellaneous' and 'Antiretroviral therapy'. Only the chapter on 'Antiretroviral therapy' attempts a more systemic approach, based on the causation rather than the clinical presentation, when it lists a range of conditions that might erupt under antiretroviral treatment. These conditions are presented in the two sections 'Immune reconstitution inflammatory syndrome' (IRIS) and 'Cutaneous manifestations of antiretroviral drugs'.

For each condition, on the left page there are high-quality colour pictures displaying the skin condition. This is complemented by a brief description of the condition and its treatment on the opposite page. This includes a hands-on treatment recommendation with standard dosages and durations for the treatment and explicitly including both EDL (Essential Drugs List for primary health care) and non-EDL items.

With its user-friendly structure, this atlas is a valuable addition to the standard reference in a consultation room in public sector facilities. It is comprehensive enough to include the more common conditions, while at the same time concise enough to serve as a quick reference during or in between consultations. On the wish-list for future editions would be an update of the primary health care EDL reference, as the book refers to the 1998 edition of this list. Having been published before the new antiretroviral treatment guidelines came into effect in 2010, a future edition should possibly also present clinical examples of the skin presentation of the abacavir hypersensitivity syndrome (which is only mentioned in the text), as this drug is now part of the paediatric first-line regimen and skin eruptions following the initiation of this drug are a major point of concern. Similarly, tenofovir, which is now part of the adult first-line regimen, is not mentioned in the book but would probably have shown its dermatological side-effects (if any) by the time the next edition appears.

Dirk Hagemeister

Paarl



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Journal 41

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Regarding the use of antiretroviral therapy to prevent the transmission of HIV in serodiscordant partnerships:

1. True (A) or false (B):
Observational studies have suggested that the lower the average viral load in a community, the lower the incidence of new HIV infections.
2. True (A) or false (B):
The HPTN 052 trial provides evidence that initiation of ART at a threshold of 350 – 550 cells/μl reduces sexual transmission of HIV to HIV-negative partners.
3. True (A) or false (B):
The HPTN 052 trial provides clear evidence that initiation of ART at a threshold of 350 – 550 cells/μl reduces mortality and AIDS-related complications in HIV-infected individuals.
4. Evidence for the benefits of ART initiation above 500 cells/μl is mixed, and trials investigating these are ongoing within South Africa.

Regarding HIV prevention in the context of mental disorders:

5. True (A) or false (B):
Individuals diagnosed with mental illness in South Africa have a level of knowledge of HIV prevention that is similar to that of the general population.
6. True (A) or false (B):
Standard HIV prevention messages and interventions may not be adequate for this group, as they have an increased risk of HIV infection compared with the general population.

Regarding the use of microscopy to diagnose a febrile HIV-infected infant:

7. True (A) or false (B):
High *Candida* fungal loads may lead to abnormal results of white cell count quantification in peripheral blood.
8. True (A) or false (B):
Peripheral blood smears may be useful in interpreting unusually rapid changes in full blood count parameters.

Regarding primary breast lymphoma in the context of HIV/AIDS:

9. Primary extranodal lymphoma is the most common presentation of non-Hodgkin's lymphoma.
10. Non-Hodgkin's lymphoma is the most common AIDS-associated malignancy.

11. Which of the following are common presenting symptoms of non-Hodgkin's lymphoma in HIV/AIDS:
A. Pain
B. Fever
C. Sweating and weight loss
D. All of the above.

Regarding invasive obstetric procedures in HIV-infected women:

12. Most current guidelines recommend that pregnant women with higher CD4 cell counts (e.g. >350 cells/μl) do not require any form of prophylaxis or therapy to prevent mother-to-child transmission of HIV before undergoing an invasive obstetric procedure such as amniocentesis.
13. If a woman is established on effective antiretroviral therapy and has an undetectable viral load, invasive obstetric procedures do not appear to significantly increase the risk of mother-to-child transmission of HIV.
14. In contexts where the invasive obstetric procedure is urgent and an HIV-infected woman has not received any form of antiretrovirals, initiation of therapy immediately before or after the procedure may still provide some measure of protection against HIV transmission.

Regarding HIV prevention and treatment interventions for men who have sex with men (MSM):

15. In terms of post-exposure prophylaxis, unprotected anal intercourse is a low-risk activity for HIV transmission, and it is appropriate to use 2-drug PEP.
16. There is evidence that pre-exposure prophylaxis using antiretroviral medications (PrEP) can help to protect MSM from sexually transmitted HIV infection, but adherence is an important consideration.
17. Anal intra-epithelial neoplasia (AIN) is recognised as an AIDS-related malignancy that is associated with the human papillomavirus.
18. Existing evidence suggests that the predominant subtype of HIV circulating in MSM in South Africa is subtype B (also the most common subtype among MSM in Europe and North America), while subtype C is more common in heterosexual populations in SA.
19. HIV prevention messages aimed solely at heterosexuals invariably include the risks associated with anal sex.
20. Recreational drugs can cause drug-drug reactions and side-effects in HIV-positive individuals taking antiretroviral medication.