



Management of fertility preservation in young patients with Turner syndrome

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ISFP

The 5th World congress of the
INTERNATIONAL SOCIETY FOR FERTILITY PRESERVATION
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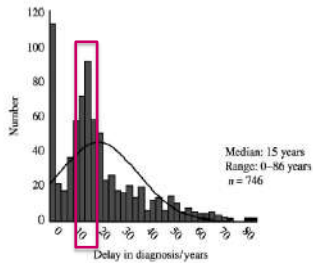
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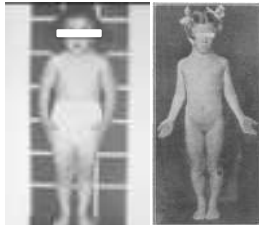
Nothing to declare

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Turner syndrome diagnosis



- 1/2500 / 1/3000 female newborns
- 10 - 20% spontaneous abortion
- <1% of 45,X viable
- **Mostly prenatal diagnosis or childhood (~12 years)**
- **~ 50% before 12 years**
- **Short stature / Ovarian insufficiency (puberty retardation)**



[Stocholm al., 2006 - Trovo de Marqui et al., 2014 - Silvia D'Ippolito et al., 2017 - Culen et al., 2017 - Gravholt et al., 2017]

Puberty / Fertility

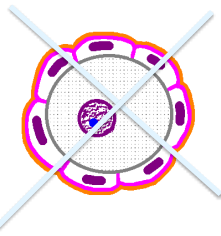
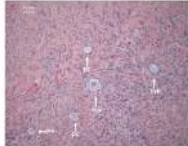


- | | | |
|---|-------------------------------------|--|
| Spontaneous puberty | ~40-50% (mosaic form +++) | [Hädnott, 2011] |
| Spontaneous menarche | 10% | [Hövatta, 1999 - Welt, 2008 - Hädnott, 2011 - Hewitt, 2013] |
| <ul style="list-style-type: none"> - 45,X/46,XX - Xp distal deletion (>Xp11.1, Xp21.1, Xp22.1.22) | 😊 | |
| <ul style="list-style-type: none"> - 45,X - Xq deletion Xq (Xq13.2, Xq26, Xq27) - Chromosome X ring - Y chromosome material | 😞 | |
| Premature ovarian failure | 29.3 years (TS mosaic) | [Reindalo RH 1996] |
| 1.8 to 7.6 % of spontaneous pregnancy | | [Hövatta, 1999 - Hädnott, 2011 - Chakhtoura, 2013 - Hewitt et al., 2013] |
| <ul style="list-style-type: none"> - Birth rate - Age at pregnancy | <p>3 à 40%</p> <p>[22;24] years</p> | |

[Reynaud, 2004 - Lachlan, 2006 - Kamman, 2008 - Kavoussi, 2008 - Punushothaman, 2010 - Mercier et al., 2013 - Bernard et al., 2016]

Natural history of TS ovary development

From prenatal life to puberty

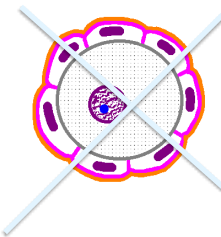
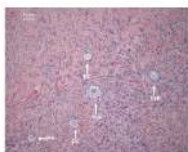


- Decreased number of oogonia
- Accelerated degeneration of primordial follicles ~ 18 Weeks
- Follicular loss depending on chromosome abnormality
 - 45,X
 - Chromosome X ring
 - Xp21 / Xp11.1
 - Xq26 / Xq28

[Weiss, 1971 - Pasquino et al., 1997 - Hreinsson et al., 2002 - Reynaud et al., 2004 - Kammoun et al 2008 - Kavoussi et al., 2008 - Borgström et al., 2009 - Lachlan et al., 2006 - Mercer et al., 2013]

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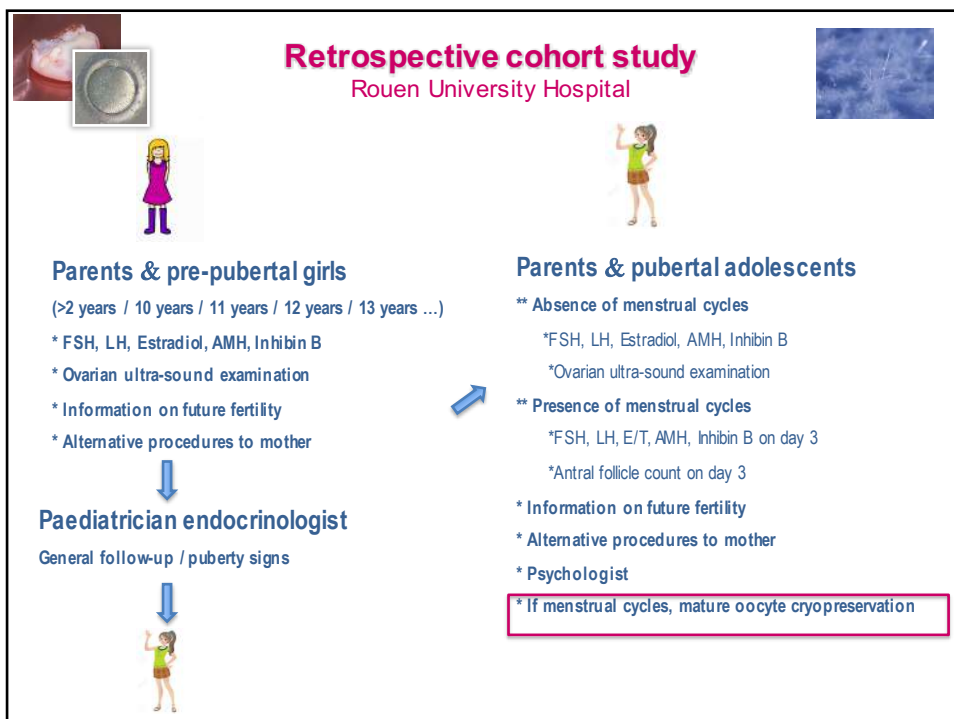
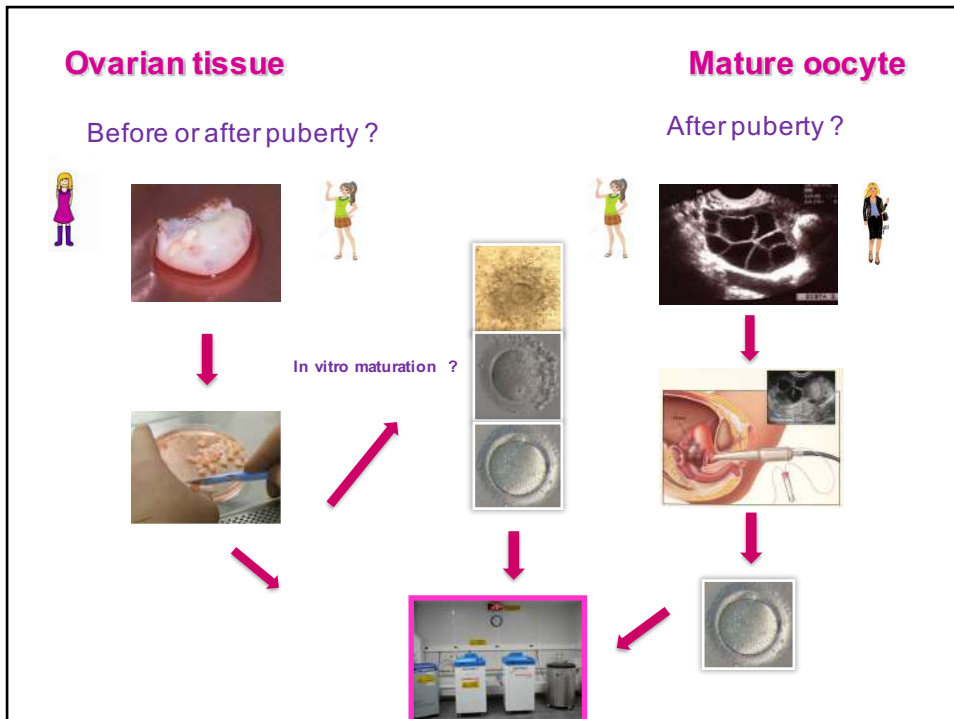
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➔ Fertility preservation ?





Chromosome abnormalities




□ **25 patients** **[3;27] yrs**
Median : 12±5 yrs

□ **Chromosome abnormalities**


45,X	(3)	
46,X,i(X)(q)	(2)	
45,X/46,X i(X)(q)	(2)	
45,X/46,X r(X)	(1)	
45,X/46,X i(Y)	(2)	
45,X/46,XX,del(X)(p)	(1)	
46, XX,del(X)(q)	(1)	
45,X/46,X,+marY	(1)	
45,X/46,XX	(9)	
45,X/47,XXX	(1)	
45,X/46,XX /47,XXX	(1)	
46,XX,del(X)(p)	(1)	


Fertility prognosis

13/25 (52%)




12/25 (48%)







Clinical features




- **Context of diagnosis**
 - Prenatal diagnosis
10 (40%)
 - Growth retardation
12 (48%)
 - No pubertal development
1
 - POF/ Growth retardation
2
- **Malformations**
 - Heart
5
 - Kidney
6
- **Learning disorder** 10 (40%)
- **Psychosocial problem (Emotional immaturation)** 25




Puberty



- Pre-pubertal 52% (13/25 ⇒ 4/25)
- Spontaneous 48% (10/21) [11;15] yrs
- Spontaneous menarche 48% (10/21) [11;15] yrs
- POF 44% (11/25)



Fertility preservation



Authors/Patients	Stimulation	Karyotype	Age of spontaneous menarche	Contexte of diagnosis	FSH D3 (IU/l)	AMH D3 (IU/l)	AFC	Age stimulation (years)	Protocol	Frozen oocytes matures	Frozen ovarian tissue	Histologic analysis (follicles/mm ²)
P1	1	45,X/46,XX	12	Prenatal diagnosis	5.6	5.6	10	15	antagonist	14		
	2								antagonist	11	LO	80
P7	1	45,X/46,XX	15	Short stature	4	8.2	40	16	antagonist	6		
P11	1	45,X/46,XX	13	Short stature	4.32	0.9	3	14	agonist	2	LO	21.65
P12	1	46,XX,delXp	15	Prenatal diagnosis	6.86	2.3	16	15	antagonist	5		
P15	1	45,X/46,XX	13	Short stature	7.28	1.1		15	antagonist	12		
P21	1	45,XX/47,XXX	15	Short stature	7.3	1	9	28	antagonist	3		
	2								antagonist	4		

- Mature oocyte freezing
 - 6 patients with at least one oocyte banking cycle
 - 2 patients awaiting fertility preservation [45,X ; 45,X/47,XXX]
 - 2 patient refusals [parents, « fear » of the patient]



Fertility preservation



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■ Ovarian tissue banking

- 2 patients in addition to oocyte banking
 - 1 patient with POF (10 yrs)
 - 3 patients with bilateral gonadectomy (Y chromosome material)
- 1 with gonadoblastoma (3 yrs)



Parents' point of view



- Present ["23/25" ; 2 patients > 25 yrs]
- Complete agreement with the procedure (21/23)
- The "syndrome" was too present
- They feel guilty and were not completely objective
- No question on future sexuality of their daughter
- Experimental nature of the procedure



Patients' point of view



- 24 patients (>3 yrs)
 - Future fertility was a high priority for 20/24 patients
 - 5 patients did not have any knowledge about TS and fertility
 - 4 patients expressed some hesitations about fertility preservation with two refusals
 - Absolute necessity to discuss the possibility of POF
 - Absolute necessity to discuss alternative procedure to mother (adoption – oocyte donation – living without children)
 - 12 patients did not have any knowledge on oocyte donation
 - 3 patients talked spontaneously about oocyte donation
 - 4 patients talked spontaneously about adoption
 - We impose the necessity of parenthood to children ?
 - Informed consent ?





Clinical Practice Guideline

C. H. Gravholt and others

Turner syndrome clinical practice guideline

1773 68-678



Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting

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On behalf of the International Turner Syndrome Consensus Group¹

R 3.2. We suggest that young mosaic TS women with persistent ovarian function should be counseled that oocyte cryopreservation after controlled ovarian hyperstimulation is a possible fertility preservation option (⊕○○○).

R 3.3. We recommend against routine oocyte retrieval for fertility preservation of young TS girls before the age of 12 years (⊕○○○).

R 3.6. We suggest that other options for motherhood such as adoption or using a gestational carrier should be mentioned during preconception counseling (⊕○○○).