

Sex

Sex



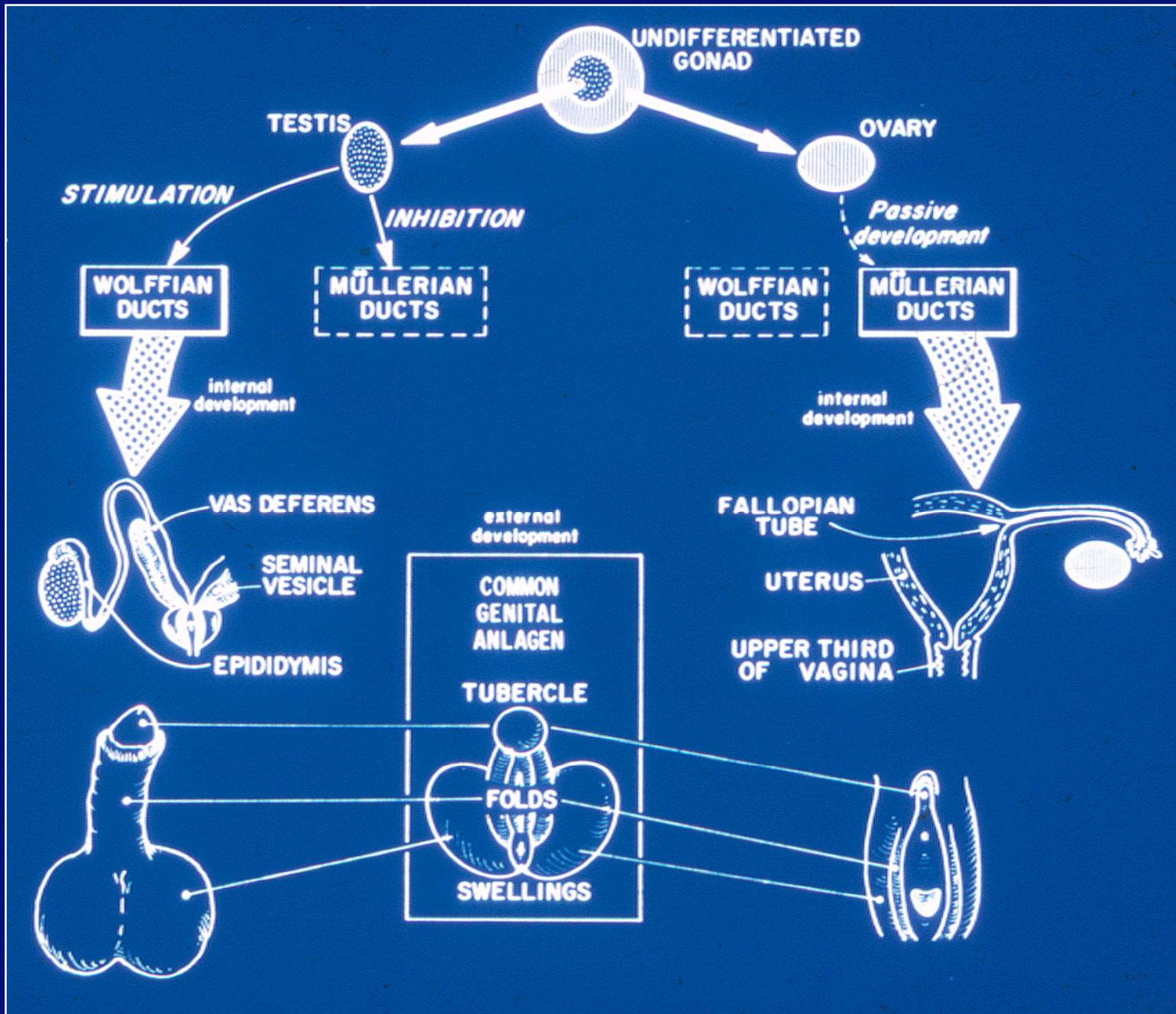
Genetic Sex



Gonadal Sex



Phenotypic Sex



Early Testicular Organogenesis

Y Chromosome



SHORT
ARM
CODES:

GERM CELLS



SEX
CORD



SEMINIFEROUS
CORD



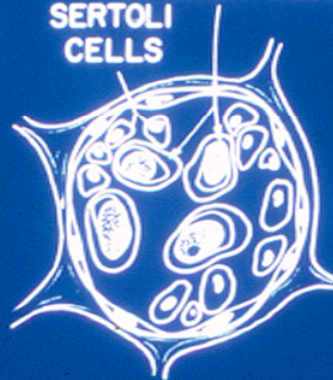
ANDROGEN
PRODUCTION

Late Seminiferous Tubule Maturation

LONG
ARM
CODES:



SPERMATOGONIA
SERTOLI
CELLS

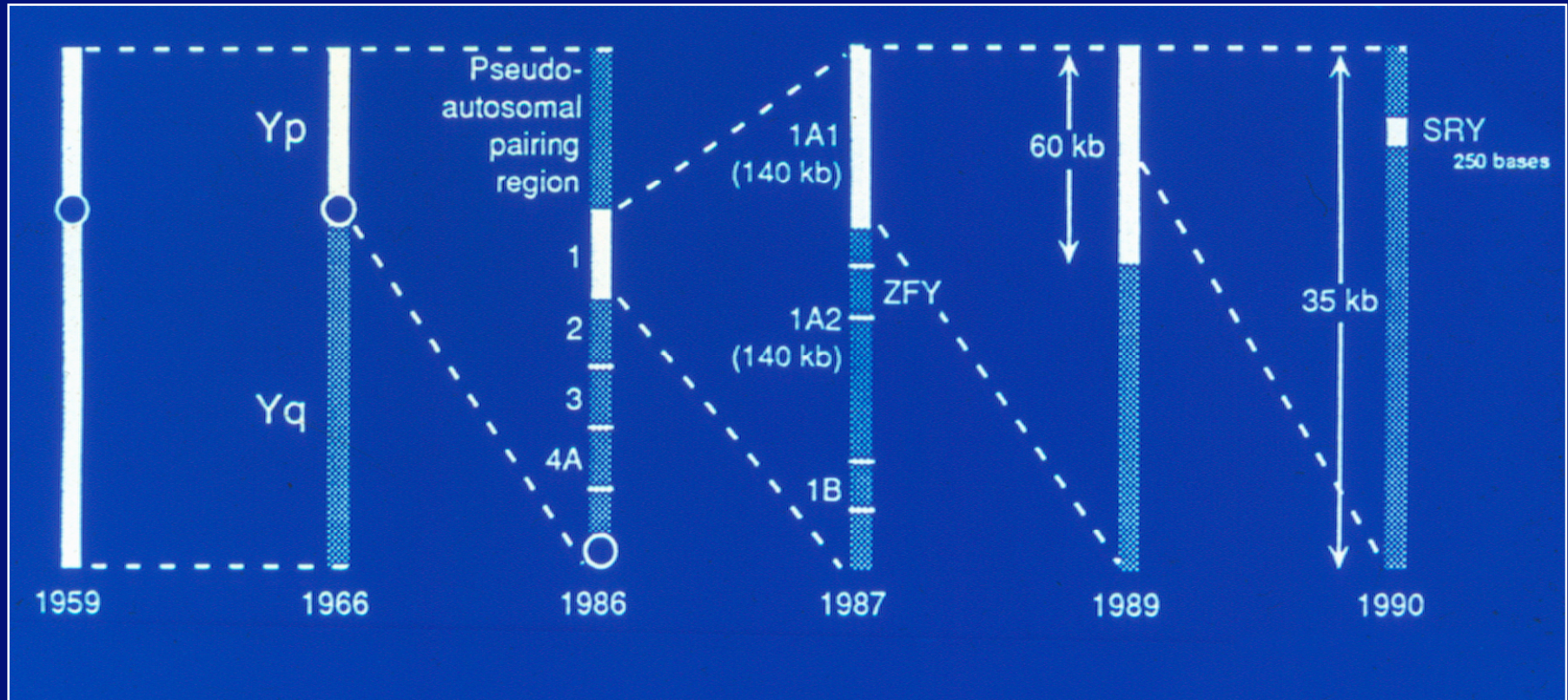


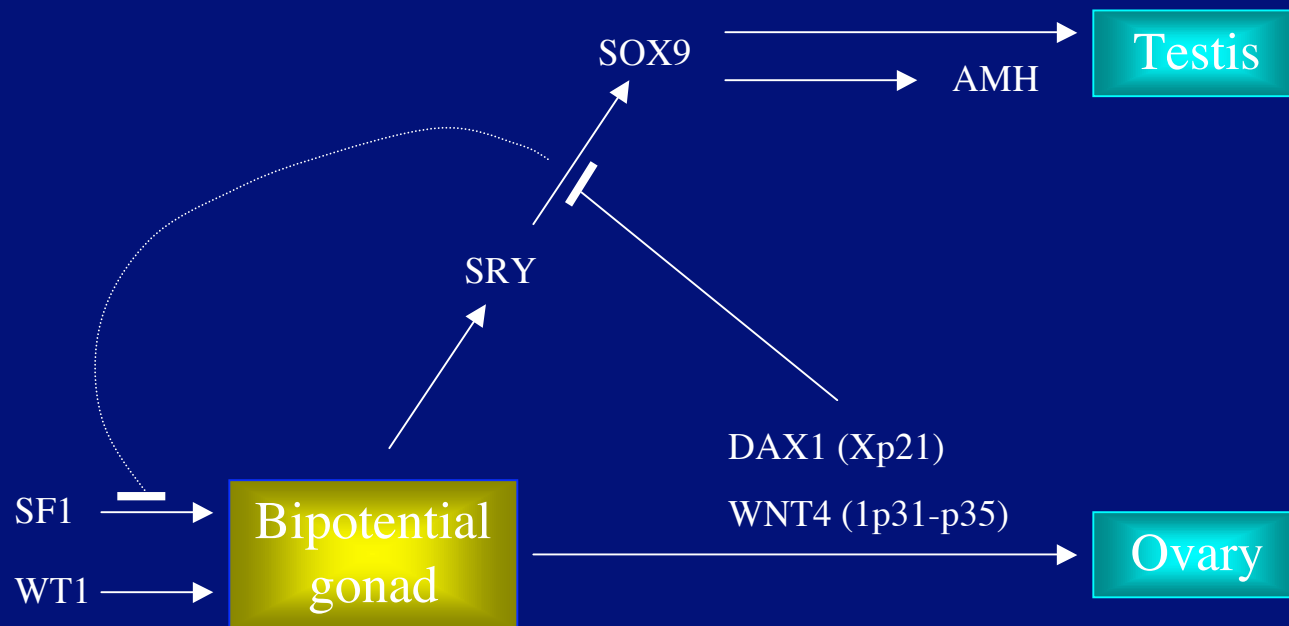
MATURATION

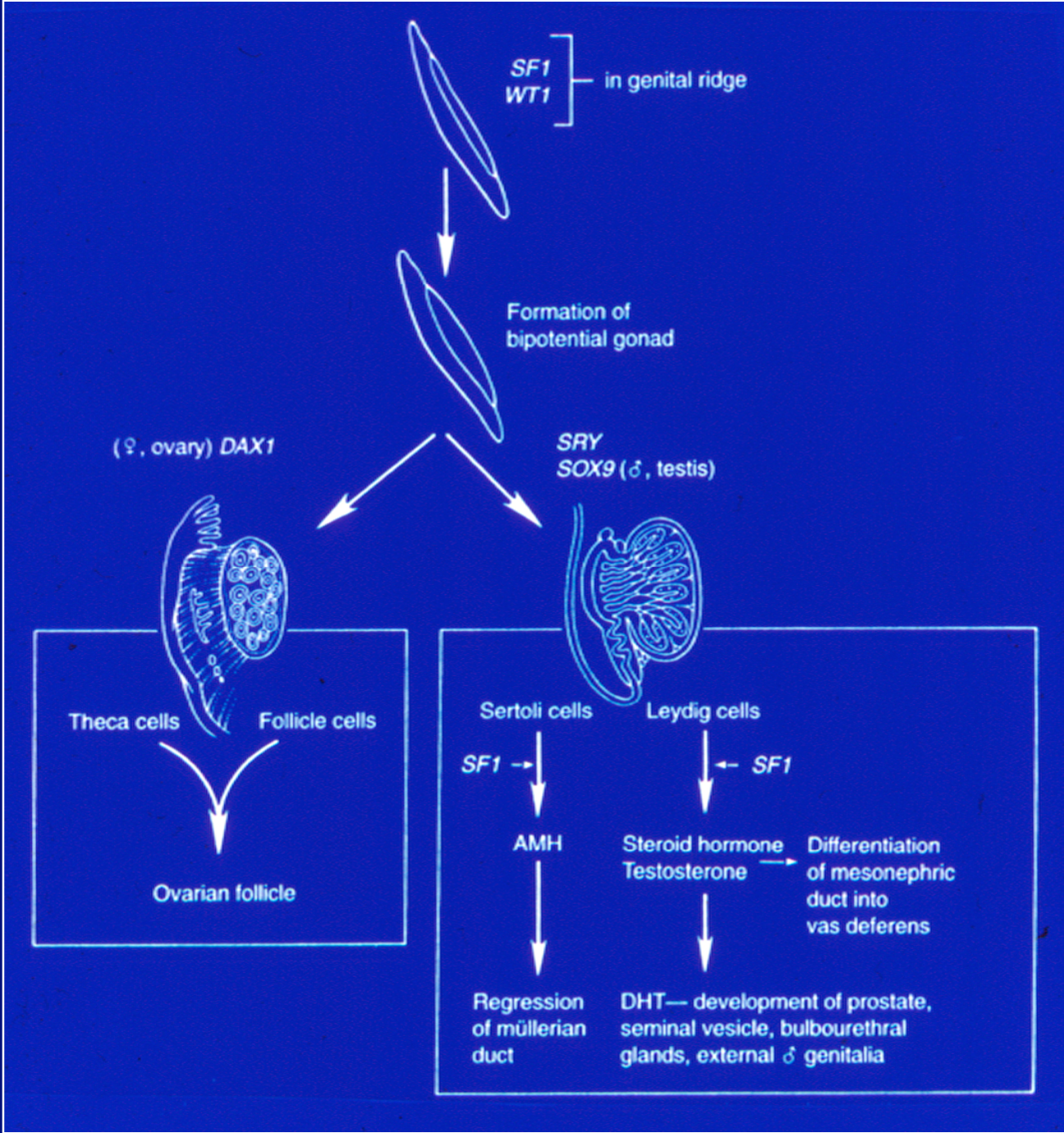
SPERMATIDS

SERTOLI
CELLS









Undifferentiated Gonad

Ceolomic Epithelium



Seminiferous Tubules
(Male)



Primary Ovarian Follicles
(Female)

Mesenchyme



Leydig Cells
(Male)



Theca & Sromal Cells
(Female)

Germ Cells



Spermatogonia
(Male)



Ova
(Female)

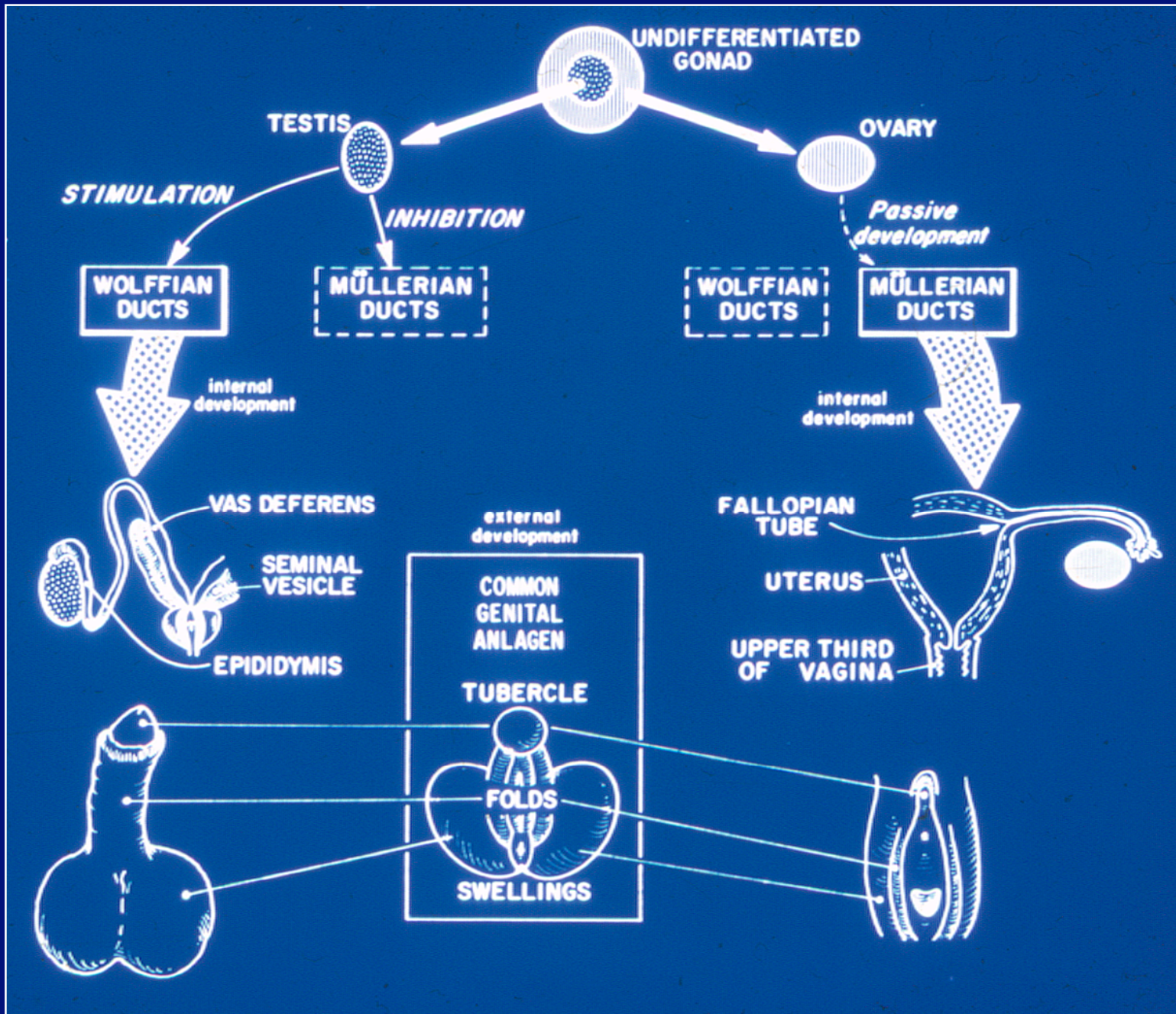
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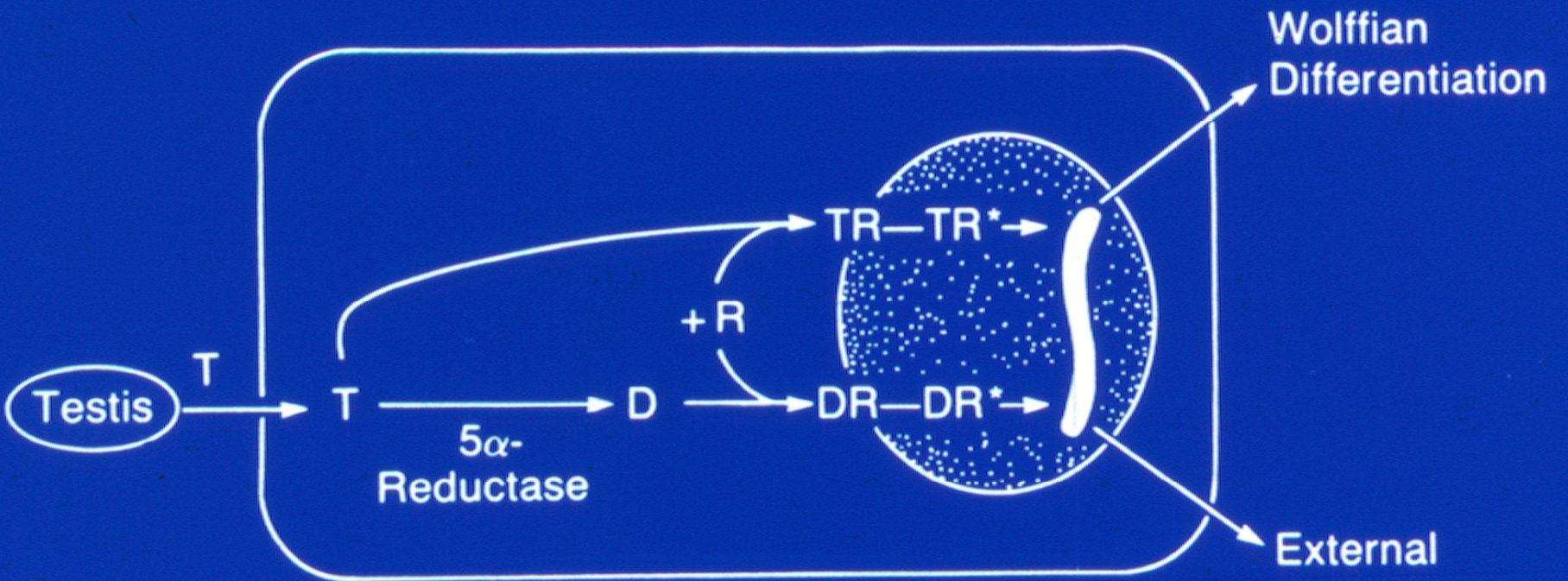
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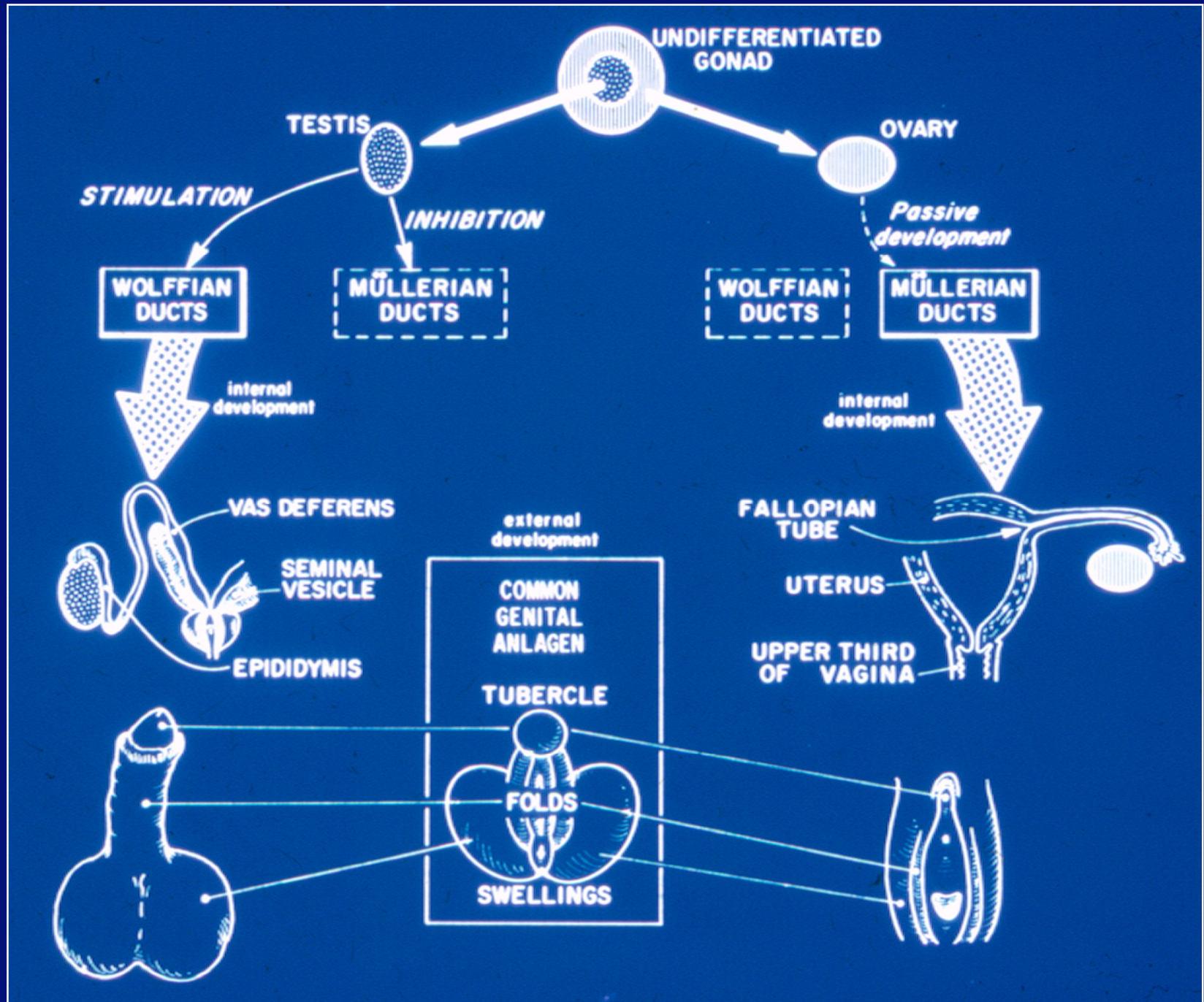


Gonadal Sex



Phenotypic Sex





Genetic Control of Male Phenotype

- Y Chromosome
 - ◆ Testicular Differentiation
- X Chromosome
 - ◆ End Organ Receptor
- Autosome
 - ◆ Enzymatic Control of Testosterone Biosynthesis
 - ◆ Conversion of T to DHT
 - ◆ Control of MIS Action

Intersex Questions

- What gene is integral in development of the bipotential gonad from the urogenital ridge?
- What gene is responsible for differentiation of the bipotential gonad into fetal testis?
- What is the major androgen of the fetal testis?
- What is the timing of its action?
- What stimulates fetal testis to produce androgen?
- What is the receptor site in fetal testis?
- What causes differentiation of external genitalia & U-G Sinus?

Intersex - Differential Diagnosis

- True Hermaphrodite
- Mixed Gonadal Dysgenesis
- Female Pseudohermaphrodite
- Male Pseudohermaphrodite

True Hermaphrodite

- 60% Look Male
- Most Will Have at Least a Rudimentary Vagina
- Internal Duct Structures Will Correspond to the Gonad on the Ipsilateral Side

PEEL
HERE

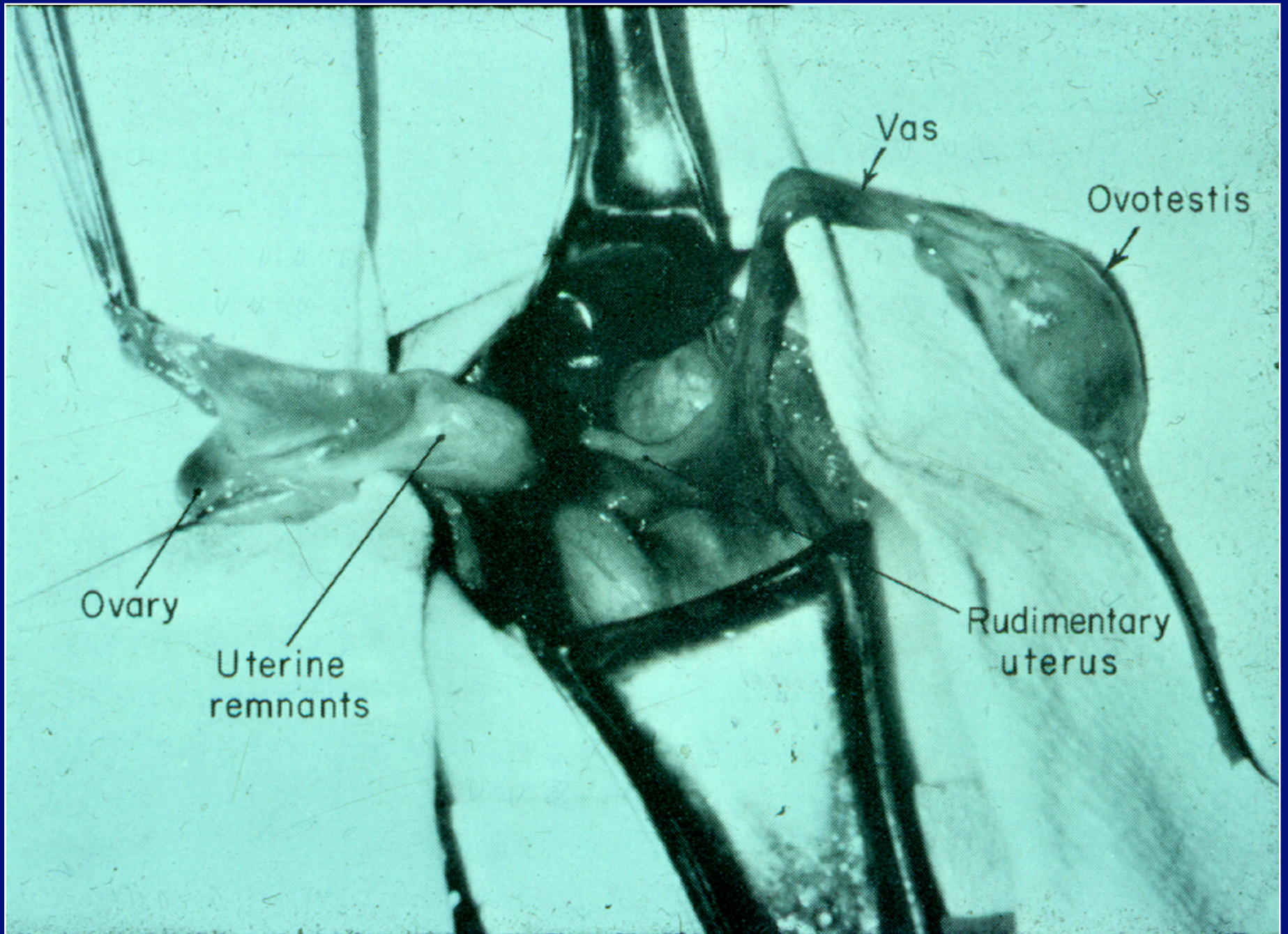
118a

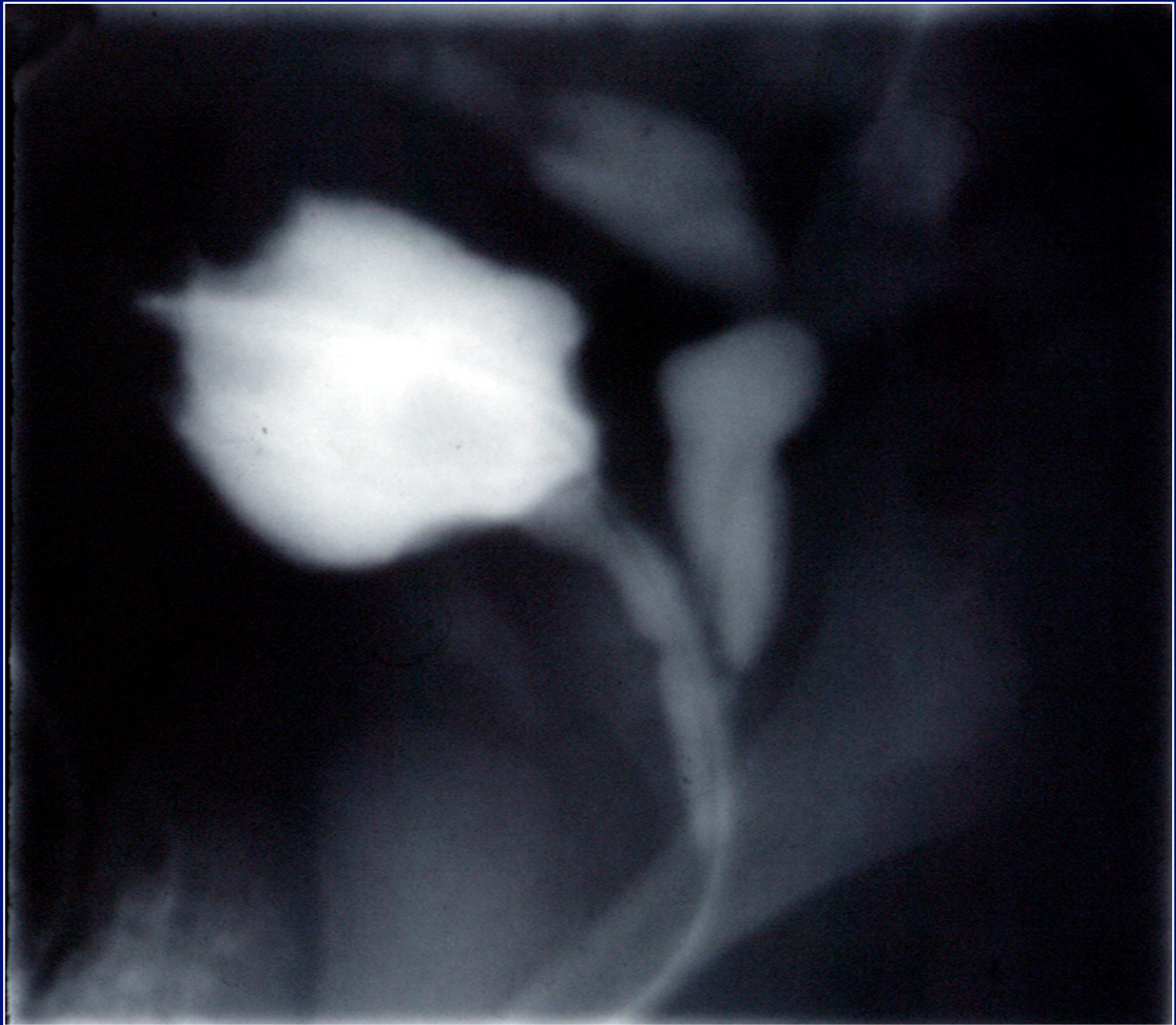
GARBAGE PAIL KIDS



HALF- NELSON







Mixed Gonadal Dysgenesis

- 45 XO/XY
- Streak+Testis (OVO)
- Poorly Virilized
- Sterile Male
- Short Stature
- High Incidence of Testis Tumor







Gender Assignment Decision

45-46 XO/XY

Male

Female

Orchiopexy
Orchiectomy
1st Stage Hypospadias Repair

E
A
R
L
Y

Gonadectomy
and
Clitoral Recession

Hormonal Stimulation

Hormonal Management

2nd Stage Hypospadias Repair

Vaginoplasty

Female Pseudohermaphrodite

- 46 XX - Virilized
- The Most Common Cause of Ambiguous Genitalia (AGS)
- DX
 - ◆ Karyotype
 - ◆ Biochemical Markers
 - ◆ No Surgery Necessary

Normal ♀

I

II

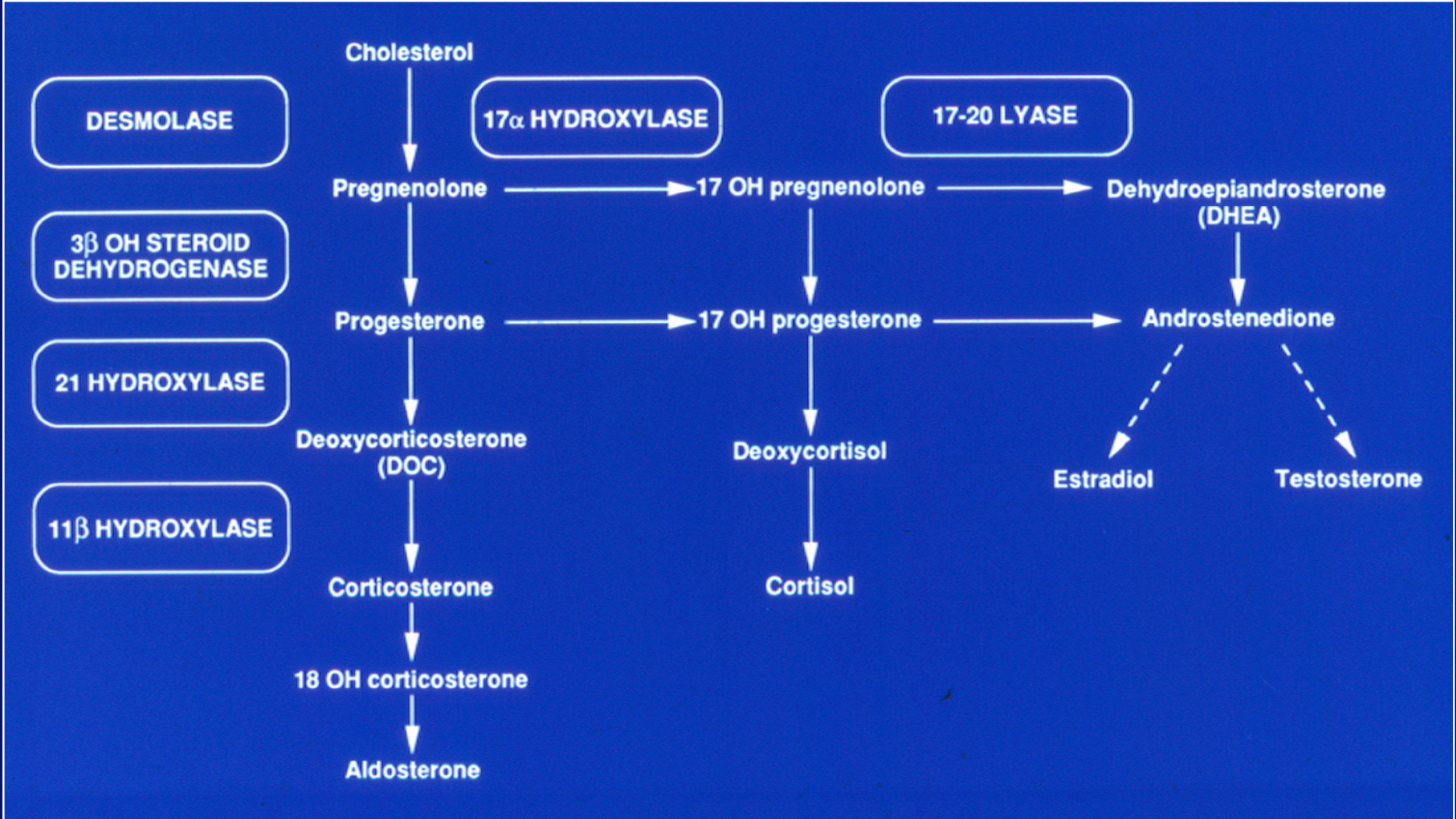
III

IV

V

Normal ♂



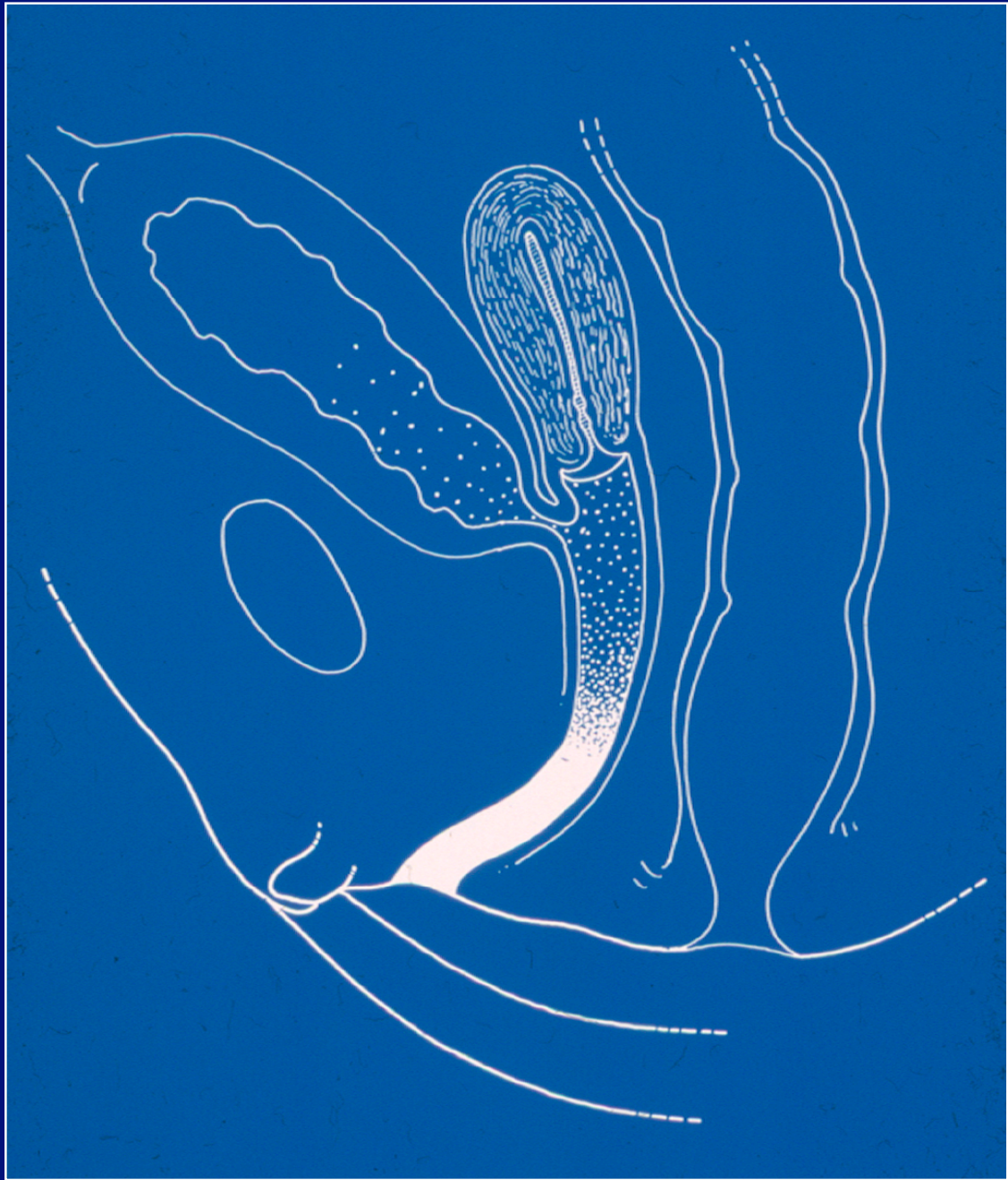




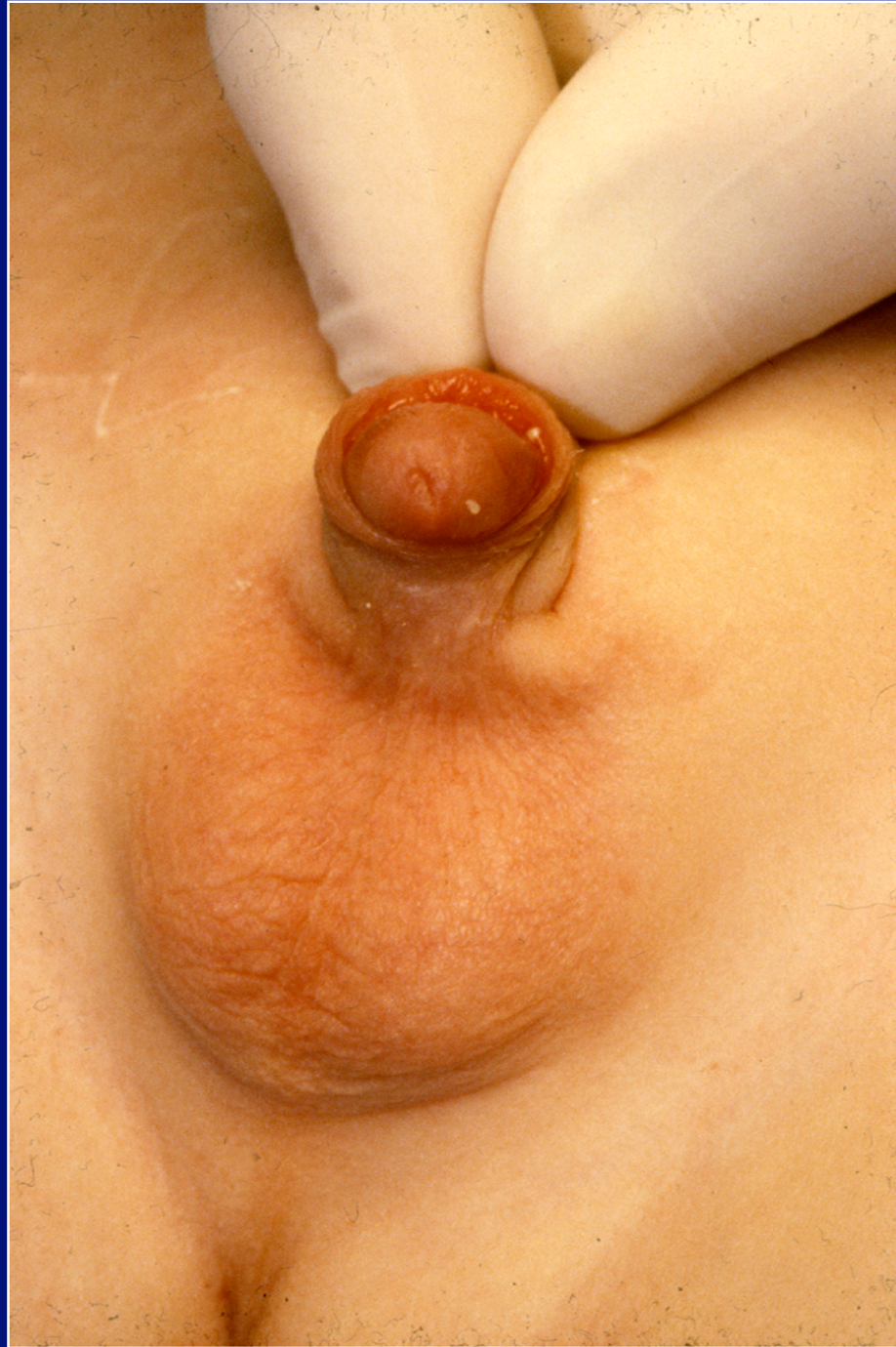




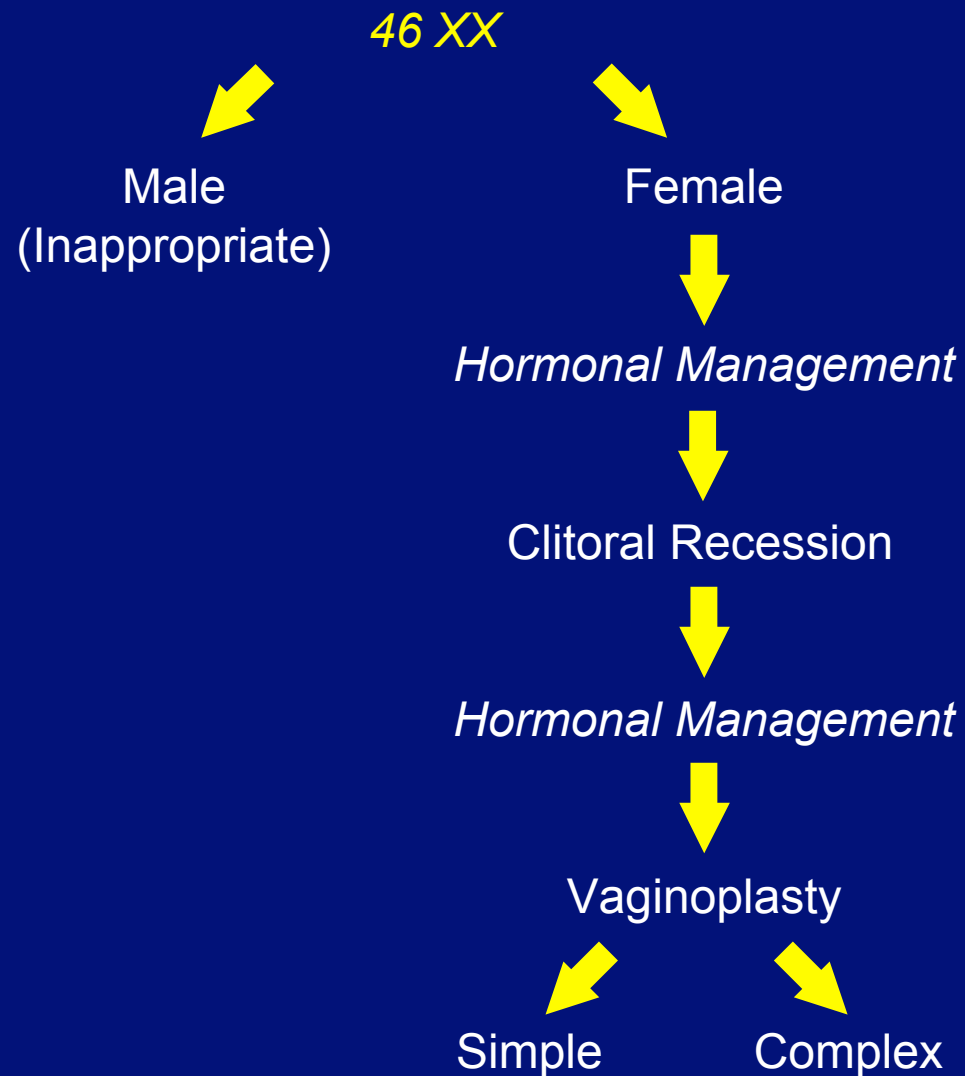
UROGENITAL SINUS
IN THE FEMALE







Gender Assignment Decision



Male Pseudohermaphrodite

- XY Individual
 - ◆ Poorly Virilized
 - ◆ Diminished Androgen Production
 - ◆ Diminished Androgen Response (Spectrum)
 - ◆ Diminished DHT

BUCCAL SMEAR →

KARYOTYPE →

URINARY KETOSTEROIDS →

GONADAL BIOPSY →

ETIOLOGY →

CHROMATIN +

CHROMATIN -

XX

XX
(60%)

XO
XO/XY

XY

XO/XY

FEMALE PSEUDOHERMAPHRODITE (VIRILIZED FEMALE)

TRUE HERMAPHRODITE

MALE PSEUDOHERMAPHRODITE

MIXED GONADAL DYSGENESIS

elevated

normal

Adrenogenital Syndrome
AUTOSOMAL RECESSIVE

Enzyme deficiencies:
21 Hydroxylase
11 Hydroxylase
3β Hydroxysteroid dehydrogenase

Maternal ingestion of androgens or maternal tumors

Mixed testes & ovaries

Testes

Testes

Testes

Testes + streak ovaries

? Undetected Y of mosaicism

Diminished androgen production
AUTOSOMAL RECESSIVE

Enzyme deficiencies:
20,22 Desmolase
20α Hydroxylase
3β Hydroxysteroid dehydrogenase
17α Hydroxylase
17,20 Desmolase
17β Ketosteroid reductase

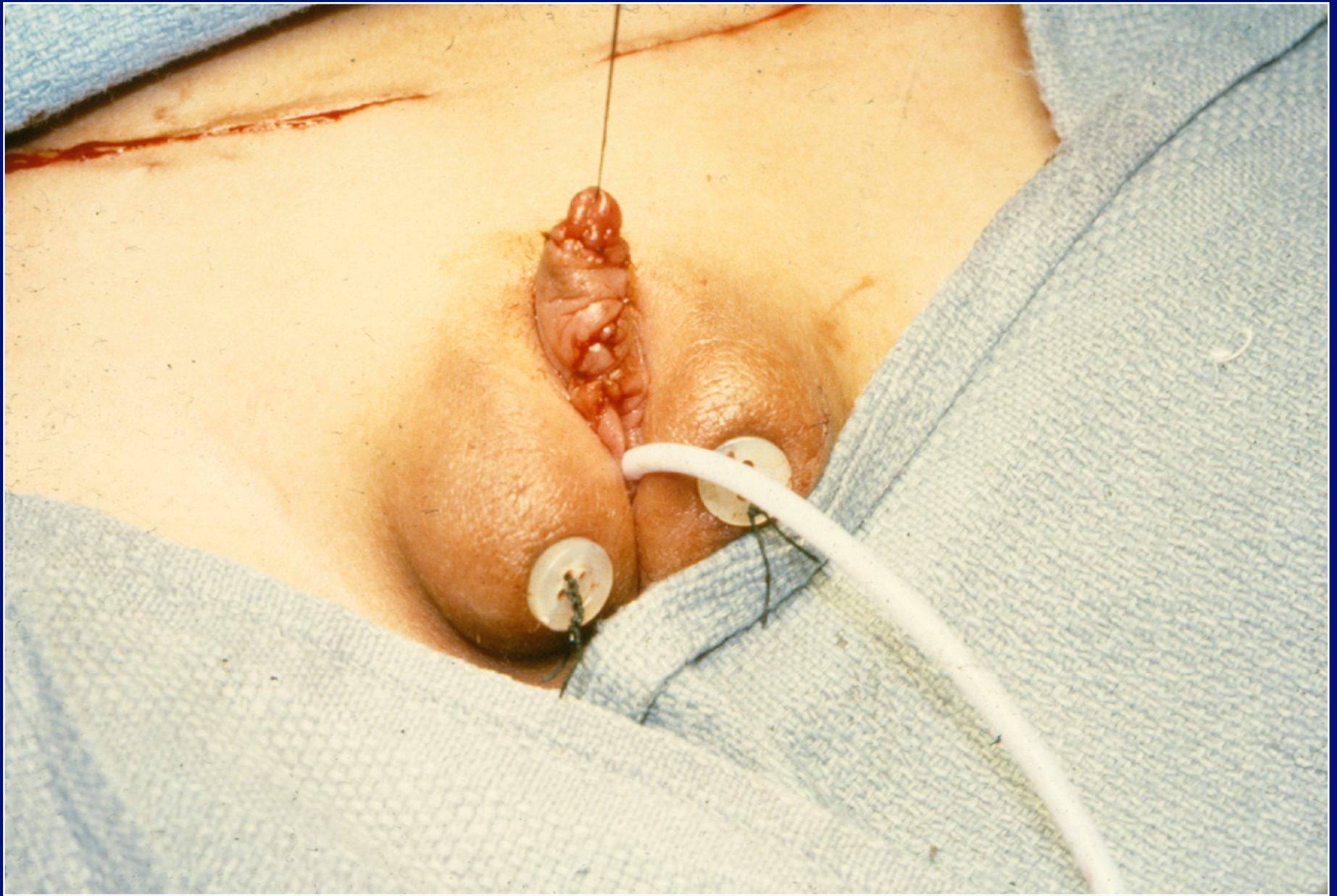
Diminished androgen response
X-LINKED RECESSIVE

↓ Androgen binding protein
Testicular feminization (Classic type)
Familial Incomplete ♂ pseudohermaphroditism (Type I)
• Lubs' syndrome
• Reifenstein syndrome
• Gilbert-Dreyfus syndrome
• Rosewater syndrome

Diminished 5-dihydro-testosterone
AUTOSOMAL RECESSIVE

5α Reductase deficiency
Familial Incomplete ♂ pseudohermaphroditism (Type II)
• Pseudovaginal perineoscrotal hypospadias





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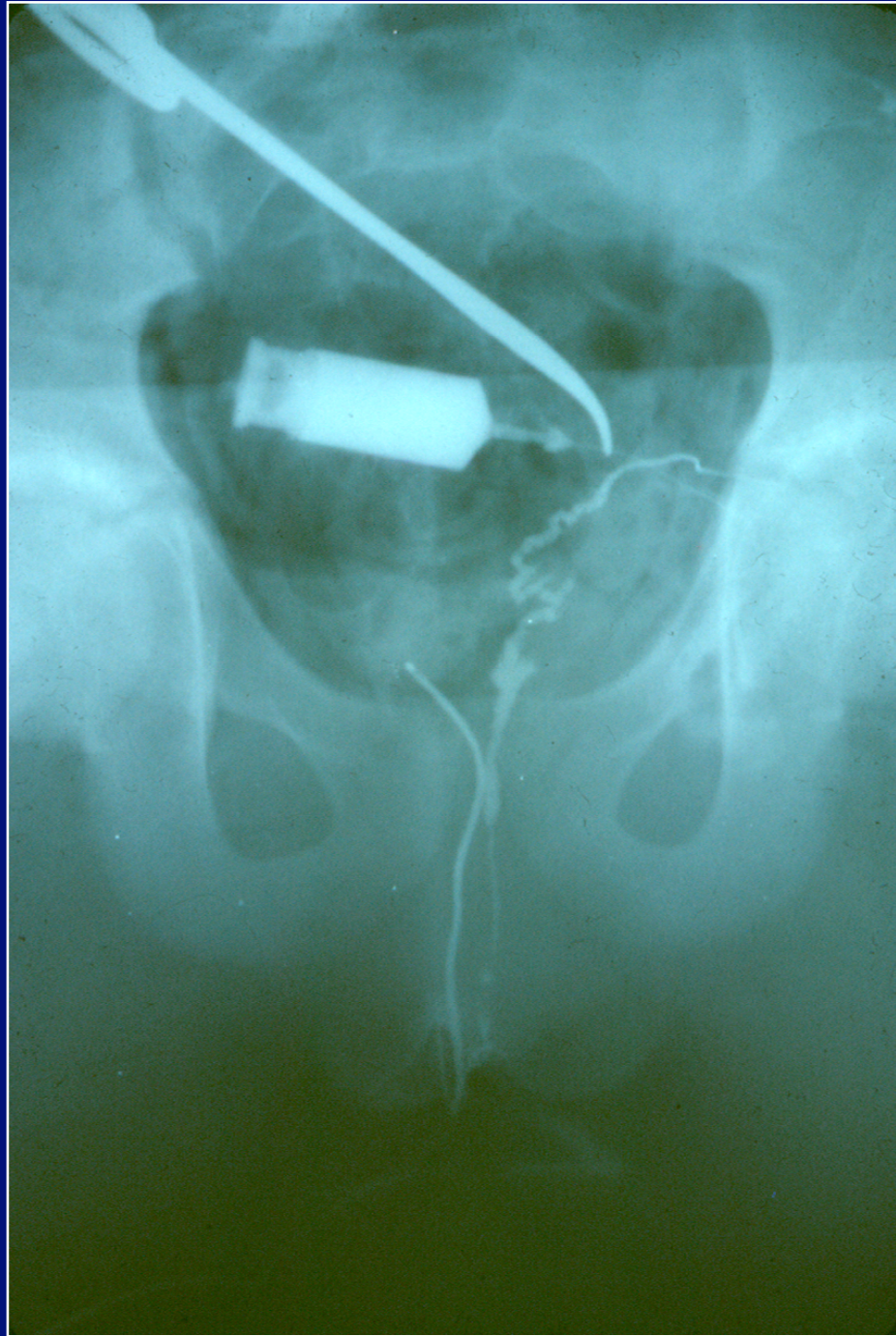
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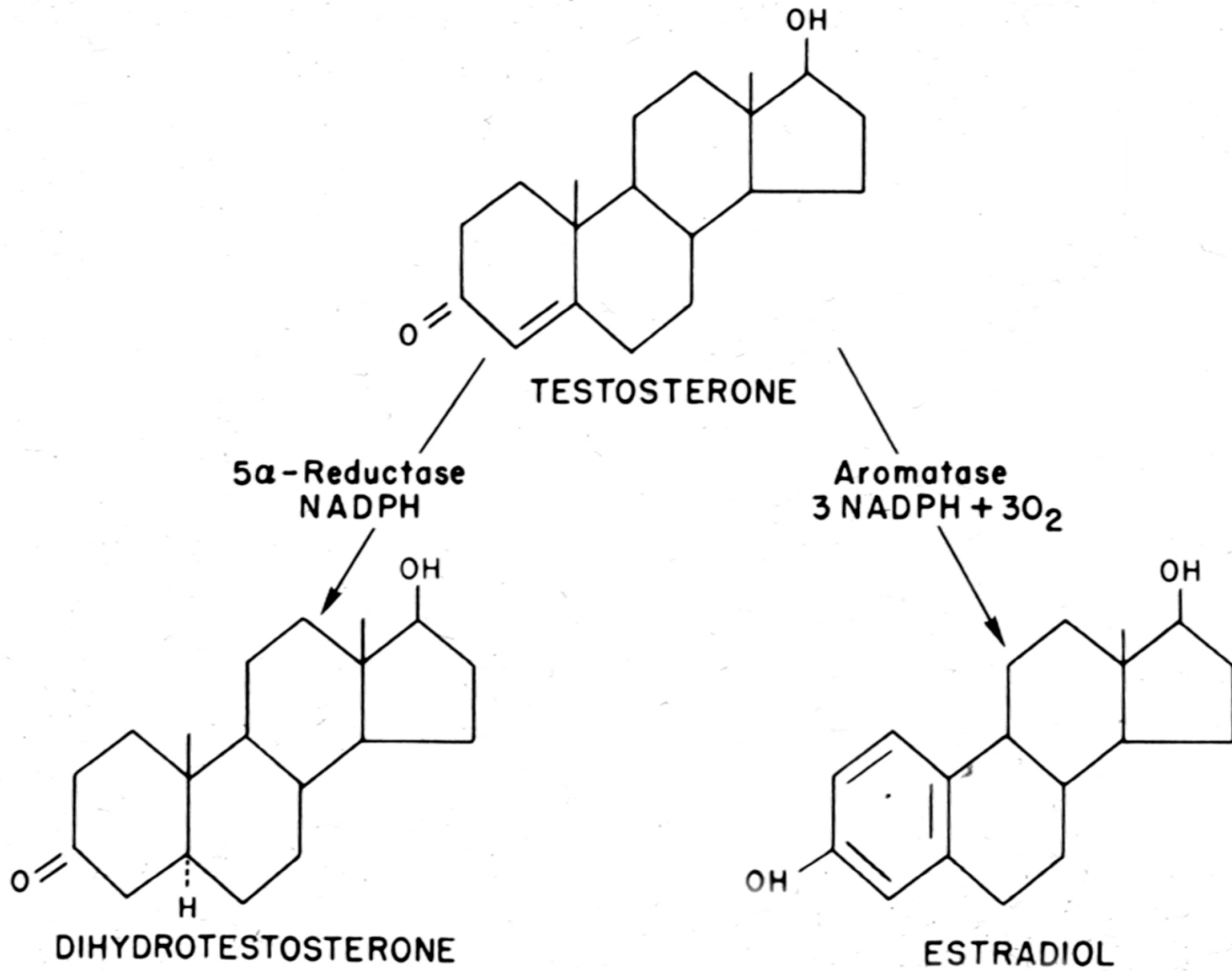
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XO/XY

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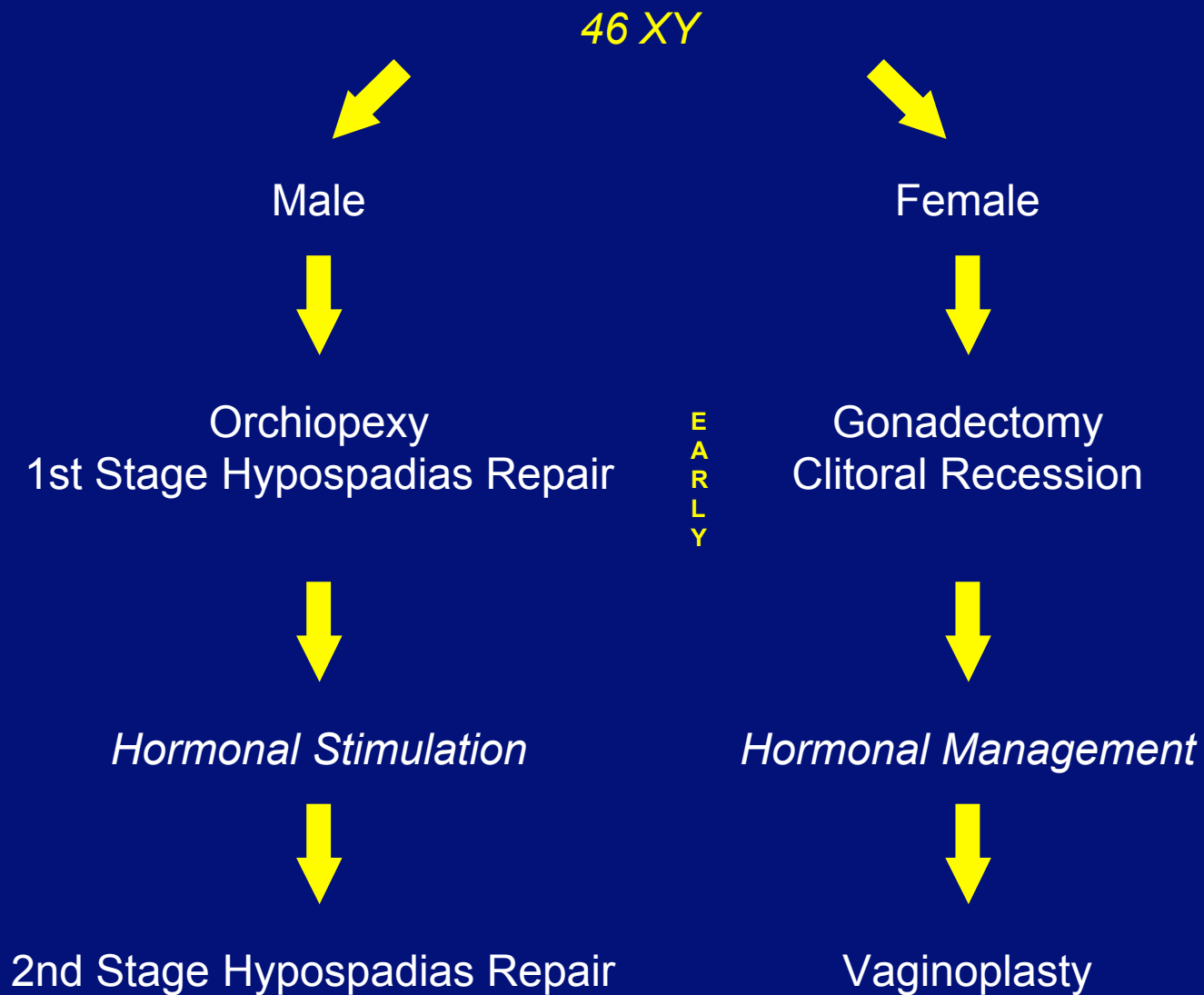
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Gender Assignment Decision



Gender Assignment Decision

Conclusions:

1. Maintain gonadal sex whenever possible
2. Gonads inappropriate for gender assignment should come out early.
3. Clitoral Recession, Orchiectomy and Hypospadias Repair are best done early.
4. Vaginoplasty can be delayed.
5. Long-term follow-up and management are essential.

Treatment

Early

- Gender Assignment - By Committee
- Steroid Replacement

Later (if necessary)

- Gonadectomy
- Clitoral Recession
- Vaginoplasty
- Psychotherapy

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**"For the last time, Junior, Mrs. Burda doesn't
want a sex change!"**

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9	5
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8	5
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9	2
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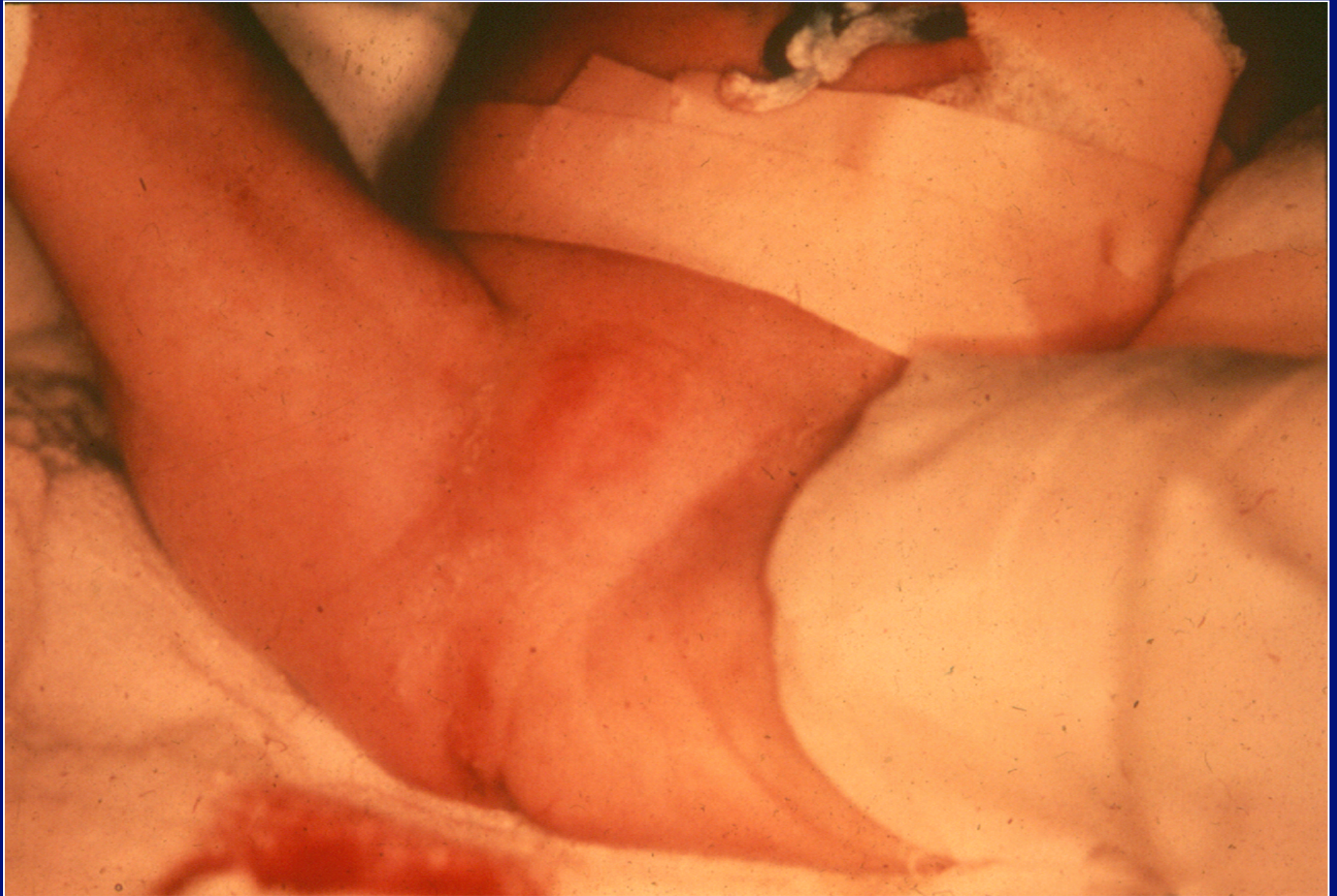
~~Keay, Baby Boy~~ ^{GIRL}

CAL CENTER
ERSEY 07601

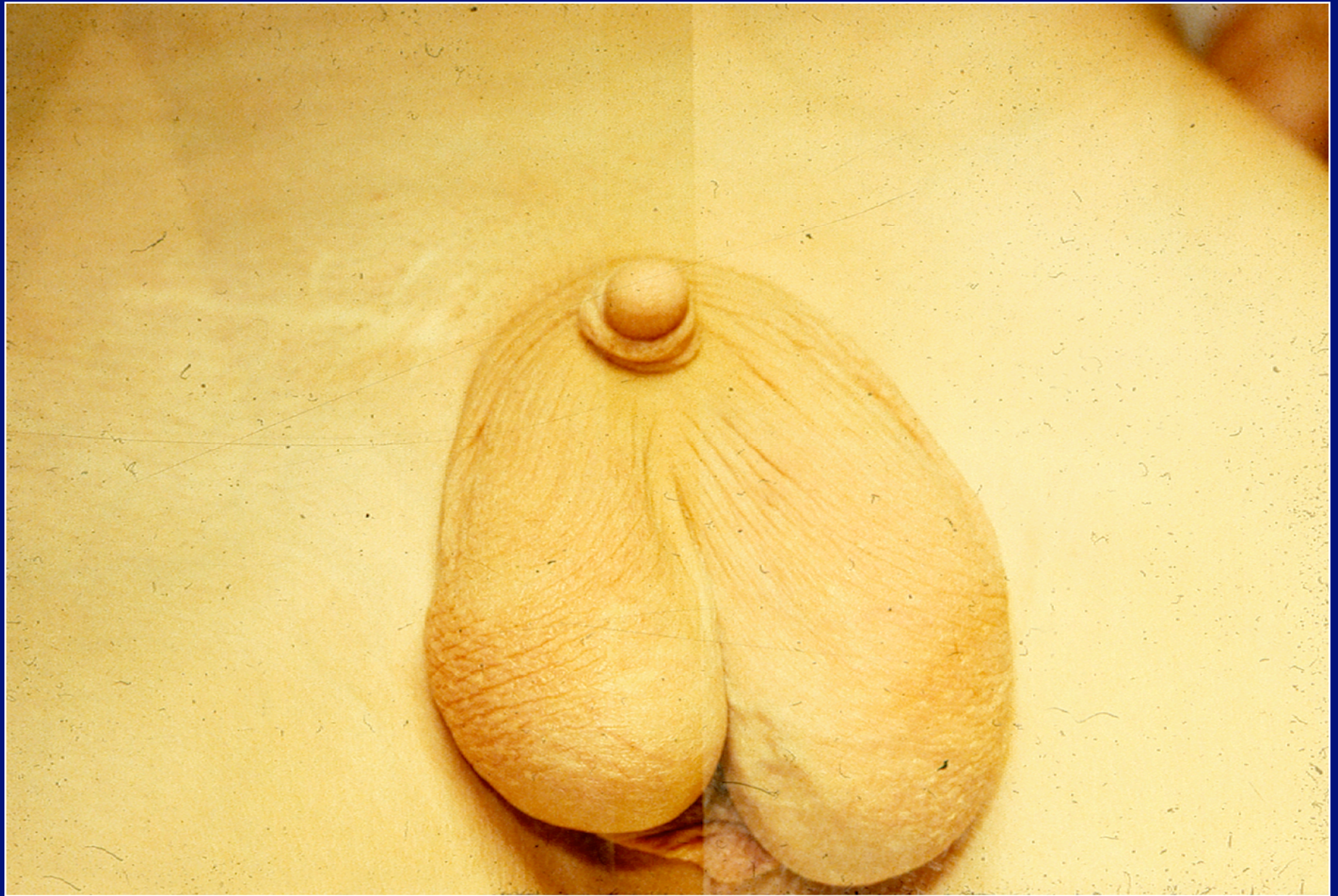
Some originals in LF.

OR	REMARKS	DOB
	Repeat - by uterine ultrasound	
	original sinus - bladder	















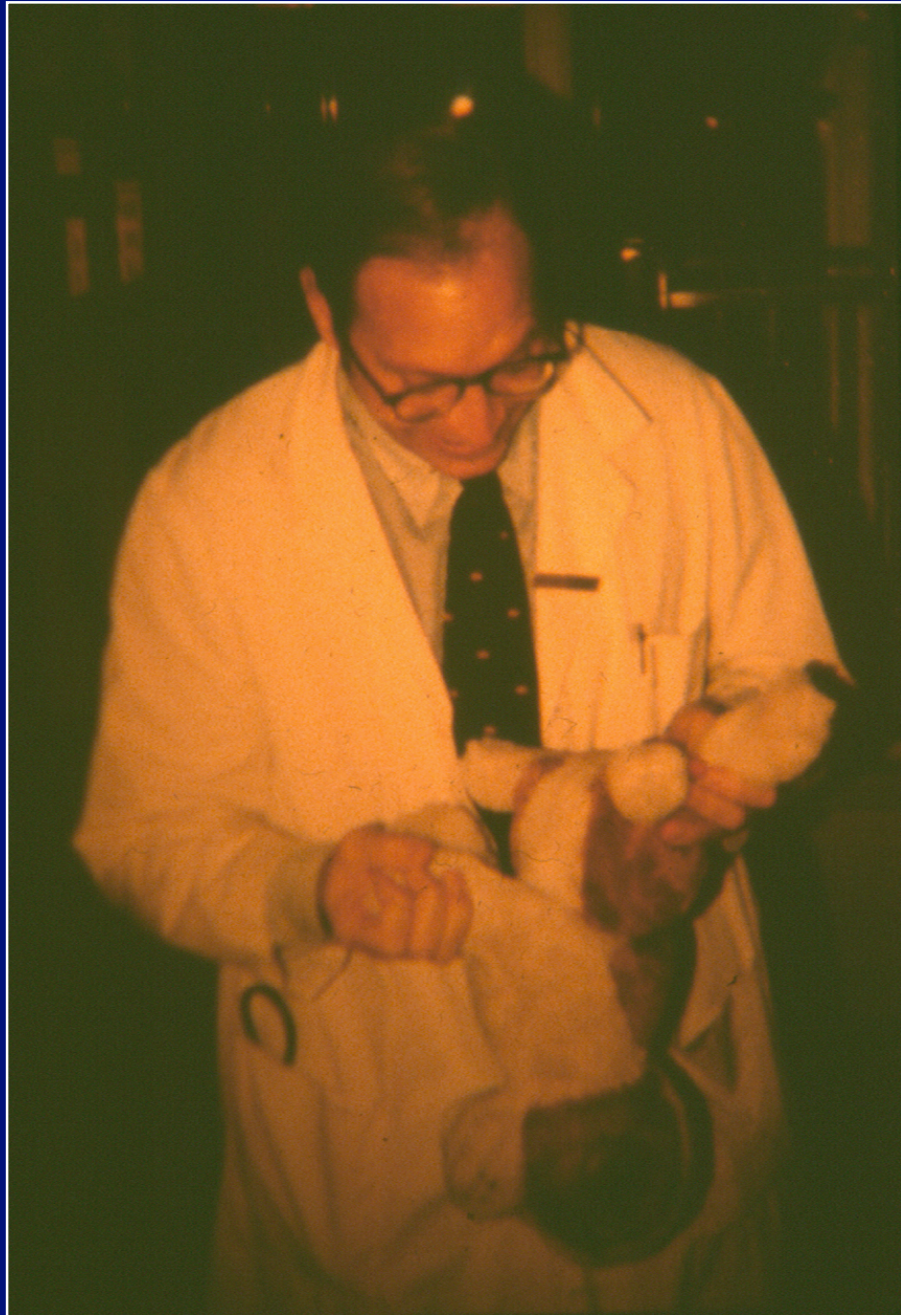
Workup

History

- Maternal Androgen
- Family History

Physical Exam

- How Many Openings
- Size of the Phallus
- Palpable Gonads
- Presence of a Uterus



Stretched penile length in normal males. Values are expressed in cm.

S.D.	Mean \pm S.D.	Mean - 2.5
Newborn, 30 weeks	2.5 \pm 0.4	1.5
Newborn, 34 weeks	3.0 \pm 0.4	2.0
Newborn, term	3.5 \pm 0.4	2.4
0-5 months	3.9 \pm 0.8	1.9
6-12 months	4.3 \pm 0.8	2.3
1-2 years	4.7 \pm 0.8	2.6
2-3 years	5.1 \pm 0.9	2.9
3-4 years	5.5 \pm 0.9	3.3
4-5 years	5.7 \pm 0.9	3.5
5-6 years	6.0 \pm 0.9	3.8
6-7 years	6.1 \pm 0.9	3.9
7-8 years	6.2 \pm 1.0	3.7
8-9 years	6.3 \pm 1.0	3.8
9-10 years	6.3 \pm 1.0	3.8
10-11 years	6.4 \pm 1.1	3.7
Adult	13.3 \pm 1.6	9.3



Workup - Later

- Urethrogram
- Karyotype
- Biochemical Markers
- SRY Gene
- Laparoscopy +/- Gonadal BX

Surgical Goals

- Sexually Functional
- Cosmetically Acceptable

Conclusions

- Gender Assignment Is a Medical Emergency
- A Gender Assignment Committee Should Be Utilized
- The Gonadal Sex Should Be Maintained If Possible
- If Gonadal Sex Is Not Maintained, Early Gonadectomy Is Important



There is a difference