

## ARTICLE

## Focus on adolescents with HIV and AIDS

L Fairlie,<sup>1</sup> MB ChB, DCH (UK), FCPaed (SA), MMed; N Sipambo,<sup>1,2</sup> MB BCh, FCPaed (SA);  
C Fick,<sup>1</sup> MB BCh, Dip HIV Man; H Moultrie,<sup>1</sup> MB BCh, MSc

<sup>1</sup> Wits Reproductive Health and HIV Institute (WRHI), University of the Witwatersrand, Johannesburg, South Africa

<sup>2</sup> Department of Paediatrics, Chris Hani Baragwanath Hospital, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Corresponding author: L Fairlie (lfairlie@wrhi.ac.za)

Adolescents living with HIV, including those infected perinatally and non-perinatally, bear a disproportionate burden of the HIV epidemic in South Africa. This article discusses HIV management in adolescents including the following aspects: (i) burden of HIV disease, modes of HIV acquisition and implications for management; (ii) initiation of combination antiretroviral therapy (ART), outcomes and complications of ART in adolescents, including virological failure and switching regimens; (iii) adherence in adolescence, including factors that may contribute to poor adherence and advice to improve adherence; (iv) issues particular to adolescents, including sexual and reproductive health needs, disclosure to adolescents and by adolescents, and transition to adult care. This article aims to provide insights based on the literature and experience to assist the clinician to navigate the difficulties of managing HIV in adolescence and achieving successful transition to adult care.

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### Epidemiology

There are few routine data on the health of South African (SA) adolescents (defined by the World Health Organization (WHO) as aged 10 - 19 years), partly a result of the age bands used in the District Health Information System. This is cause for concern. Many of the determinants of adult ill health, such as harmful alcohol use, tobacco use, unhealthy diet, and lack of physical activity, have their origins in adolescence. Critically, female adolescents bear a disproportionate burden of the HIV epidemic in SA. In 2012, the estimated HIV prevalence (range) in 15 - 24-year-old SA women and men was 13.9% (12.9 - 16.8%) and 3.9% (2.5 - 5.7%), respectively,<sup>[1]</sup> equating to ~720 000 adolescents and young people living with HIV.<sup>[2]</sup> The population of adolescents living with HIV in SA is comprised of adolescents with perinatal HIV infection (PHIV) who have moved into adolescence (PHIA) and those who acquired HIV at an older age through sexual activity, intravenous drug use or other less common modes of transmission (non-PHIV).

The prevention of mother-to-child-transmission programme (PMTCT) in SA has led to a massive reduction in perinatal HIV infections in the last decade. As a result, combined with high coverage and early initiation of combination antiretroviral therapy (ART) with concomitant reductions in morbidity and mortality, the SA population of children with perinatally acquired HIV

is rapidly moving into adolescence, with adolescents possibly already forming the bulk of paediatric HIV patients.<sup>[3]</sup> Some PHIA will have been diagnosed with HIV and started on ART early in childhood, with some already on second- or third-line ART by the time they reach adolescence. Other PHIA who are diagnosed in late childhood or in early to mid-adolescence are often severely immunocompromised and urgently require ART at the time of diagnosis, though up to half may be asymptomatic.<sup>[4]</sup> These late presenters represent ongoing missed diagnostic opportunities, the result of numerous factors beyond the scope of this article, but which include poor record keeping contributing to subtle chronic symptoms not being appropriately identified or investigated by healthcare workers despite numerous clinic visits, and the lack of child- or youth-friendly services hampering accessibility.

The prevention and diagnosis of HIV infection acquired in adolescence continues

to require urgent attention. Nearly a quarter (24%) of all new HIV infections in SA in 2012 occurred in 15 - 24-year-olds, with the incidence in women in this age group almost 4 times greater than that in men (2.5% v. 0.6%).<sup>[2]</sup> Adolescents living with HIV acquired during adolescence are likely to have early-stage disease, higher CD4<sup>+</sup> counts, and fewer opportunistic infections, and are less likely to meet current criteria for initiation of ART than PHIA. An exception is pregnant adolescents, who would qualify for ART regardless of CD4<sup>+</sup> count and time of infection. Measures to address HIV testing and access to care in children and adolescents are imperative.

### Combination ART and monitoring

Table 1 tabulates the indications for ART initiation in adolescents. Table 2 describes first-, second- and third-line regimens currently used in adolescents.

Table 1. Criteria for ART initiation in ALHIV

Criteria for initiation of ART in ALHIV	Criteria for fast-tracking (starting ART within 7 days of being eligible)
WHO stage 3 or 4	CD4 <sup>+</sup> count of ≤200 cells/mm <sup>3</sup>
CD4 <sup>+</sup> count ≤500 cells/mm <sup>3</sup>	WHO stage 4 disease
	Pregnancy or breastfeeding (PMTCT started urgently)
	MDR/XDR-TB

ART = antiretroviral therapy; ALHIV = adolescents living with HIV; WHO = World Health Organization; PMTCT = prevention of mother-to-child transmission; MDR/XDR-TB = multidrug-resistant/extensively drug-resistant tuberculosis.

**Table 2. ART regimens in ALHIV**

First-line regimen	
Weight <40 kg or age <15 y	ABC + 3TC + EFV*
Weight ≥40 kg, age ≥15 y and Tanner stage ≥3	Fixed-dose combination (FDC): <sup>†</sup> TEE (TDF + FTC <sup>‡</sup> + EFV)
Pregnant adolescents	
Age >12 y and weight >40 kg	FDC: TEE <sup>†</sup> TDF + 3TC/FTC + EFV (individual drugs can be given and nevirapine can replace EFV)
Second-line regimen	
If first-line regimen was: ABC/TDF + 3TC/FTC + EFV	Recommended second-line regimen: AZT +3TC + LPV/r
Third-line regimen	
Failing second-line regimen	Consult a specialist Regimen should be based on genotype resistance testing and expert opinion with supervised care Access to third-line ART managed centrally by the National Department of Health Third Line Committee, email jamalk@health.gov.za

ART = antiretroviral therapy; ALHIV = adolescents living with HIV; ABC = abacavir; 3TC = lamivudine; EFV = efavirenz; TEE = tenofovir, emtricitabine and efavirenz; TDF = tenofovir; FTC=emtricitabine; AZT= zidovudine; LPV/r = lopinavir/ritonavir.  
\*Nevirapine can replace EFA if necessary.  
<sup>†</sup>If FDC not used, individual drugs can be given.  
<sup>‡</sup>3TC can replace FTC.

Monitoring of clinical, immunological and virological indicators on ART for adolescents is the same as for children. In addition, given the high risks of poor adherence and virological failure in this group, 6-monthly viral load (VL) testing should be considered.

### Outcomes on ART

Longitudinal cohorts, mainly from well-resourced settings, report good clinical health with weight, height and body mass index approximating population norms.<sup>[5]</sup> Reductions in mortality rates of up to 76% in PHIV children and adolescents receiving ART have been reported in well-resourced settings.<sup>[6]</sup> All-cause mortality rates are similar when adolescents (9 - 19 years) and young adults receiving ART (20 - 29 years) are compared in reports from sub-Saharan Africa.<sup>[7,8]</sup> Immunologically, cohorts from resource-rich and resource-limited settings demonstrate robust CD4<sup>+</sup> improvement on ART, sustained to at least 5 years of follow-up.<sup>[6,8]</sup> Adolescents, however, generally have lower virological suppression rates (HIV VL <400 copies/mL) on ART compared with adults. Suppression rates range between 27% and 78% in longitudinal cohorts with low rates in both PHIV and non-PHIV adolescents in

sub-Saharan Africa.<sup>[8-10]</sup> Table 3 describes challenges with ART that are unique to adolescents.<sup>[11]</sup>

### Adherence

Adolescence is a period of physical, sexual, emotional and psychological change associated with developing autonomy, increased impulsivity and risk taking, increased peer influence and potentially reduced parental oversight. Poor adherence in adolescence has been described in many chronic conditions including diabetes, asthma, cystic fibrosis and HIV. Poor adherence may be related to a number of factors including: simple lifestyle barriers such as forgetting or struggling to fit ART into a busy school and extramural schedule; medication-related factors such as complex twice-daily regimens with high pill burdens; drug-drug interactions, and side-effects; patient-related factors such as treatment fatigue, lack of disclosure to the adolescent and by the adolescent to others, fear of stigma, unresolved psychosocial problems or substance abuse; and socioeconomic constraints limiting access to the clinic.

Since both adherence and barriers may change over time, it is necessary to assess adherence and modifiable barriers at each

visit and, together with the adolescent, tailor interventions to support adherence (Table 4). At each visit the following adherence reinforcements are necessary: identify and resolve any confusion with the regimen; manage any emerging drug side-effects; enquire about changes in lifestyle and need for adjustments; and provide ongoing psychosocial counselling and management of new or unresolved issues. A multidisciplinary approach including social workers, nurse, mental health professionals and counsellors may be required where available.

### Approach to an adolescent with virological failure

An elevated HIV VL is the most sensitive, though not necessarily specific, measure of non-adherence in HIV-infected patients as individuals with significant non-adherence will have detectable VLs. However, highly adherent individuals may have elevated VLs as a result of drug resistance, inappropriate regimens, drug interactions or incorrect doses. VL blips are defined as an unexplained VL between 50 and 1 000 copies/mL with VL suppression on repeat sampling, and are of limited clinical significance. Virological failure is defined as a VL >1 000 copies/mL on two consecutive assays taken at least 1 month apart from a patient on ART for at least 6 months. Virological failure precedes immunological failure which, in turn, usually precedes clinical failure, and allows early detection of adherence problems potentially prior to development of resistance mutations. Table 5 outlines management of adolescents with virological failure.

Not all adolescents with virological failure will have developed resistance. Resistance is more likely in regimens containing nevirapine, efavirenz and lamivudine as single mutations confer high-level resistance to these drugs. Since cross-resistance between nevirapine and efavirenz and other non-nucleoside reverse-transcriptase inhibitor (NNRTI) drugs occurs, adolescents failing an NNRTI-based regimen need to be switched to the standard second-line regimen as soon as possible to prevent accumulation of additional NRTI and/or NNRTI resistance mutations that may compromise NRTIs and second-generation NNRTIs like etravirine that could be used in later regimens.<sup>[12]</sup> Adolescents can safely be switched to the second-line regimen without HIV drug-resistance testing (DRT) (if not available), as the resistance mutations are largely predictable if early switch occurs.<sup>[12]</sup> Adolescents with virological failure on a protease inhibitor (PI)-based regimen can continue intensive adherence counselling for longer

**Table 3. Challenges of ART treatment in PHIV adolescents\***

<b>Problem</b>	<b>Implication</b>	<b>Solution</b>
<b>Physiological</b>		
Rapid growth and puberty	Exposure to inadequate ART dose as a result of growth	Routine dose adjustment per weight and Tanner stage assessment
Weight stunting and delayed puberty	Overdosage of ART with potentially increased toxicity	Routine dose adjustment per weight and Tanner stage assessment
Orofacial motor abnormalities or lesions (e.g. candidiasis, poor dentition)	Difficulty with swallowing ART leading to decreased adherence	Select regimens with ART agents available in liquid or powder formulations (e.g. AZT, 3TC, ABC), or crushable or dissolvable, or allow the capsules to be opened (e.g. ATV, DRV, EFV, FTC, TDF) Note: co-formulated agents cannot be crushed
Poor palatability	Decreased adherence	Same as above; consider masking taste using soda, juice, apple sauce
<b>Adverse effects</b>		
GI intolerance (e.g. nausea, diarrhoea)	Decreased adherence	Take with meals Alter timing of administration (e.g. night-time dosing) Anti-emetic, antidiarrhoeal agents Consider alternative regimen
Central nervous system side-effects (e.g. altered sensorium, dreams, headache)	Decreased adherence	Alter timing of administration (e.g. night-time dosing) Consider alternative regimen
Change in physical appearance (e.g. scleral icterus with ATV, facial lipoatrophy with d4T)	Decreased adherence	Consider alternative regimen
<b>Drug-drug interactions</b>		
Rifampicin-based TB co-treatment with LPV/r	Suboptimal LPV levels	Increased boosting with ritonavir or double dosing with LPV/r
Hormonal contraceptives and ritonavir-boosted PIs	Suboptimal hormonal levels with increased risk of pregnancy	For females using ritonavir-boosted PIs and combination hormonal contraceptives (pills, patches and rings) or progestin-only pills, the use of an alternative contraceptive method with dual contraceptive method use is recommended
<b>Comorbid conditions</b>		
Malaria, low nutritional status and advanced HIV disease	Increased risk of anaemia with certain ARVs (e.g. AZT)	Regular assessment of haemoglobin levels at initiation, 1 month, 3 months and then every 6 months or symptomatic
Cognitive impairment due to HIV encephalopathy, longstanding HIV infection	Decreased adherence	Simplified regimens, cognitive age-appropriate education, regimens with a high barrier to resistance
<b>Developmental stage</b>		
Concrete thinking and emotional immaturity	Decreased adherence	Simplified regimens, cognitive age-appropriate education, regimens with a high barrier to resistance

ART = antiretroviral therapy; PHIV = perinatally acquired HIV; AZT = zidovudine; 3TC = lamivudine; ABC = abacavir; ATV = atazanavir; DRV = darunavir; EFV = efavirenz; FTC = emtricitabine; TDF = tenofovir; GI = gastrointestinal; d4T = stavudine; TB = tuberculosis; LPV/r = lopinavir/ritonavir; PI = protease inhibitor.  
\*Adapted from Agwu and Fairlie.<sup>[11]</sup>

periods to try to achieve virological suppression, as PIs have a high resistance barrier and are associated with less accumulation of NRTI resistance mutations even with high VLs >30 000 copies/mL.<sup>[12]</sup> Most patients with virological failure on a boosted PI will resuppress on this regimen with optimal adherence.

Where possible, it may be appropriate to have a specific clinic day with multidisciplinary team support for adolescents with adherence problems, virological failure and resistance.

In some cases virological failure secondary to poor adherence may prove intractable despite adherence interventions, and the resultant immunological and clinical failure could constitute a relative emergency. In such instances a period of inpatient directly observed therapy should be considered to stabilise the adolescent, identify critical clinical, psychosocial and mental health issues, and provide intensive interventions.<sup>[13]</sup> This should only be done in a multidisciplinary team setting in consultation with the adolescent and caregiver.

**Table 4. Strategies to address non-adherence in HIV-infected adolescents**

**Medication-related barriers**

Reduced pill burden (e.g. once daily/fixed-dose combinations)  
 Palatable formulations (liquid, powder, crushing)  
 Management of side-effects  
 Anti-nausea, anti-diarrhoeal agents  
 Change timing of dosing (e.g. night-time dosing)  
 Regimen change

**Patient-related factors**

Disclosure  
 Counselling to deal with loss/trauma  
 Treatment of concurrent psychiatric diagnosis (e.g. anxiety, depression, substance abuse)  
 Education about HIV and benefits of ART

**Behavioural interventions**

Motivational interviewing  
 Counselling, support groups  
 Life-skills education with time-management and prioritisation  
 Parental/caregiver involvement  
 Buddy systems  
 Adherence clubs  
 Peer motivators/educators  
 Activity triggers (e.g. meals)  
 Calendars  
 Technological interventions (e.g. cell phone, SMS texts, watches, beepers)  
 Pill boxes  
 Pharmacy clinic  
 Directly observed therapy

**Structural barriers**

Address barriers such as transportation, insurance, child care, clinic hours  
 Education of clinic staff about cognitive and development stage of adolescents

Adapted from Agwu and Fairlie.<sup>[11]</sup>

**Indications for HIV DRT**

The following are suggested criteria for DRT in adolescents: failing an NNRTI-based regimen

for more than 1 year (although should ideally have been switched to a PI-based regimen earlier); or failing a boosted PI-based regimen (especially with a history of rifampicin-

based tuberculosis (TB) co-treatment). To optimise results, DRT should be done only if VL  $\geq 1\ 000$  copies/mL; and if the adolescent has received ART for at least the past 4 weeks. Unfortunately it may not be possible to ensure adherence, and thus drug pressure, at the time of DRT if the adolescent claims adherence to be good. This will limit the interpretability of DRT as the resistant viral subpopulation may not be at adequate levels required for the DRT. The current DRT and all previous DRTs need to be combined with the treatment history to guide new regimen choices in treatment-experienced adolescents.

**Drug-drug interactions**

Table 6 summarises the most important drug-drug interactions in children and adolescents. It is advisable to consult an up-to-date medicines formulary and available online resources ([www.hivdrug-interactions.org](http://www.hivdrug-interactions.org)) prior to the prescription of any new agent where there is uncertainty about potential drug interactions.

**ART side-effects and toxicities**

Table 7 highlights the most significant side-effects and toxicities in adolescents. The clinician needs to be aware of the risks of using tenofovir in adolescents <15 years of age and <40 kg weight, with a low glomerular filtration rate (GFR) and Tanner staging of  $\leq 3$ . Gynaecomastia, which is common in pubertal adolescent males in general, may be associated with efavirenz; careful management to avoid psychological distress and subsequent adherence problems is required.

**Table 5. Management of VL results in adolescents**

VL	Response
Lower than detectable limit	Congratulations! Adherence support/reinforcement as needed Continue annual VL monitoring
<400 copies/mL	Annual VL monitoring and adherence support
400 - 1 000 copies/mL	Step-up adherence package Repeat VL in 6 months
>1 000 copies/mL – virological failure	Adherence counselling/review Full review of ART history including PMTCT, past regimens (duration and virological response), current regimen duration and response, CD4 <sup>+</sup> count and clinical stage Repeat VL in 3 months <ul style="list-style-type: none"> <li>• If &lt;400, return to routine 6 - 12-monthly monitoring</li> <li>• If 400 - 1 000, continue step-up adherence and repeat VL after 6 months</li> <li>• If NNRTI regimen and VL &gt;1000 despite stepped-up adherence, switch to second-line therapy after adherence ensured</li> <li>• If PI regimen and VL &gt;1 000 but &lt;30 000 despite stepped-up adherence, continue with same regimen while monitoring VL every 3 months</li> <li>• Continue stepping up adherence and consult an expert</li> <li>• If PI regimen and VL &gt;30 000, refer to an expert for further management</li> </ul>

VL = viral load; ART = antiretroviral therapy; PMTCT = prevention of mother-to-child transmission; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor.

**Table 6. Antiretroviral drug interactions for agents commonly used for the management of adolescents living with HIV**

Drug class	Drug	ARV interacts	Effect of interaction	Management of interaction
Antibiotics	Rifampicin	LPV/r	Reduced level of EFV	Superboost with additional RTV, to bring the ratio of LPV:RTV to 1:1 or double the LPV/r dose if RTV not available
		NVP	Cumulative toxicity, may have reduced NVP levels	Avoid concurrent use
	Clarithromycin	EFV	Reduced level of clarithromycin	Avoid concurrent use; consider azithromycin as an alternative
		AZT	Reduced level of AZT if administered together	Give clarithromycin and AZT at least 2 hours apart
	Aminoglycosides	TDF	Cumulative renal toxicity	Avoid concurrent use where possible; monitor renal function and discuss with expert where necessary
Antifungals	Fluconazole	NVP	Elevated NVP levels, may have cumulative hepatotoxicity	Monitor for NVP side-effects
Anticonvulsants	Carbamazepine Phenytoin Phenobarbitone	PIs, NNRTIs	Altered ART drug levels	Valproate/lamotrigine are preferred anticonvulsants in combination with ART
	Valproate	AZT	Increased AZT level	Monitor for AZT side-effects; consider alternatives
Psychotropic drugs	Benzodiazepines (NB midazolam, triazolam)	PIs	Delayed clearance of the benzodiazepine may result in increased sedation	Lorazepam is the preferred agent
	Fluoxetine Paroxetine	PIs	Drug levels may increase to dangerous level	Avoid concurrent use – citalopram preferred.
Contraceptives	Oral contraceptives (COCs, POPs)	PIs, NNRTIs	Contraceptive efficacy may be reduced	Avoid concurrent use. Strongly reinforce condom use and advise on alternative methods (IUCD or injectable)
Others	Warfarin	NNRTIs, PIs	Warfarin level altered	Monitor INR closely and adjust warfarin dose accordingly
	Corticosteroids (NB: fluticasone, budesonide)	PIs	Increased level of corticosteroids	Monitor closely for systemic effects of corticosteroids; consider dose reduction
	Simvastatin and lovastatin	PIs	Increased level – may lead to dangerously toxic levels	Consider substitution with low-dose atorvastatin (in consultation with an expert)
	Ergotamine	PIs	Increased level, may lead to toxicity	Avoid concurrent use
	St John's wort	PIs, NNRTIs	Reduces levels of antiretroviral agents	Avoid concurrent use

ARV = antiretroviral; LPV/r=lopinavir/ritonavir; EFV = efavirenz; RTV = ritonavir; NVP = nevirapine; AZT = zidovudine; TDF = tenofovir; PI = protease inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; COCs = combined oral contraceptives; POPs = progestin-only pills; IUCD = intrauterine contraceptive device; INR = international normalised ratio.

### Disclosure to adolescents

In order to fulfil their developing autonomy adolescents require accurate information regarding their health, including their HIV status. WHO recommends that disclosure occurs before 12 years of age, but this needs to be applied to each individual context.<sup>[14]</sup> Consideration of the maturity and level of insight is essential. A child who enquires about their treatment and their health indicates a desire for further information and a need to start the disclosure process. Disclosure should be complete long before sexual activity begins. Disclosure may result in improved adherence, acceptance of the

diagnosis and improved clinical outcomes.<sup>[15]</sup> Moreover, disclosure of maternal HIV status to the child may strengthen the relationship and build trust between mother and child.<sup>[16]</sup>

Caregivers need supportive counselling in order to prepare them for the disclosure process. Disclosure is not a once-off event, but a process, built on a foundation of health education, aiming to teach the child about maintaining their health, understanding their condition and beginning to take ownership of their own healthcare. Disclosure is never urgent, and is best done by the caregiver after adequate preparation. Many tools are available for facilitating

Table 7. ART-associated side-effects

Adverse event	Associated drugs and causes	Clinical signs and symptoms	Adolescent-specific considerations	Diagnosis	Management
<b>Lipatrophy</b>	Mitochondrial toxicity with inflammatory changes Associated with d4T, ddI, AZT	Loss of subcutaneous fat occurs in all areas of the body, most notable in the face, limbs and buttocks	Body image may be affected by the changes -> negative self-esteem Disfiguring -> affect adherence	Clinical, may be aided by photographs Anthropometric measures impractical	If suppressed VL in past 3 months, switch to either ABC or TDF depending on age, weight and renal function
<b>Lipohypertrophy</b>	Combination of ageing and treatment of HIV Not associated with individual/class ART	Fat accumulation centrally May include buffalo hump	Body image -> negative self-esteem Disfiguring -> affect adherence	Clinical, may be aided by photographs Anthropometric measures are impractical	Little evidence to support drug switches Lifestyle changes (aerobic exercise and healthy diet)
<b>Dyslipidaemia</b> Increased total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL)	PI-based therapy, d4T	Usually asymptomatic, identified on routine monitoring investigations	Future risk for atherosclerosis, and cardiovascular and cerebrovascular disease	Fasting serum LDL and cholesterol are the standard but non-HDL cholesterol possibly more useful The AAP thresholds for interventions LDL >4.9 mmol/L if no known CVD risk factors LDL >4.1 mmol/L for children with 2 or more CVD risk factors	Lifestyle modifications: diet low in lipids, regular exercise, referral to a dietician Switch ART (see above lipatrophy) 6-monthly LDL after intervention If no response, discuss with an expert, consider ATZ for patients on LPV/r <i>Note: The use of statins should be discussed with an expert</i>
<b>Gynaecomastia</b> Growth of breast tissue in male clients	Associated with EFV, mechanism unclear. May be HIV-related. May be normal pubertal development	Lipomastia (fat deposition in the breast region) may be similar in appearance Lipomastia is a manifestation of lipodystrophy Uni/bilateral	Most common cause of gynaecomastia in adolescents is physiological (i.e. puberty)	Clinical Ultrasound may differentiate lipomastia	Observe - may resolve spontaneously If progressive/causing distress, refer to expert care and consider switching EFV to alternative
<b>Renal toxicity</b> Proximal renal tubular toxicity	Associated with TDF	May present acutely (as acute kidney injury, with a reduced GFR) May present as chronic disorder, with proteinuria and glycosuria on dipstick testing, with GFR changes appearing later If patient develops muscle symptoms or weakness, check K <sup>+</sup> and other electrolytes	<i>It is not recommended that TDF be used early in adolescence (avoid use if &lt;15 years of age or &lt;40 kg)</i> Regular urine dipstick monitoring essential for all adolescents receiving TDF Regular creatinine with GFR calculated GFR = (height (cm) x 40)/serum creatinine (µmol/L)	Proteinuria or glycosuria on dipstick are early signs Reduction in the GFR	Abnormal urine dipstick tests or a GFR below 80 mL/min per 1.73 m <sup>2</sup> needs urgent referral for expert review
<b>Bone toxicity</b> Reduced BMD	Lower overall BMD associated with both HIV infection and ART TDF associated with a reduction in BMD exceeding other ART, particularly in combination with PIs	Most adolescents asymptomatic Need to optimise bone health and prevent possible future complications Future risk for osteoporosis Theoretical increased risk for pathological fractures	Use of TDF in early adolescence not recommended (avoid if <15 years or <40 kg) Adolescence is a time of high bone turnover (due to rapid growth), affects measures of serum ALP	On DEXA scanning (seldom done in clinical practice) Clinician to maintain awareness that reduced BMD is possible	General measures to ensure bone health Avoid alcohol and cigarette use Weight reduction if overweight Regular exercise (preferably high impact) Adequate calcium and vitamin D Avoid medications with adverse effects on bone (e.g. NSAIDs and corticosteroids)

ART = antiretroviral therapy; d4T=stavudine, ddI=didanosine, AZT = zidovudine; VL = viral load; ABC = abacavir; TDF = tenofovir; LDL = low-density lipoprotein; HDL = high-density lipoprotein; PI = protease inhibitor; AAP = American Academy of Pediatrics; CVD = cardiovascular disease; LPV/r = lopinavir/ritonavir; ATV = atazanavir; EFV = efavirenz, GFR = glomerular filtration rate; BMD = bone mineral density; ALP = alkaline phosphatase; DEXA = dual-energy X-ray absorptiometry; NSAIDs = non-steroidal anti-inflammatory drugs.

disclosure, including talking books, picture books and comic books, some aimed at educating the adolescent, others guiding the caregiver. Adolescents also require support in connection with disclosing to sexual partners, friends, parents or any other individual, if and when this becomes desirable.

## Transition to adult care

Transition of adolescents from child-focused care to adult-focused care may involve physical transfer to a different clinical space or may be a developmental shift with the adolescent moving from a supported to an independent, autonomous role within the same clinic. Regardless, planning to ensure safe and successful transition is required, as transition may be accompanied by significant anxiety and may result in disruption of care. All adolescents who transition to adult care must have undergone a disclosure process with ongoing support, information and reassurance.<sup>[17]</sup> Full communication to the adult-care practitioner, of all previous medical, sexual and reproductive health and psychosocial history, is essential. Ongoing attention to sexual and reproductive health needs, particularly access to contraception, is important for the transitioning adolescent.

In settings receiving these transitioning youth, familiarity with the complexities of managing HIV-infected youth from a medical and psychosocial perspective, a multidisciplinary team with co-ordination of all aspects of care, and appropriate linkage to other services including sexual and reproductive health services, psychological and psychiatric care are required.<sup>[17]</sup>

In conclusion, although many adolescents living with HIV have good outcomes on ART, adolescence is a high-risk period for non-adherence and associated virological failure. Clinicians need to be aware of adolescent-associated problems, and mechanisms to assist this population with a successful transition to adult care.

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