

Patient Case Studies

**Adapted from 1917 Case Conference
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History

- **46 yo AAM with advanced AIDS diagnosed in 11/08 after presenting to the ER with fever, productive cough, chest pain, and pancytopenia**
 - **Presented to multiple places for care**

History

- **Patient started on Atripla during initial 11/08 hospitalization + adherence**
 - **1/09 admit dx and Rx HIV aphthous esophageal ulcerations with weight gain**

History

- **PMH**
 - **AAA**
 - **(L) iliac and common femoral vein thromboses, on coumadin Rx**
- **PSH**
 - **IVC placement**
 - **AAA repair with graft 3/09**

History

- **SHx**
 - **3 lifetime sexual partners (all women)**
 - **3 children from previous marriage; aged 19, 21, and 23**
 - **Remarried 3/08, works at Mercedes plant supply department**

History

- **Unprotected intercourse with current wife prior to HIV diagnosis**
 - **No seroconversion in HIV negative wife**
- **Not currently sexually active, but frequently requests viagra during clinic visits**

History

- Labs
 - CD4
 - 11/98: 1
 - 9/09: 133 on Atripla
 - VL
 - 11/08: 775,000
 - 9/09: <48 on Atripla

Questions

- The HIV negative wife of the HIV+ patient asked
 - “How can we safely try to conceive to have a baby?”
 - “We had sex before his HIV was diagnosed, so it’s OK for us to try now that I’m on HAART?”

Questions

- Wife’s gynecological history
 - Normal menses at age 43
 - One previous pregnancy that ended in miscarriage at 9 weeks when she was younger

How Do You Address Reproductive Issues in HIV-serodiscordant Couples Wishing to Conceive?

Background

- We have established that the life expectancy of HIV positive patients continues with the use of ART
- A large proportion of HIV-positive adults are of reproductive age
- Many serodiscordant couples are reconsidering parenthood as an option

Background

- If couples do not receive sufficient information on reproductive options to reduce viral transmission risk, the use of preventive barrier methods may decrease

Considerations

- Are you dealing with an
 - HIV discordant couple where the male is infected, OR
 - HIV discordant couple where the female is infected, OR
 - HIV concordant couple (both are infected)
- Possible therapeutic options differ and opinions on best treatment strategies differ as well

HIV-discordant Couple, Male Infected

- The female partner of an HIV infected male runs a 0.1-0.2% risk of acquiring HIV in an act of unprotected sex
 - The risk of transmission is not zero if HIV-infected male is undetectable on HAART

HIV-discordant Couple, Male Infected

- Options available to prevent transmission to uninfected female partner
 - Insemination using donor (HIV neg) sperm
 - Adoption
 - Sperm washing

Sperm Washing

- HIV is present in semen as free virus in the seminal plasma and as cell-associated virus in the non-sperm cells
- It is still controversial whether HIV is able to attach or infect spermatozoa, although most evidence indicates that this is not the case

Sperm Washing

- Sperm washing involves
 - Centrifuging the semen to separate motile, HIV free sperm from the infected seminal plasma and non-sperm cells
 - The remaining sperm pellet is then re-suspended in fresh medium and centrifuged twice before preparation for a final swim-up

Sperm Washing

- Requires a separate laboratory facility within specialty OB-GYN reproductive endocrinology centers to prevent contamination of other HIV negative clinical specimens
 - UAB doesn't have this

Clinical Work-Up

- Before proceeding with sperm washing and assisted reproductive techniques, couples should receive counseling
 - Description and risks associated with sperm washing
 - Impact of possible treatment failure

Clinical Work-Up

- Coping with the possibility of becoming a single parent when one parent is HIV positive and subsequently expires
- In addition, a sexual health screen and fertility screen of both partners should be performed
 - HIV testing of the partner

Clinical Work-Up

- Screening for evidence of any genital lesions
- Semen analysis
- Female endocrine profile to ensure female partner fertility
- Non-invasive test of tubal patency

Assisted Reproductive Techniques

- IUI (intrauterine insemination)
 - Most common method
 - Performed in those couples without significant fertility issues
 - Outcome improved if VL is undetectable and patient is receiving HAART

Assisted Reproductive Techniques

- IVF (in vitro insemination) and ICSI (intra-cytoplasmic sperm injection)
 - Performed when the fertility screen reveals anovulations, tubal blockage, or suboptimal semen analysis
 - Significant cost difference when compared to IUI as well as increased risks

Evaluation of Sperm Washing as a Potential Method of Reducing HIV Transmission in HIV-discordant Couples Wishing to Have Children

Louise U. Kim, Mark R. Johnson*, Simon Barton†, Mark R. Nelson‡, Glenn Sontag†, J. Richard Smith*, Frances M. Gotch, and Jill W. Gilmour

Sperm Washing Evaluation

- Evaluated amount of HIV viral RNA present in each component of semen (seminal plasma, NSC, sperm) and compared it to plasma viral loads
- Also evaluated the possibility of sperm infection by checking for HIV receptors

Sperm Washing Evaluation

- Findings
 - No detection of CD4 or CCR5 receptors on spermatozoa
 - Low expression of CXCR4 receptors on spermatozoa
 - Spermatozoa were negative for viral RNA and proviral DNA

Sperm Washing Evaluation

- There was poor correlation between the viral load found in semen and that found in peripheral blood
- Although this correlation was low, it is still recommended that patients receive ART prior to participating in this type of program

Sperm Washing Evaluation

Table 1. Viral load in semen and blood

Patient number	Date of diagnosis	Treatment	CD4 (no. cells μl^{-1})	Blood plasma (copies ml^{-1})	Seminal fluid (copies ml^{-1})	Seminal plasma (copies ml^{-1})	NSC (no. cells)	Spermatozoa (no. cells)
1	1.8.91	d4T, lamivudine, zidovudine, zalcitabine, zalcitabine	425	150	LDL	LDL	LDL (10^6)	LDL (10^6)
2	1.1.86	d4T, lamivudine, zalcitabine, zalcitabine	786	LDL	LDL	LDL	LDL (5×10^5)	LDL (6×10^5)
3	1.1.86	NI	187	8300	LDL	LDL	LDL (10^6)	LDL (1×10^6)
4	1.3.85	ZDV, lamivudine, didanosine, zalcitabine	279	LDL	LDL	LDL	LDL (5×10^5)	LDL (5×10^5)
5	1.1.93	ddl, lamivudine, zidovudine, zalcitabine	131	380 000	LDL	7600	LDL (5×10^5)	LDL (4×10^5)
6	21.3.89	d4T, lamivudine, zalcitabine, zalcitabine	369	1500	5000	LDL	LDL (10^6)	Invalid
7	1.1.94	NI	93	400 000	11 000	5200	1700 (3×10^5)	LDL (10^6)
8	1.8.89	ZDV, ddl	364	8600	21 200	2080	780 (5×10^5)	LDL (6×10^5)
9	15.1.92	d4T, lamivudine, didanosine, zalcitabine	187	1200	56 000	2000	24 000 (5×10^5)	LDL (5×10^5)
10	9.8.94	ddl, d4T, nevirapine	247	69 000	176 000	68 000	54 000 (10^6)	LDL (10^6)
11	6.6.94	ddl	281	200 000	200 000	68 000	LDL (10^6)	LDL (6×10^5)

Whole semen was separated into its cellular components and the level of viral RNA determined by NucliSens. All samples were successfully amplified except the spermatozoal fraction for patient 6, which inhibited the amplification (two tests). A number of samples were tested on more than one occasion resulting in comparable values.

Safety and Efficacy of Sperm Washing in HIV-1-serodiscordant Couples Where the Male Is Infected: Results From the European CREAThE Network

Louis Bujana, Lital Hollanderb, Mathieu Couderta, Carole Gilling-Smith, Alexandra Vucetichb, Juliette Guibertd, Pietro Vernazzae, Jeanine Ohlf, Michael Weigelg, Yvon Englerth and Augusto E. Sempriniib, for the CREAThE network

Safety and Efficacy of Sperm Washing

- CREAThE network is the Centre for Reproductive Assisted Techniques for HIV in Europe
- This retrospective study: 8 centers in 6 European countries to study the safety and efficacy of assisted reproduction with sperm washing

Safety and Efficacy of Sperm Washing

- Information obtained from each couple
 - Variables of the man's HIV infection
 - Age of the woman at the time of treatment
 - Past gynecological history

Safety and Efficacy of Sperm Washing

- The possible assisted reproductive techniques were
 - IUI (intrauterine insemination)
 - IVF (in vitro insemination)
 - ICSI (intra-cytoplasmic sperm injection)
 - FET (frozen embryo transfer)

Safety and Efficacy of Sperm Washing

- HIV screening was performed at the time of the procedure and 6 months after the last assisted treatment for all HIV negative female partners
- 1036 couples participated in 3390 assisted reproductive techniques

Safety and Efficacy of Sperm Washing

Table 2. Results of assisted reproduction attempts according to the different procedures used.

Procedures	IUI	IVF	ICSI	FET	Total	p ^d
Couples	853	76	262	40	1231*	
Cycles	2840	107	394	49	3390	
Pregnancy per cycle (%) ^b	15.1	29.0	30.6	20.4	17.5	<0.001
Multiple pregnancy rate (%)	4.9	17.2	20.8	20.0	9.12	<0.01
Delivers per cycle (%) ^c	11.5	20.8	15.8	14.3	12.3	<0.05
Pregnancy per couple (%)	42.7	38.2	43.1	25.0	41.9	>0.05
Delivery per couple (%)	35.1	26.3	21.0	17.5	30.9	<0.01

FET, frozen embryo transfer; ICSI, intra cytoplasmic sperm injection; IUI, intra-uterine insemination; IVF, in-vitro fertilization.
 *The total was over 1036 couples as a couple could have different assisted reproduction procedures (for example four IUI + two IVF).
^bMissing information in 66 IUI and seven IVF cycles.
^cMissing information in 91 IUI, 11 IVF and 40 ICSI cycles.
^dP-value for comparison between procedure groups.

Safety and Efficacy of Sperm Washing

- 580 pregnancies (47 cases with unknown outcome)
- 533 pregnancies resulted in 410 deliveries (80%), resulting in 463 live births
- 967 women had negative HIV tests 6 months after their last assisted reproductive technique

Other Considerations

- Until recently, the American Society of Reproductive Medicine did not advise the use of assisted reproductive techniques or sperm washing in HIV infected patients
- The majority of studies and literature available has been performed in Europe (primarily Italy and the UK)

Other Considerations

- **Risk of cross-contamination to uninfected samples from HIV negative patients or to healthcare workers is increased when samples are handled in the same lab**
- **It is recommended that there be a separate lab to perform these procedures within the facility**