Adolescents-problem areas

Dr Lee Fairlie
HIV Symposium
9 May 2015
SS

• 17 year old female
• First presentation to care 31/1/2005 (8 years)
• Perinatally HIV-infected
• WHO stage 1; Immunologically stage 3 CD4 198 (11.9%)
• Started D4T/3TC/EFV on 27/5/2005
• Did well initially: remained virally suppressed
• Bloods 8/2/08: VL < 25 copies/ml and CD4 562 (27.4%)
Continued....

Ongoing adherence concerns:
- Living with aunt, mom looking after her ill mother
- Little in way of treatment support
- Only disclosed to when 12y6m

<table>
<thead>
<tr>
<th>Date</th>
<th>Jul 08</th>
<th>Aug 08</th>
<th>Dec 08</th>
<th>Mar 09</th>
<th>Oct 09</th>
<th>Feb 10</th>
<th>May 10</th>
<th>Oct 10</th>
<th>Feb 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>12y4m</td>
<td>12y5m</td>
<td>12y7m</td>
<td>12y11</td>
<td>13y6</td>
<td>13y10</td>
<td>14y1</td>
<td>14y7</td>
<td>14y10</td>
</tr>
<tr>
<td>CD4 #</td>
<td>261</td>
<td></td>
<td>198</td>
<td></td>
<td>247</td>
<td>205</td>
<td>221</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td>CD4%</td>
<td>14</td>
<td></td>
<td>14.6</td>
<td></td>
<td>14.5</td>
<td>12.9</td>
<td>12.47</td>
<td>17.72</td>
<td></td>
</tr>
<tr>
<td>VL</td>
<td>15000</td>
<td>150</td>
<td>37000</td>
<td>18000</td>
<td>25</td>
<td>1800</td>
<td>1200</td>
<td>46888</td>
<td>1577</td>
</tr>
</tbody>
</table>

DRT on 25/08/2008: No resistance detected
Changed to second line 16/3/2011
(ABC/TDF/Aluvia)
True/false

1. As SS had no resistance she should not have switched regimens
2. AZT/3TC & LPV/r would have been a superior choice of 2\textsuperscript{nd} line
3. Adolescents of 12 years and younger can use TDF without any concern
4. TDF can safely be used in pregnant adolescents > 12 years and > 40 kg
On second line....

• Well clinically

<table>
<thead>
<tr>
<th>Date</th>
<th>Oct 11</th>
<th>April 12</th>
<th>June 12</th>
<th>Sep 12</th>
<th>Nov 12</th>
<th>May 12</th>
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<tbody>
<tr>
<td>CD4#</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>167</td>
<td>214</td>
<td></td>
<td>228</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>CD4%</td>
<td>11.9</td>
<td>15.8</td>
<td></td>
<td></td>
<td></td>
<td>11.2</td>
</tr>
<tr>
<td>VL</td>
<td>188</td>
<td>4130</td>
<td>11958</td>
<td>154122</td>
<td>1347</td>
<td>124293</td>
</tr>
</tbody>
</table>

Vomiting and unable to swallow alluvia 200/50, switched to 100/25mg
Ongoing poor adherence and missed appointments
Seen in July 2013

- LMP April 2013
- Pregnant, does not want to explore option of TOP
- O/E HOF about 16 weeks
- Has not taken ART since realized she was pregnant
- Advised by her sister that ART may be harmful to the baby......
Further progress…

<table>
<thead>
<tr>
<th>Date</th>
<th>VL</th>
<th>CD4 (%)</th>
<th>3m: Baby admitted: kwashiorkor, GE, LRTI(diluting formula) PCR negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 Oct 2013</td>
<td>59894</td>
<td>106 (9.9%)</td>
<td></td>
</tr>
<tr>
<td>21 Nov 2013</td>
<td>137025</td>
<td>163 (11.7%)</td>
<td></td>
</tr>
<tr>
<td>23 Dec 2013</td>
<td>135174</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 Jan 2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Mar 2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 Apr 2014</td>
<td></td>
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</table>

- Male infant born
- Birth PCR negative
- Received kal/AZT/3TC
- Booked ANC

- Has defaulted visits again since May
- Changed to combivir and aluvia
- DRT: No resistance detected
Options for contraception in SS are: (choose as many as applicable)

1. CU-IUD
2. COC or progesterone only pill
3. DMP
4. Implanon
5. Condoms
Issues.....

- Teenage pregnancy
- High transmission risk with high VL and low CD4
- ? Resistant virus most likely
- Difficulties with managing these HIV-exposed infants (Maternal VF)
- Failed opportunities for FP
- Disclosure
Why are adolescents different?

- Transition period from childhood to adulthood characterized by physical, psychological, social and emotional maturation
- Changing body
- Changing mind
- Not happening together
- Sexual awakening
- Risk-taking, impetuous
- Autonomy
- Peer influence
- ‘Hot cognition’
A complex set of issues in HIV+

Specific issues in adolescence
- Timing of infection – viral dynamics, exposure to ART
- Effects of infection/ART on developing organs
- Developmental stage – autonomy, risk-taking
- Family structure and stability – orphanhood
- Peer pressure

Developmental outcomes are altered
- ADHD/PTSD
- Learning disorders
- Behavioural issues
- Mental health problems
- Sexual maturity
- Stigma which may be detrimental to identity development

May impact on behaviours in adolescence
- Adherence
- Disclosure
- Substance use, violence
- Sexual behaviour, risk-taking

Secondary transmission
Approaching adolescents...

- Dress down 😊
- Always talk about sex
- Always talk about alcohol/drugs (rock n roll optional!)
- Have no expectations....
- But expect to be surprised
- Give whatever support you can.....you may be this young person’s ONLY role model
Adherence

- Adolescence is increased risk period for poor adherence
- Poor adherence in adolescents not restricted to HIV
- Adherence is the single most challenging aspect of successful HIV care
- Non-adherence may be caused by any combination of structural, patient-related, provider-related, medication-related, disease related and psychologically-related factors
- Adherence is not stagnant and requires continuous reassessment
Factors associated with non-adherence

- Many factors are simple and practical
- Forgetting
- “Reminds me of HIV”
- Wanting a break from ART
- Complications in day-to-day routines
- Pill burden (“too many pills”)
- AIDS diagnosis/Advanced HIV disease
- Advanced age > 15 years
- Depression and PTSD
- Poor self image (stunting)
- Alcohol/substance abuse
- Dropping out of school
- Adverse effects of ART
- Structural barriers such as poverty and stigma
- Poor social support – orphans

MacDonnell *AIDS Behav* 2013; Rudy *AIDS PAT CARE & STDs* 2010; Mills *PLoS Med* 2006
Mechanisms to improve adherence

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<th><strong>Medication-related barriers</strong></th>
<th><strong>Behavioural interventions</strong></th>
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<td>Reduced pill burden (OD dosing, FDC)</td>
<td>Motivational interviewing</td>
</tr>
<tr>
<td>Palatable formulations</td>
<td>Counselling, support groups</td>
</tr>
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<td>Management of side effects</td>
<td>Life skills education</td>
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<tr>
<td>Anti-nausea, anti-diarrhoeal agents</td>
<td>Parental/caregiver involvement</td>
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<td>Change timing of dosing</td>
<td>Buddy systems</td>
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<td>Regimen change</td>
<td>Adherence clubs</td>
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<th><strong>Structural Barriers</strong></th>
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<td>Disclosure</td>
<td>Address barriers such as transportation, child care, clinic hours</td>
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<tr>
<td>Bereavement and trauma counselling</td>
<td>Education of clinic staff</td>
</tr>
<tr>
<td>Treatment of concurrent mental illness</td>
<td>Address stigma and discrimination</td>
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<td>Intensive HIV and ART education</td>
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Resistance

• NNRTIs (NVP and EFV) and lamivudine low genetic barrier to resistance
• Continued failure on this regimen accumulation of resistance to NRTIs
• PI resistance is uncommon and high levels of viremia for prolonged periods before increased resistance
• Need to address adherence issues before any switch to 2\textsuperscript{nd}/3\textsuperscript{rd} line regimens

PENPACT -1 \textit{Lancet Infectious Disease} 2011
Potential solutions

- Need to try and get the non-adherent child and adolescent through with minimal damage!!
- Drug holidays (this may be the worst option immunologically)
- Holding regimens
  - 3TC monotherapy
  - Combination NRTIs
- New regimens (may require access to third line drugs)

Siberry JAIDS 2011; Abadi JAIDS 2006; Fairlie 2013 (unpublished)
Risk-taking behaviour

- PHIV+ mixed findings regarding risky sexual activity and substance abuse
- May delay sexual activity because of concerns regarding HIV, may also be developmentally and neurocognitively delayed
- PHIV+ lower rates of substance abuse and risky sexual behaviour than general adolescent population
- High levels of transactional sex amongst AIDS orphans
- Both groups: those who are sexually active frequently engage in unprotected sex (up to 65%)
- Low rates of disclosure to sexual partners (about a third)
- High risk sexual behaviour and substance abuse associated

Burungi H *AIDS CARE* 2009; Mellins C *AIDS PATIENT CARE and STDs* 2011; Bauermeister J *Sex Res* 2012; Cluver *JAIDS* 2011; Elkington *J Adol Health* 2009; Youth Risk Behaviour Surveillance 2012 *MMWR.*
Pregnancy and SA adolescents

Table 1: Percentage of females aged 13–19 who were pregnant during the year preceding the survey, 2009–2011 (source: Stats South African General Household Survey 2012:18)
Pregnancy rates in adolescent women

• Up to 30% of adolescents in SA report ever having been pregnant

• QA Karim et al: Open cohort recruited from FP and STI clinic for longitudinal HIV risk reduction study 2004-2007; KZN

• 27% of women under 18 years HIV+

• Of HIV-
  
  o Pregnancy rates 23.7 (>18) and 16.4/100wy (<18)
Factors Contributing to teenage pregnancy

Contributing factors

- Poor educational attainment
- Cultural, religious beliefs
- Limited or inconsistent contraceptive use
- Barriers to accessing contraceptives
- Gender norms
- Gender-based violence
- Early marriage
- Sexual activity
- Poverty

Source: Flanagan et al, 2013, Teen pregnancy in South Africa: A literature review examining contributing factors and unique interventions
The law and adolescent sex

Sexual offences act:

• Section 15: criminalises acts of sexual penetration by adults with children between the ages of 12 and 16 years, despite their consent

• Section 16 criminalises sexual penetration between consenting young people between the ages of 12–16 years

• Court case 2013: Teddy bear clinic and partners vs Minister of Justice: “Constitutional Court found that sections 15 and 16 of the Act are unconstitutional in that they infringe the rights of adolescents (12- to 16-year olds) to dignity and privacy, and further in that they violate the best-interests principle”

Children’s Act 2010
CRIMINAL LAW (SEXUAL OFFENCES AND RELATED MATTERS) 
AMENDMENT ACT 32 OF 2007 

* eliminating the differentiation drawn between the age of consent for different consensual sexual acts and providing for special provisions relating to the prosecution and adjudication of consensual sexual acts between children older than 12 years but younger than 16 years;

1. In Teddy Bear Clinic for Abused Children and Another v Minister of Justice and Constitutional Development and Another 2014 (2) SA 168 (CC), ss. 15 and 16 were found to be inconsistent with the Constitution and invalid to the extent that they impose criminal liability on children under the age of 16 years. The declaration of invalidity was suspended for a period of 18 months in order to allow Parliament to correct the defects. A moratorium was placed on all investigations into, arrests of, prosecutions of, and criminal and ancillary proceedings against, children under the age of 16 years in relation to these provisions, pending Parliament's correction of the defects. Furthermore, children under the age of 16 years who have been convicted of an offence referred to in s. 15 or 16, or issued a diversion order following a charge under those provisions, are not to appear in the National Register of Sex Offenders, and are to be issued certificates of expungement.

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The law and contraception

• Adolescents 12 years by law should receive condoms at their request
• Other contraception:
  - at least 12 years of age and
  - proper medical advice is given
  - medical history is taken
  - appropriate examinations
  - ? Medical exclusions
• Right to confidentiality unless concern about physical or sexual abuse, or deliberate neglect
The law and HCT

• Able to consent to HIV testing if:
  • > 12 years old
  • < 12 years old and able to demonstrate sufficient maturity to understand benefit, risks and social implications
• Maturity assessment (*difficult!!!*)
  - Age
  - Knowledge
  - Views
  - Personal circumstances

Children’s Act 2010
Contraception use

- Gaps in the literature regarding pregnancy intentions and contraception
- US-based review article
  - 51% PHIV+ adolescents use condoms
  - Injectables alone 21%
  - Condoms & injectables/oral 16%
  - Overall HIV+ more likely to consistently use contraception compared to HIV- (56% vs. 44%)
  - 83% pregnancies unintended
QA Karim et al:
  - Contraception use 43.8% (6m); 51.6% (12m)
  - Any STI symptoms 11.4% (6m); 9.7% (12m)

Carter et al. AIDS PATIENT CARE and STDs. 2013
58.3% 15-24 year olds using condoms, highest percentage age-wise
What are the barriers to accessing contraception?

- HEALTH CARE WORKER ATTITUDES
- Side effects especially weight gain and mood changes
- Fears of using IUD
- Drug-drug-interactions
- Stopping/irregular periods
- Misinformation or poor education regarding contraception
- Not integrated into HIV care (hospital-based clinics)
Contraceptive options in young women

- WHO:

<table>
<thead>
<tr>
<th>MEC categories for contraceptive eligibility</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A condition for which there is no restriction for the use of the contraceptive method</td>
</tr>
<tr>
<td>2</td>
<td>A condition where the advantages of using the method generally outweigh the theoretical or proven risks</td>
</tr>
<tr>
<td>3</td>
<td>A condition where the theoretical or proven risks usually outweigh the advantages of using the method</td>
</tr>
<tr>
<td>4</td>
<td>A condition which represents an unacceptable health risk if the contraceptive method is used.</td>
</tr>
</tbody>
</table>

MEC = Medical Eligibility Criteria for Contraception

WHO 2014
Summary of recommendations for adolescent contraception

- Abstinence
- Delay sexual debut
- Barrier method (strong reinforcement of condom use) with highly effective contraception:
  - combined hormonal contraception
  - progestogen-only injection
  - Cu IUD
  - LNG-IUS
  - progestogen-only implant
- Emergency contraception to be promoted and accessible in the event of unprotected intercourse, method misuse or failure
## Summary of options for contraception for adolescents living with HIV

<table>
<thead>
<tr>
<th>Method</th>
<th>Common side effects</th>
<th>Common contraindications (not all-inclusive)</th>
<th>Drug interactions: TB Rx</th>
<th>Drug interactions: ART</th>
<th>Prevention</th>
<th>Comment/recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male condom</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
<td>Promote condom use for all adolescents. Consistency, correct use and with confidence</td>
</tr>
<tr>
<td>Female Condom</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td></td>
<td>Promote condom use for all adolescents. Consistency, correct use and with confidence</td>
</tr>
<tr>
<td>CCs</td>
<td>Nausea, intermittent bleeding, mild headaches, breast tenderness</td>
<td>History of thrombosis, hypertension</td>
<td>Rifampicin - do not use together (WHO MEC 3)</td>
<td>RTV-boosted PIs – do not use together (WHO MEC 3) NNRTIs – generally can be used, add condom (WHO MEC 2)</td>
<td>X</td>
<td>Client-dependent contraception: adherence essential. Can be used where adherence ensured. Combine with condom use</td>
</tr>
<tr>
<td>Injectable (DMFP/NET-EN)</td>
<td>Changes in menstruation (irregular, prolonged, heavy, amenorrhoea) and weight gain</td>
<td>Undiagnosed vaginal bleeding</td>
<td>DMFP: none (WHO MEC 1) NET-EN: mild interaction with rifampicin. To add condom (WHO MEC 2)</td>
<td>DMFP: none (WHO MEC 1) NET-EN: mild interaction with PIs and NNRTIs. To add condom (WHO MEC 2)</td>
<td>X</td>
<td>Recent studies have shown that DMFP may increase HIV transmission risk (until further research has been conducted, WHO stance: condom use is strongly recommended (WHO MEC 1). Client-Independent contraception</td>
</tr>
<tr>
<td>Cu IUD</td>
<td>Menstrual changes (bleeding may be heavier, longer and more cramps)</td>
<td>Current AIDS and unwell, current cervicitis/PID</td>
<td>None</td>
<td>None</td>
<td>X</td>
<td>Reliable, long acting reversible contraceptive method. Client-independent method. May be used as emergency contraception. Combine with condom use. Can be inserted if client is well (WHO MEC 2). Note: Unwell HIV positive – WHO MEC 3.</td>
</tr>
<tr>
<td>LNG IUD</td>
<td>Irregular and infrequent bleeding initially with development of amenorrhoea later</td>
<td>Current AIDS and unwell, current cervicitis/PID</td>
<td>None</td>
<td>None</td>
<td>X</td>
<td>Not currently available in the PHC setting. Reliable, long acting reversible contraceptive method, client-independent method. Cannot be used for emergency contraception. Combine with condom use. Can be inserted if well (WHO MEC 2). Note: Unwell HIV positive – WHO MEC 3.</td>
</tr>
<tr>
<td>Progestogen-only implants</td>
<td>Irregular bleeding and amenorrhoea, but less pronounced than with injectables</td>
<td>Undiagnosed vaginal bleeding</td>
<td>Mild interaction with rifampicin. Avoid concurrent use. (See comment)</td>
<td>Mild interaction with PIs and NNRTIs. Avoid concurrent use. (See comment)</td>
<td>X</td>
<td>Note: recent evidence has shown that EFV, rifampicin and certain anticonvulsants should not be used with the implants due to reduced contraceptive efficacy. If already inserted, it may be removed and an alternative method used, or an additional non-hormonal method should be added (such as IUD or condom use).</td>
</tr>
<tr>
<td>Emergency contraceptive pills</td>
<td>Nausea, vomiting, headaches, fatigue, cycle irregularities</td>
<td>Incident occurred more than 120hrs ago</td>
<td>With Rifampicin. No dose adjustment recommended</td>
<td>With PIs. No dose adjustment recommended</td>
<td>X</td>
<td>All clients should be aware of the availability of this method. Consider emergency IUCD use where pill use is inappropriate</td>
</tr>
<tr>
<td>CONDITION</td>
<td>COC</td>
<td>DMPA</td>
<td>Implant</td>
<td>Cu-IUD</td>
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<td></td>
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</tr>
<tr>
<td>Pregnancy</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NC</td>
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<tr>
<td>Breastfeeding</td>
<td>Less than 6 weeks postpartum</td>
<td>6 weeks to &lt; 6 months postpartum</td>
<td>6 months postpartum or more</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postpartum (non-breastfeeding)</td>
<td>&lt; 21 days with other risk factors for VTE*</td>
<td>&gt; 21 to 42 days with other risk factors for VTE*</td>
<td>&lt; 48 hours including immediate post-placental</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTE - deep venous thrombosis (DVT) and pulmonary embolism (PE)</td>
<td>History of DVT/PE</td>
<td>Acute DVT/PE</td>
<td>DVT/PE, established on anticoagulant therapy</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known thrombogenic mutations</td>
<td>History of ischemic heart disease (current or history of) or stroke (history of)</td>
<td>History of deep venous thrombosis (DVT) and pulmonary embolism (PE)</td>
<td>Major surgery with prolonged immobilization</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Known hypertrophic cardiomyopathy</td>
<td>Elevated BP (systolic ≥ 140 - 159 or diastolic ≥ 90 - 99)</td>
<td>Elevated BP (systolic ≥ 160 or diastolic ≥ 100)</td>
<td>Vascular disease</td>
<td>NA</td>
<td></td>
<td></td>
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<tr>
<td>Known hyperlipidemias</td>
<td>Hyperlipidemia</td>
<td>Hyperlipidemia</td>
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Emergency contraception

- Need to inform adolescents that this is an option for them
- CU IUD: Inserted within five days of unprotected intercourse, most effective form of emergency contraception available
- Emergency contraceptive pill: one dose of levonorgestrel 1.5 mg, taken within five days (120 hours) of unprotected intercourse
- Opportunity for intervention: unprotected intercourse/misuse or failure contraception or sexual assault
Specific points.....

- Concern regarding EFV and Implanon-> may be up to 12 % reduction in efficacy
- PI and COC
- With CU IUD, increased bleeding, may be increased risk factor for transmission of HIV
- DMPA may increase risk of HIV acquisition
- WHO:

  “Given the importance of this issue, women at high risk of HIV infection should be informed that progesterone-only injectables may or may not increase their risk of acquisition.”

WHO 2014 updates
Adolescents and PMTCT

• Horwood et al:
  o HIV prevalence, health care usage (ANC&PNC) women age 12-39 attending 6 EPI clinics in KZN
  o Adolescent women compared to over 20 years
  o Higher numbers adult women reported being HIV+; having a CD4 count done; receiving the result and access to PMTCT
  o Higher transmission rate in adolescent mothers: 10.8% vs 6.1%
  o Worrying: this despite adolescent mothers being as likely as adults to attend 4 clinic visits

= SYSTEM FAILING YOUNG HIV+ MOTHERS AND THEIR CHILDREN
Potential impact of risky sexual behaviour

• Recent study PHIV+
  – 28% reported sexual intercourse; median age of coitarche of 14 years; 62% reported unprotected sexual intercourse, and only 33% of youth disclosed their HIV status to their partners
  – For those not sexually active at baseline ART non-adherence was associated with sexual debut
  – Genotypic resistance in the 42% of sexually active youth with viral loads ≥5,000 copies/mL, identifying 62%, 57%, 38%, and 22% to NRTIs, NNRTIs, PIs, and all 3 ARV classes, respectively
  – Concern for secondary transmission (horizontal and vertical) multi-resistant HIV

Tassiopoulos CID 2013
STI management

• Syndromic approach: WHO/local guidelines
• Opportunity for education regarding STI and prevention (including HIV)
• Opportunity for HIV testing
• Opportunity to offer contraception and re-enforce condom use
• Offer treatment of current sexual partner
• Need to handle sensitively
# STI: Syndromic Approach

<table>
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<td>• Male urethritis syndrome</td>
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<tr>
<td>• Genital ulcer syndrome</td>
<td>• Candidiasis/bacterial vaginosis</td>
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<td>• Scrotal swelling/pain</td>
<td>• Lower abdominal pain</td>
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<td>• Balanitis/balanoposthitis (BAL)</td>
<td>• Genital Ulcer Syndrome</td>
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<tr>
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Pre-and post exposure prophylaxis

• PrEP studies have not included adolescents because of issues around consent

PEP:
• Offer post a sexual assault
• Offer to the partner of a discordant couple if burst condom or unprotected sex
• Follow PEP guidelines
Conclusions

• Adolescents are sexually active and need full access to SRH services
• This requires youth friendly services and the correct attitude from HCW
• Many contraceptive options available
• Recognise and treat STIs
• Beware the contradictions in the law!
The special needs of HIV-infected adolescents

- Simplification of ART as far as possible
- Addressing adherence and other risk-taking behaviour
- Assistance with disclosure both to and by the adolescent
- Support for sexual and reproductive health issues especially regarding contraceptive use and safer sex practices
- Support for mental health issues including unresolved grief, depression, anxiety, ADHD, PTSD and substance abuse
- Facilitation of psychometric testing where necessary to ensure appropriate education
- Transition to adult care
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