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FROM THE EDITOR

With the national ARV roll-out underway, despite being somewhat slower than was hoped, antiretrovirals (ARVs) are now recognised as the standard of care for appropriately staged HIV-infected South Africans in both the private and public health care sectors.

As American and local experts point out in their article 'Managing HIV as a chronic disease' (p. 7), highly active antiretroviral therapy (HAART) results in significantly better survival rates but requires a streamlined system, a multidisciplinary approach, accurate data collecting and statistical analyses, and the full support of clinics and the community.

Clearly the public hospitals cannot carry on taking the brunt of the pandemic, as shown in research conducted at Red Cross Children's Hospital in Cape Town (p. 32) confirming that current admission policies regarding inpatient treatment of HIV/Aids appear unsustainable. This is of great concern, as the HIV prevalence in the Western Cape lags behind that of other provinces and sub-Saharan Africa. With finite resources (including money, health care workers and hospital beds) this is another compelling reason to speed up the ARV roll-out in all provinces, i.e. to reduce the present high admission rates for opportunistic infections and terminal care.

In developing countries there is a huge need to incorporate HIV/AIDS into the health care system as another chronic disease, as opposed to creating parallel structures for HIV infection, which is time consuming and unnecessary. Optimal use of human resources and appropriate division of labour, coupled with adequate training in the long-term management of HIV infection, is essential. This means the full continuum, from voluntary counselling and testing (VCT) through the early (pre-ART) stages, to HAART and eventually terminal care. With this in mind, a Society guidelines committee met in Johannesburg recently to formulate pre-ART guidelines to assist health care workers through the phases before HIV-positive patients require HAART (p. 18). Any comments on this document would be welcomed.

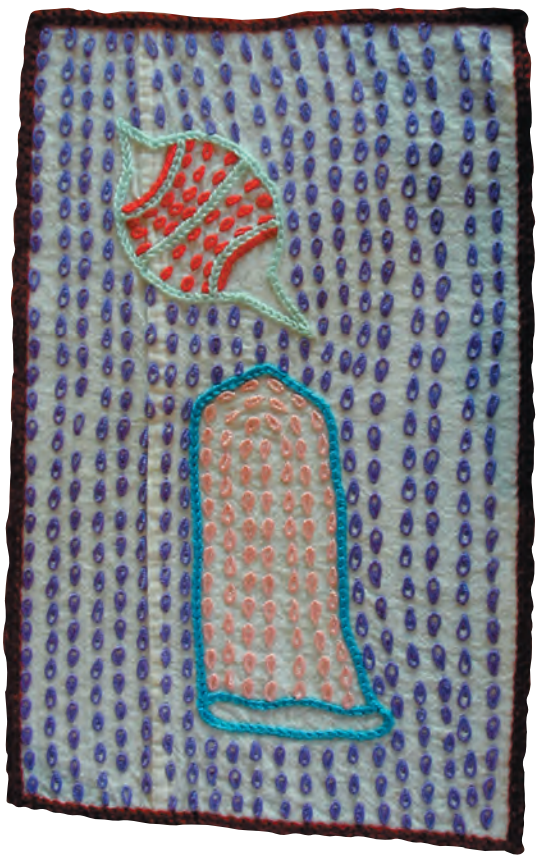
Approximately 90% of patients will develop one or more skin diseases during the course of their infection. KZN dermatologist, Dr Ncoza Dlova, shares her experience and visuals of HIV-associated dermatological conditions with us in a series of articles. In Part 1 (p. 12), Dr Dlova points out that the course of cutaneous manifestations is completely different in patients on antiretroviral therapy and those who are not, generally being less severe and chronic in patients on HAART. Another compelling reason to hope for a stepping up of the provision of ARVs at approved public sector sites.

Constant talk about ARVs in both the private and the public sector is certainly not all that is on our minds. Reduction of transmission is a vital part of any successful HIV/AIDS plan. Two articles in this issue deal with different aspects of this problem, which seems to confound us in South Africa. In the first, Steve Andrews and Marilyn Keegan address the well-known role of transport workers in global and national spread of HIV in a novel way. They stress the importance of interventions at rest places, lending credence to the importance of the PLACE method (which aims to improve prevention programme coverage at geographical sites at which HIV transmission is most likely to occur). Another prevention of transmission issue, the breast-feeding debate, is addressed in an article and a letter to the Editor, so read on ...

DES MARTIN

Editor, Southern African Journal of HIV Medicine

President, Southern African HIV Clinicians Society



ADHERENCE ISSUES

The HIV epidemic has led to a burgeoning number of journals devoted to HIV disease, social impacts, management, etc. I was interested to receive an inaugural copy of *Leadership in HIVAIDS*, sponsored by, among others, the Department of Trade and Industry. A very nice glossy mag it is too, with lots of interesting reading material aimed not only at the health professional but civil society in general. One piece reported on an open letter from the Hudson Institute, Washington, and including a number of authors from around the world, challenging the Global AIDS Coordinator, Randy Tobias, and calling for safe proven AIDS drugs for Africa. The World Health Organization was formed in 1948 and its constitution drafted then included the elimination of substandard pharmaceutical production and improving the quality and safety of health care infrastructure in developing countries throughout the world. This letter questions quality and safety of pharmaceutical standards and implementation of guidelines in general of the WHO in recent times. It asks for a clearer plan from the WHO on exactly how 3 million people should be treated with antiretroviral (ARV) therapy by 2005, claiming that the present plan is vague on medical supervision and follow-up. It also highlights the concerns around the WHO's recommendation for fixed-dose combination (FDC) ARV drugs.

While fixed-dose drugs are attractive in simplifying therapy and promoting adherence, they should undergo stringent human bioequivalence testing verified by a rigorous regulatory body. The pre-qualification system employed by the WHO, which is *not* a regulatory agency, does not mean that adequate quality control has been performed on these drugs. The generic FDCs are also attractive for reasons of cost. However, it should not always be assumed that generics and FDCs are cheaper than patent drugs – the latest price comparisons done by Médecins Sans Frontières show that in many cases single-component patented drugs are cheaper than the equivalent generics. Sobering lessons learnt in treating malaria are that cheaper copies may not be as effective and may thus lead to more morbidity and mortality than before. Thompson Ayodele, director for public policy analysis in Lagos, Nigeria, makes the following salient statement: 'the extent of the HIV epidemic and the emergence of resistant strains makes the need for testing more, not less acute. HIV medicines, whether original or generic, should meet the most stringent rigorous clinical and testing reviews. If the proposed drugs are rejected by pharmacies in Brussels, Geneva, London, Tokyo or Washington, accepting the use of the same drugs in Africa, with little resources and lack of equipment to do proper clinical and scientific evaluation, may further compound the woes of HIV/AIDS victims.'

Another factor that may well have a negative impact on adherence, and thus the success of the '3 by 5 Initiative', is the high rates of alcohol use in communities also needing widespread implementation of ART. Alcohol abuse has been associated with poor adherence to highly active antiretroviral therapy (HAART). The relationship between adherence to HAART and alcohol consumption at baseline and over a 6-month follow-up was investigated by the CARE unit in Boston.[1] In this group of 267 HIV-infected participants, alcohol consumption was the most significant predictor of adherence, with better adherence associated with recent abstinence from alcohol compared with at-risk level use (OR = 3.6) or moderate use (OR = 3.0). The study concluded that any alcohol use in HIV-infected persons with a history of alcohol problems is associated with worse ART adherence, and surmised that addressing alcohol use may improve clinical outcomes. In a further study by Ena *et al.*[2] from Spain, which looked at risk and determinants of developing severe liver toxicity during therapy with nevirapine- and efavirenz-containing regimens in HIV-infected patients, multivariate analysis showed the association of severe liver toxicity with hepatitis C antibody positivity (RR = 7.64), combination of non-nucleoside reverse transcriptase inhibitor with a protease inhibitor (RR = 3.07) and alcohol intake greater than 40 g/d (RR = 3.09). The study concludes that alcohol should be avoided during ART therapy.

Two good reasons why we need more support for our communities where ART programmes are happening. In any of these communities, shebeens, beer halls and bottle stores far outnumber alcohol support groups such as Alcoholics Anonymous. In one of the communities where we work there is not a single NGO devoted to alcohol support, yet alcohol use continues to be one of the big social problems cited by our therapeutic counsellors, who often consider it a significant factor in possible non-adherence. As the national ARV programme rolls out, perhaps SANCA needs to be looking at a parallel 'roll-out' of services throughout South Africa.

LINDA-GAIL BEKKER
Managing Editor

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MANAGING HIV AS A CHRONIC DISEASE: USING INTERACTIVE DATA COLLECTION TO IMPROVE CLINICAL CARE

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As South Africa and the rest of the developing world respond to the AIDS crisis, a critical task will be to develop scalable systems for sustainable and effective delivery of antiretroviral (ARV) drugs in a variety of resource-restricted settings. With the emergence, from national governments, the World Health Organization (WHO) and major international donors, of the political will and funding to support treatment programmes, it has become urgent that we consider how ARVs will be delivered. In this review, we consider how ARVs allow us to manage HIV/AIDS as a chronic disease, and the data systems that are required to support this approach to therapy.

MANAGING HIV/AIDS AS A CHRONIC DISEASE

With modern ARV treatment regimens, sustained high survival rates can be expected.[1,2] However, effective management of patients who qualify for ARVs entails a lifetime commitment by both patient and providers to complex treatment with significant side-effects. A system of efficient chronic care may require comprehensive clinic redesign and a division of labour that allows non-physicians to take greater responsibility for routine care. This model has been used successfully in the developed world for a number of chronic diseases (diabetes, asthma and hypertension).[3] While the AIDS pandemic in the developing world presents a unique set of challenges, the expected prolonged and healthy survival of patients treated with ARVs in resource poor-settings necessitates the development of a comprehensive management strategy for this disease.[4] A number of highly successful ARV pilot programmes have been reported from the developing world, including from South Africa.[5,6] The challenge now is to develop effective programmes that are replicable and scalable within the resource-poor public health sector. Scalable disease management programmes have been implemented successfully in the developing world for perinatal diseases, tuberculosis (TB)[7] and HIV[8,9] in co-operative projects with health improvement organisations supporting national and provincial health programmes.

The outcome of chronic diseases has been most successful in situations where a structured programme of care delivery results in an informed, activated patient population and knowledgeable, proactive, protocol-driven care providers who work collaboratively with their peers.[10] In the Chronic Care Model described by Ed Wagner,[11] this interaction can be supported best by harnessing and integrating the contributions to care from both the community and the clinic (Fig. 1). The design of care in the clinic should take into account the varied needs of the patients, utilise fully the spectrum of skills of the clinic

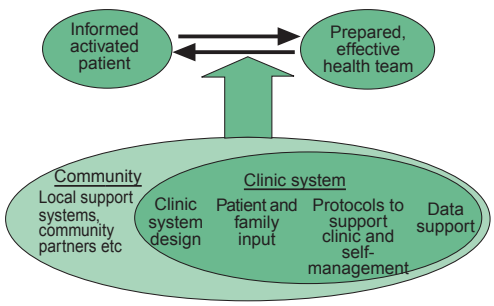


Fig. 1. The chronic care model, adapted from Wagner.[11]

personnel, and strive to accomplish the six attributes of care identified by The Institute of Medicine, i.e. care that is patient-centred, effective, safe, efficient, timely, and equitable.[12] To achieve this, several components of the health care delivery system need to be considered.

HEALTH CARE ORGANISATION (HCO)

While the introduction of new services may stress an already overstretched health system, the introduction of sound disease management practices for ARV delivery provides an opportunity to strengthen the system. To assist in this process HCO leadership should make excellent HIV/AIDS care a goal of the health system, and provide the resources to initiate ARV care (e.g. data systems, data entry personnel, counsellors), remove barriers to clinic redesign, and actively support implementation and ongoing improvement of ARV treatment programmes.

CLINIC SYSTEM DESIGN

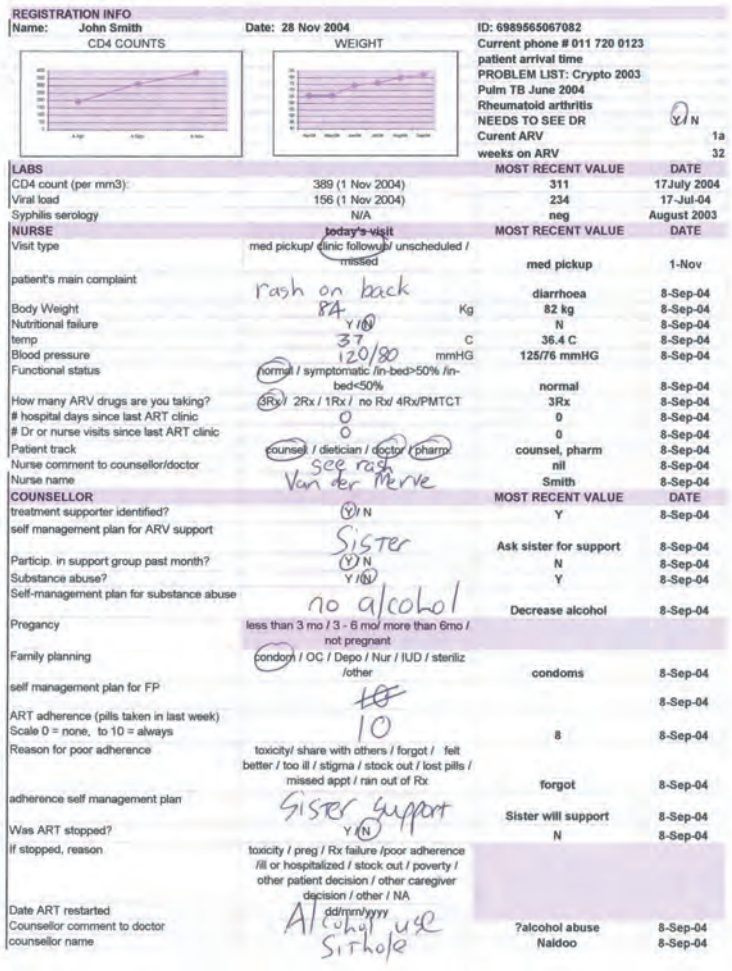
As clinics make the transition from palliative care of AIDS to comprehensive management of HIV/AIDS, the structure of care delivery needs to be redesigned. While many of the reported pilot programmes and initial phases of the South African ARV roll-out are mostly doctor-based, a more nurse-based focus will need to emerge as the service devolves into more of a primary care setting, As suggested by South African Government guidelines,[13,14] new and existing patients who are being prepared for ARVs will have different needs from patients who are being seen repeatedly for ARV maintenance therapy, or patients with HIV who do not qualify for treatment. Patients on chronic therapy can be triaged in streams that stratify patients who need routine care and surveillance ('fast-track') from those who require more complex care or a change in management (e.g. consideration for up- and down-referral). Reassessment of the role of different caregivers often reveals additional human resources that can be harnessed to increase clinic capacity. For instance, as clinics become overburdened and progressively more dysfunctional, caregivers are consumed with inappropriate tasks (e.g. nurses are diverted from patient care to traffic control, directing and placating patients), and time and effort is wasted on data entry that is duplicated throughout the clinic (e.g. pharmacists re-enter demographic data in order to dispense drugs). Clinic efficiency is significantly enhanced when the roles of every member of the care unit are clarified.

CLINIC PROTOCOLS

Management can be organised to support the best available guidelines of ARV therapy and HIV care. The South African guidelines have clear algorithms, which can be incorporated into disease management.[13,14] Patient encounter forms can support these algorithms by promoting information collection and prompt care that relates to the specific needs of the particular stage of a patient's management. Protocols should be adapted periodically through a systematic process that is informed by data collected in the clinic.

SELF-MANAGEMENT SUPPORT

Patients can be given an active role in the management of their disease. The process whereby patients become informed and involved is incorporated into routine clinic management in many HIV clinics with the use of counsellors and teaching sessions. Self-management strategies should be documented and can be reinforced



REGISTRATION INFO

Name: John Smith	Date: 28 Nov 2004	ID: 6989565067082	
CD4 COUNTS / WEIGHT		Current phone # 011 720 0123	
		patient arrival time	
		PROBLEM LIST: Crypto 2003	
		Pulm TB June 2004	
		Rheumatoid arthritis	
		NEEDS TO SEE DR	Y/N
		Curent ARV	1a
		weeks on ARV	32
LABS		**MOST RECENT VALUE**	**DATE**
CD4 count (per mm3):	389 (1 Nov 2004)	311	17July 2004
Viral load	156 (1 Nov 2004)	234	17-Jul-04
Syphilis serology	N/A	neg	August 2003
NURSE	**today's visit**	**MOST RECENT VALUE**	**DATE**
Visit type	med pickup/ clinic follow up/ unscheduled / missed	med pickup	1-Nov
patient's main complaint	rash on back	diarrhoea	8-Sep-04
Body Weight	84 Kg	82 kg	8-Sep-04
Nutritional failure	Y/N	N	8-Sep-04
temp	37 C	36.4 C	8-Sep-04
Blood pressure	120/80 mmHG	125/76 mmHG	8-Sep-04
Functional status	normal / symptomatic /in-bed>50% /in-bed<50%	normal	8-Sep-04
How many ARV drugs are you taking?	3Rx/ 2Rx / 1Rx / no Rx/ 4Rx/PMTCT	3Rx	8-Sep-04
# hospital days since last ART clinic	0	0	8-Sep-04
# Dr or nurse visits since last ART clinic	0	0	8-Sep-04
Patient track	counsel / dietician / doctor / pharm	counsel, pharm	8-Sep-04
Nurse comment to counsellor/doctor	see rash	nil	8-Sep-04
Nurse name	Van der Merve	Smith	8-Sep-04
COUNSELLOR		**MOST RECENT VALUE**	**DATE**
treatment supporter identified?	Y/N	Y	8-Sep-04
self management plan for ARV support	Sister	Ask sister for support	8-Sep-04
Particip. in support group past month?	Y/N	N	8-Sep-04
Substance abuse?	Y/N	Y	8-Sep-04
Self-management plan for substance abuse	no alcohol	Decrease alcohol	8-Sep-04
Pregancy	less than 3 mo / 3 - 6 mo/ more than 6mo / not pregnant		
Family planning	condom / OC / Depo / Nur / IUD / steriliz /other	condoms	8-Sep-04
self management plan for FP	~~US~~		8-Sep-04
ART adherence (pills taken in last week)			
Scale 0 = none, to 10 = always	10	8	8-Sep-04
Reason for poor adherence	toxicity/ share with others / forgot / felt better / too ill / stigma / stock out / lost pills / missed appt / ran out of Rx	forgot	8-Sep-04
adherence self management plan	Sister support	Sister will support	8-Sep-04
Was ART stopped?	Y/N	N	8-Sep-04
If stopped, reason	toxicity / preg / Rx failure /poor adherence /ill or hospitalized / stock out / poverty / other patient decision / other caregiver decision / other / NA		
Date ART restarted	dd/mm/yyyy		
Counsellor comment to doctor	Alcohol use	?alcohol abuse	8-Sep-04
counsellor name	Sithole	Naidoo	8-Sep-04

Fig. 2a. Data collection sheet.

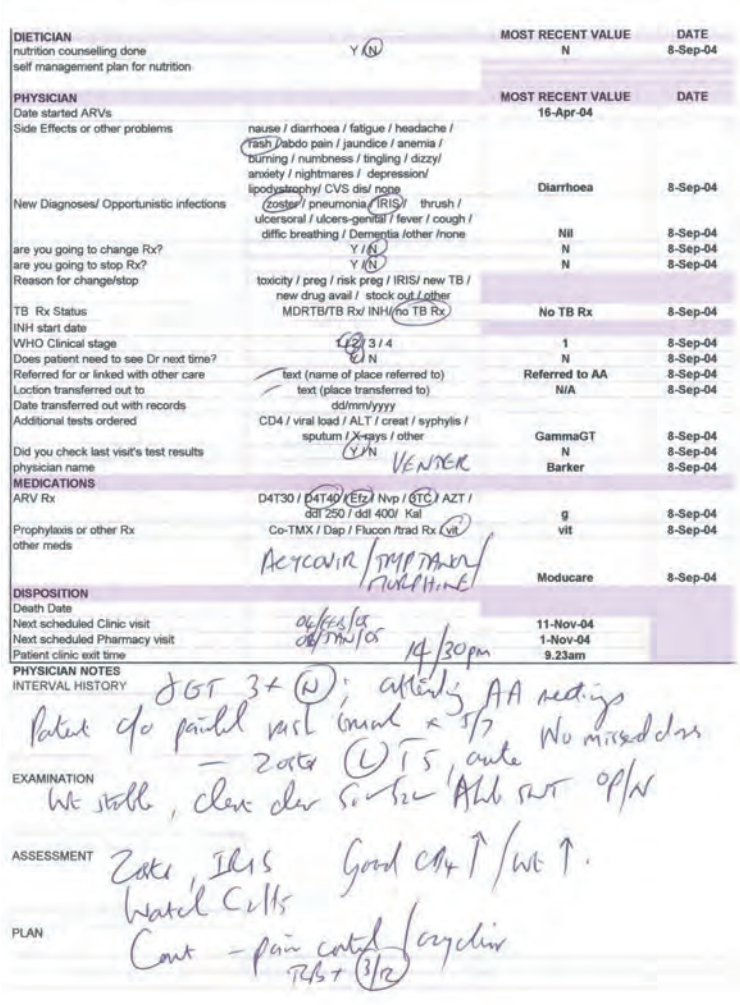
at subsequent visits. Standardised assessments of patient knowledge and barriers to care can be used to design better care. Patients can be motivated, and their adherence can be promoted by seeing their disease indices, including 'improvements' in weight, CD4 counts, and other parameters (Fig. 2a and b). These act as important adherence support tools.

COMMUNITY RESOURCES

The South African programme strongly emphasises the role of community organisations, ranging from support for disclosure and stigma reduction to assistance with palliative care and adherence support. Effective chronic disease management should include linkage of clinic care to community resources (e.g. home visits and partnerships with community activist groups).

ROLE OF DATA SYSTEMS FOR CHRONIC MANAGEMENT OF HIV/AIDS

A key component of chronic disease management is a data collection system that both supports and drives optimal care of the individual patient *and* the treated population. A number of data information capturing systems of varying degrees of sophistication and complexity have been demonstrated to support ARV management in a variety of resource-rich and poor settings. Many of these use a combination of paper- and computer-based record keeping[15] and some have demonstrated the ability to network remote rural clinics with satellite and web-based technology.[9] As South Africa and other sub-Saharan countries grapple with the need to standardise and record data in a variety of settings, there has been an explosion of proposed technology-rich solutions to accomplish this task. Unfortunately, there is often a tension between the needs of data collection systems that allow national and regional health planners to analyse and improve programmes, and the needs of clinicians on the front lines who require a targeted set of measures to help manage their large workloads. While it is possible to integrate these needs, the needs of patient care can become subservient to those of central planners, and caregivers often end up with time-consuming data collection forms that seem to have little relevance to disease management. Setting up a chronic disease registry and a set of measures that support good care is a simple task compared with the complexities of establishing a comprehensive medical record. We propose an interactive data support model that has immediate relevance to the clinician *and* provides data to central planners. In addition, collected data can be used to drive improvement in chronic management of HIV.



DIETICIAN		MOST RECENT VALUE	DATE
nutrition counselling done	Y (N)	N	8-Sep-04
self management plan for nutrition			
PHYSICIAN		**MOST RECENT VALUE**	**DATE**
Date started ARVs		16-Apr-04	
Side Effects or other problems	nause / diarrhoea / fatigue / headache / rash /abdo pain / jaundice / anemia / burning / numbness / tingling / dizzy/ anxiety / nightmares / depression/ lipodystrophy/ CVS dis/ none	Diarrhoea	8-Sep-04
New Diagnoses/ Opportunistic infections	zoster / pneumonia / IRIS / thrush / ulcersoral / ulcers-genital / fever / cough / diffic breathing / Dementia /other /none	Nil	8-Sep-04
are you going to change Rx?	Y / N	N	8-Sep-04
are you going to stop Rx?	Y / N	N	8-Sep-04
Reason for change/stop	toxicity / preg / risk preg / IRIS/ new TB / new drug avail / stock out / other		
TB Rx Status	MDRTB/TB Rx/ INH/no TB Rx	No TB Rx	8-Sep-04
INH start date			
WHO Clinical stage	1 / 2 / 3 / 4	1	8-Sep-04
Does patient need to see Dr next time?	Y / N	N	8-Sep-04
Referred for or linked with other care	text (name of place referred to)	Referred to AA	8-Sep-04
Loction transferred out to	text (place transferred to)	N/A	8-Sep-04
Date transferred out with records	dd/mm/yyyy		
Additional tests ordered	CD4 / viral load / ALT / creat / syphylis / sputum / X-rays / other	GammaGT	8-Sep-04
Did you check last visit's test results	Y / N	N	8-Sep-04
physician name	VENTER	Barker	8-Sep-04
MEDICATIONS			
ARV Rx	D4T30 / D4T40 / Efz / Nvp / QTC / AZT / ddI 250 / ddI 400/ Kal	g	8-Sep-04
Prophylaxis or other Rx	Co-TMX / Dap / Flucon /trad Rx / vit	vit	8-Sep-04
other meds	ACYCLOVIR / TMP DAPSONE	Moducare	8-Sep-04
DISPOSITION			
Death Date			
Next scheduled Clinic visit	06/Dec/04	11-Nov-04	
Next scheduled Pharmacy visit	06/Dec/04	1-Nov-04	
Patient clinic exit time	14/30pm	9.23am	

PHYSICIAN NOTES

INTERVAL HISTORY: IGT 3+ (N); attending AA meetings. Patient c/o painful vaginal ulcers x 1/7. No missed doses. — Zoster (L) T5, acute.

EXAMINATION: Ulcers still, clear discharge. Abd soft NAD. OP/N

ASSESSMENT: Zoster, IRIS. Good CD4 ↑ / wt ↑. Watch Cells

PLAN: Cont - pain control / acyclovir. TRS + (3/12)

Fig. 2b. Data collection sheet.

Data collection that is tied to disease management needs to be integrated into clinical practice, and should be perceived as providing obvious benefit to patient care. The system will fail if the perception is that the system generates additional 'work'. Feedback of patient progress and provider performance is a critical requirement for acceptance of the system. As medical record systems become more sophisticated, laboratory and pharmacy data systems can be fed electronically into the chronic disease registry. The HIV/AIDS disease registry can ultimately be integrated electronically into other chronic disease registries and the comprehensive medical record.

CORE FEATURES OF A CHRONIC DISEASE REGISTRY (TABLE I)

The data collection system should support a streamlined, high-throughput chronic disease management system that promotes excellent

treatment of patients with HIV/AIDS, and continuous improvement of care delivery. In addition to improvement in patient outcome, the disease management programme can improve efficiencies (e.g. triage into fast-track and intensive care track care pathways) to allow much greater flexibility of care and higher throughput of patients in clinics with limited human resources. Core data collection should be standardised to allow for expected migration of patients from one site to another and mechanisms established for easy transmission of core data from one ARV site to another, both through user-held information (e.g. card) and connectivity between ARV sites. Standardisation of data collection is a laudable focus of the provincial and national programmes, but this goal should not delay implementation of sound disease management practices at a local level.

An example of a collection form for chronic AIDS management in the era of ARV therapy is shown in Fig. 2. This is a form that has been designed for use in a specific urban Johannesburg ARV clinic and has been extensively modified and improved through continuous in-clinic testing. Although the core data requirements for ARV clinics are universal, each clinic presents a unique set of resources, staffing and structural elements, so no single form is likely to be suitable for all clinics. In addition, this form is likely to undergo significant further transformation as it is repeatedly evaluated by the clinic staff. Data are transferred from the sheet to the computer database at the end of this clinic, and, apart from prompting excellent care, has been found to promote rather than hinder clinic flow. Although the primary focus of this set of measures is disease management, all of the provincial and government required indicators can be reported on through monthly queries of the database. Since the task of filling in the fields can be shared by the various caregivers and administrative personnel the patient encounters during the visit, no single person is saddled with the responsibility of collecting data. If computer-generated forms are used, fields that are not relevant to the current visit (e.g. detailed demographic data) can be suppressed. Duplication of fields can be eliminated by programming the data system to derive information from pre-existing fields (Fig. 2).

The lack of easily accessible historical patient information systems in consultation rooms represents a major obstacle to improving care. A simplified historical graphic of core measures, e.g. weight, CD4 counts, can be displayed on the form as a 'snap-shot' of disease status for the provider and patient (Fig. 2). The disease management form can be pre-filled (by the computer database) with some historical data displayed in adjacent columns, allowing current patient condition to be evaluated in its historical context and avoiding time-consuming searches for previous data.

TABLE I. CORE FEATURES OF A DATA REGISTRY THAT SUPPORTS CHRONIC DISEASE MANAGEMENT FOR HIV/AIDS

- Collection of a core set of measures that promote the best available HIV/AIDS/ARV treatment guidelines, track HIV/AIDS management of the individual patient and the clinic population, and comply with standardised measures for ART reporting as laid out by national Department of Health guidelines
- Collection of data that track the processes of clinic care delivery and historical patient data (including self-management strategies)
- Promotion of streamlined clinic function that allows triaging of care and prompts specific tasks to be completed in sequence as the patient moves through the clinic
- Integration of clinical and pharmacy information that promotes streamlined (non-duplicative) drug-dispensing practices
- Provision of data reports that assist caregivers in the management of individual patients
- Provision to the patient of a portable document that summarises core elements of patient management to date (this document will allow for self-referral or transfer of patient care away from the clinic)
- Provision of data reports that allow evaluation of clinic population outcomes *and* the processes of care delivery in the clinic and community
- Provision of data reports that flag patients who are attending clinic, have missed clinic visits, and/or require specific tasks to be completed at a clinic visit

Restriction of data fields to a minimum set of measures that are perceived to be useful for patient management can promote acceptance and utilisation of this tool.

REPORTING DATA AS A PEER-REVIEW MECHANISM TO IMPROVE CARE

Data represent a powerful tool that can be used to rapidly improve care. Care providers are used to evaluate data, and simple, accessible reports of patient and population data can accelerate change. Allowing staff to see clearly how well they are providing care, against national benchmarks or even against nearby clinics, allows for interrogation of reasons for poor or good performance. Once the patient data are entered into the registry, this information needs to be fed back to providers, not only to prompt excellent individual patient care as described above, but also as a powerful tool to improve clinic performance. The collected data should be easily accessed and filterable so that lists of patients and aggregates of data can be sorted by patient sub-type, patient provider, clinic day, etc. These data can then be used to inform, activate and prepare both the patient and the providers in a way that closes the gap between current clinic practice and ideal care delivery for HIV/AIDS. In addition to the requirement to feed specific fields of data back to the provincial and national health departments, aggregate data should be reported to senior leaders of the health care system to sustain support and enthusiasm for the programme.

CONCLUSION

In the era of ARVs, HIV and AIDS should be managed as a chronic disease. Management of this condition requires thoughtful use of data systems that promote and improve excellent care and improve clinic efficiency. Data collection for AIDS management should supplement, rather than replace, the medical record. The system should facilitate patient flow, promote patient self-management, promote excellent care pathways, provide caregivers ready access to critical historical information, and allow improvement through feedback of patient and clinic populations to clinic providers. It should also fulfil data reporting requirements of national programmes. Introduction of improved disease management practices for HIV provides an opportunity to strengthen the overall health system and the data systems that support care delivery for other diseases.

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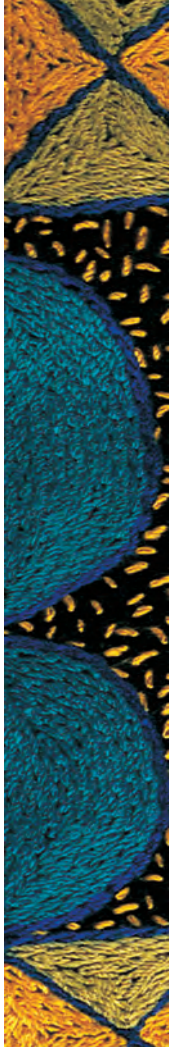

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CUTANEOUS MANIFESTATIONS OF HIV/AIDS: PART I

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Human immunodeficiency virus (HIV) infection can lead to a variety of clinical cutaneous manifestations. These cutaneous disorders occur universally during the course of HIV infection. Cutaneous manifestations of HIV are very diverse. The course and clinical presentation of HIV in individuals who have access to highly active antiretroviral therapy (HAART) is completely different from that in those who do not. Many of the HIV cutaneous presentations seen in South Africa become chronic and progressive. There is a marked reduction in the incidence of opportunistic infections and neoplasms in North America, Western Europe and Australia, where there is access to HAART.

Approximately 90% of patients will develop one or more skin diseases during the course of their illness. It is therefore crucial that health professionals become familiar with and are able to recognise the various skin manifestations of HIV.

Thirty-seven per cent of patients present with skin lesions as a marker of HIV infection. As the CD4+ lymphocyte cell count decreases, the severity of the skin condition increases, multiple skin lesions are seen, and frequent relapses are encountered. There tends to be increased severity of infections with known pathogens and occurrence of infection with unusual and exotic pathogens.

Patients often present with florid clinical patterns which fail to respond to conventional therapy. Correlation between skin disorders with CD4+ lymphocyte count in patients with HIV/AIDS in an American study is illustrated in Fig. 1.

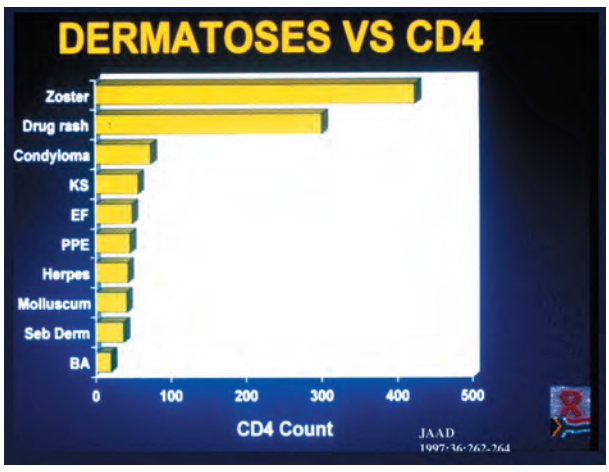

Fig. 1. Correlation between mean CD4 cell count and incidences of specific skin disorders in patients with HIV infection.

ACUTE SEROCONVERSION ILLNESS

The incubation period from the time of exposure to the development of an acute febrile syndrome is about 2 - 6 weeks. It is estimated that 50 - 70% of patients will have the acute syndrome after infection, however, of these only 25% have symptoms severe enough to warrant medical attention. Patients present with an infectious mono-nucleosis-like picture characterised by fever, sore throat,

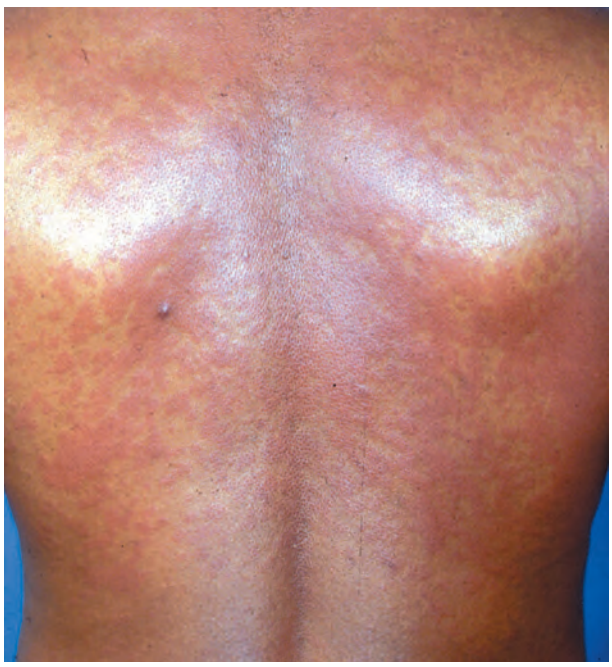

Fig. 2. Morbilliform rash of acute seroconversion illness.

myalgia, malaise, headache and enlarged cervical lymph nodes.

The cutaneous manifestations may take the form of a diffuse morbilliform rash (Fig. 2), a papular exanthem or a maculopapular rash with central petechiae, with occasional involvement of the palms of the hands and soles of the feet.

In one-third of patients the picture may include an enanthem characterised by ulcerations, aphthous-like lesions and candidiasis.

The duration of the acute episode is about 1 - 2 weeks, and it may be complicated by hepatitis and neurological symptoms.

FUNGAL INFECTIONS

Cutaneous fungal infections are common in both HIV-infected and uninfected individuals. They are the commonest infectious manifestation of immunosuppression related to HIV, ranging from superficial mucocutaneous candidiasis to life-threatening disseminated infections like histoplasmosis. Fungal infections occur early in the course of HIV infection, when they manifest with oral candidiasis, and later on as AIDS-defining conditions like histoplasmosis and cryptococcosis. A thorough knowledge of the diagnosis and treatment of these conditions is therefore important to decrease the significant morbidity associated with cutaneous fungal infections in HIV/AIDS.

CANDIDIASIS

This is the commonest mucocutaneous manifestation, affecting 20 - 70% of individuals with HIV.[1] Asymptomatic colonisation of the oropharynx occurs in up to 60% of HIV-infected patients. The incidence of oral candidiasis increases as the CD4+ count declines, and it is a marker of rapid HIV progression. As oral candidiasis is common in infants under 6 months of age, other clinical markers of HIV should be sought in this age group. However, recurrent and severe oral candidiasis in the older child (over 6 months of age) is indicative of immunosuppression. The incidence has declined with the use of fluconazole prophylaxis for cryptococcal meningitis.

Candidiasis most often affects the tongue and buccal mucosa, causing thick, whitish plaques, but may also present as angular cheilitis. (Fig. 3). Less common manifestations are paronychia (Fig. 4), onychomycosis, recurrent vaginal and urethral involvement and cutaneous involvement, predominantly of the flexures. Children may present with candidiasis in the napkin area and other flexures (axillae and neck folds) and chronic paronychia with nail dystrophy. Severe oral involvement with dysphagia indicates oesophageal candidiasis. Disseminated candidiasis, although rare, is often fatal and should be considered in ill patients with fever and severe immunosuppression.

Fig. 3. Oral candidiasis.

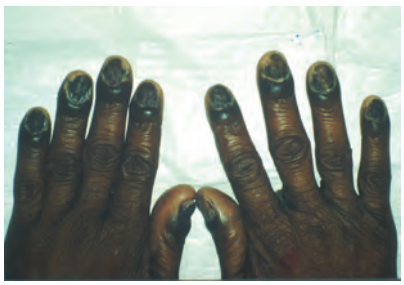

Fig. 4. Chronic paronychia.

Therapy is aimed at clearance and prevention of dissemination. Good oral hygiene is important, together with the use of topical azoles in the form of pastilles, troches or lozenges twice daily for 14 days. For refractory cases or where oesophageal involvement is suspected, oral azoles are indicated: itraconazole 200 mg daily for 5 days or fluconazole 100 mg daily for 5 days. The therapeutic dose in children is 3 - 6 mg/kg. Higher doses and longer duration of treatment may be necessary for recurrent episodes in severely immunosuppressed individuals. Cutaneous candidiasis may regress on HAART alone, in the absence of specific antifungal agents.

DERMATOPHYTOSIS

Dermatophytosis involving the skin, hair and nails is a common opportunistic infection in patients with HIV/AIDS. Although the frequency is not necessarily increased in these individuals, they are prone to more extensive and atypical forms which may be resistant to therapy. The commonest pathogen causing tinea infections is *Trichophyton rubrum*. Tinea corporis, pedis and capitis (Figs 5, 6 and 7) may present as typical 'ringworm' infection with active edges and central clearing, or present in atypical forms (extensive scaling, lack of an active edge, interdigital tinea pedis spreading to the dorsa of the feet, and 'two feet, one hand' syndrome with bilateral tinea manum and pedis). Folliculitis on hair-bearing areas may be complicated by Majocchi's granulomas and deep abscesses.

Certain types of onychomycosis (Fig. 8) are prevalent in HIV infection. Proximal white superficial onychomycosis and peri-ungual involvement are the commonest, and tend to spread to involve multiple fingers and toes as the CD4+ count declines.

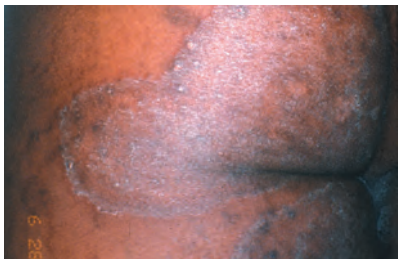

Fig. 5. Tinea corporis.

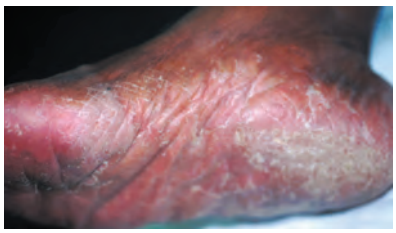

Fig. 6. Tinea pedis.

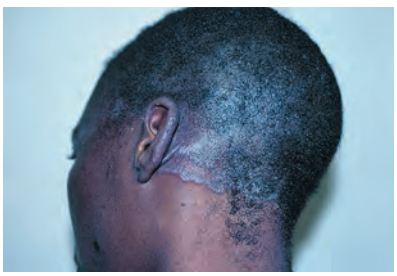

Fig. 7. Tinea capitis.

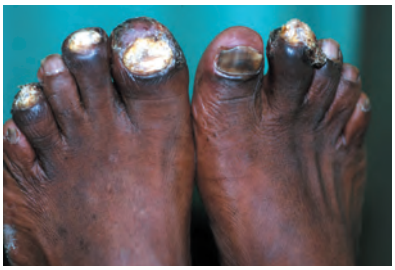

Fig. 8. Onychomycosis.

In children, HIV can present with painful tinea capitis, e.g. kerion, and may progress to scarring alopecia.

Since the diagnosis of superficial fungal infections may be difficult, confirmation with potassium hydroxide (KOH) microscopy is essential to exclude other pathologies. Therapy is important, as fungal infections are persistent and may act as a portal of entry for secondary staphylococcal and streptococcal infections.

Dermatophyte infections in HIV-infected adults and children are ideally treated with oral antifungals. The choice of antifungal agent depends on other concomitant therapies, as drug interactions are significant. Therapy may be required for longer than normal and HIV-infected patients are prone to relapse.

Tinea corporis is treated with either griseofulvin 500 mg - 1 g daily for 28 days, itraconazole 200 mg/day for 7 days or terbinafine 250 mg/d for 14 days.

Onychomycosis is more resistant to therapy and treatment needs to be of longer duration. Terbinafine 250 mg/d should be given for 3 months for fingernail infections and for 4 months for toenail infections, and itraconazole in a pulsed dosage of 400 mg/d for 1 week per month is necessary for 3 months for fingernail infections and for 4 months for toenail infections. Itraconazole should be taken with fatty food or an acidic drink to enhance absorption and also to combat the hypochlorhydria or achlorhydria to which HIV-infected individuals are susceptible. Itroconazole is a p450 enzyme inhibitor, so the prescribing physician needs to be aware of the danger of co-administration of other drugs metabolised by this enzyme system, e.g. protease inhibitors (PIs). In very ill patients with onychomycosis on multiple drugs it is best simply to keep the nails short and resort to topical therapy, e.g. amorolfine nail lacquer.

Primary and secondary prophylaxis is important to prevent relapse and re-infection. This may be achieved by benzoyl peroxide washes of the feet, drying carefully between the web spaces, and application of an antifungal cream or powder.

The first line of therapy for tinea capitis in children is micronised griseofulvin at 10 - 15 mg/kg for 6 - 8 weeks. Shorter duration of therapy can be achieved with itraconazole (5 mg/kg/d for 28 days) and terbinafine (250 mg > 40 kg, 125 mg 20 - 40 kg and 62.5 mg < 20 kg for 28 days). Compliance is best with shorter duration of therapy.

Patients on HAART will experience less frequent infections, which could clear without specific antifungal therapy. If treated with antifungals they will respond better to therapy and experience fewer relapses.

SYSTEMIC FUNGAL INFECTIONS

Disseminated cutaneous histoplasmosis and cryptococcosis are AIDS-defining conditions as they occur with profound immunodeficiency. Skin lesions signify dissemination via the bloodstream, the primary infection being in the lungs.

Cryptococcosis

This is a common systemic mycosis due to the yeast *Cryptococcus neoformans*. Skin involvement occurs in 10% of patients with systemic disease. The lesions are polymorphous and may present as papules, nodules, pustules or ulcers (Fig. 9).

The site most commonly affected is the head and neck, although lesions may be widespread. They may be confused with molluscum contagiosum, so biopsy is important to make a definitive diagnosis. Cryptococcosis is a life-threatening condition if untreated. Treatment involves intravenous injections of amphotericin B for 2 weeks followed by lifelong maintenance therapy with fluconazole

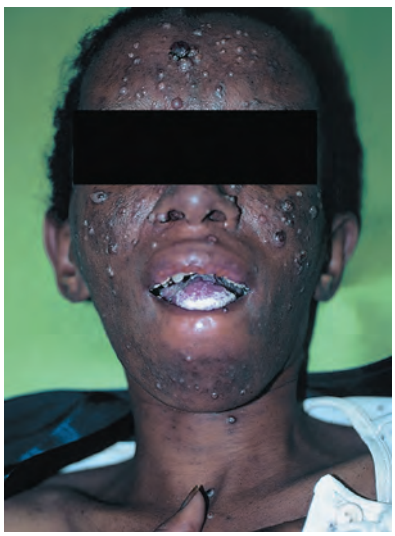

Fig. 9. Cryptococcus – umbilicated lesions resembling molluscum contagiosum.

200 mg daily. Patients on HAART may present with headache due to immune reconstitution of cryptococcal meningitis.

Histoplasmosis

Cutaneous histoplasmosis is associated with advanced immunosuppression, usually at a CD4+ lymphocyte count of < 75 cells/µl. Patients are usually ill, with fever, anaemia, respiratory symptoms, lymphadenopathy, hepatosplenomegaly and skin lesions. Histoplasmosis is therefore often misdiagnosed as tuberculosis, and patients are started on empiric anti-TB therapy, without response.

Skin involvement occurs in 5 - 10% of patients (Figs 10 and 11), and mucosal involvement is characteristic with gingival ulcers, plaques, nodules and abscesses. Owing to the polymorphous presentation, a high index of suspicion is required and biopsy and culture of lesions is mandatory. In the absence of skin lesions, blood and bone marrow culture are sensitive methodologies. Therapy in the acute stage is amphotericin B 15 mg/kg by intravenous injection or itraconazole 400 mg daily for 8 weeks. Lifelong maintenance therapy should be given, with itraconazole 200 mg/d or fluconazole 200 mg/d.

Sporotrichosis

Sporotrichosis is caused by the organism *Sporothrix schenckii* and can be classified as lymphocutaneous, fixed cutaneous, disseminated cutaneous or systemic. In HIV/AIDS, skin lesions may consist of widespread ulcers, papules, nodules and plaques, often with systemic involvement (Fig. 12). Local cutaneous infection is more likely to disseminate. Biopsy and culture is important to make a diagnosis, and therapy with itraconazole is effective.

Other systemic mycoses that may occur but are rare in South Africa are

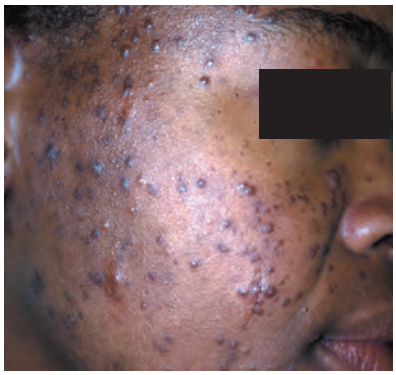

Fig. 10. Disseminated histoplasmosis – facial lesions.

Fig. 11. Disseminated histoplasmosis.

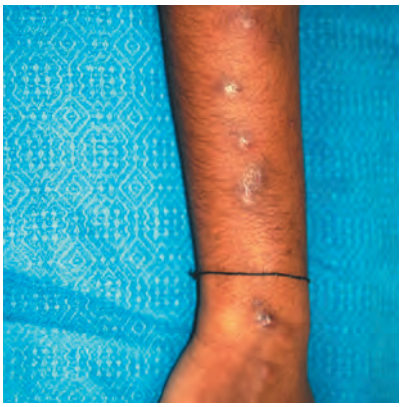

Fig. 12. Linear sporotrichosis.

blastomycosis, penicilliosis and coccidioidomycosis. Accurate diagnosis can only be made utilising pathological and mycological investigations. As more patients are being treated with HAART, the incidence of systemic fungal infections will decline.

BACTERIAL INFECTIONS

The most common bacterial infections in HIV-infected patients are due to *Staphylococcus aureus* and *Staphylococcus epidermidis*. These are common in the general population, but in HIV-infected individuals may be more widespread, recurrent and resistant to therapy. *S. aureus* is the most common cutaneous and systemic bacterial pathogen in adults. HIV-infected patients have increased *Staphylococcus* carriage in their nares. Infection presents with folliculitis, impetigo, ecthyma and cellulitis. In addition to *S. aureus*, Gram-negative infections such as ecthyma gangrenosum caused by *Pseudomonas* occur.

FOLLICULITIS

This common bacterial infection presents with acneiform papules and pustules, which may be excoriated. The common causative organisms are *S. aureus, S. epidermidis* and *P. aeruginosa*.

IMPETIGO

These lesions begin as macules that progress to vesicles and pustules, which then rupture leaving honey-coloured crusts. They are particular common in the perioral and perinasal areas. The causative organism is *S. aureus*, which is a common cause of cutaneous infection in the general population. In HIV infections, however, lesions may be seen more commonly in the intertriginous areas.

SOFT-TISSUE INFECTION

This presents as a warm, red and tender swelling which may progress to necrotising fasciitis.

Therapy for a first episode is the empiric use of antibiotics that will treat staphylococcal and streptococcal infections, and taking a specimen for a Gram stain. Deeper and recurrent infection warrants samples for microscopy and culture. If the patient is severely ill, admission for intravenous antibiotic therapy should be considered and longer duration of therapy may be required. If the infection is recurrent, therapy of staphylococcal carriage with mupirocin may be effective.

BACILLARY ANGIOMATOSIS

This rare condition caused by the spirocheate *Rochalimea henselae* presents with angiomatous papules, nodules and abscesses (Fig. 13). It occurs in patients with severe immunosuppression and may be clinically confused with Kaposi's sarcoma. Systemic involvement may occur with pulmonary, hepatic, bone and central nervous system symptoms. Histology is important as it is a fastidious organism and hence difficult to culture. Patients respond well to erythromycin 500 mg 6-hourly or doxycycline 100 mg twice a day until the lesion resolves. If the condition is recurrent, secondary prophylaxis is necessary. Alternative drugs are the cephalosporins and quinolones.

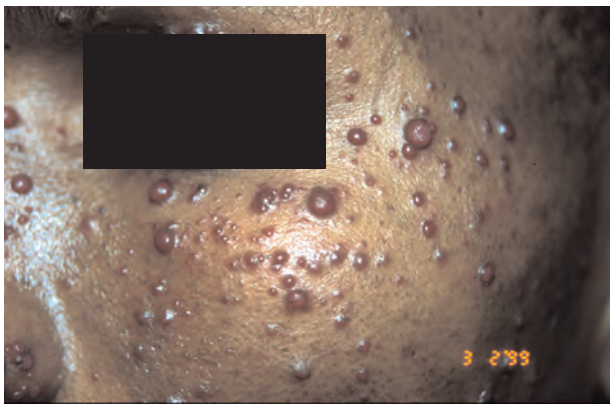

Fig. 13. Bacillary angiomatosis.

SYPHILIS

In HIV disease, syphilis progresses more rapidly through all of the stages. Syphilis may present atypically or be refractory to therapy, and laboratory investigations may be difficult to interpret owing to unusual serological responses. The primary chancre may consist of multiple lesions and may be extensive. Secondary syphilis presents as in the immunocompetent patient, with scaly plaques on the trunk, muzzle area of the face, palms and soles (Figs 14 and 15). However, it may mimic any other cutaneous disease and hence a high index of suspicion is required for diagnosis. Progression to neurosyphilis occurs more rapidly even if the patient has had optimal treatment. Lues maligna, an unusual form of secondary syphilis with ulcers, has been described. False-positive VDRL and RPR tests and delayed titre responses occur more commonly in HIV-infected patients. Treatment for primary, secondary and early latent syphilis is one dose of 2.4 million units of benzathine penicillin G, and for late latent syphilis or syphilis of unknown duration 2.4 million units of penicillin G weekly for 3 weeks.

MYCOBACTERIAL DISEASE

Tuberculosis

HIV-infected adults are susceptible to tuberculosis and

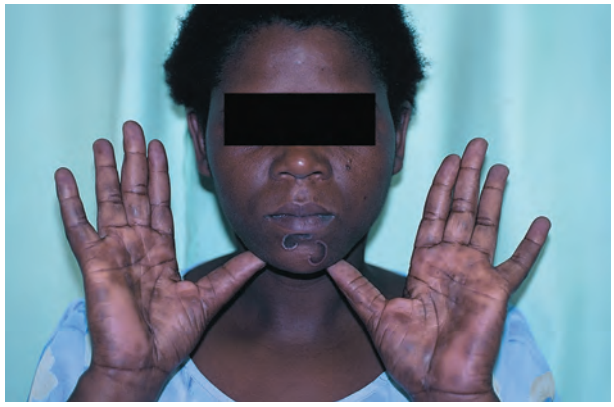

Fig. 14. Secondary syphilis, face and palms.

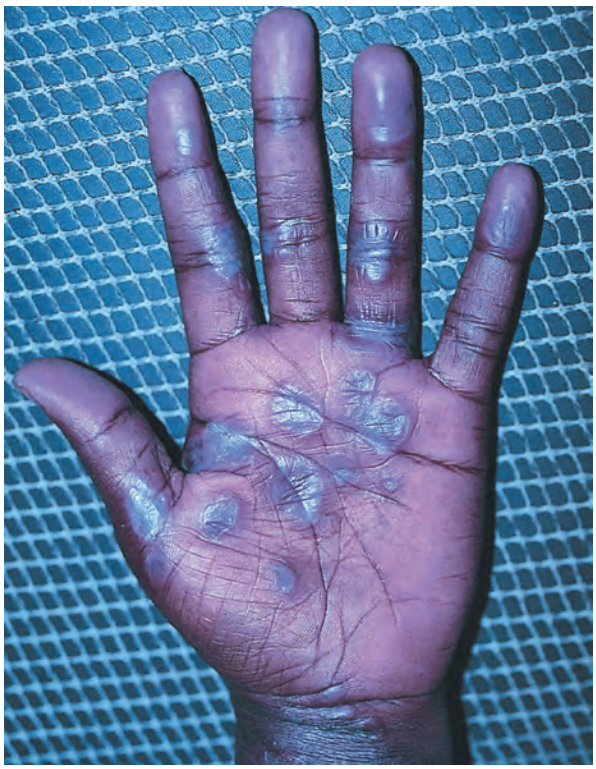

Fig. 15. Secondary syphilis with typical palmar lesions.

therefore at increased risk of presenting with cutaneous hypersensitivity reactions.

Papulonecrotic tuberculid can present with papules and pustules which ulcerate, usually involving the acral sites (earlobes, elbows, knees, extensors and buttocks) (Figs 16 and 17).

Lichen scrofulosorum presents as grouped papules on the trunk (Fig. 18) in patients with underlying lymphadenopathic and bone tuberculosis.

Erythema induratum/nodosum causes ulcers and painful nodules on the lower limbs, with a bluish edge (Fig.19).

Diagnosis of any of the above hypersensitivity reactions to tuberculosis is supported by a strongly positive Mantoux test, histology and investigation for underlying tuberculosis. Treatment with standard antituberculosis therapy for 6 months is effective.

Atypical mycobacteria

Mycobacterium avium, haemophilum and *bovis* may cause skin lesions with systemic mycobacterial disease in 10% of HIV-positive individuals. These infections are associated with advanced immunosuppression and are uncommon, partly because of the widespread use of antituberculosis therapy. Cutaneous lesions can present as papules, pustules, abscesses and ulcers. Lesions may present as nodules involving ascending lymph nodes of a limb. Biopsy and culture is essential for an accurate diagnosis, and therapy with clarithromycin and rifampicin is effective.

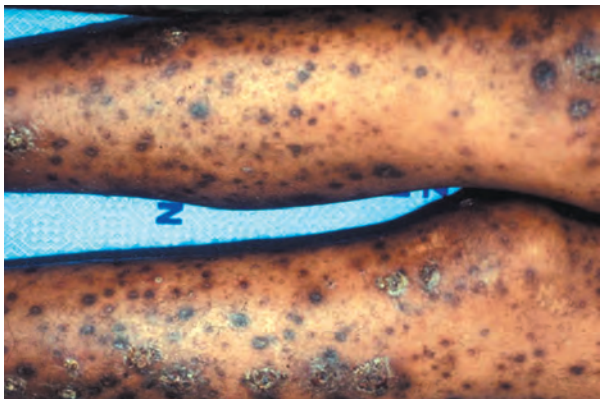

Fig. 16. Papulonecrotic tuberculid.

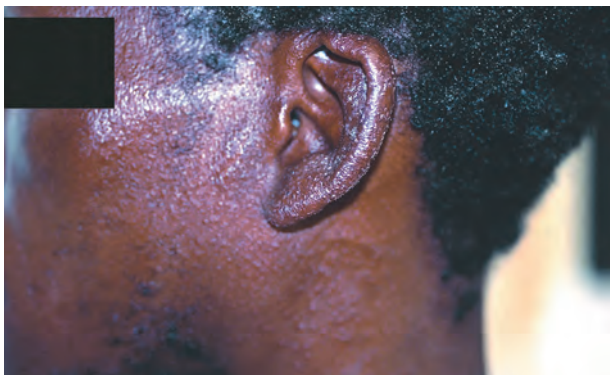

Fig. 17. Papulonecrotic tuberculid with classic earlobe lesions.

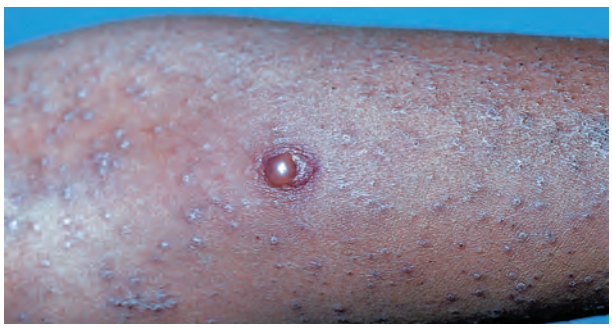

Fig. 18. Lichen scrofulosorum with blistering mantoux.

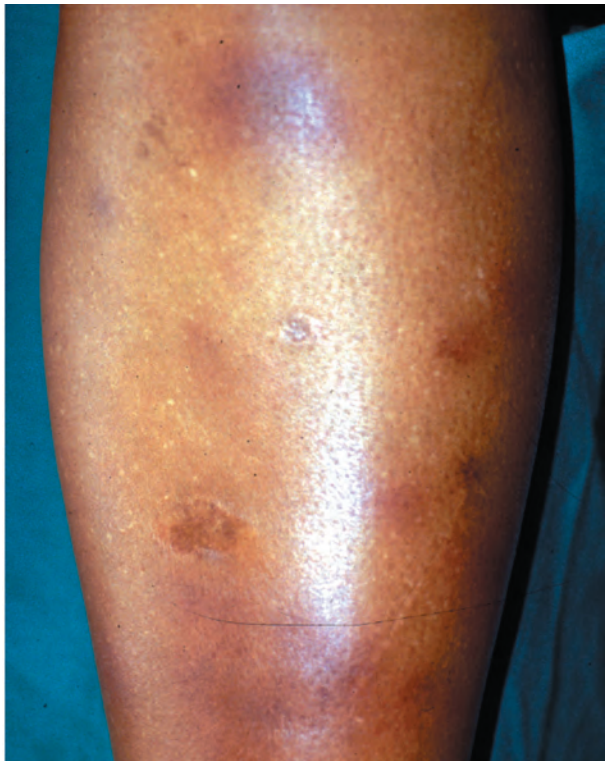

Fig. 19. Erythema nodosum, lower limbs.

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GUIDELINE

PRE-ART GUIDELINES

Amended November 2004

South African HIV Clinicians Society Expert Committee

Introduction

As southern Africa has finite medical resources and the public sector roll-out of antiretrovirals (ARVs) is in its infancy, it is incumbent on medical practitioners to attempt to preserve the immune status of the patient for as long as possible so as to delay the initiation of antiretroviral therapy (ART).

These guidelines attempt to address the factors which are important in the holistic approach to patient management and which could also influence the progression and outcome of disease, including:

- natural history of HIV infection
- primary prophylaxis and immunisations
- nutrition
- support and counselling.

PRIMARY PROPHYLAXIS AND IMMUNISATION

Most morbidity and mortality in HIV-infected patients is the result of opportunistic infections (OIs). **Primary prophylaxis** and immunisation can reduce the risk of these occurring. **Secondary prophylaxis** is given to prevent *recurrences* of OIs. Progressive immunosuppression is associated with a wide variety of OIs, but some OIs can occur when the CD4+ cell count is relatively high, e.g. 500 cells/µl.

As these guidelines address pre-ART issues, only conditions that occur at CD4+ above 200 cells/µl will be discussed, as patients with CD4+ counts of 200 cells/µl or with a slightly higher CD4+ count and the presence of an OI(s) are likely to be on antiretroviral therapy.

PRIMARY PROPHYLAXIS

Co-trimoxazole

Co-trimoxazole markedly reduces hospitalisation and mortality and provides protection against:

- *Pneumocystis jiroveci* (formerly known as *P. carinii* pneumonia (PCP)
- toxoplasmosis
- many bacterial infections, and
- diarrhoea caused by *Isospora belli* or *Cyclospora* species.

Indications

- All HIV-infected adults who are immunosuppressed, i.e. World Health Organization (WHO) stages 3 & 4 and/or CD4+ count < 200 cells/µl or total lymphocyte count of < 1.25 x 10^9/l.
- Co-trimoxazole can be discontinued in patients on ART when the CD4+ count has risen above 200 cells/µl and has remained above that level for 3 months or more.

Dosage

Co-trimoxazole 960 mg/d. This dosage is the best-studied and the *only* regimen used in randomised controlled trials conducted in Africa. Lower dose regimens (480 mg/d or 960 mg 3 times per week) have been shown to have equivalent efficacy to the 960 mg/d with less toxicity, but all these studies were conducted in developed countries.

Side-effects

The commonest side-effect of co-trimoxazole is maculopapular rash. Treatment may be continued in the presence of mild rash or interrupted and then re-challenged with antihistamine cover. Treatment should not be continued in the presence of fever, hepatitis or mucous membrane lesions, e.g. Stevens-Johnson syndrome. Neutropenia is a rare side-effect of prophylactic co-trimoxazole – routine blood count monitoring is not necessary.

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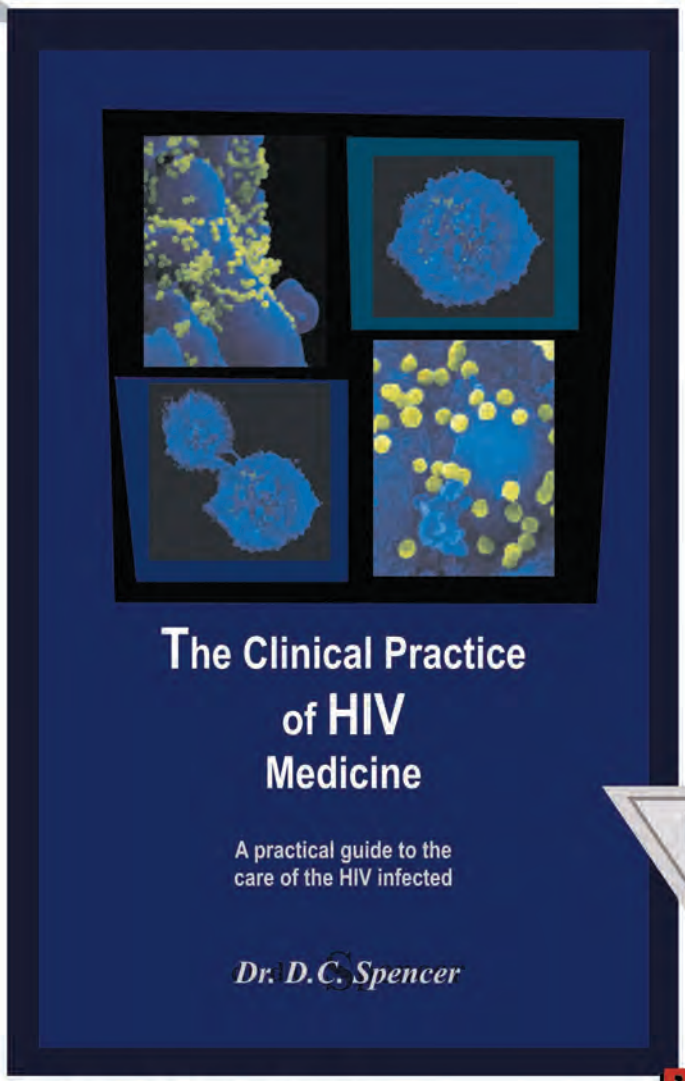

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Alternative drug

Dapsone 100 mg/d.

Note: Dapsone does not provide protection against bacterial infections and provides only limited protection against toxoplasmosis.

Drugs to prevent tuberculosis (TB)

Isoniazid (INH) given at a dose of 300 mg/d for 6 months is the most studied of the prophylactic regimens and recommended in South African Department of Health (DoH) guidelines.

Notes:

- Before commencement of preventive TB treatment, active TB should be excluded by using current DoH guidelines.

  Further investigations to exclude TB must be done if any of the following symptoms are present:
  - cough > 2 weeks
  - drenching night sweats or fever for > 2 weeks
  - observed weight loss > 1.5 kg/month.

  If any of the above symptoms are present, two sputum smears and one sputum for TB culture should be sent to the laboratory.

  It is not necessary to do a screening chest X-ray before initiating preventive therapy.
- Preventive therapy reduces the risk of active TB by about 60% in HIV-infected patients with a tuberculin skin test (Mantoux test) reaction of ≥ 5mm.
- There is no significant benefit in giving prophylaxis to patients with a negative skin test unless they fall into a high-risk category, i.e.:
  - people who have been in contact with TB including health care workers
  - underground miners and prisoners.
- In communities with a high TB prevalence the benefit of prophylaxis does not extend beyond about 2 years. It is therefore recommended that HIV-infected health care workers should not work in areas with a high risk for TB.
- TB preventive therapy should not be administered at TB clinics, as HIV-infected patients may be exposed to multidrug-resistant TB. In addition, the capacity of TB clinics is limited.
- It is essential to monitor for symptoms of hepatotoxicity on a monthly basis. Patients *must* immediately report any symptoms of nausea, vomiting, abdominal pain and jaundice.
- Pyridoxine 10 - 50 mg daily must be given concomitantly with isoniazid (INH) to prevent neuropathy (25 mg tablets are available in the public sector). As other supplements and multivitamin preparations may also contain pyridoxine, patients should be warned not to take over 100 mg per day.

ADULT IMMUNISATIONS

HIV infection is associated with a multifaceted suppression of both humoral and cell-mediated immune response, which may impair the response to vaccinations, reducing their efficacy. The safety of vaccination is also modified by HIV infection and the live vaccines of varicella, rotavirus and oral polio are contraindicated. HIV infection increases susceptibility to the diseases immunisation can protect against. Therefore HIV infection alters both the risks and benefits of vaccination. While the aim of vaccination is to prevent clinical disease, trials of vaccine efficacy frequently rely on the surrogate marker of antibody titre. The antibody titres required to prevent disease are not always well established for immune-competent individuals and may differ in HIV-infected people. Particularly if severe, immune suppression is associated with impaired responses to sub-unit, toxoid and killed vaccines. The efficacy of vaccination is therefore lowest in those most susceptible to the disease against which protection is sought. The decision to use a vaccine must be based on best assessment of risks and benefits.

Response to vaccination when the CD4+ count is < 200 cells/µl is very poor.

It is mandatory to report all suspected vaccine-related adverse events and vaccine failures.

PNEUMOCOCCAL VACCINATION

Although pneumococcal vaccination is recommended routinely and as early as possible by the Centers for Disease Control and Prevention (CDC) for patients who are HIV-seropositive, this is not currently recommended in South Africa. The recommendation by the CDC was not based on studies but on the premise that while efficacy is not proven, the potential benefit and safety of the vaccine justify its use in this situation. There is currently insufficient evidence to support this recommendation. Plasma HIV levels have been found to be transiently elevated in some studies in HIV-seropositive individuals following pneumococcal vaccination. The significance of these elevated levels is uncertain. The polyvalent Pneumovax® has been shown to be ineffective and in fact increased the risk of pneumonia in a large Ugandan study of patients not on ART, and is therefore not advised.[1]

INFLUENZA VACCINATION

The Southern African influenza vaccine recommendations for 2004[2] recommend that people with mild to moderate immunosuppression should be vaccinated because of the greater liability to complications associated with secondary

infection. However, because of the poor efficiency of the vaccine in severely immunosuppressed persons, i.e. those with CD4+ counts < 200 cells/µl, there is little point in immunising them. Instead one would need to rely on chemoprophylaxis with either amantidine or (preferably) the newer neuraminidase inhibitor drugs, Zanamavir or Oseltamavir, for protection against influenza.

Limited data are available with regard to the effects of influenza on the HIV-infected individual but there is some evidence that symptoms may be prolonged and complications more common, and severe, at least in some cases. Transient (2 - 4-week) increases in replication of HIV-1 in the plasma or peripheral blood mononuclear cells of HIV-infected persons after influenza vaccination have been noted in some studies. These increases are of uncertain significance. Responses are sub-optimal if CD4+ counts are very low.[2]

TRAVEL AND OTHER SPECIAL SITUATIONS

- **Hepatitis A and B vaccination** can be given to all HIV-positive patients if necessary.
- **Yellow-fever vaccination** can be given to patients with early HIV infection (WHO stage 1 or 2) and patients who have a CD4+ cell count of > 200 cells/µl, *but* is contraindicated in patients with symptomatic HIV infection (WHO stage 3 or 4 disease) and if the CD4+ count is less than 200 cells/µl.
- **Rabies vaccination** should be given to HIV-infected people working with animals and at game parks. Immunoglobulins should be used in the event of a significant exposure.
- **Cholera.** No role other than for health care workers involved in an epidemic.
- **Typhoid and oral polio vaccination** is endorsed (inactivated polio vaccine (Salk) should be given if this is available).

MALARIA

Most cases of malaria in sub-Saharan Africa are due to *Plasmodium falciparum*, the most severe and only life-threatening form of malaria. All the remarks that follow apply to this species. South Africans are generally at increased risk of developing severe malaria as they do not develop protective immunity because transmission is of low intensity, and is seasonal. Falciparum malaria has higher mortality rates and is more common in HIV-infected persons, especially those people with low CD4+ lymphocyte counts. Pregnant women in areas of high transmission of malaria are at risk of severe forms of the disease, generally when they are primigravidas, but all gravidities of HIV-infected women are at risk. There is evidence that placental infection by malaria increases the risk of mother-to-child transmission of HIV.

Preventing malaria

- **Avoiding mosquito bites.** All HIV-infected individuals living in malaria transmission areas should be protected by adequate vector control. Malaria control programmes in these areas are responsible for vector control, particularly spraying the interior of dwellings with residual insecticides, the use of larvicides, and reducing standing water. At an individual level, the simplest and most cost-effective way to minimise mosquito bites is by using insecticide-impregnated bed nets, and ensuring that these are regularly re-impregnated. The use of topical insect repellents is also effective, provided that 10 - 20% diethyltoluamide (DEET) preparations are used (other preparations have minimal or no effect). Repellents should be applied to all exposed skin (sparing the face) especially between dusk and dawn. Travellers should also use mosquito coils or plugs.
- **Chemoprophylaxis.** All HIV-infected travellers to malaria transmission areas should be given chemoprophylaxis, according to National Department of Health Guidelines for the prevention of malaria in South Africa. Either mefloquine or doxycycline is recommended. The combination of atovaquone and proguanil (Malanil) is also effective, but is expensive and there are potential drug interactions with ARVs that do not apply to either mefloquine or doxycycline (see below).

  Malaria chemoprophylaxis should be offered to HIV-infected pregnant women living in malaria endemic areas, irrespective of their gravidity. Chemoprophylaxis must be accompanied by the non-drug measures to avoid mosquito bites. Mefloquine is the agent of choice in pregnancy (as doxycycline is contraindicated), but its safety in the first trimester is still unclear.
- The role of mefloquine or doxycycline chemoprophylaxis outside of pregnancy in adults living in endemic areas is unclear. HIV-infected patients with CD4+ lymphocyte counts < 200 cells/µl are at highest risk of malaria. These patients should all receive co-trimoxazole, which has been shown to reduce the risk of malaria in several studies of HIV-infected groups in sub-Saharan Africa. However, resistance to sulfadoxine-pyrimethamine (Fansidar) has become widespread among *P. falciparum* in southern and eastern Africa. Co-trimoxazole has the same mechanism of action as Fansidar and it is therefore likely that it will have limited chemoprophylactic efficacy in most areas.

Treating malaria

Since HIV-infected individuals are at increased risk of severe or fatal malaria it is essential that the diagnosis is

made early. HIV-infected patients living in or travelling to malaria transmission areas should be encouraged to present to a health care facility where they can be tested immediately should they develop fever or flu-like symptoms. Falciparum malaria in the HIV-infected patient should be treated with the most effective antimalarial available, i.e. either quinine (combined with doxycyline or clindamycin) or artemesinin-based combination therapy (in South Africa artemether-lumefantrine (Coartem) is the only available product). Fansidar resistance is now so widespread in sub-Saharan Africa that this agent should no longer be used alone to treat malaria in patients at high risk of severe malaria – this includes all those with HIV infection. There are potentially significant interactions between ARVs and quinine and Coartem (see ARV guidelines).

NUTRITION

In all stages of HIV infection emphasis on nutrition is very important and should focus on recommending a normal, healthy eating pattern and a balanced diet. The objective is to maintain a healthy body weight by eating a wide variety of healthy foods and exercising regularly. Moderate exercise is recommended but intensive/vigorous exercise should be avoided as it may increase the metabolic rate and thus accelerate wasting.

Owing to the large number of people living in poor socio-economic conditions in southern Africa, health care practitioners treat many underweight individuals. Malnutrition itself compromises immunity, which in turn affects HIV-related immune deficiency.

The pathogenesis of malnutrition in HIV is multifactorial. Reduced food intake because of socio-economic factors, anxiety, depression and oral or oesophageal thrush, and diarrhoea (in the later stages of HIV infection), are associated with acute periods of weight loss because of malabsorption of nutrients and an increased metabolic rate due to opportunistic infections.

MEASURING NUTRITIONAL STATUS/BODY CELL MASS

Nutritional status, specifically the maintenance of protein stores (body cell mass) does impact on the ability to survive the ravages of HIV. Body weight fluctuates within 3% over time in stable healthy adults. Physical performance has been shown to decline after a weight loss of >10% of initial body mass, and weight loss of > 20% is associated with increased hospitalisation. At a level of 54% of normal body cell mass, death is likely to occur regardless of the presence or absence of OIs.

A depletion of the intracellular component of mass – the body cell mass – has been linked to shortened survival, increased risk of OIs and poorer quality of life, independent of the level of immune depletion (CD4+ cell count).

At each visit the nutrition status should be assessed and the following recorded:

- Body weight.
- Weight loss indicators (WHO):
  - < 10% unintentional weight loss (WHO clinical stage 2)
  - > 10% unintentional weight loss (WHO stage 3).
- In the absence of reliable previous weight, the body mass index (BMI) can be calculated by dividing the patient's weight (kg) by height squared (m^2). A BMI of ≤ 18.5 is associated with a high mortality risk. In the absence of a stadiometer, height can be measured by measuring the distance between the tip of one middle finger to mid-sternum and multiplying this by two.
- Additional screening criteria:
  - changes in dietary intake
  - assessment of clinical status (wasting)
  - medication regimen (drug-nutrient interactions) and
  - exercise habits.

HIV-RELATED WASTING SYNDROME

There are two types of HIV-related wasting syndrome:

- Starvation-related wasting resulting from food deprivation (voluntary/involuntary) in clinically stable patients who have not yet presented with OIs. The macronutrient status reflects the total body mass and the micronutrient status the body's cellular functioning. Micronutrient deficiency may exist without macronutrient deficiency, but macronutrient deficiency is almost always associated with micronutrient deficiency. These people respond well to nutritional support and feeding which usually reverses the starvation.
- Cachexia-related wasting is a disproportionate depletion of lean body mass (LBM) as a result of alterations in metabolism. In fighting disease, metabolic output is redirected to energy requirements and substrate needed to fuel the body's response instead of normal maintenance of the body mass. In the long term this leads to protein (especially skeletal muscle) loss. Feeding is not a sufficient intervention to reverse the effects of cachexia.

FOOD SECURITY

In the African setting, household food security and the ability to implement food safety measures should be considered as important determinants of the development of AIDS wasting syndrome.

Large and small food donations require appropriate storage facilities and an efficient distribution network.

Further studies on the impact of malnutrition and food supplementation are urgently needed.

DIETARY SUPPLEMENTS

There are no data to support the routine use of supplements in HIV-infected individuals with *no evidence of nutritional deficiencies*. Evidence does, however, suggest that micronutrient deficiencies are common in patients with HIV and are associated with disease progression.

Regarding vitamin supplementation in *poor, developing countries*:

- Use of the following vitamins and minerals has been demonstrated to help slow disease progression:
  - Vitamin B complex, C and E. A recent study by Fawzi *et al.*[3] conducted on 1 078 pregnant women in Dar es Salaam, Tanzania, compared the following regimens: vitamin A alone; a multivitamin (vitamin B complex, C and E) alone, vitamin A plus the multivitamin; and placebo. The results showed that multivitamins (vitamin B complex, C and E) helped to slow down disease progression, but that the addition of vitamin A actually reduced the benefit at the end point.[3] Vitamin B complex had been shown to be useful in earlier studies.[4-6]
  - Selenium. Little work has been conducted on selenium apart from Willumsen's work in 2003[7] and more work is required to confirm that selenium may reduce the incidence of OIs, improve immune function and slow disease progression.
- Benefit demonstrated in identified deficiency:
  - Vitamin A[8] (**Note:** not more than 20 000 IU/4 000 µg RE – increased disease progression).
  - Zinc[9] (**Note:** > 20 mg/d = increased disease progression; ≥ 14 mg/d = decreased survival.)
- Vitamins and minerals not recommended in HIV-infection – associated with possible worsening of the condition:
  - Vitamin A[10]
  - Iron: no published reports of iron supplementation studies.

Where possible all patients should be on multivitamins that include the nutrients in dosages indicated in Table I. A supplement which provides 100% to 150% of the recommended dietary allowances (RDAs) of current dietary reference intakes (DRIs) is advisable since it is most unlikely

TABLE I. DIETARY SUPPLEMENTS

Nutrient	RDA (range for female and male)	Maximum dose for supplementation in HIV/AIDS	Toxic on higher dose (upper limit (UL) — do not exceed)
Vitamin E (mg TE)	15	25 α-TE*	1 000 TE
Selenium (µg)	55	100	400
Folate (µg)	400	400 - 800	1 000
Niacin B_3 (mg)	14 -16	25	35
Thiamin B_1 (mg)	1.1 - 1.2	5.5 - 6.0	None
Riboflavin B_2 (mg)	1.1 - 1.3	5.5 - 6.8	None
Vitamin B_6 (mg)	1.3	6.8	100
Vitamin B_{12} (mg)	2.4	5 - 10	None
Vitamin C (mg)	75 - 90	250	2 000
β-carotene (mg)	No RDA	15 mg	
Magnesium (mg)	280	200	350
Chromium (mg)	25 - 35 µg	25 µg	
A-lipoic acid	No RDA	10 - 15 mg	100 mg
Glutathion	10 mg	50 mg	None

α-TE = α-tocopherol equivalents or mg of RRR-α-tocopherol; DRI = Dietary Reference Intakes, which has four categories: EAR (estimated average requirements – needed to set RDA), RDA (recommended dietary allowances), AI (adequate intakes), UL (tolerable upper limits).

Notes:

- Patients receiving rifampicin treatment may require additional vitamin D supplementation.
- Patients receiving isoniazid therapy should receive 10 - 15 mg pyridoxine (vitamin B_6) to prevent peripheral neuropathy. Pyridoxine has monoamine oxidase inhibitor (MAOI)-like activity. Avoid high tyramine or histamine foods:[8]
  - **Foods that must be avoided (high content of tyramine, dopamine, histamine, phenylethylamine):** aged cheese (e.g. cheddar, blue); aged meat (e.g. dry sausage, salami, biltong); soy sauce; fermented soy beans, soybean paste; tofu; sauerkraut; tap beer; concentrated yeast extract (Marmite); banana peel; all casseroles made with aged cheese.
  - **Foods that may be used with caution:** red or white wine 60 - 120 ml per day; coffee, cola; pizza (homemade or gourmet pizza may have higher content); bottled beer, 2 X 350 ml bottles maximum; alcohol-free beer, 2 X 350 ml bottles maximum.
  - **Foods not limited (based on current analyses):** unfermented cheese (cream, cottage, processed); smoked white fish, salmon, anchovies, pickled herring; fresh meat, poultry or fish; canned figs, raisins; fresh pineapple; beetroot, cucumber; sweetcorn, mushrooms; salad dressings, tomato sauce; Worcestershire sauce; baked raised products, plain cookies; boiled egg, yoghurt, ice cream; avocado, figs, banana, raspberries; Brewer's yeast (vitamin supplements); curry powder; peanuts, chocolate.

  All packaged processed meats, e.g. hot dogs, bologna, liverwurst, should be stored in refrigerator immediately and eaten as soon as possible. Histamine content is highest in improperly stored or spoiled fish, e.g. tuna.

that a person with HIV/AIDS will be able to meet the requirements for vitamins and minerals with diet alone owing to poor appetite and/or possible financial constraints.

FOOD CHOICE ADVICE

In HIV-infected people, the emphasis is on ensuring adequate energy and protein intake to maintain body weight and, more specifically, lean body tissue. This advice should commence early in the infection and include (where the patient can afford it):

- Food variety.
- Plenty of fruit and vegetables.
- Starch as the basis of all meals.
- Daily portions of meat and dairy products.
- Sugars, fats and oils should be included in the diet, especially following periods of weight loss.
- Regular intake of dried beas, peas, lentils, peanuts or soya.
- Salt should be used sparingly (as in South Africa there is a high prevalence of hypertension and stroke).
- Alcohol should be avoided.
- During times of loss of appetite and/or nausea, small frequent meals should be advised. The patient should avoid lying down after a meal, and should eat foods at room temperature.
- When symptoms of sore mouth or throat appear, soft foods moistened with margarine or gravy can be advised and sticky, spicy and acidic foods should be avoided, e.g. peanut butter, dry rough foods, citrus fruits.
- When diarrhoea or vomiting is present advise isotonic fluids (see box), diluted fruit drinks, and avoidance of caffeine products (coffee, cola drinks), dairy products (although fermented dairy, e.g. maas, may be tolerated) and high-fat foods. Encourage high soluble fibre foods, e.g. bananas, oats porridge.
- Intake of lots of clean, safe water.
- As much physical activity as possible.

Oral rehydration solution (ORS)

- 1 litre clean, safe water
- add 8 level teaspoons sugar
- add half teaspoon salt
- mix well
- store in clean and covered container
- keep in cool place
- make fresh solution every day

This suffices if nothing else is available, but contains no potassium. ORS with potassium is on the primary care EDL.

Fig. 1. The food pyramid.

THE FOOD PYRAMID

The food pyramid (Fig. 1) illustrates the above dietary guidelines.[11]

- Choose at least 1 portion (or more) from the last 3 levels of the pyramid for each meal as indicated in example meal plans (see below).
- Eat at least 6 meals (where possible) – 3 main meals and 3 snacks in between meals.
- Use fats, sweets and alcohol sparingly (top level).

EXAMPLE MEAL PLANS

Choose foods from the different levels of the pyramid within the financial constraints of the given individual, including culturally accepted foods.

Morning meal

- Porridge (1 cup)/2 slices wholewheat bread with sugar/jam (2 t)
- Milk (1 cup)/cheese (30 g)/1 egg/cooked beans (1/2 c)/ meat or fish (30 g cooked)
- Fruit/vegetable – raw/cooked/juice (1 portion)

Mid-morning snack

- Cottage cheese (2 tbsp) + 1 slice wholewheat bread *or*
- Cheddar cheese (30 g) + 3 crackers *or*
- Yoghurt, low fat, fruited (175 ml)

Lunch/light meal

- Porridge/rice/samp (1 - 2 cups)/2 - 3 slices wholewheat bread with sugar/jam (2 - 3 t)
- Milk (1 cup)/cheese (60 g)/eggs (1 - 2)/1/2 c cooked beans/30 - 60 g cooked meat or fish
- Fruit/vegetable – raw/cooked/juice (1 portion)

Mid-afternoon snack

- Cottage/gouda cheese (125 ml) + 1/2 banana *or*
- Pudding (175 ml) *or*
- Bean/egg filling + 1 slice wholewheat bread

Dinner/main meal

- Meat/fish/poultry/cooked dry beans or lentil dish (one 60 - 90 g portion cooked)
- Samp/rice/porridge/potato/sweet potato (1 - 2 cups)
- Vegetables (cooked and/or raw) (1 - 2 cups) *and/or*
- Fruit 1 - 2 portions

Late evening meal

- 1 slice wholewheat bread + filling *or*
- Fruit yoghurt (175 ml) *or*
- Fruit raw/cooked/juice + milk/maas

NUTRITIONAL BENEFITS OF HERBS AND OTHER UNCONVENTIONAL TREATMENT STRATEGIES

More information on unconventional treatment strategies is available on **www.sun.ac.za/nicus**.

- **Garlic.** No human studies to date have consistently and conclusively documented that garlic can improve immunity or the immune response. Various deleterious side-effects are associated with the use of garlic supplements.
- **Virgin olive oil.** Although the substitution of saturated fat or polyunsaturated fat with extra-virgin olive oil may have health benefits for people living with HIV/AIDS, there is no convincing or consistent scientific evidence that virgin olive oil boosts immunity or alters the course of HIV/AIDS, adversely or beneficially. For financially insecure patients the purchase of a relatively expensive product such as virgin olive oil may limit the purchase of other affordable wholesome foods.
- **African potato (Hypoxis hemerocallidea corm).** HIV/AIDS patients should avoid any supplements containing African potato or the hypoxis plant. It is a rich source of phytosterols, but *it has been found to be a toxic agent causing bone marrow toxicity and worsening immune suppression in HIV-infection* as well as in feline immunodeficiency virus infection. This agent should therefore be avoided.
- **Onion.** Onions are a food source of phytochemicals such as flavonoids and organosulphur compounds. In terms of safety the ingestion of large quantities of onions is known to cause gastrointestinal discomfort and distension and they should be used with caution by individuals with chronic diarrhoea and gastrointestinal discomfort.
- **Spirulina.** This extract of blue-green algae has some immunomodulatory activity:
  - inhibits mast cell-mediated allergic reactions
  - increases the activity of macrophages
  - increases phagocytosis
  - increases the concentration of interleukin-1 (IL1).

  Blue green algae extracts can be contaminated with toxic species (*Microcystis aeruginosa*) that are hepatotoxic. Heavy metal contamination has also been reported. A protein (cyanovirin-N) with anti-HIV properties has been isolated from another species (*Nostoc ellipsosporum*) by the National Cancer Institute, USA. Research is needed to confirm efficacy in humans.
- **Sutherlandia frutescens.** This traditional herbal remedy is widely used in South Africa. Animal studies conducted by the Medical Research Council failed to show any significant toxicity. No published studies exist on human toxicity *or* use for any indication.
- **Immune modulators (e.g. phytosterols)**

  A mixture of the plant sterols (phytosterols) beta-sitosterol and its glycoside, Moducare, is widely promoted as an 'immune booster' in HIV infection. Studies conducted by researchers at the University of Stellenbosch have shown several effects on immunity *in vitro*:
  - lymphocyte proliferation in response to mitogenic stimulation is enhanced
  - increased lytic ability of natural killer cells
  - increased Th1 immune response and unchanged or inhibited Th2 response
  - inhibition of the pro-inflammatory cytokines, Interleukin 6 and TNF-α.

  Effects are therefore both stimulatory and inhibitory. It is more accurate to call it an immune modulator rather than an immune booster. The net effects in HIV-infected individuals are difficult to predict. The stimulatory effects (e.g. on lymphocyte proliferation) could be harmful, leading to increased HIV replication.

  A small unpublished feline study has shown that CD4+ cell counts remain higher during treatment. An uncontrolled unpublished human study claimed reduced viral load but provides no specific figures. Researchers stated that Moducare has no antiviral effects and ascribed the reduction in viral load to reduced immune activation.

  A small controlled human trial carried out in adults with tuberculosis showed no improvement in sputum conversion rates, but subjects gained weight. Elevated eosinophil counts were noted in the treatment arm, which could indicate hypersensitivity.

  There are therefore grounds for believing that the product might be beneficial *but* equally a concern that it could be harmful. Further randomised controlled trials need to be conducted.
- **Other alternative diet therapies and supplements.** These diets have not been subjected to formal clinical research and many of these diets may imply, or result in, some ill-advised food elimination and/or restriction. It is best to eat a varied diet, within the financial constraints of the given individual, and include culturally accepted energy- and protein-rich foods.

SUPPORT AND COUNSELLING

The importance of the role comprehensive counselling plays in the management of patients living with HIV/AIDS cannot be overemphasised. Such counselling has a demonstrably beneficial effect upon the subsequent quality of life of people living with the virus.[12] The aim of counselling is to provide each individual with sufficient information to manage his/her condition well and to access the support required to deal with all aspects relating to their infection: medical, social, psychological and emotional. In this context counselling may be termed a 'structured conversation aimed at facilitating a client's (patient's) quality of life in the face of adversity'.[13]

Counselling is performed by a suitably trained health care professional or counsellor. The latter may be someone from the client's own community.[14,15] Additional care may be given in a 'support group' where overall supervision remains in the hands of a trained and accountable member of the group. Counsellors too require access to support for the purpose of processing and debriefing sensitive information and feelings. Burnout and emotional fatigue are common problems among workers in the health field.[16-18]

SPECIFIC FORMS OF COUNSELLING

Voluntary counselling and testing (VCT) and pre-test counselling

VCT is a *voluntary* programme that provides *confidentiality* and *ease of access* to the HIV test and result. Pre-test counselling focuses on the value of knowing one's HIV status and the consequent lifestyle and social change that such knowledge will bring. The possibility of a positive test result is discussed together with the consequent need to inform (sexual) partner(s) and to disclose one's HIV status to significant others such as family members. How would I respond to such news? How will I inform my partner? How do I deal with stigma and rejection? The counsellor anticipates the patient's responses and aims to provide sufficient support to enable the patient to cope. A downside to testing positive is coping with societal restrictions and personal shame: exclusion from or 'loading' of insurance policies and home loans, retrenchment or harassment in the workplace, the curtailing of emigration and restrictions on international travel, the banning of blood and organ donation, rejection from family and friends. However 'forewarned is also forearmed'. Knowing one's HIV status is a 'first' step in preventing viral transmission and in ensuring good health in the future. Wise counsel will assist the patient to manage his/her personal affairs and make provision for the long-term care of dependants.

A return date for obtaining the result is set at the initial visit. The actual blood or saliva test may be done at or after the counselling has been completed. The test measures the presence of antibodies in the patient and is usually an HIV ELISA and/or Western blot test. Some centres are able to perform 'rapid' HIV-antibody tests: the patient can be given his/her result almost immediately. Pre-test counselling is regarded as a prerequisite to performing an HIV test. Persons doing the test without the patient's consent are liable to prosecution in South Africa. The patient must give his/her consent to the test.[19-21]

Post-test counselling

In this context the patient has had an HIV test but has not yet received the result. It presupposes that pre-test counselling has been performed. The counsellor assists the patient in understanding his/her test result. The patient must be *shown* his/her result. The test result will be either negative or positive. An 'indeterminate' result means that the test needs to be repeated. If it is persistent over subsequent follow-up, an alternative means of verifying infection is indicated. Where the result is negative, both truly negative and falsely negative results are possible. Test results that are falsely negative occur either soon after exposure, mostly within 6 weeks – the so-called 'window period' – or late in the course of HIV infection. In both situations the patient's level of anti-HIV antibodies is below the limit of detection by the laboratory. Repeat antibody testing where the suspicion of infection is very high or the use of an alternative means of detecting the virus – by measurement of the p24 antigen, or directly measuring the virus with a viral polymerase chain reaction (PCR) test (a 'qualitative' viral load) – and the practice of 'safe sex' until clarification of status are indicated. False-negative tests are rare *and seldom a cause of anxiety to either the patient or the counsellor.*

In 2000, an average of 24.5% of South African antenatal clinic attenders tested HIV-positive. Prevalence rates in the community as a whole are in excess of 11 - 17%.[22,23] This is sufficiently high to make false-positive HIV-antibody tests unusual. The patient who tests HIV-positive but who is uninfected is not difficult to differentiate from those who are truly infected and whose tests are truly positive. False-positive tests occasionally result from technical or laboratory errors. Where uncertainty exists the test must be repeated. Alternative tests, if required, will clarify the patient's status.

Where the patient tests positive, instill hope. Deal with immediate feelings, particularly where he/she has been poorly prepared. It is always good to have a close friend or family member with the patient or in the waiting room outside. In Africa, the involvement of the family and

sometimes community members is a cultural norm and may be requested by the patient. Review the 'hows' with the patient: how to notify partners and/or family, how to practise safe sex, and how to introduce the use of condoms into a relationship when these were previously taboo. Recall the ways in which the virus can be spread and indicate what to do when blood spills occur in the home. There is no need for social isolation. Young patients wishing to have a family will need advice regarding pregnancy.

Encourage the patient to plan for the future. Detail the support that is available to him/her. Access to ART has altered the previously bleak picture. Patients can expect to live for many years after starting ARV drugs. Even in resource-poor settings, patients show a response to ARV drugs that is similar to that in highly developed communities.[24,25]

Post-test counselling is always done in private and never 'over the telephone'. Do not leave test results on an answering machine or cell phone. Never give results to a 'friend' or a third party. Post-test counselling is generally not repeated unless the patient requests further assistance. The latter is most frequently given in the form of 'life-skills' counselling.

Life-skills, crisis intervention and family planning counselling

Growing the skills to meet the challenges of life is a long-term necessity we all face. Those who are HIV infected encounter these challenges when least prepared. They are young. Sexual relationships and the nuclear family are incomplete. Permanent employment and financial security are many years away. Peer pressure and a culture that is itself in transition, drive youth – like lemmings – into the web of an epidemic that offers little chance of escape.

Patients express shame, guilt, anger, betrayal, blaming, denial, depression, bargaining, loss. What do I do with myself? How do I deal with my feelings? How do I mend the relationships that have been broken? How do I change? Can I accept my situation and move on? Who am I? Time and listening skills are needed but seldom available in busy clinics and practices. Suicidal thoughts must be taken seriously, although suicide remains rare. Nevertheless suicide is more frequent in the HIV infected and particularly around the time of diagnosis.[26,27] The counsellor assists the patient in setting goals and encourages him/her to implement these. The virus must not be allowed to define who the patient is.[28]

Have sexual partners been notified? Do these partners need assistance and are they supportive of the patient? Is the patient employed and are there work-related problems: unlawful dismissal, HIV testing without consent or with coercion, undue absenteeism, inability to work and the need to procure pension benefits and/or disability grants? From time to time patients or their families will ask for legal assistance: with physical and other forms of abuse in the home, advice regarding separation or divorce, work-related issues, problems with the payout of funeral benefits or insurance cover. Obtaining bank loans and insurance remains difficult for many patients. Support groups are often very helpful in this long-term form of counselling. Patients learn from one another.

Family planning may need to be addressed. Infected parents want an HIV-negative baby. Ideally both partners should be counselled together and each encouraged to take personal responsibility for his/her own sexual health. Discussion on contraception must include barrier methods, particularly condom use, and the role of injectable and oral hormonal contraceptives. Condom use is recommended at all times, even where both partners are already HIV infected. Super-infection with 'new' HIV strains has been recorded in such circumstances.[29,30] Nonetheless those who plan to become pregnant need to be listened to sympathetically and assisted where possible.

Discordant couples (where one is HIV-negative and the other positive) may question why one remains uninfected. Such couples need clear scientific advice and must be encouraged to persist in condom use.

Life-skills and crisis counselling usually takes place in a situation where privacy and time are available to the counsellor and the patient. Where time and opportunity do not permit, the physician must refer to an appropriately skilled caregiver. Severe depression, suicidal talk, domestic violence, and psychotic and irrational behaviour, must be regarded seriously. Patients and their families must be assisted with obtaining the help they need.[31]

Management-related counselling

Patients often ask the difference between being HIV-positive and having the acquired immunodeficiency syndrome (AIDS). The various staging systems – WHO or Centers for Disease Control (CDC) – can be explained briefly in a non-technical manner.

THE ART OF COUNSELLING

- **Empathy.** Indicate concern, be non-judgemental and accepting. Where possible sit alongside the patient and not on the other side of the desk, and at the same height as the client. Avoid emotional and physical distance.
- **Trust.** Maintain confidentiality at all times, keep (brief) notes/records of the interview. Keep the interview private and attempt to prevent interruptions, e.g. cell-phone calls. Where feasible, ensure that the same

counsellor and patient/client meet during follow-up visits.

- **Listen.** Be an informed and an attentive listener. When information is needed, provide scientific knowledge in a manner that can be understood by the client. Provide information on the costs involved and the accessing of affordable medicines. Encourage long-term budgeting. Listen to the patient – attempt to hear what is being said behind the words.
- **Sensitivity.** Be client-centred. Attempt to understand the culture and belief system. Encourage family or partner involvement. Enquire about feelings: What need is being expressed? What emotion is being experienced? Provide a sense of hope and indicate the next step – what can be done. Deal with specific medical problems without delay. 'How are you coping?'
- **Right questions.** 'Why do you want to know your HIV status?' Encourage the patient to voice his/her concerns and questions. Avoid 'closed-ended' questions: e.g. 'Do you ..., Did you ..., Have you ....' Use instead 'open-ended' questions that allow for interaction between the client and yourself. Begin the discussion with 'Why ..., What ..., When ..., How ..., Describe ...'.

EDUCATION: PROVIDING PATIENTS WITH KNOWLEDGE

The counsellor needs to be able to address the following topics comprehensively and clearly:

- Scientific data about HIV and the effects of infection on the human system.
  - What is a virus? The natural history of the virus (HIV) and where it has come from.
  - How is HIV infection contracted? Through contact with blood, sexual contact and mother-to-child transmission. How can viral transmission be prevented?
  - How does the virus damage the human body/immune system? The viral life cycle within the human lymphocyte, i.e. within the immune system of the host.
  - Survival data as they relate to the patient. The control of the virus by the host immune system, medication, and lifestyle modification.
- Laboratory monitoring of the infection and the effects of medication.
  - The CD4 cell count: measuring the immune system. *Aim*: to build up the CD4 cell count and to maintain it within the normal range indefinitely. The normal CD4 cell count is between 500 and 2 000 cells/µl.
  - The viral load: measuring the virus itself. *Aim*: to ensure tight control of the virus to minimise the damage to the human body/immune system.
  - Other laboratory tests, e.g. full blood count (FBC).
  - Cost and frequency of tests. *Aim*: where possible, to ensure an affordable and reliable source of scientific information on the patient's progress.
- The medical management of the patient.
  - The diagnosis of HIV and AIDS. The taking of a medical history and the examination of the patient. Confirmatory blood (saliva) tests.
  - Follow-up visits and blood tests. Emphasise adherence with the follow-up schedule. Follow-up visits offer the opportunity to ensure that the viral infection is under control.
- The role of lifestyle and diet (nutrition) in maintaining health.
  - A healthy diet and lifestyle makes good sense and should be encouraged.
  - There is, however, little supportive evidence-based data for the use of special diets and nutritional supplements. These can prove very expensive to the consumer.
  - Where documented or anticipated deficiencies of vitamins or trace elements exist, these can be replaced.
  - It is possible that a mixture of vitamins B, C and E may be of benefit. (See section on nutrition.)

CONCLUSION

Adequate counselling requires time and commitment. This is often difficult in a busy or understaffed clinic or medical practice. Many successful HIV practices have delegated much of the counselling to trained nursing staff or willing and skilled community members. To view the HIV epidemic purely as a plague that requires the adoption of health precautions and drugs is to miss the point. The epidemic continues to grow each year despite scientifically appropriate messages. Lifestyles are not changing. For the latter to occur significant changes in relationships between people must occur. In an article on concurrent relationships as a reason for the high rate of HIV infections in Africa, the authors comment: 'as soon as one person in a network of concurrent relationships contracts HIV, everyone else in the network is placed at risk. By contrast, serial monogamy traps the virus within a single relationship for months or years.'[30]

We need a more caring society. The HIV epidemic offers that opportunity. Good counselling helps to open that door.

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Chairperson of the Pre-ART Guidelines Committee: Dr Des Martin.
Expert panel members: Professor Gary Maartens, Dr Dave Spencer, Dr Lynne Webber, Dr Leighton McDonald, Professor Andre Dannhauser, Professor Derick Veldman, Dr Francois Venter, Professor Robin Wood and Dr Steve Andrews.

These guidelines pertain to the Republic of South Africa.

LETTER • LETTER • LETTER • LETTER • LETTER

To the Editor: The article in this issue of the *Southern African Journal of HIV Medicine* by Anna Coutsoudis entitled 'Breast feeding and HIV: an update' (p. 45), illustrates that there is still a great deal of debate in South Africa around this topic.

Coutsoudis correctly points out in her article that the randomised controlled trial of breast versus formula feeding carried out in Kenya had limitations; in particular an intent-to-treat analysis was performed that would have underestimated transmission in the breast-feeding and over-estimated transmission in the formula-feeding populations. This given, why would it be unethical to repeat this trial with prevention of mother-to-child transmission (PMTCT) antiretroviral prophylaxis in the intrapartum period? There is ethical equipoise, since most women still breast-feed in South Africa and formula feeding is not without risk. This paper also cites a suggested 4% assumed risk of transmission for every 6 months of breast-feeding, and this high transmission rate must beg the question of the circumstances under which breastfeeding is justified and when it is feasible to avoid this risk.

There should be an analysis of risk benefit – what are child survival risks in South Africa if infants are not breast-fed, compared with survival in those infants who become infected with HIV?

Francois Dabis has reported from Cote d'Ivoire on the use of triple regimens such as AZT/3TC/NVP to reduce intrapartum as well as breast-milk transmission and other strategies such as the regimen used by Lallemant in Thailand which have shown a large reduction in transmission. Since South Africa and Thailand share similar infrastructure and socio-economic status, perhaps a similar regimen should be adopted here.

Coutsoudis also does not comment on the local PMTCT programmes and the fact that breast-milk substitutes are available. She does not comment on whether high rates of exclusive breast-feeding are feasible, and indeed whether high rates have been attained in a variety of communities in South Africa. Finally, the paper does not give formula feeding as a option in PMTCT strategies and yet does not clarify why not or the conditions under which it should be considered.

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COST OF INPATIENT CARE FOR HIV-POSITIVE PATIENTS AT RED CROSS CHILDREN'S HOSPITAL, CAPE TOWN

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There is anecdotal evidence that certain categories of patients at Red Cross War Memorial Children's Hospital (RCH) are thought to be utilising more resources than others. Faced with an ever-increasing demand for care, shrinking budgets and tough measures by government to force health managers to operate within budget, bold decisions need to be taken regarding future admission policy. The *aim* of this retrospective record-based study was to assess the cost of inpatient care for paediatric HIV-positive patients at RCH over a 1-year period (January - December 2001). The *objectives* were (*i*) to determine the cost of inpatient care for paediatric HIV-positive patients; and (*ii*) to provide baseline data for health managers to develop future admission policy and to plan for future needs in terms of management and budgetary protocols.

Methods. The study population consisted of HIV-positive inpatients admitted to RCH. Information on patients' demographic details, date and duration of admission, reason for admission, additional diagnosis, nutritional status, laboratory investigations done, surgical procedures performed and medication prescribed were obtained from the patient records. Direct costs were recorded for admissions (bed costs), X-rays, laboratory and surgical procedures. The tariff fees charged for these services were obtained in consultation with management at RCH.

Results. There were 16 032 admissions to RCH in 2001. Of these patients 616 (4%) were HIV+. A 25% random sample (N = 154) with a mean age of 1.75 years was analysed. Almost 80% were admitted with diarrhoea and vomiting and/or chest problems. The mean number of previous admissions was 2.0. The most common conditions diagnosed clinically were failure to thrive (64%), pneumonia (54%), gastroenteritis (43%), oral thrush (42%) and tuberculosis (22%). Over half were found to be underweight for their age, 20% were marasmic and 87% suffered some form of malnutrition at admission. HIV+ patients were 4.7 times more likely to die in hospital than HIV-ve patients. Their average length of stay in hospital was 9 days, compared with 4 days for HIV-ve patients. HIV+ patients consumed 12%, 61% and 9% of the total budgets allocated for antibiotics, antifungals and analgesics, respectively (7% of the total budget for medicines). The average cost (direct cost) for each HIV+ inpatient amounted to R18 765.76. Admission (bed) costs formed the bulk of this amount (84%) followed by laboratory costs (9%), medication (3%), surgical (2%) and X-rays (2%). Alarmingly, HIV+ patients, who formed 4% of the total admissions, consumed 26% (R11.56 million) of the total budget for direct treatment costs (R44.65 million).

Conclusion. The current admission policies regarding HIV+ patients to RCH appear unsustainable, given the continued high demand for care, an ever-increasing HIV pandemic, the non-availability of antiretroviral therapy, lower health budgets and the continued inability of these patients to pay for health services.

The prevalence of HIV infection in the Western Cape lags behind that of the rest of the country and sub-Saharan Africa.[1,2] However, the prevalence rate for women attending antenatal clinics in this province has almost doubled from 3.09% to 6.29% between 1996 and 1997,[3] indicating a significant increase in the rates of new infection of HIV. This trend has continued (8.6% – Provincial Administration of the Western Cape, annual antenatal survey results, 2001)[3] and has major cost implications for public hospitals that provide specialised care for paediatric HIV patients. One simply has to look beyond the debate of government's failure to provide antiretrovirals to reduce mother-to-child transmission of HIV and deal with the realities and cost implications of providing care for children with HIV. This

scenario must be seen in the context of a decision taken by the National Department of Health to cut the budget for highly specialised services by R50 million from 1 April 2002.[4] It is envisaged that these cuts in the budget will be more than quadrupled in the next 5 - 8 years. The implications for Red Cross War Memorial Children's Hospital (RCH) are tremendous – it now has to provide specialised quality care for growing numbers of paediatric HIV-positive patients in an environment where financial resources are constantly being reduced by government so that other priority areas can also receive funding.

The specialised care offered to paediatric HIV-positive patients at RCH needs to be costed to provide administrators of the hospital with detailed information as to how much of the current budget is used up in providing care for these patients. Future planning in terms of patient admission protocols, laboratory services, length of stay in hospital, medicine costs, surgical procedures, home-based care initiatives and priorities for non-HIV patients will be directly affected by this costing exercise and ultimately administrators will have to make bold decisions on the best way to spend scarce resources in providing quality care for children admitted to RCH.

LITERATURE REVIEW

Most health economists and HIV/AIDS experts support the view that antiretroviral (ARV) drugs are a cost-effective alternative when compared with the costs of providing care for infected infants who are born HIV positive.[5] Havens *et al.*[6] investigated the lifetime cost of care for children with HIV infection. Based on a median survival time of 120 months, the mean lifetime charges for hospital-based care for children with HIV infection was approximately U$408 307. Their data suggested an extremely beneficial economic impact of the implementation of CDC recommendations for universal counselling and voluntary testing of pregnant women, coupled with AZT treatment of pregnant women with HIV infection and their newborn infants to reduce perinatal mother-to-child transmission (MTCT). In a similar study in the Cape Town Metropole, Roux *et al.*[7] investigated the burden and cost of inpatient care for HIV-positive paediatric patients. They found that 106 (8.3%) HIV patients occupied these beds at the time of the survey. Furthermore, 25% of the HIV-infected children received oxygen, 46% received intravenous foods or drugs, 81% had some form of malnutrition and 46% were underweight for their respective ages. Tuberculosis (TB) was diagnosed in 20% of the HIV-positive children. This was a higher prevalence than previously found in hospitalised children in this region and was thought to be related to the effect of immunodeficiency on susceptibility to TB.

Based on a daily bed cost of R280 per day, the annualised cost of paediatric beds for a constant number of 57 HIV-positive inpatients was found to be R5 825 400. The estimated lifetime hospitalisation cost for an infant diagnosed at 13 months (the median age for acute admissions in this study), surviving for 32 months from the time of diagnosis and requiring 2.4 admissions per annum for a mean of 11 days per admission, would cost R19 712 per infant (based on a paediatric bed cost of R280 per day). In comparison, the cost of the MTCT Prevention Programme in Khayelitsha, Cape Town, was calculated at between R624 520 and R810 520 per annum, based on a rate of 5 000 births each year. The cost included serological screening for infection, treatment for an expected 10% of infected women according to the Thai regimen,[8] *Pneumocystis carinii* pneumonia (PCP) prophylaxis, follow-up serotesting at 15 months of age and formula milk feeds up to age 6 months for infants at risk. On the basis of a vertical transmission rate of 30% and an effective 50% protection rate, the cost per infant protected from infection lies between R8 326 and R10 806, which is much more cost effective than the R19 712 per infant required for care of paediatric inpatients in a specialised hospital.

Hussey *et al.*[9] examined the survival patterns of 193 children in Cape Town known to be vertically infected with HIV. The median survival of children with HIV was 32 months from time of diagnosis (median age at diagnosis was 5 months) and survival time was influenced by age and disease severity. For children over the age of 12 months, the cumulative proportion surviving 48 months was 78%. This compares poorly with survival rates in developed countries such as the USA (where an HIV-infected infant has 75% chance of surviving in excess of 5 years) and Italy (70% of perinatally infected children were alive at 6 years and 50% at 9 years). The difference in survival times can be attributed to availability and access to medical care, access to ARV therapy and other supportive care often lacking in developing countries.

A recent count at the RCH[10] revealed that toddlers with AIDS occupied 25% of the general paediatric beds. The authors questioned the logic of spending 25% of the hospital's scarce resources on treating an inevitably fatal affliction, i.e. denying access to these patients to alleviate the chronic shortage of hospital beds for children with other diseases.

The European Collaborative study[11] that reported on the hospitalisation of children born to HIV-infected women in Europe found that uninfected children had 0.5 admissions per 5 child years compared with 2.4 for infected children. It was found that infected children were 4 times more likely to be hospitalised than uninfected children of the same age. Nearly 60% of the total inpatient days of HIV-infected children occurred after AIDS diagnosis. This places a heavy

burden on the health care system and has implications for planning and admission protocols in resource-poor countries. Medscheme, the country's largest private medical scheme administrator, undertook a number of studies[12] in which they demonstrated that the hospital treatment arising from complications of AIDS-defining illnesses was more expensive than providing double or triple ARV therapy for the rest of the patient's life. Medscheme calculated that it cost R60 000 per annum (average first 2 years) to manage a patient with HIV/AIDS on double ARV therapy, R70 000 per annum for triple therapy, and R230 000 per annum on patients who were unmanaged (not receiving ARV therapy).

Studies done elsewhere in Africa[13-15] report that drug costs and consumption among paediatric HIV patients will continue to increase, resulting in shortages of essential medicines because of financial constraints, and that the impact of AIDS in the sub-Saharan region will result in less treatment available to all patients – those with AIDS and those without AIDS. The clinical spectrum of HIV disease in children is similar in most African studies where ARVs are not available to infected patients. These include respiratory infection, malnutrition, anaemia, diarrhoea, malaria, meningitis, pneumonia and TB.[16-18]

In summary, the literature shows clear evidence of an increasing burden of costs placed on institutions and governments in developing countries where paediatric inpatient care occurs in the continued absence of ARV therapy.[19] There is much evidence that MTCT programmes reduce infection rates and the provision of ARV therapy is more cost effective than treating unmanaged patients symptomatically for the wide spectrum of disease associated with paediatric HIV/AIDS. Alternatives such as home-based care for HIV/AIDS patients have been shown to reduce the medical utilisation costs of HIV/AIDS cost by between 28% and 50%, depending on which stage of the disease the patient is at.[20] These are difficult times for health planners in developing countries, and difficult decisions will have to be made regarding future inpatient admission protocols and management protocols for paediatric HIV-positive patients admitted to financially strapped tertiary hospitals for care.

AIM

To assess the cost of inpatient care for paediatric HIV-positive patients at RCH.

OBJECTIVES

- To determine the cost of inpatient care for paediatric HIV-positive patients over a 1-year period at RCH.
- To provide baseline data for health planners to develop/modify admission and management protocols for patients with paediatric HIV.
- To provide baseline data for health planners at RCH to plan for future needs in terms of budget allocation for the management of paediatric HIV-positive patients.

METHODOLOGY

The study population included all paediatric HIV-positive children admitted to RCH for inpatient care between January and December 2001. HIV positivity was confirmed by means of a laboratory test. Patients who had clinical signs and symptoms strongly associated with HIV/AIDS infection but whose serological status was unknown were excluded from the study. Similarly, patients who tested negative for HIV, were awaiting retest or had not been tested because consent had been refused, were not included in the study population. Another inclusion criterion was that admission as an inpatient must have occurred within the specified study period of January - December 2001 (Table I). A retrospective 25% random

TABLE I. TARIFF FEES AND OTHER DATA USED IN THIS STUDY

Item	Source	Additional notes
Amounts for budgets	RCH Budget for 2001/2002	Supplied by financial director for RCH
HIV+ statistics	RCH Laboratory	
Patient admission statistics	Administration office	
Medicine costs	Hospital pharmacy	Tender price list for 2001. These amounts are much lower than RAMS tariffs
X-ray costs	RAMS schedule of fees 2001	These tariffs were used after consultation with department head
Admission costs	High care/general ward R1 685.30 per day ICU R2 631.00 per day	RAMS fees for 2001
Surgical costs	RAMS schedule of fees	Same as above
Laboratory costs	BHF tariff fees for 2001	Same as above

sample of all paediatric HIV-positive inpatients was chosen for inclusion into the study.

Information describing the patient's demographic details, date and duration of admission, reason for admission, additional diagnosis, nutritional status, laboratory investigations done, surgical procedures performed and medication prescribed were obtained from patient records.

Only the direct costs attributable to patient care were recorded. The costs for occupation of a paediatric bed (admission costs – high care and intensive care), laboratory investigations, medication obtained at the hospital pharmacy, X-ray costs and costs for surgical procedures were recorded as direct costs for each patient. Tariff fees charged for these services were obtained after broad consultation with the medical superintendent, director of finances for RCH, senior nursing staff, department managers, and hospital administrators in charge of patient billings. Table I provides more detail as to how figures used in this costing exercise were obtained. Ethical approval for this survey was obtained from the Ethics Committee of RCH and Stellenbosch University.

Indirect costs such as personnel costs, physicians' fees, etc. were excluded from this cost analysis because of the inherent difficulties of estimating such costs. Data analysis was done using Microsoft Excel Data Analysis and Data Analysis Plus software packages and results are presented in the form of graphs, tables and free text. Statistical analyses (*p*-values, *t*-tests, confidence intervals, means, etc.) are fully described where applicable. The limitation of this study was that direct costs attributable to patient care was dependent on the quality and accuracy of information recorded in the patient files selected for analysis in this study.

RESULTS

Table II provides a summary of the demographics of the study population for this retrospective costing analysis.

Almost 80% of the patients (Fig. 1) were admitted to RCH with either diarrhoea and vomiting (42%) or cough, fever and/or chest problems (37%) as the main complaint. Fig. 2 shows that the majority of the patients (62.3%) had no previous admissions to RCH, but over 25% of HIV+ patients who had previous admissions were admitted two or more times as inpatients. About 5% of HIV+ patients had previously been admitted to RCH 5 or more times for in-hospital care.

On examination at RCH, 64% of the cohort were found to be below key developmental milestones for their age (failure to thrive (FTT)) while over half (54%) of the HIV+ patients were diagnosed as having pneumonia (Fig. 3).

TABLE II. PATIENT STATISTICS FOR RCH, 2001

Medical admissions	8 614
Surgical admissions	7 418
Total inpatient admissions	16 032
No. of confirmed HIV+ inpatients	616
25% random sample for analysis	*N* = 154
Percentage of HIV+ inpatients against total admissions	4%
Race	Black =141 (91.6%) Coloured = 13 (8.4%)
Gender	Male = 83 (53.2%) Female = 72 (46.8%)
Mean (average) age	21 months (1.75 years)
Median age	14 months (1.2 years)

Other common conditions that were also diagnosed among this cohort of patients included gastroenteritis (43%), oral thrush (42%), nappy rash (32%), TB (22%), and anaemia (12%).

Fig. 4 shows the nutritional status of HIV+ patients at the time of admission to RCH. A large proportion were reported to suffer from some form of malnutrition (87%) at the time of admission. Over half of the study sample (53%) were

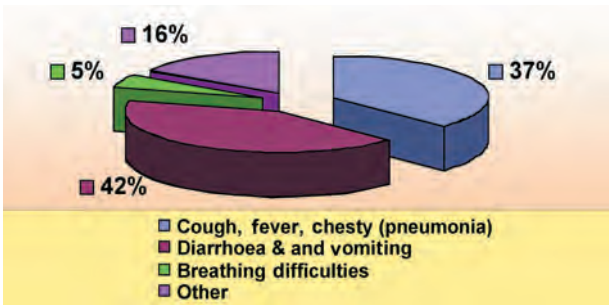

Fig. 1. Reason for admission to RCH (HIV+ paediatric patients).

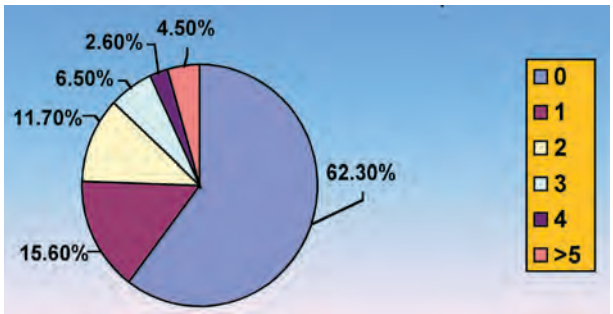

Fig. 2. Number of previous admissions to RCH.

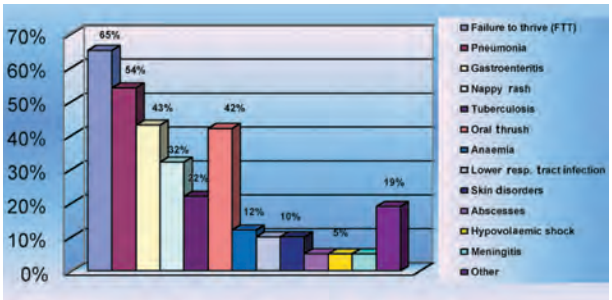

Fig. 3. Clinical diagnosis for HIV+ paediatric inpatients at RCH.

found to be underweight for their age at admission and almost 20% were found to be marasmic. In terms of in-hospital deaths, 8% of the HIV+ patients died during their stay at RCH. Although this figure seems low, it becomes significant when compared with the overall death rate at RCH for the similar period (8% v. 1.7%) – this means that HIV+ patients were 4.7 times more likely to die in hospital than their HIV-ve counterparts.

Table III provides information on the average length of stay in hospital for HIV+ patients versus all admissions to RCH. It was found that HIV+ patients stayed in hospital more than twice as long as the HIV-ve patients (9 v. 4.03 days).

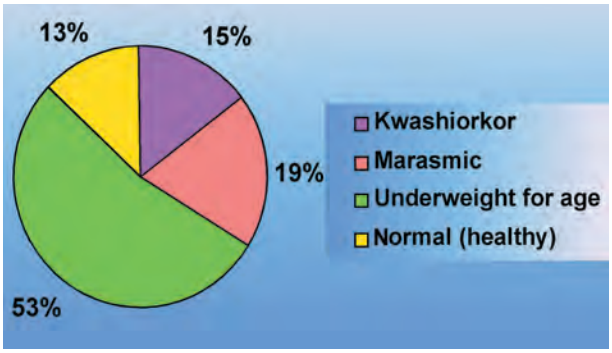

Fig. 4. Nutritional status at admission of HIV-positive patients.

TABLE III. AVERAGE LENGTH OF STAY IN HOSPITAL (DAYS) FOR HIV+ PATIENTS VERSUS ALL ADMISSIONS TO RCH

Average duration of stay in ICU	3.89
Average duration of stay (high care + ICU = total stay)	9
Average duration of stay for ALL patients	4.03

MEDICATION COSTS FOR HIV+ INPATIENTS

Table IV provides a summary of the medication costs of HIV+ inpatients at RCH. Medicines were essentially used to treat infections in these immunocompromised individuals and for prophylactic cover against further infection. Table V gives a breakdown on the average cost per patient of each of the groups of drugs costed, the budget available for that group of drugs and the percentage of budget consumed per group of drug by HIV+ patients admitted to RCH.

Fig. 5 is a graphic representation of Table IV.

Since HIV+ patients are prone to opportunistic infections, it was expected that the use of antifungal drugs among these patients would be high. However, it must be noted that these patients, who comprised only 4% of the total number of patients admitted to RCH in 2001, consumed 61% of the budget allocated for the purchase of antifungal medication. Similarly, they consumed 12%, 9% and 3% of the budgets allocated for antibiotics, analgesics and other

TABLE IV. MEDICATION COSTS FOR HIV+ INPATIENTS

Antibiotic costs	
Mean	R265.96
Total antibiotic cost for HIV 265.96 x 616	R163 831.36
Budgeted total for antibiotics (A/B)	R1 352 645
Percentage of A/B budget consumed by HIV+ patients	12%
Anti-fungal costs	
Mean cost per patient	R136.72
Total 136.72 x 616	R84 219.52
Budgeted amount for antifungals	R138 750
Percentage of budget consumed by HIV+ inpatients	61%
Analgesic costs	
Mean cost per patient	R20.63
Total spent on analgesics	R12 708.08
Budgeted expenditure	R140 787
Percentage of budget consumed by HIV+ patients	9%
Other	
Mean	R252.59
Total spent	R155 595.44
Budget (approx.)	R5 000 000
Percentage	3%
Total medication	
Mean	R591.83
Total medication	R364 567.28
Budget	7%

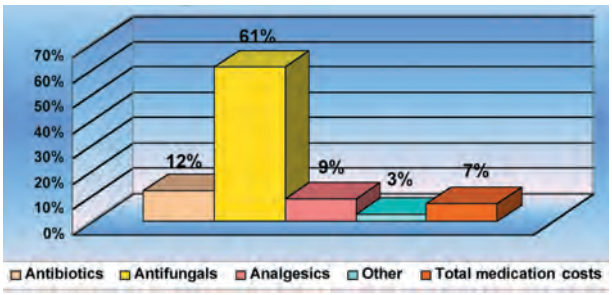

Fig. 5. Medication costs for HIV+ inpatients versus budget for medicines, 2001/2002.

medication, respectively. The total amount spent on providing medication for these patients was R364 567.28, which represented 7% of the total budget for medication in the financial year 2001/2002.

ADMISSION COSTS FOR HIV+ INPATIENTS

Table V summarises the details of the admission costs for HIV+ inpatients at RCH. The combined duration of stay (ICU + high care) was more than twice as long as that for all the other inpatients at RCH (9 days v. 4.03 days). The amount of time spent in the high-care wards differed tremendously among HIV+ patients, hence the range of 107 days for time spent in high care versus a relatively low range of 11 days for time spent in the ICU. Total admission costs amounted to approximately R9.64 million, which formed 84% of the total direct costs for HIV+ inpatients.

Approximately 12% of HIV+ patients admitted to RCH spend time in the ICU. Fig. 6 shows that 61% of these patients spend less than 1/3 of the total admission time in

TABLE V. DURATION AND COST OF STAY IN HOSPITAL (HIV+ PAEDIATRIC PATIENTS)	
Average No. of days spent in high-care wards	8.58
Median	4
Mode	2
Min.	1
Max.	108
Range	107
Average admission cost per patient in high care	R14 456.37
Average No. of days spent in ICU	3.89
Median	3
Mode	3
Min.	1
Max.	12
Range	11
Average admission cost per patient in ICU	R10 231.67
Percentage of patients admitted to ICU	11.70%
Total admission costs per HIV+ patient	R9 641 804.48
Average admission cost (high care + ICU) per HIV+ patient	R15 652.28

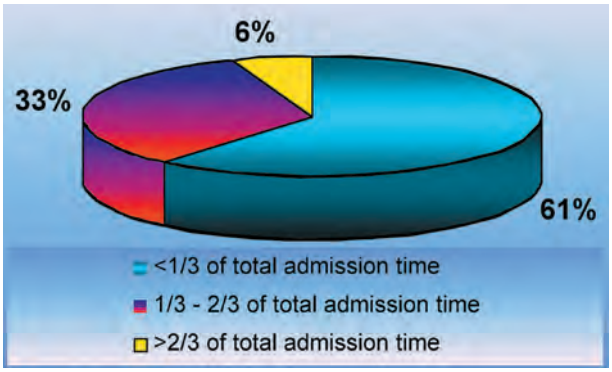

Fig. 6. Duration of stay in ICU versus total admission time.

the ICU and a relatively high percentage (33%) spend between 1/3 and 2/3 of their total admission time in the ICU. Six per cent of HIV+ patients spend more than 2/3 of their total stay at RCH in the ICU.

AVERAGE AND TOTAL DIRECT COSTS FOR HIV+ INPATIENTS

Fig. 7 provides information on the direct costs of treatment for HIV+ inpatients at RCH. The average admission cost per patient was R15 652.20, which formed 84% of the total direct costs for HIV+ inpatients at RCH. Laboratory services accounted for 9% (R1 677.42 per HIV+ patient) of the total direct costs, medication costs for 3% (R596.76 per patient), and surgical costs (R2 954.11 per patient) and X-rays (R470.00 per patient) together for the remaining 4%.

To obtain the total direct cost for all HIV+ patients admitted to RCH during 2001, the average cost per component, as shown in Fig. 5, was multiplied by 616 (N = 616). This cost is reflected in Fig. 8 below as R11.56

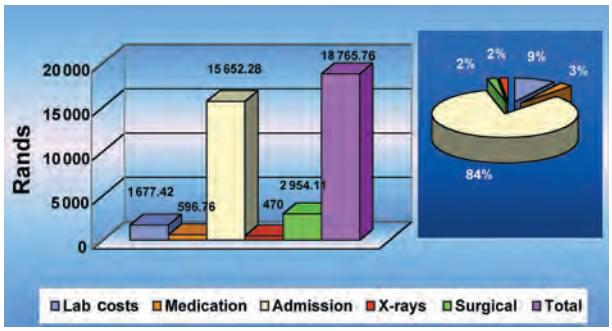

Fig. 7. Average cost per HIV+ inpatient (R).

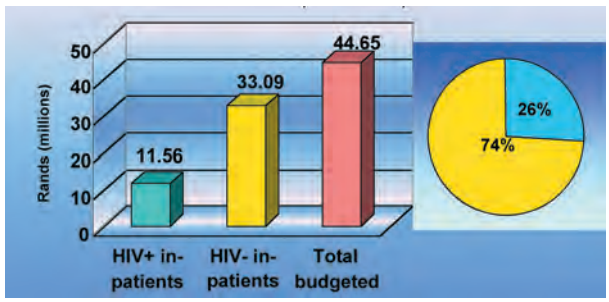

Fig. 8. Direct treatment costs for inpatients at RCH (R) (2001/2002).

million rands. The total direct cost for treating all patients at RCH (R44.5 million rands) was obtained as follows:

Budgeted item 2001/2002	Cost as per budgeted
Total budget	R152 840 000.00
Personnel expenditure	-106 318 000.00
Administration expenses	-1 291 000.00
Professional and special expenses	-5 080 000.00
Revenue	+4 500 000.00
Total direct costs	R44 651 000.00

The direct cost for HIV- patients (R33.09 million) was calculated by subtracting the total direct cost for all patients from the total direct costs for HIV+ patients (R44.65 million - R11.56 million).

Alarmingly, HIV+ patients, who formed only 4% of total admissions at RCH in 2001, consumed 26% of the total budget for direct costs for patient treatment.

DISCUSSION

The proportion of HIV+ inpatients against total patient intake for 2001 was relatively low at 4%. This low percentage is similar to prevalence figures reported by Madhi *et al.*[17] who found that 5% of children born in Soweto were HIV+. However, the 4% prevalence rate differs significantly from the findings of Leary,[21] who reported that 25% of general paediatric beds at RCH were

occupied by infants and toddlers with AIDS. This figure of 25% is misleading as it reflects the percentage for HIV+ patients in the general ward for one day only (15 of the 56 patients in the general ward). The findings of our study, which reports on prevalence of HIV+ admissions for a full year (4%), are also lower than those reported by Roux *et al.*[7] who found that 8.3% of the total beds available in the Cape Metropole Region in the second week of March 1999 were occupied by HIV+ paediatric patients (106 of the 1 264 beds). Again, the time period of this study (1 week) makes the use of this value unreliable when compared with the 4% prevalence reported in this study. Also, Roux *et al.*[7] considered patients HIV+ if they had a positive laboratory test or had suspected physical signs of HIV infection but their serological status was unknown. Our selection criteria for this study were more rigid, which could probably explain the difference in the findings between Roux *et al.* and our study. Chintu *et al.*[16] and Vetter *et al.*[18] reported prevalence rates of 28% (Lusaka, Zambia, 1991) and 8.2% (Abidjan, Ivory Coast, 1992), respectively.

Almost 80% of patients (Fig. I) were admitted to RCH with a history of diarrhoea and vomiting (42%) and pneumonia (37%). These findings are similar to those reported in other studies.[7,16,22] More than 60% (Fig. 2) of the patients admitted during 2001 were first-time admissions to the hospital. This figure is significantly higher than the 35% reported by Roux *et al.*[7] About 25% of the cohort had been admitted two or more times previously, indicating the tremendous burden that HIV+ patients can place on limited bed space at RCH, which has approximately 262 beds available for all patients. Roux *et al.*[7] also reported a mean of 2.4 v. 2.0 (our study) admissions for those who had previous admissions to hospital – however, at the time of the study patients did not have access to ARV drugs that are routinely available in most of the developed world.

The average length of stay for HIV+ patients was 9 days per patient, which is more than double the average for HIV- patients (4.03). This translates to 12% of the total bed days available at RCH (262 beds x 12 months x 30 days = 94 320 000 theoretically available – assuming that these beds are available all year round). In reality this figure of 12% will be higher as all hospitals in the Western Cape are forced to reduce the number of beds available to reduce costs and stay within their allocated budgets. Nelson *et al.*[13] reported a mean length of stay for their patient cohort of 7.9 days.

Fig. 4 provides the details on most common conditions that afflict HIV+ patients and cause them to be admitted to hospital. The percentages may vary among different studies, but most authors[7,13,16,18] report similar diagnoses in settings where ARV therapy is not available. Chan *et al.*[23] reported that 25% of their HIV+ cohort were diagnosed with TB. These findings are similar (Roux *et al.*[7] 21%, our study 22%) to studies done locally, even though Chan's cohort of patients were in a setting (Children's Medical Center, Brooklyn, New York) where ARVs were available as standard care. A key reason for the susceptibility of these children to opportunistic infections is malnutrition, which affected 87% of the patients in this study (Fig. 5). The effects of living in abject poverty, often in households with no proper sanitation or clean water, and in rural settings where access to care is limited by the ability to pay for transport, plays an important role in further complicating the ability of these patients to ward off infections. The story that is not told in this research paper is the cycle of admission to hospital of very sick patients, their 'stabilisation' in hospital by overworked staff, their early discharge (as soon as they are stabilised) back into the cycle of poverty, and then their re-entry into hospital when they are once more sick because of exposure to a hostile environment that offers little chance for their well-being. Some patients are eventually abandoned or referred to places of safety because the parents themselves are sick (or dead) and cannot care for their young. RCH also has to bear the full cost of treatment of these patients as their parents cannot afford to pay for health services. One hundred per cent of the sample randomly selected for this study were found under the 'free patient' category, which exempted them from any payment for services rendered.

The mortality rate of the cohort in this study was 8%. This figure is significant when compared with the overall death rate at RCH for the similar period (8% v. 1.7%). HIV+ patients were 4.7 times more likely to die in hospital than their HIV- counterparts. Mortality rates from studies in Ivory Coast[18] (20.8% v. 8.7%) and Zambia[16] (19% v. 9%) are similar to those of RCH. Nelson *et al.*[13] reported a mortality rate of 16% for their cohort of patients in Malawi. Hussey *et al.*[9] examined the survival patterns of children known to be vertically infected with HIV-1 in the Cape Town Metropole. The median age at diagnosis was found to be 5 months – 72% of the children were less than a year old when they were diagnosed with HIV. The median survival time of children with HIV was 32 months from the time of diagnosis. In developed countries, the median survival time was found to be in excess of 5 years (60 months),[24,25] which was more than twice that for developing countries.[9,26,27] Hussey *et al.*[9] believe that the difference in survival is clearly related to the availability and accessibility of medical and other supportive care.

The average direct cost to RCH to treat HIV+ patients was found to be R18 765.76 per admission per HIV+ patient. Eighty four per cent of this cost consisted of admission

(bed) cost alone (Fig. 7). Mkele *et al.*[28] reported in their cost analysis for HIV+ patients that bed costs comprised 82% of the total expense of inpatient care, while drugs made up only 5%, results similar to those obtained in our survey. The total amount spent on direct treatment costs for HIV+ inpatients amounted to 26% of the total direct costs for all admissions to hospital, i.e. HIV+ patients, who accounted for only 4% of total admissions to hospital, consumed 26% of the budget for direct treatment costs. It is the view of the authors that RCH is faced with tough choices if it wants to operate within its allocated yearly budget. Hospitals are being forced to operate within budgets and managers at these institutions will have to take the necessary steps (cost-cutting exercises) to make sure that they do so. This then begs the question: What are the options available to RCH in light of the ever-increasing HIV epidemic, reduced budgets, greater demand for bed space, over-worked staff and the continued inability of most patients to pay for services?

1. DEVELOP QUOTAS FOR ADMISSION OF CERTAIN CATEGORIES OF PATIENTS

To ensure that admission to RCH is available to the wider spectrum of patients, categories of patients that use up a higher amount of resources would have to be restricted. However, this is fraught with ethical dilemmas, and doctors will be forced to 'play God' with patients' lives. In addition, solutions would have to be found for those patients that the hospital refuses to admit if it has exceeded its intake quota for that category of patient.

2. DEVELOP MANAGEMENT PROTOCOLS FOR IN-HOSPITAL CARE OF HIV+ PATIENTS

There was a wide variation in terms of the direct costs assessed in this study. While a lot of this variation can be explained by the HIV+ patients admitted requiring different levels or types of care, medication, laboratory tests and surgical procedures discrepancies need to be addressed.

- Some patients were discharged as soon as they were 'stabilised', as there was pressure in the ward for bed space. Others were kept in hospital until they had fully and completely recovered.
- Some patients were discharged with 3 months' supply of medicines and multivitamins. Other patients, who appeared to need these medicines as they were discharged as soon as they were stabilised, were not given any medicines.
- Some doctors appeared to keep patients in hospital longer than others. This may be due to patient circumstances, but is probably due to a more cautious approach among certain doctors.

3. PROVISION OF ANTIRETROVIRAL THERAPY (ART) FOR HIV+ PATIENTS

The findings of this study provide strong evidence that unless something is done to reduce the transmission rates from mother to child, RCH will be faced with a greater demand for bed space from HIV+ patients who require more resources than other patients. In the USA and Brazil, highly active antiretroviral therapy (HAART) was found to reduce costs by an average of 46% and 80% for public health hospitals.[29] There is a shift of costs from hospitalisation to outpatient care. In the local context, this would imply the supply of cheaper HAART to reduce hospitalisation and number of admissions.

4. PREVENTION OF MOTHER-TO-CHILD TRANSMISSION (MTCT)

The Western Cape government has been involved in preventive MTCT programmes since 1999. Every R1 spent in the MTCT programme results in a saving of about R2.50 in hospital costs for treating an HIV-positive baby. By assuming that a single dose of nevirapine given within 72 hours after birth reduces transmission by 50%,[30] one can estimate that the proportion of HIV+ patients will be reduced by a similar figure. This translates to the number of inpatients diagnosed with HIV infection being reduced from 616 to about 308. The total direct cost for treating this group would then be around R5.77 million (R18 765.76 x 308) – a saving of R5.79 million (R18 765.76 x 308). This saving is immense when compared with the price of a single dose of nevirapine – about R10.[31] Roux *et al.*[7] calculated the lifetime cost of an HIV-infected child to be almost twice that of protecting an infant from infection through the prevention of MTCT.

5. HOME-BASED CARE INITIATIVES

The flood of HIV+ patients into tertiary hospitals (such as RCH) can be stemmed if there were more rural clinics and home-based care linked to these specialist HIV clinics.[22] Currently RCH, via its outpatient facilities, fulfils tertiary, provincial, district and primary health care functions, forcing highly trained staff often to spend too much time on patients who do not necessarily require their skills. Government needs to allocate more money for home-based care initiatives and provide more nurses and doctors in rural areas. A large majority (over 65%) of patients in this study were from rural areas. Local communities should be empowered to take charge of their own health care, and basic skills transfer and visits to these communities by trained nurses can result in much less suffering for patients and less expense for the state which bears the full cost for their care.

This study highlights the high cost of care that is required by HIV+ patients who are admitted as inpatients to RCH. RCH provides a beacon of hope for all children throughout Africa, as it provides highly specialised care that is often only available at this facility. However, it too is being affected by the HIV crisis facing the country, and is facing an untenable position of continuing to provide specialised care in an environment of lower budgets, higher demand and greater need by children, who, along with their HIV+ mothers, continue to suffer discrimination.

The managers of RCH face difficult choices requiring tough decisions that must clearly be addressed with some urgency. Decisions affecting the care of HIV-positive children must reflect choices that are sustainable, and furthermore must reflect our commitment to improving the quality of life of these children. Government must be informed that in a realistic economic sense, the pursuit of efficient practice is not merely reducing costs or budgets or avoiding costs.

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GLOBALISATION, TRANSPORT AND HIV

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Transport has changed the way the world functions. The accessibility, safety, speed and reliability of global transport make it easier for citizens to access their world, and these advances in transport are driving and changing the face of the global economy.

In South Africa '. . . transport plays an important role in the national economy as well as in the economies of several other African states. A number of countries in Southern Africa use South Africa's transport infrastructure to move their imports and exports. . .'[1]

And these imports and exports are growing, according to the latest preliminary report of the South African Receiver of Revenue Trade Statistics[2] (Table I).

'Communities which are historically displaced travel long distances to points of economic production and rely on transport benefits such as subsidies.'[3] For this reason, the Department of Transport is mandated to provide affordable transport access and mobility that is safe, reliable and internationally competitive (Table II).

Any threat to this vital system threatens not only the South African economy but also that of the entire globe.

The HIV-pandemic poses such a threat.

'July 4th 1976: Tall sails scraped the deep purple night as rockets burst, flared and flourished red, white and blue over the stoic Statue of Liberty. Ships from fifty-five nations had poured sailors into Manhattan to join the throngs for America's 200th birthday party . . . This was the part the epidemiologists would later note. They would recall that glorious night in New York Harbour, all those sailors, and recall: from all over the world they came to New York.'[4] So begins Randy Shilts' history of the San Francisco HIV epidemic, *And the Band Played On.*

The story of the global HIV pandemic is interwoven with the history of the transport industry. The rapid spread of this disease from localised African sites in the early part of the 20th century to the developed world in the 1970s and 1980s has been correlated with the rapid increase in global travel during this period. The spread of the well-documented North American homosexual epidemic of this period has been traced to a source patient, Gaetan Dugas, an Air Canada steward serving on international flights to and from Africa. International travel associated with industry, mass refugee movements and tourism have been identified as prime movers in the growth to pandemic status of this disease.

Based on an address given by Dr Steve Andrews to the South African branch of the International Chartered Institute of Logistics and Transport on 23 June 2004.

THE TRANSPORT INDUSTRY AND HIV: VULNERABILITIES AND OPPORTUNITIES

Ironically, the very success of the global transport industry as a central factor for economic development also makes this industry sector an ideal instrument for disease spread, and makes it exquisitely vulnerable internally to the ravages of these diseases. 'While new and improved infrastructure brings economic and social benefits, it can also facilitate the spread of disease.'[5]

The transport sector is staffed, managed and patronised by people who often travel long distances to work in locations away from family and friends. The sector workplace environment is a key element in contributing to increased HIV transmission risk. This environment manifests in a climate of 'virtual migrancy' and the mobile workplace, in association with multiple and often far distant places of permanent and temporary domicile, is a crucial factor in increasing sector risk to HIV. This work environment and its demands upon staff result in long periods away from home and family. In this scenario, workers interact with and meet sexual needs using the services of commercial sex workers (CSWs) and non-permanent sex partners. Male predominance in the industry, associated with relative financial prosperity of transport workers, contributes to the ability not only to purchase, but also to dictate the terms of, casual sexual encounters in areas serviced by CSWs. This increases likelihood of unsafe sexual practices, and the spread of sexually transmitted infections (STIs) and HIV. The

TABLE I. IMPORTS AND EXPORTS, SOUTH AFRICA, 2003 AND 2004

Period under review	Exports (R)	Imports (R)
January - May 2004	115 093 890 445	114 259 650 798
January - May 2003	114 301 798 452	105 100 391 972
Increase/decrease	792 091 993	9 159 258 826
Growth	0.69%	8.71%

TABLE II. TRANSPORT VOLUMES FOR SOUTH AFRICA*

	Amount of cargo	Increases
Land	56 959 (1 000 metric tons) throughout South Africa January - December 2003†	Increased by 2.9% (+19.5 million tons) compared with 2002
Air	Cargo processed through Johannesburg International Airport in 2001 was valued at R100, 1-billion‡	
Sea	Cargo handled in South African ports between April 1994 and March 1995 was 130.7 million tons, a 5.8% increase from figures for 1993/1994§	Breakbulk and bulk cargoes (including petroleum and other liquid products) handled by the seven ports in South Africa for the 2002/03 financial year totalled 166.5 million tons¶
Rail	Transnet annually handles 176 million tons of rail freight‖	By 2004 this figure had climbed to 180 million tons a year**

*This table should be viewed as a qualitative comment on the economic importance of transport to South Africa and does not attempt to provide a comprehensive or exhaustive analysis of these volumes.
†Land Freight Transport, Statistical Release P7142, Statistics South Africa, December 2003 **www.statssa.gov.za**
‡**http://www.safrica.info/doing_business/sa_trade/exporting/tradebureau.htm**
§**http://www.iss.co.za/Pubs/ASR/5No2/5No2/SAMaritime.html**
¶**http://www.transnet.co.za/BrowserDefault.aspx?tabid=600**
‖**http://www.transnet.co.za/BrowserDefault.aspx?tabid=604**
http://www.transport.gov.za/comm-centre/AfricaRailSPEECHDEL.pdf

relative difficulty of providing effective prophylactic and therapeutic health care interventions to this population compounds these problems.[6,7]

Within the sector, infected workers not only continue to spread the disease, but increasingly develop illnesses associated with HIV and eventually AIDS as the disease progresses. HIV manifests in a myriad of different ways, but begins to limit productive working time and employment periods. Because HIV cripples before it kills, working employees are increasingly less productive. If suffering from HIV dementia or peripheral neuropathy, these employees may actually be dangerous and counter-productive to industry functioning. Spread of the disease both at home and to surrounding areas limits the number of healthy non-infected economically active adults available to sustain labour requirements. In short, HIV populates the existing workplace with sick, crippled and eventually dying people, while also severely limiting options to replenish it with healthy workers.

The World Bank has identified four key groups of 'people at risk' in considering HIV interventions in the transport sector. These key areas must be specifically and appropriately targeted to reduce both the spread of HIV and its impact on industry.[8]

1. TRANSPORT INFRASTRUCTURE BUILDING AND MAINTENANCE

These activities involve groups of workers, often housed away from their families and for prolonged periods of time. The environment is usually predominantly male, with the workforce temporarily housed in an all-male environment. These employees are commonly (in comparison with the surrounding communities) relatively wealthy, able to purchase and dictate terms of sexual encounters with CSWs. This results in an increased likelihood of multiple sexual partners, increasing the likelihood of HIV and other STIs for the workforce, and for the surrounding areas. In Lesotho, the association with the Highland water project has led to an increased STI incidence in the area.[9] Studies in Malawi have correlated an increased HIV incidence with crews and communities linked to road construction.[10]

Potential interventions for this focus area include an increased use of local labour, increased frequency of home leave with personnel rotation, and exploring possibilities of

relocating entire nuclear families for prolonged operations. Government and private sector interventions must be complementary in planning and executing these programmes. Health services and disease management programmes (DMP) are required to provide education, prophylactic interventions and formal therapeutic care. Ideally, this should form an extension of the organisation's existing DMP, with local contractors required to tender in line with existing workplace DMP norms. The health care service should form part of the initial project tender documents.

2. TRANSPORT WORKERS

Improving transport services means increased time away from home for drivers, train crews, airline crews and sailors. This results in a situation of two or more semi-permanent or temporary domiciles. Long periods away from home, coupled with the ongoing displacement from a familiar environment, lead to the same likelihood of increased risky sexual behaviour as is seen in those in construction. Consequences are regional, and even international, as transport operatives move across borders. Long-haul truckers have been shown to be particularly at risk, with a 1993 Cameroon survey of 168 bus and truck drivers revealing that, in an average 14-day trip away from home, 62% had at least one episode of sex. A total of 25% reported having sex every night. Various studies of long-haul truckers have demonstrated HIV seroprevalence figures above 40% in various countries including South Africa.[11]

Interventions to control HIV transmission and spread, as well as to control the disease in infected persons in this group, must include strategies for dealing with the migrant nature of the job itself. Targeted health education and AIDS prevention strategies such as voluntary counselling and testing (VCT) have been shown to modify sexual behaviour in developing countries.[12] These must be implemented not only at home bases but also at rest points and temporary domiciles. In addition, strategies to reduce time spent away from home should be actively explored, along with the provision of controlled rest areas. The latter may also be used for health education and intervention purposes. Strategies to reduce time waiting at border posts must be explored with local and national authorities.

3. TRANSPORT SECTOR MANAGEMENT

Transport sector managers are drawn from a small group of educated professional people.

As a group they are in scarce supply, expensive to train, and very difficult to replace. In Africa, the World Bank suggests that HIV prevalence among transport managers is as high as, or higher than, that in the general population.[13]

Intervening to reduce HIV impact involves the identification of key personnel, along with development and implementation of human resource strategies to take account of increased morbidity and mortality. Education and prevention strategies, as well as therapeutic interventions in the workplace, should include, and in fact be driven by, management staff. An awareness of HIV risk regardless of workplace seniority should be built into workplace policies and intervention strategies.

4. PASSENGERS

Today vast numbers of people travel all over the world for work and leisure. Unlike previous generations, they will return home yearly or more frequently. Leisure travel is one of the fastest growing activities in the world. Over 12 million travellers – including an estimated 1.2 million business travellers – passed through Johannesburg International Airport in 2003 alone.[14] With this increase in travel comes increasing risk of exposure to, infection with and spread of a variety of diseases, including HIV.[15]

Since the demise of apartheid in 1994 South Africa has become a favourite destination for international visitors. According to Statistics South Africa, the total number of foreign travellers who visited South Africa from mainland Africa, overseas and unspecified countries, arriving through all ports of entry during April 2004, was 584 365. This is an increase of 2.1% over the April 2003 figure of 572 603.[16]

It can be argued that the transport sector has no direct responsibility for HIV transmission risks and HIV interventions for its passengers, but the sector has a responsibility to improve its communication with national AIDS control programmes and governmental structures. This will allow accurate reporting of traffic types and flows. The relevant authorities may then provide directed education, prophylaxis and therapeutic interventions that meet the specific needs of passengers.

A co-ordinated response to the threat of HIV to the transport industry is essential. The role of the health care worker is to identify and maintain a high level of awareness of the HIV risks posed by those working in and interacting with the transport sector. This will allow co-ordination with current prevention and treatment initiatives.

The South Africa Department of Transport released its Transport Sector Strategic HIV/AIDS Plan in November 2001.[17] The plan involves all sectors of the industry and identifies responsible parties, target audiences, time frames and costs. The full implementation of this and other

initiatives to combat the HIV threat to the transport industry requires urgent attention.

There is no room for complacency, for as the late Dullah Omar, Minister of Transport, said: 'There can be no pause or let-up in the battle against HIV/AIDS. So, whilst recognising the value of what has been achieved so far, government and the industry have also recognised the need to lift their joint efforts to a higher level . . . Every truck driver, taxi driver, bus operator, commuter, passenger, pilot, air steward and seafarer can either be part of the problem or become part of the solution. We are in close touch with each other and we are a potential army of millions of HIV-AIDS activists. If we do things right and act together we can reach into the heart of every home in this country. Our transport network offers us a potent weapon in this battle. It moves millions of people every day, both within and across our borders. These movements can either continue to widen the spread of HIV-AIDS or become a powerful channel for disseminating the information, knowledge and understanding upon which effective prevention depends.'[18]

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BREAST-FEEDING AND HIV: AN UPDATE

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Breast-feeding is a route of transmission of HIV from an infected mother to her infant. However, breast-feeding is an important pillar of child survival and the ideal way of feeding an infant, as well as providing a unique biological and emotional basis for child development. This article highlights the dilemma created by the risks and benefits of breast-feeding and will discuss factors that increase the risk of HIV transmission during breast-feeding as well as strategies that could be employed to reduce these risks. Many questions remain unanswered.

The subject of breast-feeding and HIV has become a highly emotive debate because of the polarisation between those whose mandate is preventing the spread of HIV, and therefore stress the importance of replacing breast-feeding, and those whose mandate is child survival, and therefore promote breast-feeding as one of the pillars of child survival.

QUANTIFYING THE RISK OF HIV TRANSMISSION THROUGH BREAST-FEEDING

DURATION OF BREAST-FEEDING

Since the advent of polymerase chain reaction (PCR) testing it has been possible to determine the risk of HIV transmission via breast-feeding more accurately. To date there has only been one randomised controlled clinical trial (RCT) of breast-feeding versus formula; however, the study had a serious limitation in terms of lack of compliance with the assigned feeding mode. This Kenyan study found a risk of transmission of 16% by age 24 months.[1] It is unlikely that any groups in the future will attempt an RCT of feeding practices, as the Kenyan trial showed that it is very difficult to randomise a behaviour, like breast-feeding, that is so inherently part of a woman's motherhood. Furthermore, it is now generally agreed that it would be unethical to repeat such a trial. In order to determine the risk of breast-feeding transmission more accurately, the Breastfeeding and HIV International Transmission Study (BHITS) Group[2] therefore conducted an individual patient data meta-analysis of 4 085 predominantly breast-fed children who participated in nine RCTs testing the effect of nutrients or antiretroviral drugs to prevent mother-to-child transmission of HIV (PMTCT). By definition, any HIV infection detected by PCR after 4 weeks of age was attributed to breast-feeding transmission. The probability of breast-feeding transmission of HIV was estimated to be 9.3% at 18 months, and the overall risk of breast-feeding transmission was estimated as 8.9 transmissions/100 child-years of breast-feeding, which is interpreted as a monthly risk of 0.74% per month of breast-feeding. The meta-analysis demonstrated that the risk of transmission was cumulative and roughly constant throughout the breast-feeding period. *A suggested figure to work with is therefore a 4% risk for every 6 months of breast-feeding.*

PATTERN OF BREAST-FEEDING

Most studies attempting to estimate the transmission of HIV attributable to breast-feeding have made no attempt to define the pattern of breast-feeding. Just as it is important to specify the duration of breast-feeding when assigning risk, so too is it important to specify the type of breast-feeding that is practised. In most studies insufficient information has been collected to enable infants to be classified as receiving exclusive breast-feeding (EBF) or breast-milk in addition to other liquids and/or solids in the first 6 months (mixed breast-fed). Many researchers have used arbitrary definitions of EBF and not the accepted World Health Organisation (WHO) definition, which defines EBF as breast-milk only, with no other solids or liquids. The only prospective study that used the correct definition of RBF was conducted in Durban.[3] In this study[3] HIV-infected women who chose to breast-feed were encouraged to practise EBF as a possible way of reducing risk of HIV infection. The study found that the cumulative probability of HIV infection was similar among never-breast-fed and EBF infants up to 6 months, i.e. 19.4% (95% CI: 13.6 - 26.0) and 19.4% (95% CI: 12.5 - 27.4), respectively, but it was higher in the mixed breast-fed group, i.e. 26.1% (95% CI 20.5 - 31.9). The results of this study suggest that the vertical transmission of HIV through

RISK FACTORS FOR BREAST-FEEDING TRANSMISSION OF HIV	
Strong evidence	**Limited evidence**
High plasma viral load	Non-exclusive breast-feeding in the first 6 months
Advanced disease/low CD4 count	High breast-milk viral load
Breast pathology – mastitis, abscesses, cracked or bleeding nipples	Subclinical mastitis as evidenced by increased breast-milk sodium levels
Primary infection/new infection	
Prolonged duration of breast-feeding – more than 6 months	Low maternal levels of vitamins B, C and E
	Infant oral candidiasis

breast-milk is dependent on the pattern of breast-feeding and not simply on breast-feeding *per se*. A limitation of the study was measuring adherence to the reported feeding practice. Measuring adherence will always be difficult and future studies have been encouraged to incorporate frequent monitoring, in order to improve the validity of the maternal recall.

Several, large, well-designed, prospective cohort studies in South Africa, Zimbabwe, Cote d'Ivoire and Zambia are currently in progress to examine more closely the effect of EBF on the risk of breast-feeding transmission. Preliminary results of the Zimbabwean[4] and Cote d'Ivoire[5] studies presented at the International AIDS Conference in Bangkok, (July 2004) have confirmed the finding that *exclusive breast-feeding carries a much lower risk of HIV transmission than mixed breast-feeding.*

IMPACT OF BREAST-FEEDING ON THE HIV-INFECTED MOTHER

Considerable evidence suggests that breast-feeding may be associated with maternal health benefits.[6] These include decreased postpartum bleeding and decreased menstrual blood loss during the months following labour; delayed resumption of ovulation with increased child-spacing; improved postpartum bone remineralisation and decreased postmenopausal hip fractures; and decreased rates of ovarian and breast cancer.

In contrast to these maternal health benefits, Nduati and colleagues reported that 24-month maternal mortality among breast-feeding HIV-seropositive mothers they followed up in Kenya was significantly increased relative to formula-feeding counterparts.[7] The accompanying commentary by Newell[8] pointed out that the data needed to be interpreted with caution because of limitations in the study. Furthermore, the results of this study were dissimilar to the results of the Durban study,[9] which failed to show an increase in either mortality or morbidity in the breast-feeding group.

Following the reporting of these two studies, the WHO convened an expert meeting and concluded that there was insufficient evidence to suggest that breast-feeding by HIV-infected women increases their mortality risk.[10] Subsequent to this WHO statement, a Tanzanian study,[11] a Zambian study,[12] and a meta-analysis involving nine large studies[13] have shown clearly that *breast-feeding does not pose any mortality or other health risk to the HIV-infected mother.*

MORBIDITY AND MORTALITY RISKS OF NOT BREAST-FEEDING

As mentioned earlier, simply encouraging women not to breast-feed in order to prevent postnatal transmission of HIV is not straightforward, as not breast-feeding carries its own risks. The objective of any PMTCT strategy must be to optimise overall child survival, including that of children of HIV-uninfected women. Central to this decision is determining the risk of morbidity and death associated with both breast-feeding and not breast-feeding, and what impact the recommendation and/or provision of formula milk or other replacement feeds to HIV-infected women will have on the feeding practices of uninfected mothers.

Breast-milk fulfils the infant's total nutrient requirements for the first 6 months of life and remains a valuable source of nutrition up to 2 years and beyond. Breast-feeding is obviously the most economical and safe mode of infant feeding, is important in promoting the mother-infant relationship, and may enhance the child's intellectual development.[6] The more well-known benefit of breast-feeding to the infant is reduction of the risk of infection, especially infections resulting in diarrhoea and pneumonia, and this has been reinforced by a recent meta-analysis.[14] In this meta-analysis, which included studies from Brazil, Pakistan and the Philippines, breast-feeding was shown to protect against child mortality especially in the early months (odds ratios were 5.8, 4.1 and 2.8 for infants 0 - 2, 3 - 4 and 5 - 6 months of age respectively). The odds ratios for protection against death from diarrhoea and acute respiratory infections in the first 6 months of life were 6.1 and 1.9, respectively. The authors concluded that 'it will be difficult, if not impossible, to provide safe breastmilk substitutes to children from underprivileged populations'.

The benefits of breast-feeding in terms of reduction of mortality from infections are unlikely to be as important in well-resourced developed communities where the risks of artificial feeding can be minimised. However, even in

developed countries breast-feeding may protect against bacterial and viral infections and later onset of health problems such as diabetes, cardiovascular disease and cancer.

MAKING INFORMED CHOICES ON INFANT FEEDING

Because of the paucity of well-designed prospective trials evaluating the long-term relative risks associated with breast-feeding and formula-feeding in settings of high HIV prevalence, several groups have designed mathematical models to assess the net mortality. In a recent modelling exercise Kuhn *et al.*[15] estimate that when infant mortality rates are greater than about 40/1 000 live births, providing formula milk to HIV-infected women would result in the excess number of deaths arising from formula use being approximately the same or greater than the number of HIV infections that might be prevented.

Counselling and empowering women to make an informed choice on infant feeding is not simply a matter of informing or educating them about the theoretical risks and different feeding options. Health workers need to assess the individual mother's circumstances to ascertain what is most feasible and safe for her. Time is required to explain the factors that increase breast-feeding transmission or morbidity from replacement feeds and suggestions to reduce these risks. In addition to a deep understanding of the social issues and the household situation, counsellors need to have the ability to translate complex scientific concepts on risk in a way that can be understood by women who do not grasp these dilemmas. They need to express compassion and have the ability to emotionally support women in a decision that affects themselves, their children, and the rest of their family.[16] Experience has shown that quality of counselling needs to be prioritised in all programmes if women are to be assisted to make informed choices.[17]

Now that there is growing evidence that mixed breast-feeding carries considerable risk for HIV transmission, those implementing PMTCT programmes should be cautious about the distribution of free formula milk, as this practice seems to encourage mixed breast-feeding.[17,18] If programmes are intent on providing free formula, a more equitable and safer approach would be to provide a choice of either formula milk for the infant or an equivalent value of food vouchers for the mother.

For those mothers who choose exclusive breast-feeding, a second choice will need to be made at about 6 months of age. The guidance that should be given at this stage is that if the child is infected or suspected to be infected, the child should continue being breast-fed. If the child is uninfected, and provided that the child will have access to adequate complementary food, the mother should be encouraged to stop breast-feeding in a short period of about 1 - 2 weeks. Mothers should be provided with specific guidance and support when they cease breast-feeding to avoid harmful nutritional and psychological consequences to the infant and to maintain their breast health. If the infant will not have access to adequate complementary food, the best option is probably for the mother to express and heat-treat her breast-milk,[19] and rather spend the money that would have been spent on formula milk on complementary food.

STRATEGIES TO REDUCE BREAST-FEEDING TRANSMISSION AND IMPROVE CHILD SURVIVAL

Until more data are available to inform these issues, what can be done to minimise breast-feeding transmission and optimise child survival? Counselling skills and opportunities should be improved so that health workers are more able to assist women to make informed choices that they are committed to follow. For women who choose or need to breast-feed, experienced support should be available to ensure good exclusive breast-feeding practices so as to minimise breast pathology, HIV viral load and disruptions to the gut environment, and therefore to reduce risk of HIV transmission. Breast-feeding should be discouraged for those women who have progressed to AIDS and have very low CD4 counts.

Strategies that should be employed to minimise risk of transmission include the following:

- Exclusive breast-feeding during the first 6 months.
- A shorter duration of breast-feeding – about 6 months.
- Good lactation management must be provided, so that breast-feeding problems such as cracked nipples, engorgement and mastitis are prevented.
- If the mother does develop mastitis or abscesses, she must express milk from the affected side frequently and discard it, and continue feeding from the unaffected side.
- Condoms must be used throughout the lactation period.
- If the infant has oral thrush it must be treated promptly.

Pasteurisation of expressed breast-milk, using a method that is practical and feasible even at home, can be used to effectively kill all cell-free HIV.[19] This strategy is likely to be difficult to implement from birth but may be more relevant after 6 months or as a temporary measure to sustain exclusive breast-feeding where the mother is unwell or away from her child.

For those mothers who choose replacement feeding, support should be available to demonstrate preparation and safe storage of commercial infant formula to minimise the risks of diarrhoeal morbidity and malnutrition.

Communities need to be engaged to be supportive of mothers with HIV infection and accept the varied approaches to infant feeding that may occur.

USE OF ANTIRETROVIRALS TO PROVIDE INFANT PROPHYLAXIS DURING BREAST-FEEDING

Recent animal trials and clinical trials suggest that antiretrovirals given to the infant during the first few weeks after delivery may protect the infant from HIV transmission during the breast-feeding period. In order to provide more conclusive evidence on the efficacy of antiretrovirals given to the infant, several studies are currently underway testing the use of single or dual antiretroviral drug regimens given for periods from 1 week to 6 months.[20]

BREAST-FEEDING IN THE HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) SETTING

As already mentioned, maternal HIV viral load has consistently been shown to be an important risk factor for breast-feeding transmission. It therefore seems very likely that giving HAART to the mother during the lactation period could reduce transmission. For women in the developing world, providing HAART during the pregnancy and lactation period is emerging as a cost-effective option that is currently under investigation in several trials.[20] It is likely that in the near future many women may already be on HAART, and the question that is often posed is: 'Can a woman on HAART safely breast-feed?' Unfortunately we do not yet have enough information to answer this question definitively, and can only suggest that given that the viral load in women on HAART will be very low (at undetectable levels), there should be no or minimal risk of breast-feeding transmission. Other considerations to bear in mind in this decision would be safety issues. We know that most antiretrovirals will be excreted into the breast-milk and the infant will be exposed to small quantities. For those drugs that have been widely used in infants, such as nevirapine (NVP), zidovudine (ZDV) and lamivudine (3TC), there are unlikely to be safety concerns. The most obvious concern will be the fact that infants will be exposed to subtherapeutic levels of antiretrovirals through the breast-milk, and if some infants escape protection and become HIV-infected, they may have developed resistance to the drugs used that will impact on their future HIV treatment. Several trials are currently investigating these issues.[20]

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CPD QUESTIONS

Journal 17

Two CPD points are awarded for the correct completion and submission of the questions below.

Please complete and post to: Southern African HIV Clinicians Society, Suite 233, PostNet Killarney, Private Bag X2600, Houghton, Johannesburg, 2041, or fax to (011) 453-5059

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PLEASE INDICATE WHICH OF THE FOLLOWING STATEMENTS ARE TRUE:

1. (a) There is strong evidence that the risk factors for transmission of HIV during breast-feeding are: high plasma viral load, advanced disease/low CD4+ count; breast pathology — mastitis, abscesses, cracked or bleeding nipples; primary infection/new infection; prolonged duration of breast-feeding — more than 6 months.
   (b) There is no evidence that risk factors for transmission of HIV during breast-feeding are: non-exclusive breast-feeding in the first 6 months; high breast-milk viral load; sub-clinical mastitis as evidenced by increased breast milk sodium levels; low maternal levels of vitamin B, C and E; infant oral candidiasis.
   (c) Exclusive breast-feeding carries a much higher risk of HIV transmission than mixed breast-feeding.

2. (a) At Red Cross Children's Hospital, HIV-positive patients comprise 40% of total admissions and consume 26% (R11.56 million) of the total budget for direct treatment costs (R44.65 million).
   (b) At Red Cross Children's Hospital, HIV-positive patients comprise 14% of total admissions and consume 26% (R11.56 million) of the total budget for direct treatment costs (R44.65 million).
   (c) At Red Cross Children's Hospital, HIV-positive patients comprise 4% of total admissions and consume 26% (R11.56 million) of the total budget for direct treatment costs (R44.65 million).

3. (a) The most common bacterial infections in HIV-infected patients are due to *Staphylococcus aureus* and *S. epidermidis*. These are common in the general population, but in HIV-infected individuals may be more widespread, recurrent and resistant to therapy.
   (b) The most common bacterial infection in HIV-infected patients is due to *Staphylococcus aureus* but not *S. epidermidis*. The former is common in the general population but in HIV-infected individuals may be more widespread, recurrent and resistant to therapy.
   (c) The least common bacterial infections in HIV-infected patients are due to *Staphylococcus aureus* and *S. epidermidis*. These are common in the general population but not in HIV-infected individuals.

4. (a) Of patients presenting with skin lesions, 37% are found to have HIV infection.
   (b) Only 37% of patients presenting with skin lesions do *not* have HIV infection.
   (c) Of patients presenting with skin lesions, 50% are found to have HIV infection.

5. (a) Cutaneous fungal infections are common in HIV-infected and non-HIV-infected patients but are the commonest infectious manifestation of immunosuppression related to HIV.
   (b) Cutaneous fungal infections are common in HIV-infected and non-HIV-infected patients but are the least common manifestation of immunosuppression related to HIV.
   (c) Cutaneous fungal infections are common in HIV-infected and uncommon in non-HIV-infected patients but are the commonest infectious manifestation of immunosuppression related to HIV.

6. (a) Isoniazid (INH) 300 mg/d for 6 months is the most studied of the prophylactic regimens and recommended in the South African Department of Health Guidelines. Preventive therapy reduces the risk of active TB by about 60% in HIV-infected patients with a tuberculin skin test (Mantoux test) reaction of ≥ 5 mm.
   (b) Isoniazid (INH) 400 mg/d for 6 months is the most studied of the prophylactic regimens and recommended in the South African Department of Health Guidelines. Preventive therapy reduces the risk of active TB by about 60% in HIV-infected patients with a tuberculin skin test (Mantoux test) reaction of ≥ 5 mm.
   (c) Isoniazid (INH) 200 mg/d for 6 months is the most studied of the prophylactic regimens and recommended in the South African Department of Health Guidelines. Preventive therapy reduces the risk of active TB by about 60% in HIV-infected patients with a tuberculin skin test (Mantoux test) reaction of ≥ 5 mm.