



*Issues on fertility in 2020: from cradle to grave*

# **Congenital anomalies related with fertility**

**Jun Nyung Lee**

*Department of Urology  
Kyungpook National University*





# Introduction

- ❖ **Prevalence of infertility**      **15%**
- ❖ **Male-factor infertility**      **20%–70% (m/c)**
- ❖ **Congenital / acquired diseases implicated in male infertility**
  - ✓ **identification and timely treatment**
  - ✓ **↓ prevalence of male-factor infertility**



# Introduction

## ❖ Male infertility causes

- ✓ **Congenital urogenital abnormalities**
- ✓ **Malignancies**
- ✓ **Urogenital tract infections**
- ✓ **Increased scrotal temperature (ex. varicocele)**
- ✓ **Endocrine disturbances**
- ✓ **Genetic abnormalities**
- ✓ **Immunological factors**



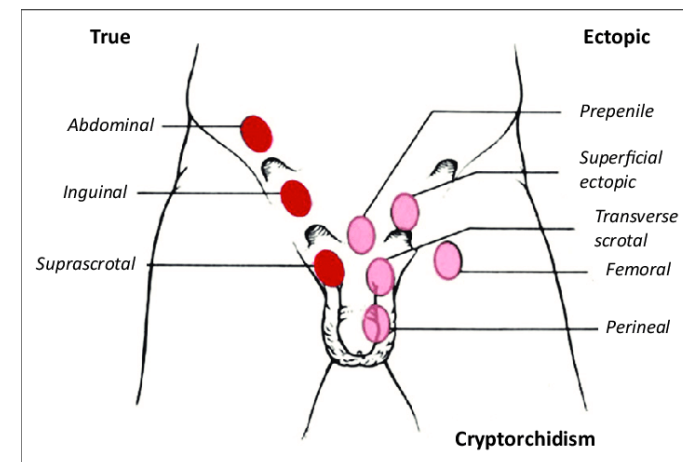
# Contents

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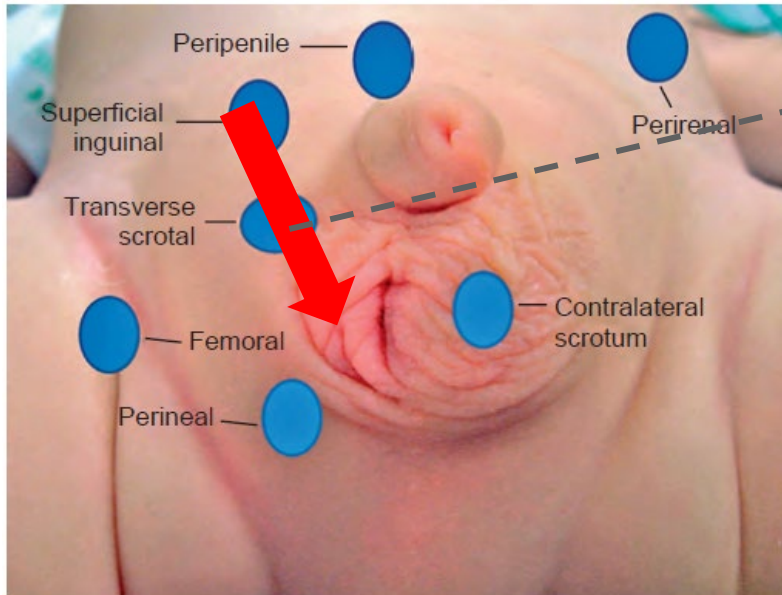
- ❖ **Undescended testis**
- ❖ **Hypospadias**
- ❖ **Hydrocele**
- ❖ **Posterior urethral valve**

# Undescended testis

- ❖ **Most common congenital abnormality of the male genitalia**
- ❖ **1% of all full-term male infants at one year of age**
- ❖ **Wide range of presentations**
  - ✓ **varying impacts on testicular development and function**
  - ✓ **intra-abdominal vs intra-canalicular (inguinal)**
  - ✓ **bilateral vs unilateral**



# Undescended testis



**Abdomen → Scrotum**  
**Benefit?**  
**2~3°C drop**

The small **temperature difference** between 33°C and 36°C is **detrimental to normal spermatogenesis and fertility in the long-term.**



# Undescended testis

## ❖ Infertility risk

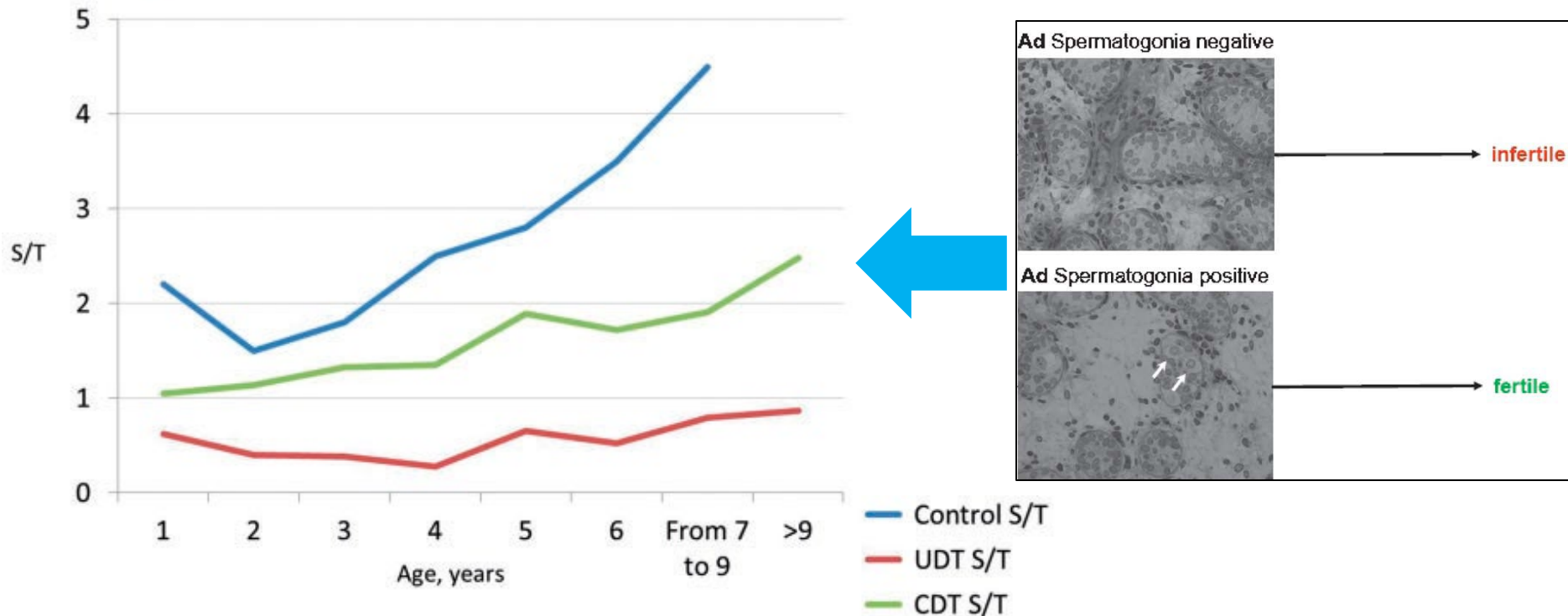
- Unilateral vs General population RR 2.0
- Bilateral vs Unilateral RR 3.5
- Bilateral vs General population RR 6.0

## ❖ Azoospermia risk in cryptorchidism

- Untreated bilateral cryptorchidism 90%
  - Medically treated cryptorchidism 32%
  - Bilateral orchiopexy 46%
- **Unilateral cryptorchidism regardless of correction 13%**
- General population 0.4-0.5%

# Contralateral side on unilateral UDT

<Age-dependent evolution of the median germ cell count>



✓ **Unilateral cryptorchidism is a bilateral disease**

Hadziselimovic F, et al. *Klin Padiatr* 2008

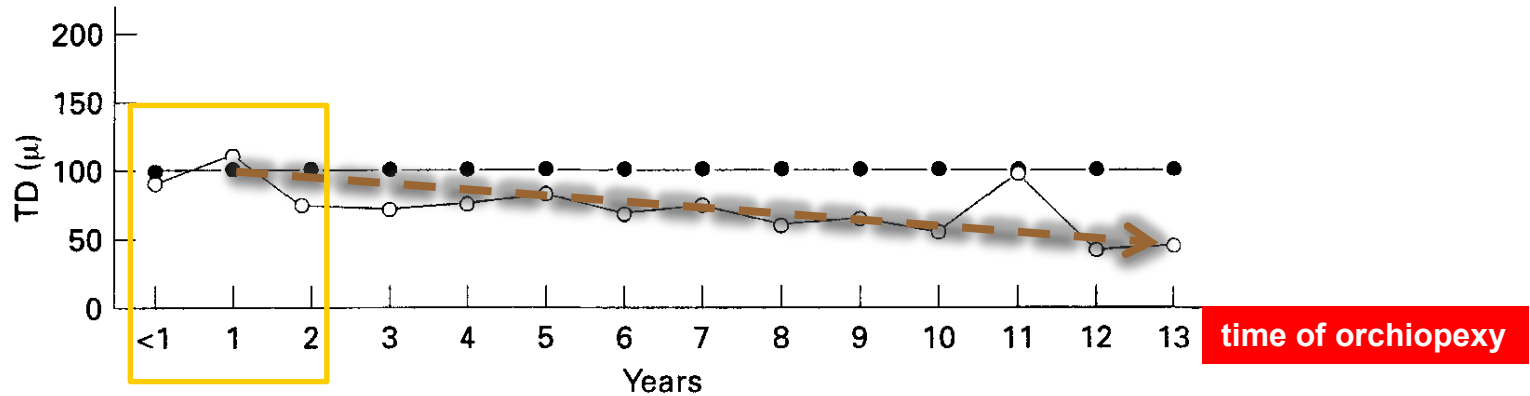
Verkauskas G, et al. *Pediatr Dev Pathol* 2019



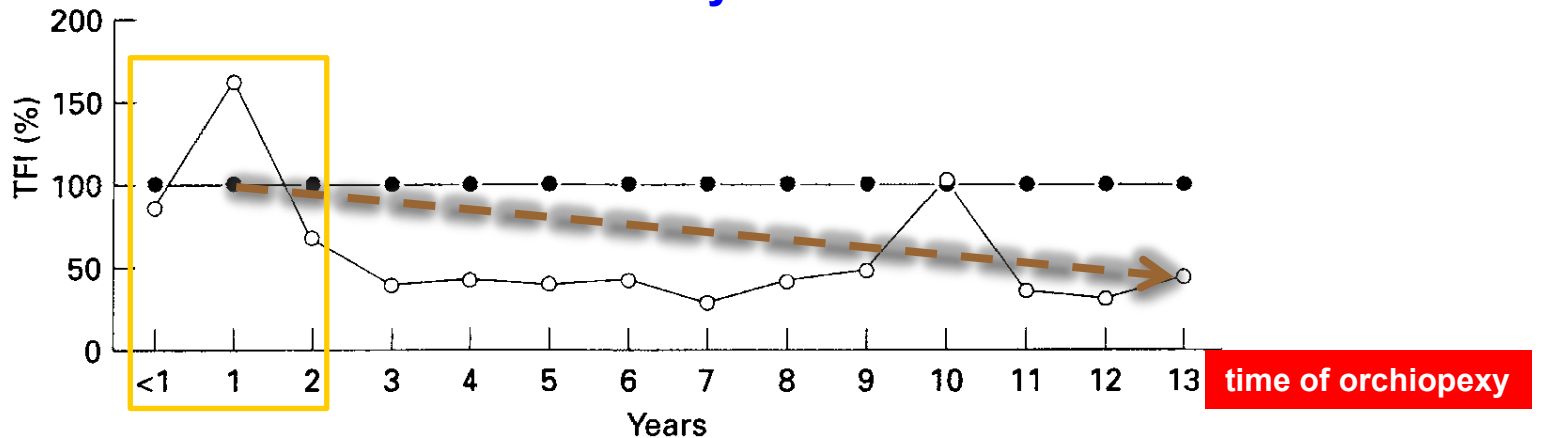


# Pathological study in UDTs

## <Tubular diameter>



## <Tubular fertility index>



○, Cryptorchid (% of the control values).  
●, Control values [9].

# Location

## <Tubular diameter according Location>

<i>Location</i>	<i>Mean</i>	<i>SD</i>	<i>No. of biopsies</i>
Intra-abdominal	44.6	11.4	37
Canalicular	44.9	11.5	310
Below external ring	47.6	11.7	31
Ectopic	47.6	11.2	73

## <Tubular fertility index according Location>

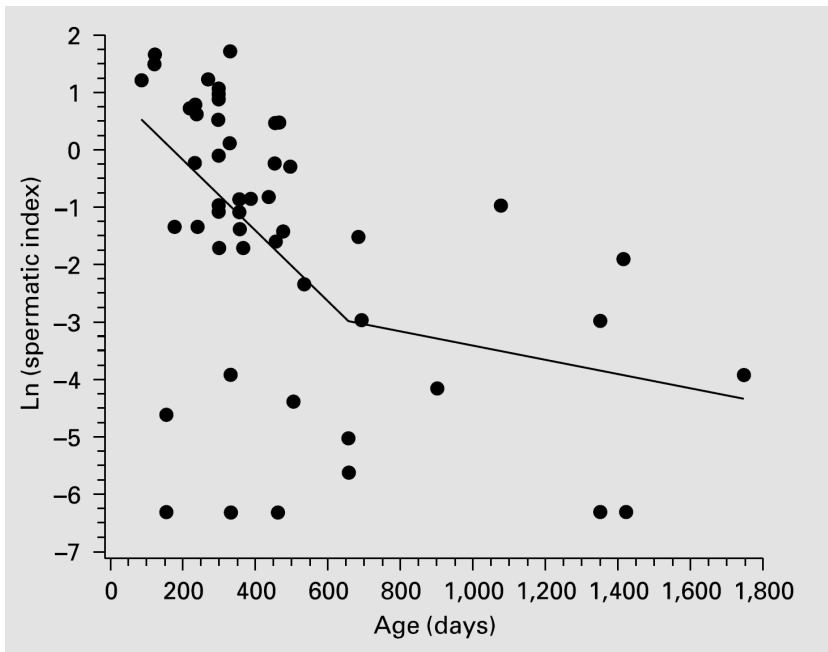
<i>Location</i>	<i>Mean</i>	<i>SD</i>	<i>No. of biopsies</i>
Intra-abdominal	23.9	30	71
Canalicular	38.3	37.4	894
Below external ring	36.1	35	72
Ectopic	38.7	33.6	138

✓ *Location* ↑ → *Tubular state* ↓

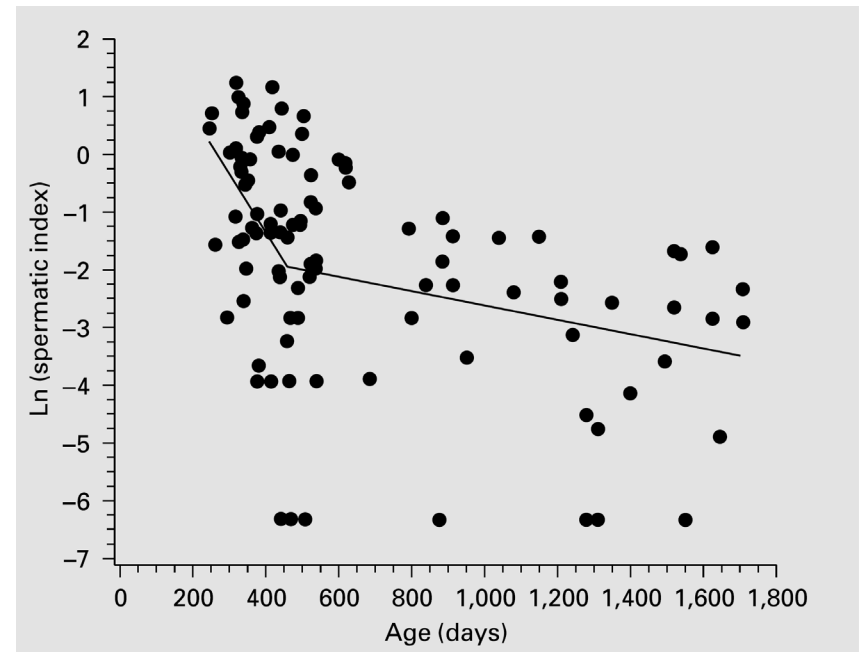


# Early surgical tx & Fertility in UDT

<Intra-abdominal type>



<Intra-canalicular type>



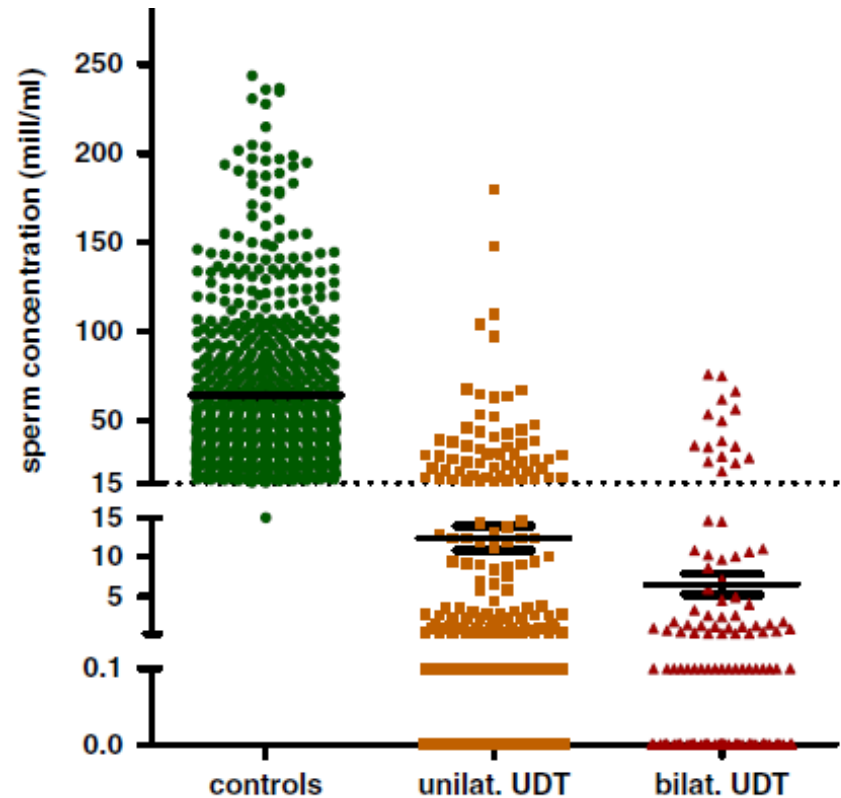
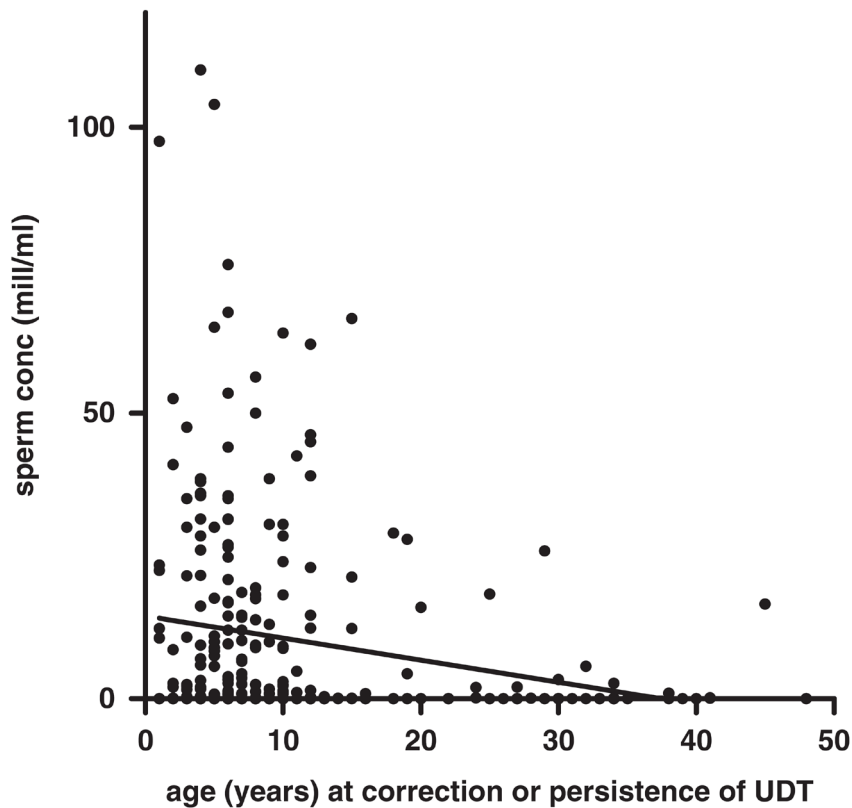
✓ **The SI appears to reach a critically low value between 8 and 9 months of age, suggesting that surgical intervention would be appropriate before this time.**





# Age at -pexy / Bilat & Sperm conc.

357 adults with prev. UDT

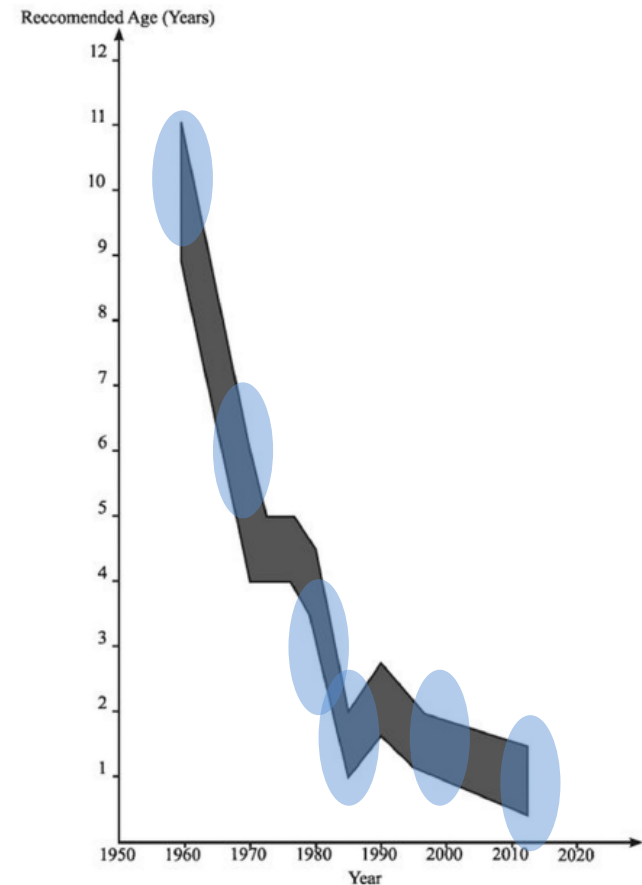




# Undescended testis

## ❖ Timing of orchiopexy

- **1950s: 10-15 yr** (suspended animation)
- **1970s: 5-6 yr** (macroscopic atrophy)
- **1970-80s: 2 yr** (microscopic degeneration)
- **1980s: 1 yr** (Early degeneration on EM)
- **2000s: 12-18 months** (germ cell count)
- **Present: 6-12 months**





# Paternity & Age at -pexy

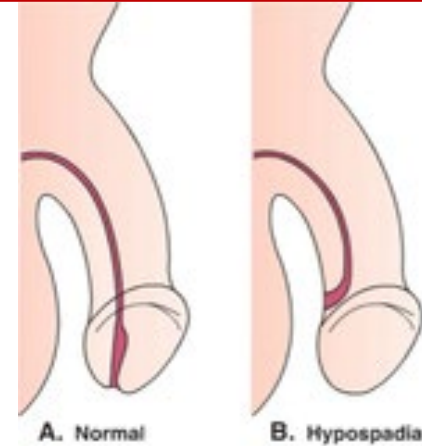
*Population based study in Australia*

	Fathered children	Hazard ratio (95% CI)	
		Crude	Adjusted*
<b>All cohort (1970–99)</b>			
Unaffected	107 006/341 000 (31.4%)	Ref (1.00)	Ref (1.00)
Undescended testes	2016/7499 (26.9%)	0.72 (0.69–0.75)	0.79 (0.74–0.85)
<u>Age at orchidopexy</u>			
Continuous†	109 471/350 835 (31.2%)	0.98 (0.98–0.99)	0.99 (0.98–0.99)
<18 months	156/1202 (13.0%)	0.68 (0.58–0.80)	0.83 (0.70–0.98)
18 months to 5 years	809/3208 (25.2%)	0.66 (0.62–0.71)	0.79 (0.71–0.87)
6 to 20 years	1038/3049 (34.0%)	0.78 (0.74–0.83)	0.78 (0.69–0.88)
Undescended testes‡	620/3288 (18.9%)	0.86 (0.79–0.93)	0.86 (0.79–0.93)
Unilateral	519/2765 (18.8%)	0.87 (0.80–0.95)	0.84 (0.77–0.92)
Bilateral	61/351 (17.4%)	0.75 (0.59–0.97)	0.58 (0.43–0.78)

❖ **Every 6 months increase in age at –pexy → 1%↓ of paternity / 5%↑ of ART use**

# Hypospadias

- ❖ 0.3%–0.8% of live births
- ❖ Underlying testicular dysfunction in utero  
→ link between hypospadias and infertility?
- ❖ Cause of subfertility
- ✓ Anatomy itself of unrepaired isolated anterior hypospadias ?

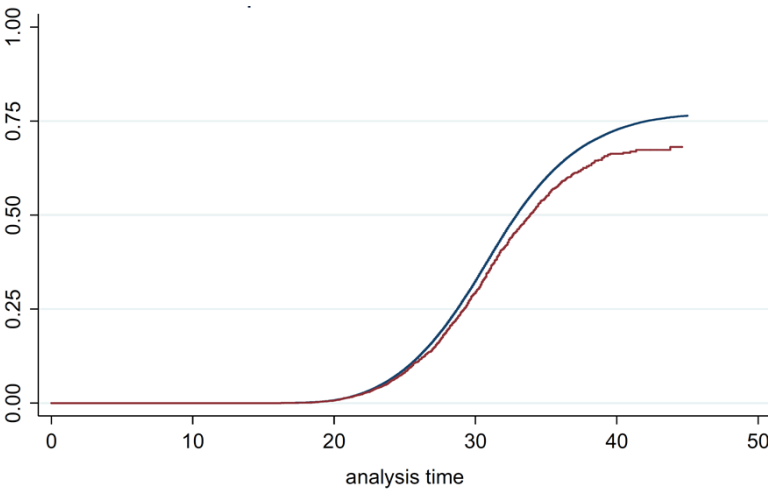


- ✓ Presence of androgen receptor mutations / partial androgen insensitivity
- ✓ Concomitant genital abnormalities (cryptorchidism - 18%)

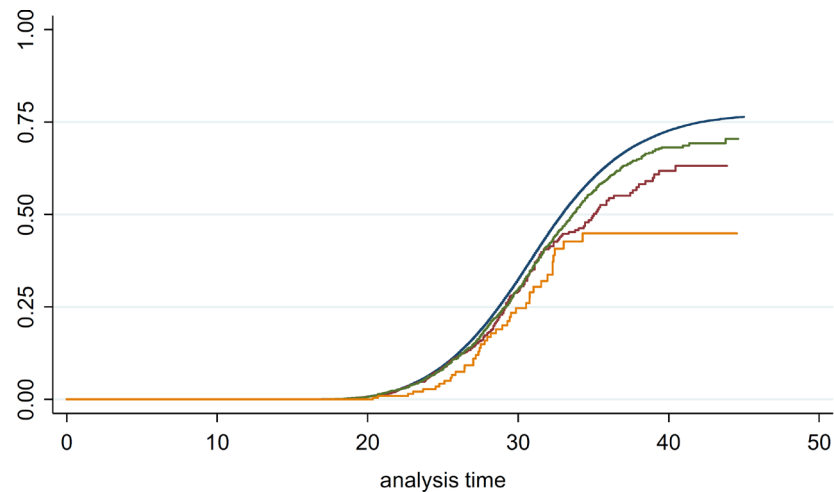
# Hypospadias

*Population based study in Sweden*

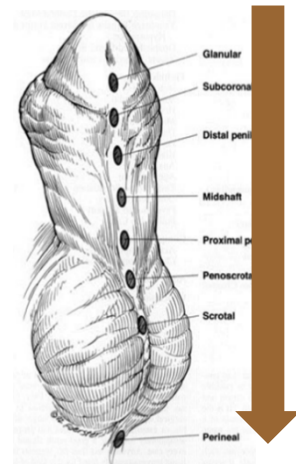
## <Paternity>



— Non-hypospadias — Hypospadias



— Non-hypospadias — Distal Hypospadias — Not Other Specified Hypospadias — Proximal Hypospadias



✓ **Fertility in men with both distal and proximal hypospadias is impaired.**





# Hypospadias

*Population based study in Australia*

	Fathered children	Hazard ratio (95% CI)	
		Crude	Adjusted*
<b>All cohort (1970–99)</b>			
Unaffected	107 006/341 000 (31.4%)	Ref (1.00)	Ref (1.00)
Hypospadias (all)	477/2484 (19.2%)	0.71 (0.65–0.77)	0.79 (0.71–0.89)
With repair	421/1941 (21.7%)	0.74 (0.68–0.82)	0.84 (0.74–0.95)
Undescended testes	2016/7499 (26.9%)	0.72 (0.69–0.75)	0.79 (0.74–0.85)
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6 to 20 years	1038/3049 (34.0%)	0.78 (0.74–0.83)	0.78 (0.69–0.88)

✓ **Hypospadias was associated with a 21% reduction in paternity.**





# Hydrocele

- ❖ Patency of processus vaginalis     **primary** vs secondary
- ❖ **Indications for surgical correction**
  - ✓ concomitant inguinal hernia
  - ✓ underlying testicular pathology
  - ✓ symptoms (discomfort)
  - ✓ parental anxiety / cosmesis
  - ✓ persistent hydrocele > 12-18 months
  - ✓ ***T damage?***



# Does hydrocele affect later fertility?

40 pts c hydrocele surgery, 3.2 yrs

## ❖ Testicular biopsy during surgery (n = 40)

- ✓ Good prognosis for fertility 75% (30 pts)
- ✓ Poor prognosis for fertility 25% (10 pts)

← Marked reduction in spermatogonia count

## ❖ Associated pathology

- ✓ 96.4% without associated pathology good prognosis group
- ✓ 75.0% with associated pathology poor prognosis group

	No. of pts
Cryptorchidism	3
Motor and mental retardation	2
Incarcerated hernia, same side	1
Testicular torsion	1
Varicocele	1
Testis/epididymis dissociation	1

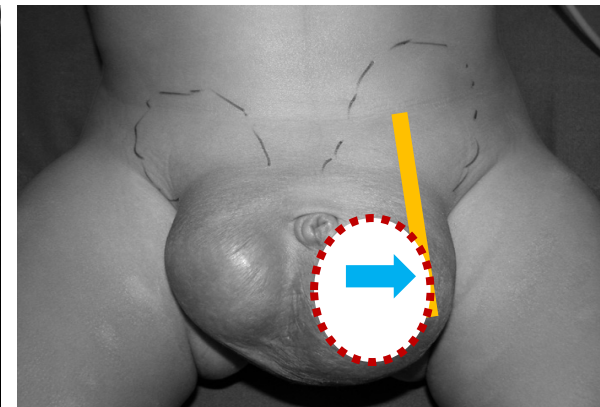
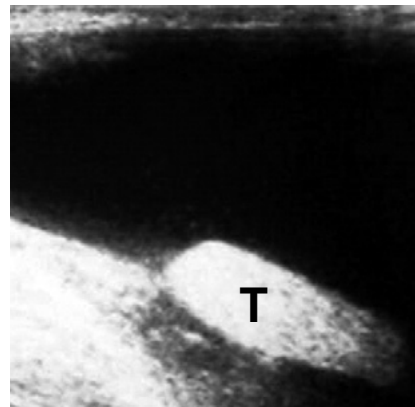


# Infantile abdominoscrotal hydrocele

## ❖ Hypothesis

- Partly obliterated processus vaginalis (valve-like mechanism)
- Excessive scrotal swelling / pressure
- Testicular dysmorphism (fusiform conf.)
- Compression damage
- **Spermatogenesis ???**

(partial / complete arrest of spermatogenesis *in adults*:18%)



*Dandapat MC, et al. Cr J Surg 1990*

*Cozzi DA, et al. J Urol 2008*



# Posterior urethral valves

Studies	P(n)	SC (NR)	pH < 8	NV	AF (NR)	MP (>32%)	AA
Woodhouse et al. [52]	9	9 (100%)	4 (44%)	4 (44%)	9 (100%)	7 (78%)	0
Puri et al. [51]	5	5 (100%)	5(100%)	3 (60%)	—	0	4 (80%)
Lopez Pereira et al. [54]	6	5 (83%)	2 (33%)	6 (100%)	5 (83%)	5(83%)	0

SC = sperm count; NR = normal range; NV = normal viscosity; AF = abnormal forms; MP = motility percentage; AA = abnormal agglutination.

- ✓ **Semen counts**                      **normal in men with a history of PUV**
- ✓ **Potential obstacles to fertility**
  - **increased semen viscosity, pH, and liquefaction time**
  - **dilated posterior urethra (ejaculatory dysfunction)**
  - **chronic renal failure / undescended testes (12%)**



# Paternity rate in PUV

*Population based study in Finland*

## <Men with children in different age groups>

Age group	General population	Patient cohort
20-29 years	14.9	2/15 (13.3%)
30-39 years	56.0	10/21 (47.6%)
40-49 years	72.2	17/22 (77.3%)
50-59 years	77.2	3/8 (37.5%)

- ✓ **Comparable fertility in PUV compared with age-matched healthy men.**



# Summary

## ❖ Undescended testis

- *Testicular damage via depletion of germ cells (Temp / Ad sperm)*
- *Early surgery for fertility preservation*

## ❖ Hypospadias

- *Testicular dysgenesis and sexual / ejaculatory dysfunction*
- *Identify and treat any concurrent risks for infertility*

## ❖ Hydrocele, Posterior urethral valve

- *Comparable fertility*
- *Concurrent testicular pathology*



***Thank you for your attention !***