Société de Médecine de la Reproduction

"Comment optimaliser la FIV jusqu'au transfert de l'embryon"

FERRING

La FIVATE dans le cadre des risques viraux

Clínica EUGIN Ginecologia i Reproducció www.eugin.net

CLÍNIC BARCELONA Hospital Universitari

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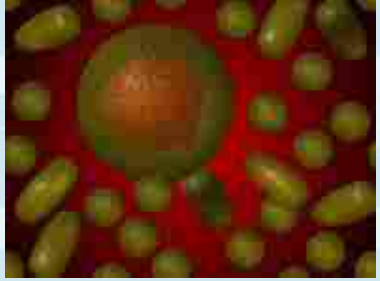
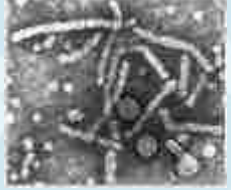
Différents aspects

- Médicaux
- Microbiologiques
- Laboratoire PMA: besoins structurels
- Formation du personnel
- Éthiques (différents selon les pays)

Différents aspects

- Diagnostique (dépistage) de la femme et du partenaire
- Risques pour
  - L'embryon
  - Grossesse
  - Partenaire
  - Health care workers
- Guidelines

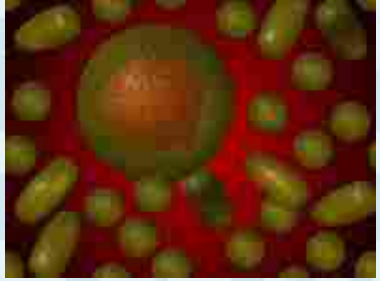


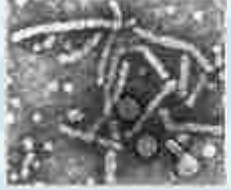


Hépatite B

Prévalence	%
• Europe et USA	2
• Europe de l'Est et Amérique Latine	2-7
• Afrique et Asie	7

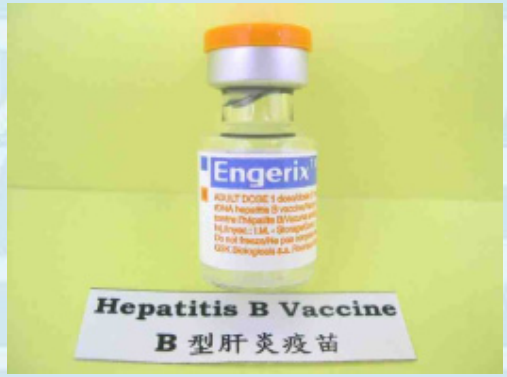
- Diagnostique. HBsAg. DNA (> 10^4 c/mL)
- Infectivité
- Risques transmission mère enfant
  2-15% à 80-90%





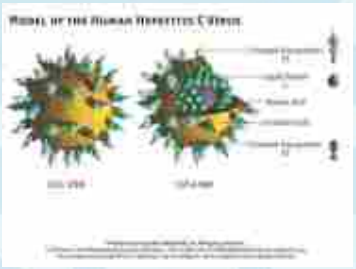
Hépatite B

Vaccin



Prévention

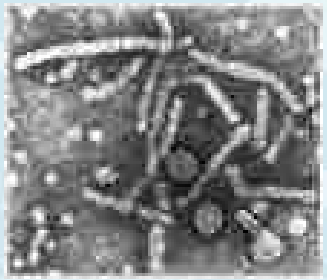
- **« Health care workers »**
- **Noveaux-nés**

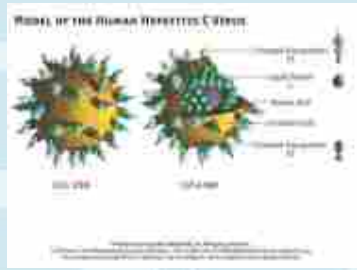


Hépatite C

Prévalence	**1-2 %**
Transmission	
Horizontale	
Mère enfant	**5% (Si VIH: 15%)**
Diagnostique	
Anti-VHC	
PCR (quantitative)	
Thérapie (IFN-α / Ribavirine)	
Efficacité / risques	

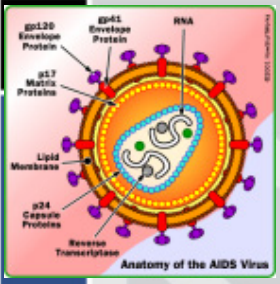
Hépatite B, C





Impact FIV?

Impact grossesse?



VIH

Épidémiologie France

Impact age reproductive

Risque transmission mère enfant:

(Historique: 15-45% Présent: 1-2%)

(Univ. De Barcelone >11/98: 0/214)

Thérapies: ARV. HAART

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VIH. Buts de la thérapie

Reconstitution du système immunitaire ➡ augmentation CD4

Diminution RNA viral

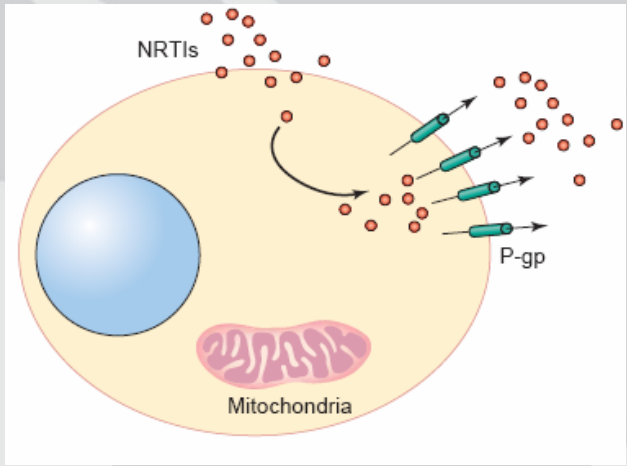
Diminution infections opportunistes

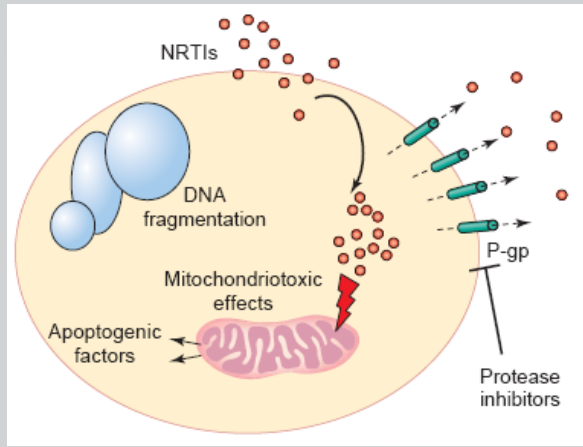
⇩ ⇩

Maladie chronique

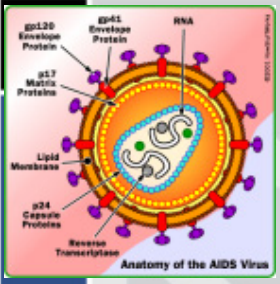
Toxicité

Toxicité





- Neuropathie périphérique
- Cardiomyopathie
- Stéatose / Insufisance hépatique
- Lypodistrophie
- Acidose lactique



HIV and fertility

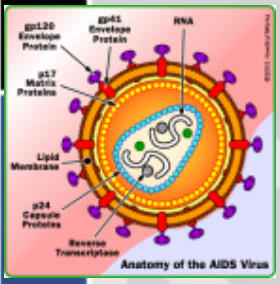
HIV-infected women may have a ↘ fertility rate

Developed countries with HAART? (↘ conception risk and ↘ abortions?)

Association menstruation disturbances with low CD4.

Risk of upper genital tract infections X 10 (and sequelae).

Ovarian dysfunction has been described



VIH

Cohorte couples avec femme VIH: 130

- <u>Hystérographie avec obst. tubaire</u>

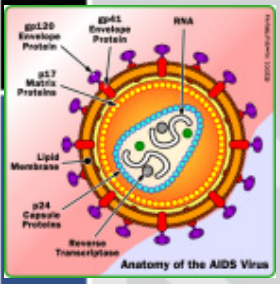
  Total 38,9%

  Sans antécédents 23,4%

Autres: « normaux » (bilan de base…)

- <u>Spermogramme anormal</u>

	VIH (N=24)	NON VIH (N=60)	OR (95% CI)
Astenospermie	17 70,8%	24 40%	6,64 (1,2-11,5)



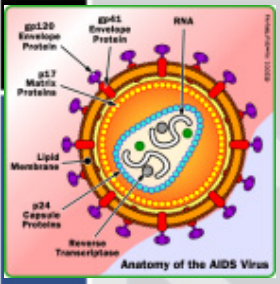
VIH et PMA

France. Critères: Journal officiel de la République Française (5/ 2001)

(discutable: CD4>200, home non infecté, évaluation psychologique)

<u>Couples avec homme infecté par VIH</u>

- **Programme de prévention de la transmission sexuelle**
- **Résultats IIU et FIV-ICSI excellents**
- **Motilité spermatique réduite (probabilité grossesse rapports non protégés?)**
- **Cycles publiés: > 3600. 0 transmissions VIH**



Couples avec femme infecté par VIH

Ohl J et al. Human Reprod Nov 2005. Single ET si < 40ans

Couples: 49 (age: 35)

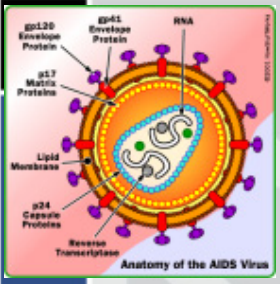
	n	Réels	Gros.	%
IUI	10	10	0	0
FIV-ICSI	62	46	11	23,9
CT	10	6	2	33,3

Bilan de base: FSH normale

ICSI: Gonadotrophines: 2793 IU ± 995 (global: 1878) Ovocytes: 8

Taux de fertilisation: 63,8%, ET: 1,8

Implantation rate: 11,8% (global: 14,5%)



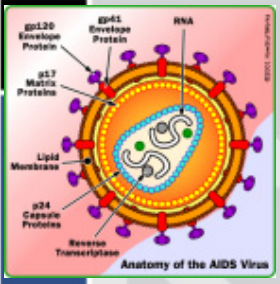
Couples avec femme infecté par VIH

Ohl et al. 2005

Résultats encourageants (??). Étude non contrôlée

IU / FIV-ICSI

Pourquoi doses gonadotrophines élevées



Couples avec femme infecté par VIH

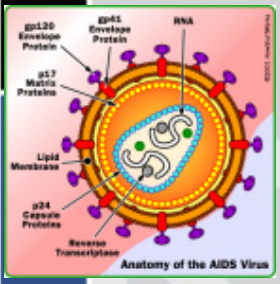
Térriou P et al (Marseille) Human Reprod Octobre 2005

Couples: 29. Cycles: 56

Matched-controlled study. Tubal indication: 52%. Age: 35yrs

Tentative et facteur masculin: $\neq$

	Cas	Contrôles	Global
Cancelled cycles (%)	15,2	4,9	6,9
Unités FSH (IU)	2898	2429	2107
E2, nº ovocytes, nº embryons, classe I, nº ET: $\approx$			
Taux grossesse (%)	16,1	19,6	26,1



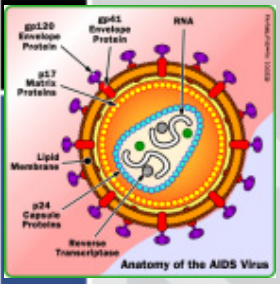
Couples avec femme infecté par VIH

Martinet V, Human Reprod Janvier 2006

Matched-controlled study. Cycles FIV: 27 (contrôles: 77)

Africaines: 52%. Age: 35,5 ans

	Cas	Contrôles		
Unités FSH (IU)	4201	3349	1	(1–1)
Ovocytes maturés	5.43	6.64	0.75	(0.51–1.10)
Nº embryons	4.38	4.77	0.87	(0.68–1.12)
Taux fertilisation	0.67	0.61	1	(0.06–16.30)
" transférés	1.3	1.94	0.32	(0.11–0.92)
Grossesses clin.	11% (3)	20.8% (16)	0.02	(0–1.65)



Couples avec femme infecté par VIH

Martinet V, Human Reprod Janvier 2006

Conclusion:
"…similar ovarian response to stimulation, suggesting the existence of a similar ovarian reserve."

Reproductive outcome in HIV infected women

Matched-control study

Coll O et al. AIDS January 2, 2006

Reproductive outcome in HIV infected women

Matched-control study

Coll O et al. AIDS January 2, 2006

Reproductive outcome in HIV infected women

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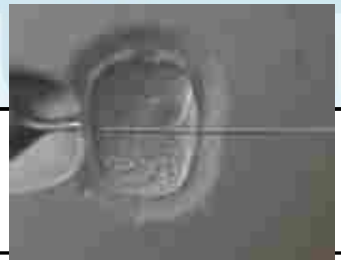

Cancelled v.s. non-cancelled cycles: homogenous

HIV-infected women vs SDC + controls
Clinical pregnancy rate

	Crude OR	95% CI	p
IVF	0.30	0.11-0.78	0.01
OD	0.68	0.27-1.71	0.42

Likelihood of an HIV infected women: 3 times lower than non-infected

Why do HIV infected women have worse outcomes?

Non-cancelled IVF cycles only

Forward stepwise variable selection procedure. Covariates

- Class I transferred embryos
- Viable embryos d+2/ embryos at 2 pronucleous stage
- Embryos at 2 pronucleous stage / inseminated oocytes
- Mature retrieved oocytes / retrieved oocytes
- Follicles by US before retrieval
- FSH units required
- Basal FSH level

Only explicative variable: FSH units required

Adjusting by age and basal FSH:

Increase of 100 FSH units: OR for pregnancy decreases by 3%

Ovarian resistance??

Why do HIV-infected women IVF have an ovarian resistance

Mean(SD)	Clinical Pregnancy				p*
	No	(n=31)	Yes	(n=6)	
Age (years)	36.2	(3.4)	34.5	(1.9)	0.25
BMI (kg/m2)	22.8	(2.4)	23.8	(2.6)	0.40
CD4 (cells/ml)	577	(250)	814	(206)	0.03
CD4 nadir (cells/ml)	338	(260)	270	(127)	0.54
Viral load (copies/ml)	74.600	(118.645)	73.258	(66.213)	0.98
Months from HIV diagnosis	89.9	(45.6)	135.2	(42.1)	0.03
Months on HAART	40.4	(26.5)	56.8	(26.2)	0.17

HAART: Highly Active Anti-Retroviral Therapy *Independent sample t-test.

Why do HIV-infected women IVF have an ovarian resistance

Logistic regression analysis ⇨ <u>CD4:</u> only significant effect on ovarian resistance

adjusted OR	95%CI	p
0.994	0.991-0.997	0.043

Conclusions
Coll O et al. AIDS. Jan 2, 2006

- Pregnancy rate after IVF is ↓ in HIV-infected women under HAART

  Oocyte donation was able to correct this defect

- This effect may be due to subclinical hypogonadism

- Subclinical hypogonadism may be mediated by immunosuppression but it does not appear to be related to therapy

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Need of a pre-IVF assessment and to optimize the immunological status of the patient before considering ART

American Journal of Obstetrics and Gynecology (2006) 194, 192–8

January 2006

American Journal of Obstetrics & Gynecology
www.ajog.org

Prenatal diagnosis in human immunodeficiency virus-infected women: A new screening program for chromosomal anomalies

Oriol Coll, MD, PhD,[a] Anna Suy, MD,[a] Sandra Hernandez, MD,[a] Sonia Pisa,[a] Montserrat Lonca, MD,[b] Claire Thorne, PhD,[c] Antoni Borrell, MD, PhD[a]

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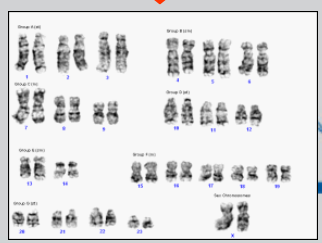
Hospital Clinic's protocol

1º or 2 trim. screening test

Risk of Down Sdr.

Under appropriate



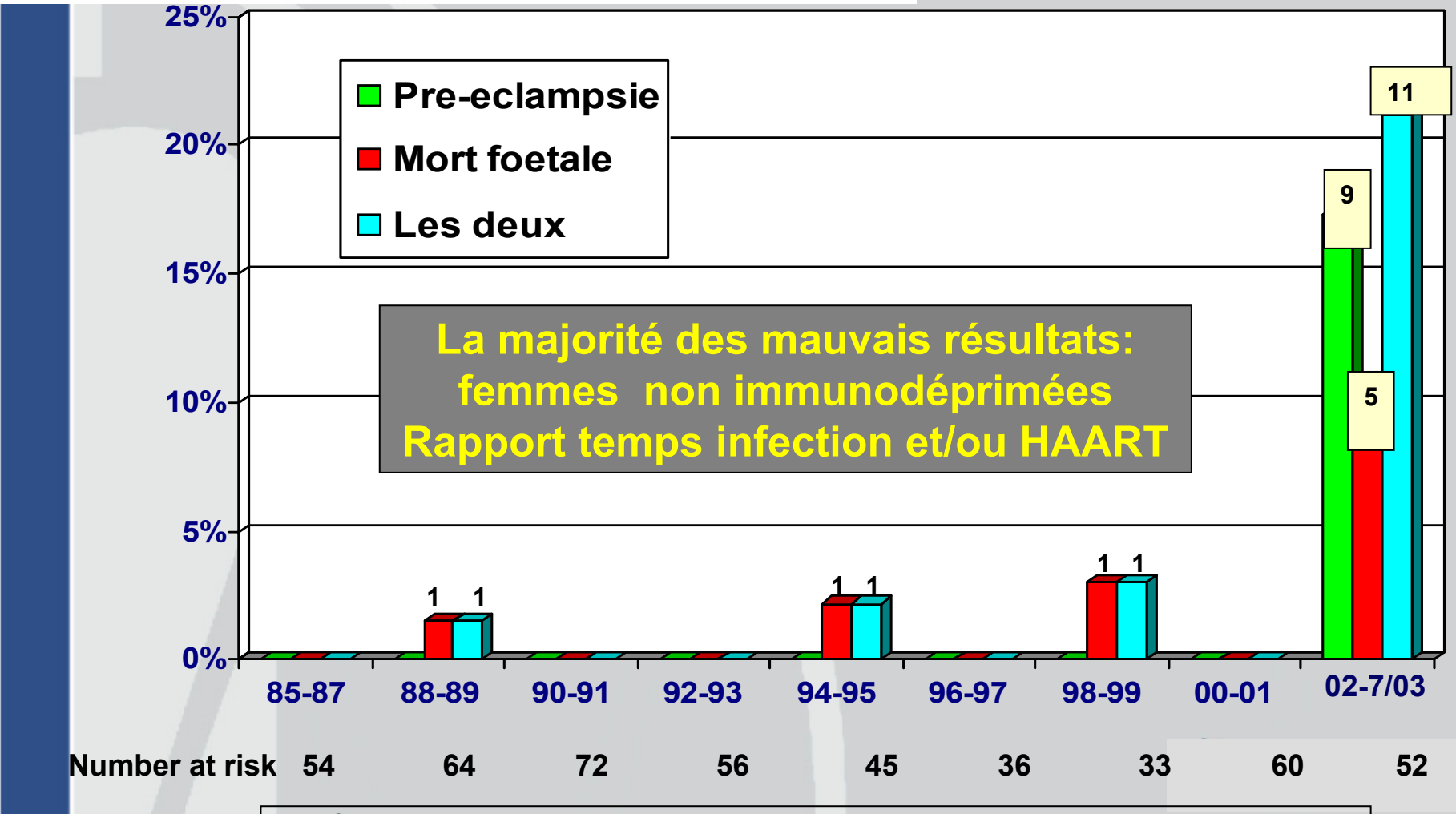
aula Clínic

Increased risk of pre-eclampsia and fetal death in HIV-infected pregnant women receiving highly active antiretroviral therapy

Anna Suy[a], Esteban Martínez[b], Oriol Coll[a], Montserrat Lonca[b], Montserrat Palacio[a], Elisa de Lazzari[b], María Larrousse[b], Ana Milinkovic[b], Sandra Hernández[a], José L. Blanco[b], Josep Mallolas[b], Agathe León[b], Juan A. Vanrell[a] and José M. Gatell[b,*]

AIDS
Official Journal of the International Aids Society

Jan 2, 2006



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"Comment optimaliser la FIV jusqu'au transfert de l'embryon"

FERRING

VIH PMA / Grossesse

- Sujet très complexe
- Fertilité réduite. Insuffisance ovarienne
- SET?

Remerciements à tous les collaborateurs

Merci de votre attention

ocoll@euvitro.com

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