

Contraceptive Options for HIV+ Women

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Presenter

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Learning Objectives

- At the conclusion of this presentation, you should be able to:
- prescribe the most appropriate contraception for your HIV + patients
- discuss contraceptive options with your HIV+ patients

Off Label Disclosure

- This presentation will not discuss any non-FDA-approved or investigational uses of any products/devices.

Contraception

Contraceptive Use Among US Women with HIV (Massad et al. *J Women's Health* 2007;16:657)

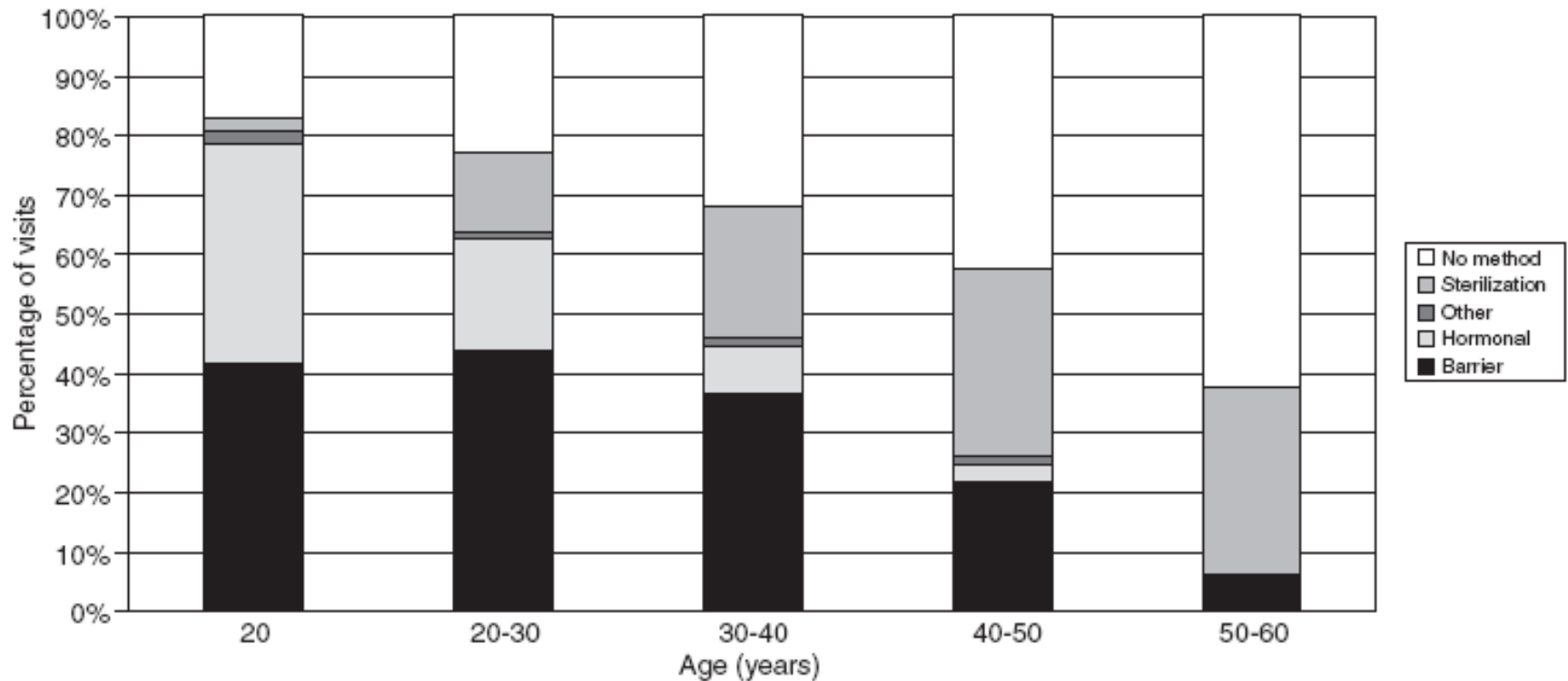


FIG. 2. Changes in contraception use with age among women with HIV at risk for pregnancy.

CASE

- Donna, is a G₁P₁, 21 year old diagnosed with HIV 10 months ago during her pregnancy.
- Her current CD₄ count is 342/19%, VL <26,500.
- She had been on lopinivir/ritonavir, epivir, and retrovir during her pregnancy but stopped post partum due to “the demands of having a newborn”.
- She requests to restart ART – and wants “the one pill a day regimen” that she has heard about “since it is so easy”.

CASE

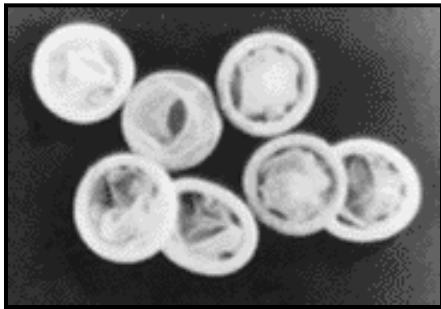
- Her partner is HIV-, he is aware of her status
- Condoms are used inconsistently.
- She had been on the nuva ring for one year prior to this pregnancy, however, she “ran out” 3 months prior to this pregnancy.
- She would like to start contraception, but is unsure which is the best method.

CASE

- You recommend testing her partner and offer an apt for him to come to your clinic.
- You plan to start ART and want to explore BC options with Donna.

The Case For Dual Method Use

- HIV+ women more likely than HIV- women to use dual methods simultaneously: (odds ratio, 2.7)
 - no alcohol use was associated with increased dual method use
- Reliance on condoms as a primary contraceptive method may increase risk of unintended pregnancy



Images courtesy of Jhpiego, an affiliate of The Johns Hopkins University. Heard I et al. *J Acquir Immune Defic Syndr.* 2004;36:714-720.

Wilson TE et al. *Sex Transm Dis.* 2003;30:809-812.

Contraception Considerations in HIV Women

- Efficacy
- Safety
- Adverse effects
- Effect on HIV progression
- Effect on HIV transmission
- Drug interactions
- Convenience/ease of use

Efficacy

- Condoms alone have higher failure rate in prevention of pregnancy with typical use than most other methods of birth control
 - Typical failure rate in first year of use: male condom (15%); female condom (21%)
- COC (8%); DMPA (3%); transdermal patch (8%); vaginal ring (8%); LNG-IUD–5 year (0.1%)
- Diaphragm (+spermicides) (16%)
- Spermicides (29%)
- Sterilization: female (0.5); male (0.15%)

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Safety

- Risk of birth defects with conception on **efavirenz (EFV)**-containing regimens
 - FDA pregnancy category D
 - Teratogenic in primates
 - Retrospective case reports of CNS defects in infants of women who received EFV at conception and during the first trimester
 - EFV should be avoided during the first trimester, and in women at risk for becoming pregnant
 - Pregnancy should be avoided in women receiving EFV
- Sufficient first trimester exposures to ART (excluding EFV) to detect 2× increase in defects have shown no increase in defects.

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Adverse Effects

- Possible negative impact on adherence to ART with use of oral contraceptives
 - Adverse effects: nausea
 - Pill burden
- Alternate routes of delivery – hormonal BC
 - Injectable (DMPA)
 - Implant (3 yr)
 - Transdermal patch (1 wk)
 - Vaginal ring (3 wk)
 - Intrauterine system (5 yr)

Metabolic Dysregulation: ART and HC

- Decreased BMD: both ART and DMPA
 - Few reported cases of fractures from both groups
- Lipid dysregulation:
 - Estrogen increases HDL and VLDL
 - Progestins decrease HDL, may increase or decrease triglycerides
- Glucose metabolism and insulin resistance

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HIV Progression

- HIV progression: conflicting data regarding CD₄ cell decline
- No evidence to date of significant effect on HIV-RNA
- Most women in studies not on ART

Use of Hormonal Contraception Does Not Affect HIV Disease Progression in 4,530 Women in MTCT-Plus

Stringer E et al. 16th CROI, Montreal, Canada Feb 2009 Abs. 175

	No/ Non-Hormonal	Injectable/ Implant	OCP
Number women	3,099	830	226
CD ₄ at Entry	432 (281-627)	418 (264-618) (p=0.25 vs no)	415 (257-605) (p=0.43 vs no)
Death and/or Becomes Eligible for ART			
Adjusted HR* (95% CI)	1.0	1.0 (0.8-1.2)	0.9 (0.8-1.1)
Time-Varying HR* (95% HR)	1.0	0.9 (0.6-1.2)	0.8 (0.6-1.1)

*Adjusted for age, parity, WHO stage, CD4 count, BMI, Hb, condom use, site

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Effect on HIV Transmission

- HC HIV Study:
 - Showed no impact of OCP or DMPA on acquisition of HIV
- Mombasa Sex Worker Cohort:
 - In a cohort of HIV- sex workers, DMPA and OCP had an increased risk of HIV acquisition

Watts DH et al. *Contraception*. 2008;77:84-90.

Morrison CS et al. *Sex Transm Dis*. 2007;34:11

Morrison CS et al. *Hormonal Contraception and HIV: An Update*. August 2004.

Baeten et al. *CID*;45:360-69,2007

HC and HIV Shedding

- Any type of HC had increase in CVL shedding
- 1993: HC compared to no HC showed increased risk of shedding
- Compared shedding with DMPA/, Low dose OCP/, and High dose OCP
 - Dose response with shedding with high dose OCP

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Interactions PIs and OCP

ARV	Effect on EE/NE	Recommendation
Atazanavir	↑ EE 48% ↑ NE 110%	Alternative methods or use back up
Darunavir/ rtv	↓ EE	Alternative methods or use back up
Fos-amprenavir	↑ EE levels APV 20%	Do not co-administer
Indinavir	↑ EE 24% ↑ NE 26%	No change
Lopinavir	↓ EE 42%	Alternative methods or use back up
Nelfinavir	↓ EE 47% ↓ NE 18%	Alternative methods or use back up
Ritonavir	↓ EE 40%	Alternative methods or use back up
Saquinavir	No data	No data
Tipranavir	↓ EE 50%	Alternative methods or use back up

Interactions: NNRTI and OCP

ARV	Effect on EE	Recommendation
Nevirapine	↓ EE 20%	Alternative methods or use back up
Efavirenz	↑ EE 37%	Alternative methods or use back up
Etravirine	↑ EE 22% No change NE	Dose unchanged

Drug Interaction Studies: ART and Hormonal Contraceptives

Slides by Dr. Jean Anderson

Drug	Hormonal Contraceptive	N	AUC	Limitations
SQV 600 mg × 2 (HGC)	EE 30 µg	8	No effect on SQV level	Effect on HCG levels not assessed; study doses nonstandard; no studies with new SQV tablet or with RTV boost
TDF 300 mg once daily	EE 35 µg/norgestimate 0.18, 0.215, 0.25 mg	20	Unchanged	Study doses unclear or nonstandard
TPV/r 500 mg/100 mg twice daily	EE 35 µg/NE 1 mg	21	Decreased EE, NE unchanged	Steady-state not likely reached; study doses unclear or nonstandard

HGC = hard gel capsule; TDF = tenofovir DF; SQV = saquinavir; TPV/r = tipranavir boosted with ritonavir.
 El-Ibiary et al. *Eur J Contracept Reprod Health Care*. 2008;13:123-132.

Drug Interaction Studies: ART and Hormonal Contraceptives

Slides by Dr. Jean Anderson

Drug	Hormonal Contraceptive	N	AUC	Limitations
Maraviroc 100 mg twice daily	EE 35 µg/LNG 150 µg	15	Unchanged	Study doses not standard
NFV 750 mg every 6 hours	EE 35 µg/NE 0.4 mg	12	Decreased EE and NE	Study doses unclear/nonstandard
NFV 1250 mg twice daily or 750 mg every 8 hours	DMPA	21	Unchanged MP, NFV; ovulation suppressed	Other medications in study
NVP 200 mg twice daily	DMPA	16	Increased NVP; no change MP	Other medications in study
NVP 200 mg once daily then 200 mg twice daily	EE 35 µg/NE 1 mg	10	Decreased EE and NE	Steady-state not likely reached; study details unclear
RTV 500 mg twice daily	EE 50 µg	23	Decreased EE	Steady-state not likely reached; study doses unclear

Drug Interaction Studies: ART and Hormonal Contraceptives

Slides by Dr. Jean Anderson

Drug	Hormonal Contraceptive	N	AUC	Limitations
APV 1200 mg twice daily	EE 35 µg/ NE 1 mg	10	Decreased EE; increased NE; 20% decrease APV	No studies with RTV boost
ATV 400 mg once daily	EE 35 µg/ NE 0.5-1 mg	19	Increased EE 48% and NE 110%	No studies with RTV boost; steady-state not likely achieved
EFV 400 mg once daily	EE 50 µg	13	Increased EE 37%	Study doses unclear/nonstandard
EFV 600 mg once daily	DMPA x 12 wk	17	Unchanged MP, EFV; ovulation suppression	
IDV 800 mg every 8 hours	EE 35 µg/ NE 1 mg	?	Slightly increased EE and NE	Study details unclear
LPV/r 400/100 mg twice daily	EE 35 µg/ NE 1 mg	12	Decreased EE and NE	Study details unclear

APV = amprenavir; ATV = atazanavir; AUC = area under the concentration-time curve; EE = ethinyl estradiol; IDV = indinavir; LPV/r = lopinavir/ritonavir; MP = medroxyprogesterone; NE = norethindrone. El-Ibiary et al. *Eur J Contracept Reprod Health Care*. 2008;13:123-132.

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Spermicides



- Possible increase in mucosal irritation and genital ulcers, especially with frequent use
- UNAIDS clinical trial in Africa and Thailand found significantly higher HIV seroconversion rates in nonoxynol-9 users

Safety of DMPA with HIV

- Women with HIV/AIDS can use without restrictions
- No evidence of decreased efficacy of DMPA with ART
- Dual method use should be encouraged
- May consider Implanon

Safety and Tolerability of DMPA Among HIV+ Women on ART: ACTG A5093

- 70 HIV+ women on ARV or no ARV given DMPA and followed for 12 weeks for adverse events, changes in CD₄ and VL, and ovulation
- No changes in CD₄ or VL with DMPA
- No ovulation detected
- Clinical profile similar to that in HIV- women
- DMPA safe to use by HIV+ women on ARV

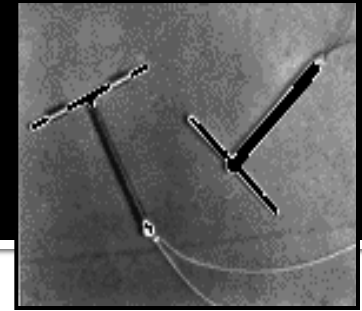
IUD: WHO, 2004

- Safe for majority of women with HIV
- IUD not associated with increased risk of HIV acquisition
- IUD not associated with increased transmission of HIV to sexual partners
- No increased risk of infectious complications; women with AIDS not on ARV therapy should be closely monitored
- Dual method use should be encouraged

IUDs vs Hormonal Contraception

- 599 PP women in Zambia randomly assigned IUD or hormonal contraception
- Women on HC were more likely to become pregnant (4.6/100 vs 2.0/100)
- PID 1 with IUD, 0 with HC (NS)
- Clinical disease progression determined by death or CD4 drop < 200
 - HC (13.2/100 woman-yrs)
 - IUD (8.6/100)

IUD Safety



- LNG-IUD: Significant reduction in menstrual blood loss and increase in hemoglobin and ferritin levels; serum E2 levels remained in follicular range; genital HIV shedding was not affected; levels of LNG similar with and without HAART (n = 12)¹
- Increased menstrual flow (up to 35%) and duration potentially increase transmission risk and risk of anemia (Cu-IUD), but in study of 563 serodiscordant couples, IUD use not associated with increased risk of transmission by males or females²

1. Heikinheimo O et al. *Hum Reprod.* 2006;21:2857-2861.

2. No authors listed. *BMJ.* 1992;304:809-813.

Diaphragm: No Added Protective Benefit

- MIRA trial: 2003-2005 in South Africa and Zimbabwe
- Control group condoms only; intervention diaphragm and condoms
- Results: No added protective benefit of diaphragm and lubricant gel in addition to male condoms.
 - Incident of HIV was same
 - However, in those who used diaphragms only, no increased incidence of HIV seen.

Emergency Contraception

- Should be considered when there is an episode of unprotected intercourse or broken condom
- Combined oral contraceptive pills with EE and norgestrel or LNG reduces pregnancy by at least 74%
 - Plan B: LNG 0.75 mg × 2 (12 hours apart)
 - Preven: EE 50 µg/LNG 0.75 mg × 2 (12 hours apart)
- Take within 72 hours
- No STI/HIV protection

Emergency Contraception

- EC should be provided to all HIV-infected women and their partners who are of childbearing potential.
- Special attention to the following groups:
 - Those who rely on condoms as primary contraceptive method
 - Those who are taking efavirenz or other agents with teratogenic potential
 - Those who are participants in clinical trials that advise subjects to avoid pregnancy

Review of Contraceptive Choices

Contraceptive	Interaction with ART	VL shedding	HIV acquisition	HIV progression
OCP	May affect EE	Some affect with high dose OCP	No increase	No affect
DMPA	None	No increase	No increase	No affect
IUD	None	No increase	No increase	No affect

CASE

- Donna opts for DMPA. If she is happy with this method she may choose to have Implanon inserted.
- Her partner tests HIV -. He does not want to use condoms. She agrees to try using female condoms.
- You discuss with her the risk of transmission and agree to revisit this at her next visit.

Conclusions

- Condoms condoms condoms used with all forms of contraception
- All forms of contraception should be offered and available to HIV+ women.
- HIV+ women should have the same access to reproductive options as uninfected women

Establishing Linkages

HIV → FP/ FP → HIV

Why are Linkages Important

- HIV integration in FP / FP integrated into HIV:
 - Normalizes and promotes testing
 - Decreases stigma
 - Allows prevention messages
 - Links newly diagnosed persons into HIV care
 - decreases M&M
 - Decreases transmission
 - Perinatal
 - Partner

Public Health Responsibility: the Broader Picture

- Provide prevention in FP clinics (primary prevention)
- Provide prevention in HIV clinics (secondary prevention)
- Prevent new transmissions to infants and partners:
 - partner testing
 - treatment of STDs
 - contraceptive availability
 - planned pregnancy
 - provision of barrier techniques

Model of Care in an HIV Clinic

- Integrate on-site Title X family planning services
- Become a Center of Excellence for HIV+ Women
- Integrate on-site GYN and colposcopy services
- Co-manage pregnant women with OB/GYN
 - HIV specific childbirth classes
- 0% Perinatal Transmission Campaign
- Secondary prevention programs
- Linkage with FP clinic if unable to provide FP services

Every Woman, Every Visit

- Ask about pregnancy intentions *every woman, every visit*
- Integrate family planning services into HIV clinics.
- Develop referral relationship with local family planning clinics
- Provide HIV testing for all partners

Great Communication with Good Science Promotes Excellent Outcomes

The next step is yours.. engage women living with HIV in options-based dialogues because together you can create healthy women, healthy children, and healthy communities.

We are counting on YOU!

Ebony Johnson: Community Advocacy,
Education & Empowerment Specialist