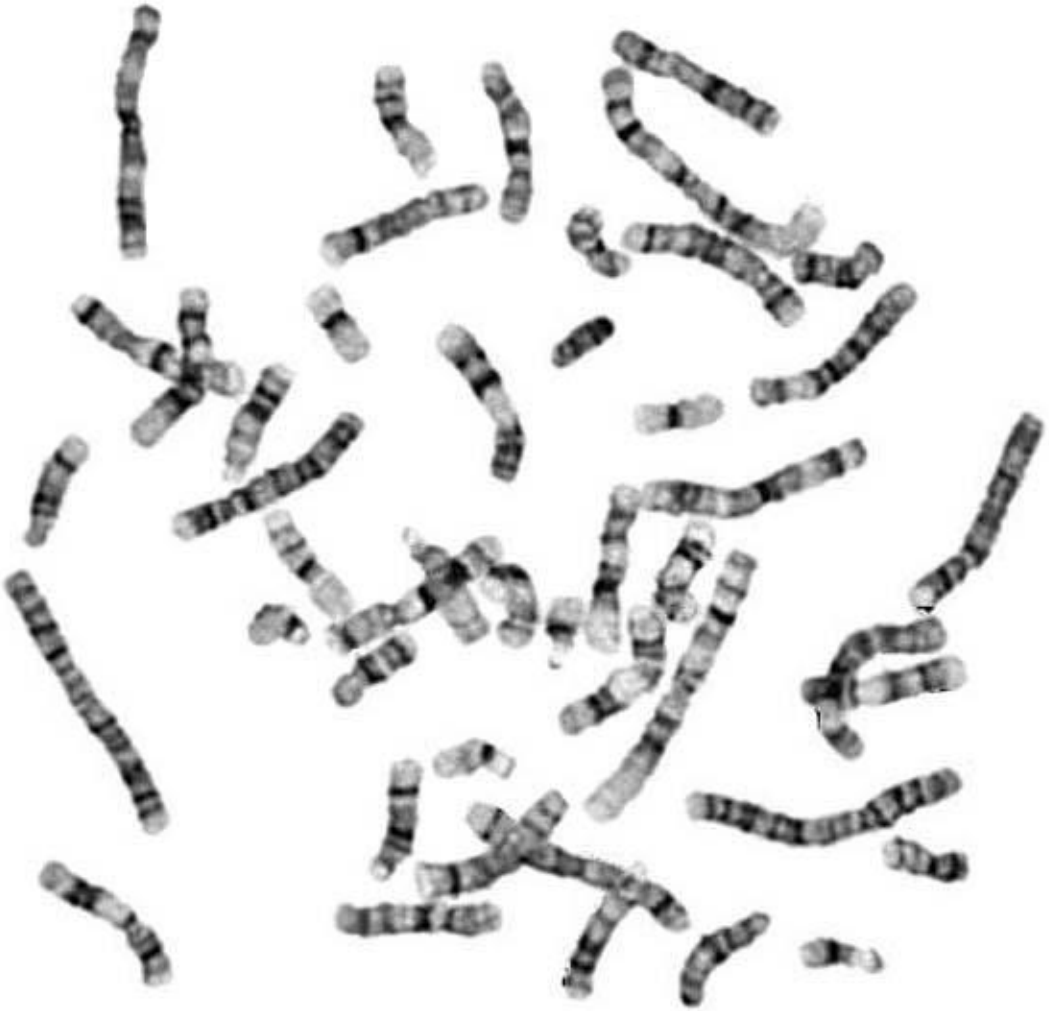
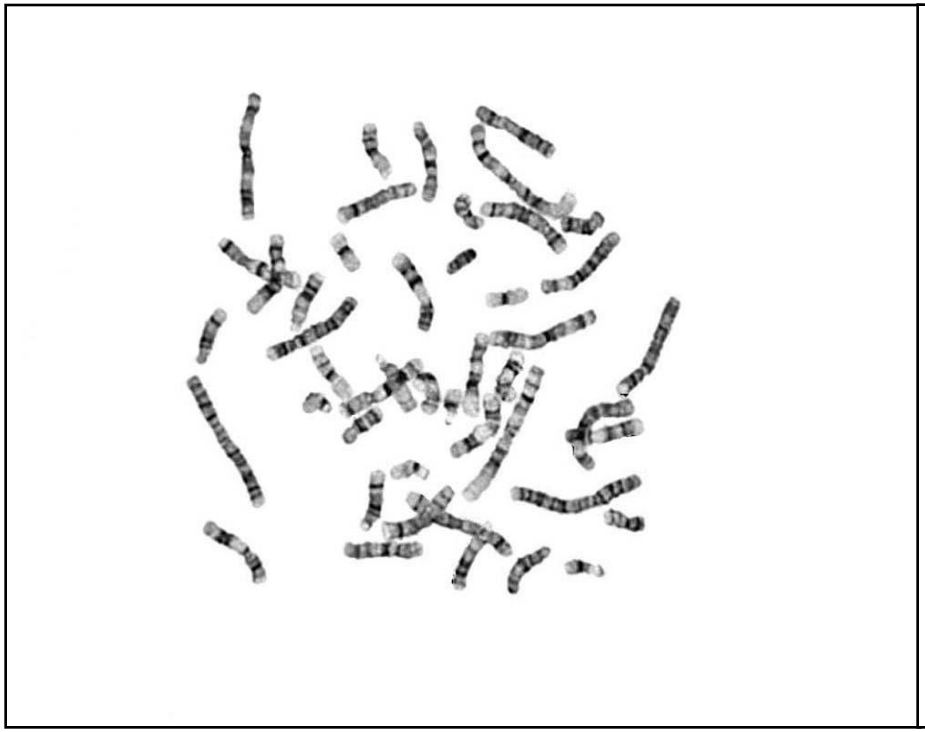
ABERRAÇÕES CROMOSSÔMICAS

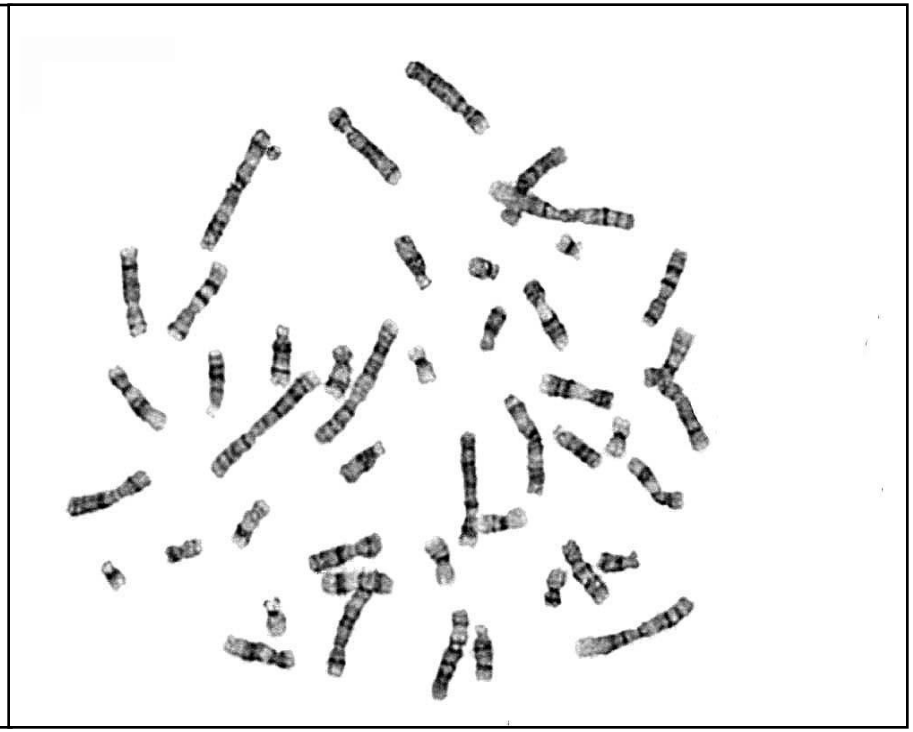
0.7% **nascimentos** **(1/160);**

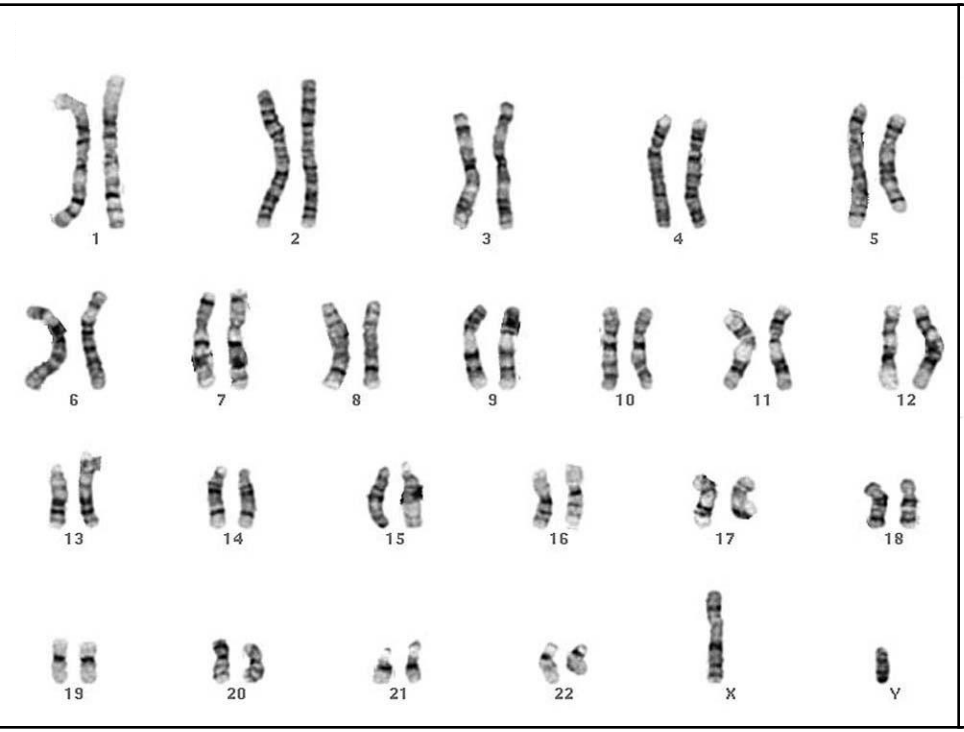
2% **gravidezes (>35 anos);**

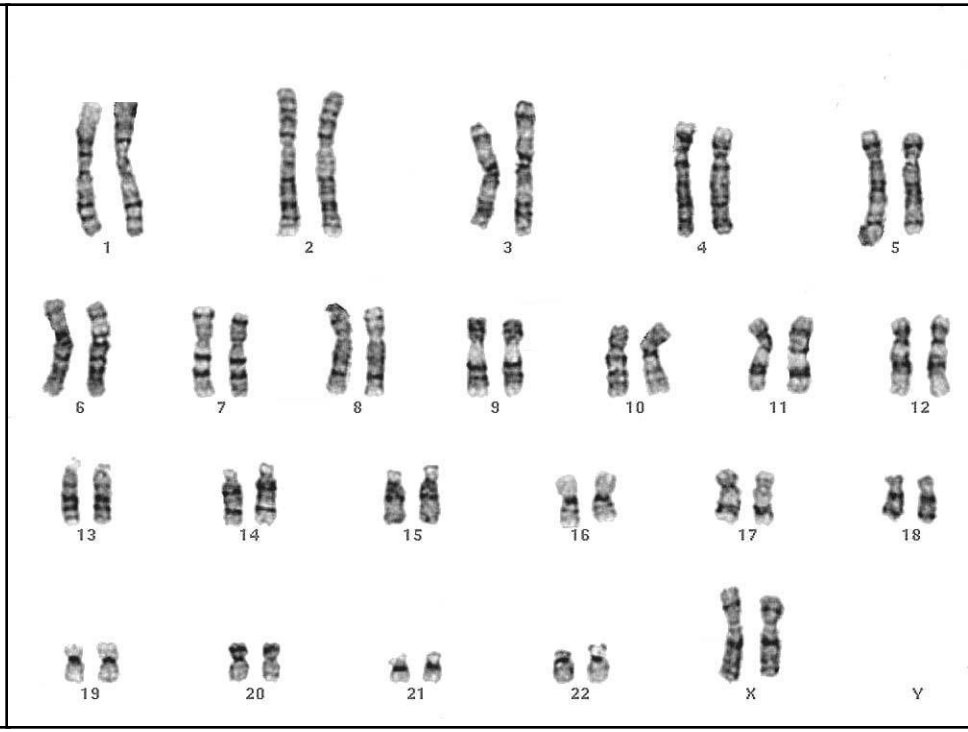
50% **abortos espontâneos 1º trimestre;**








1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y


1
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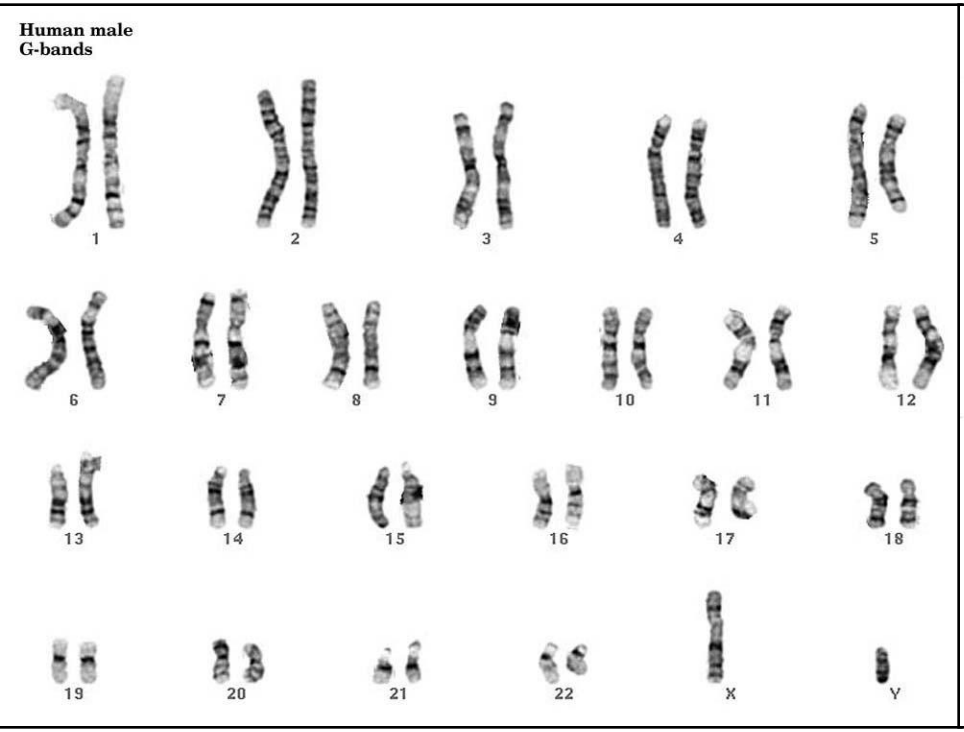
14
15
16
17
18
19
20
21
22
X
Y

46,XY


Human male
G-bands
1
2
3
4
5
6
7
8
9
10
11
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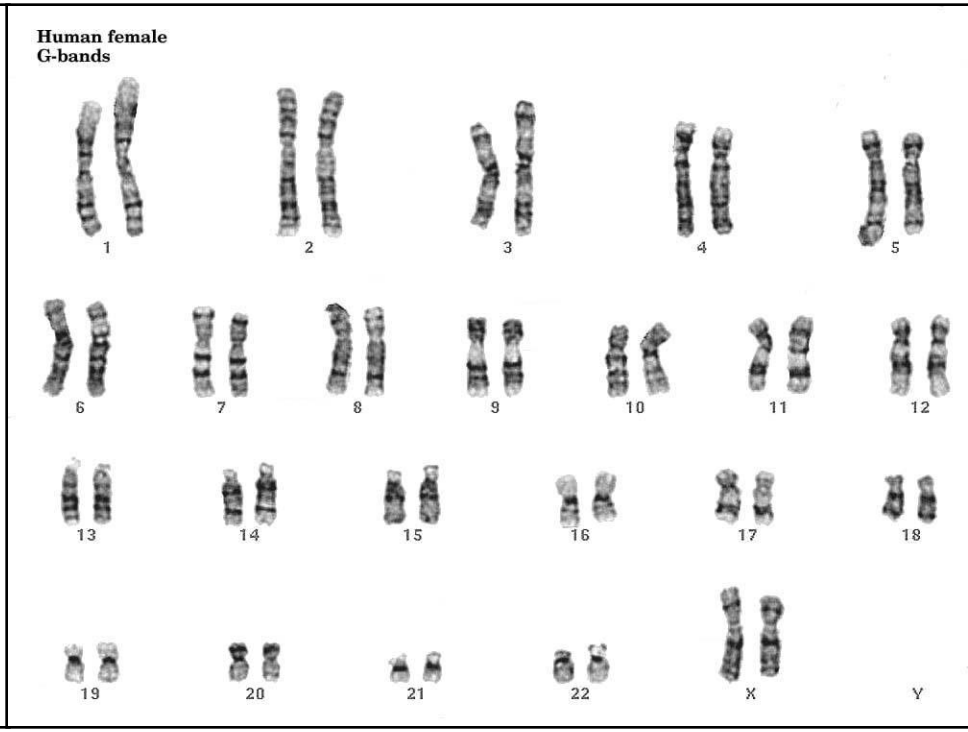
13
14
15
16
17
18
19
20
21
22
X
Y

46,XX


Human female
G-bands
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y

MECANISMOS DE DETERMINAÇÃO SEXUAL

- Cromossomos sexuais diferentes
(♀ XX, ♂ XY)

- Razão X/autossomo
(♀ XX, ♂ X0)

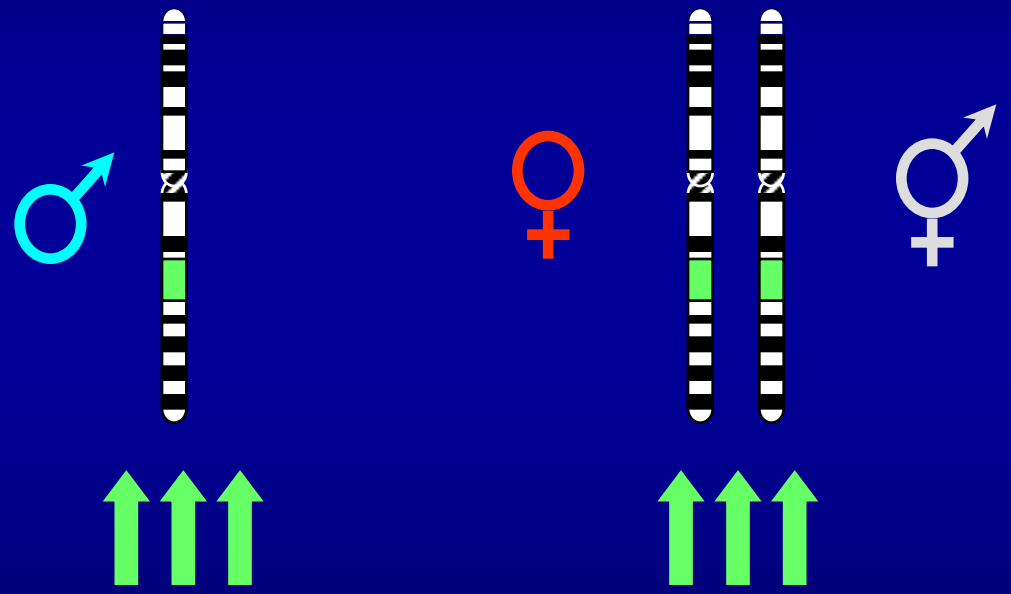
X

Y

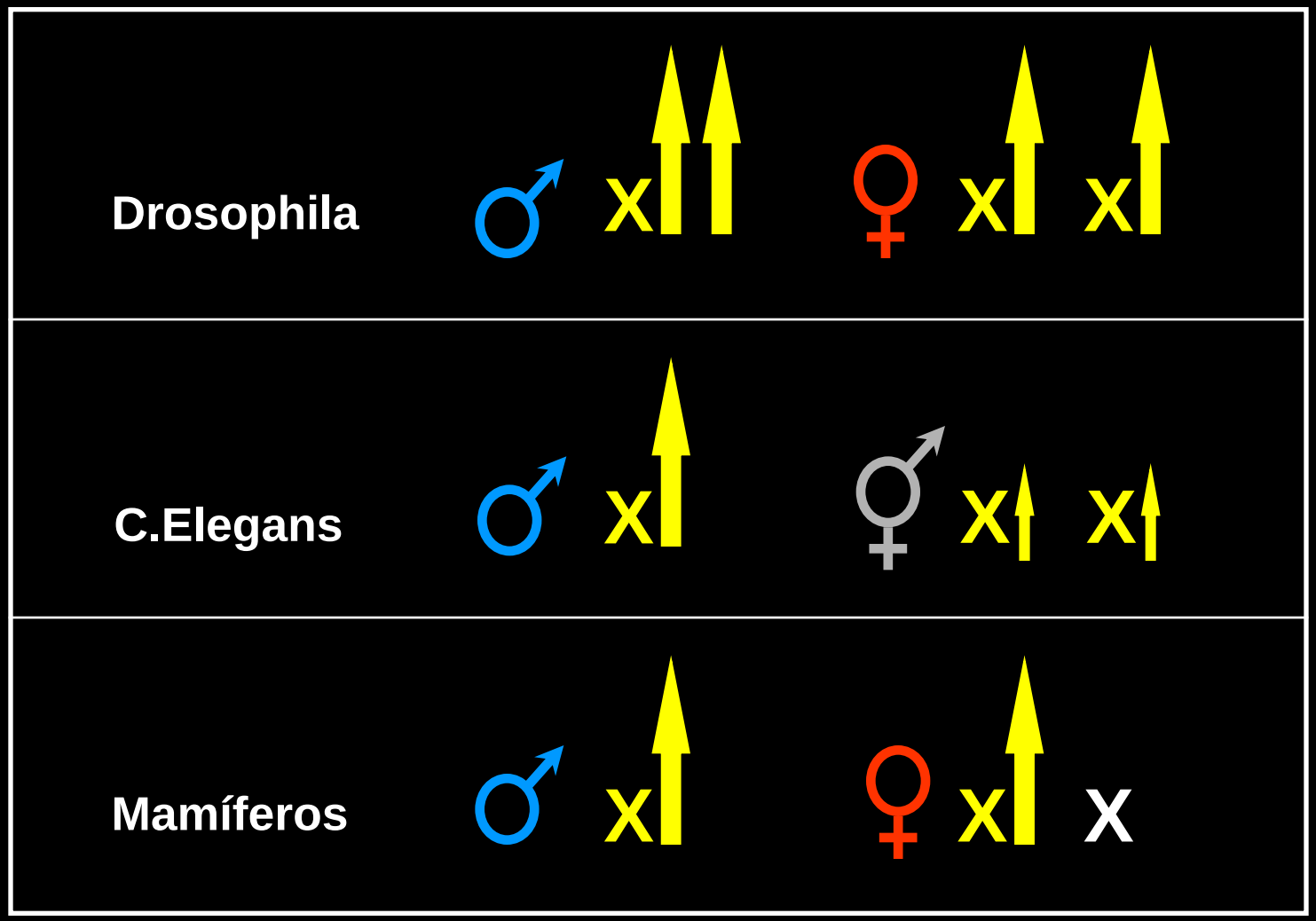
região
pseudo-autossômica

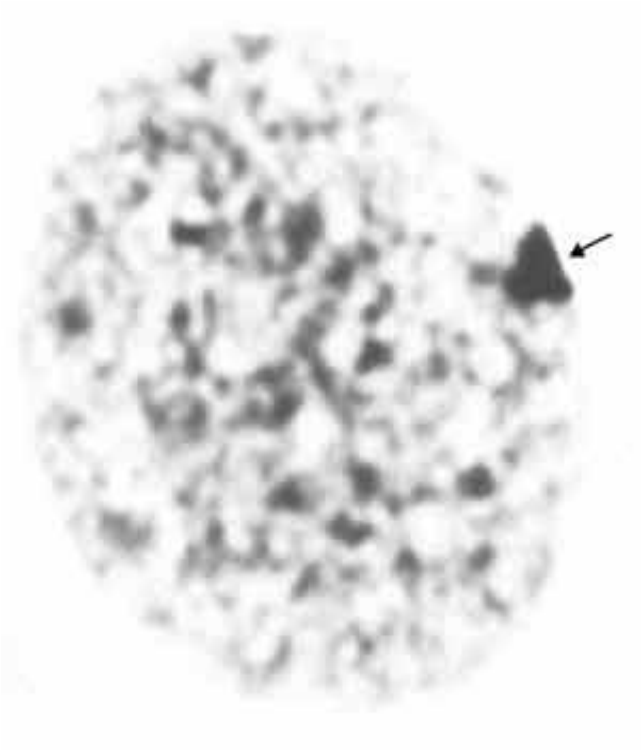
poucos genes

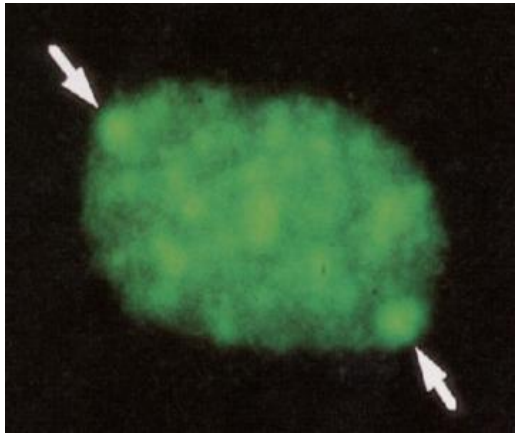
COMPENSAÇÃO DE DOSE



MECANISMOS DE COMPENSAÇÃO DE DOSE

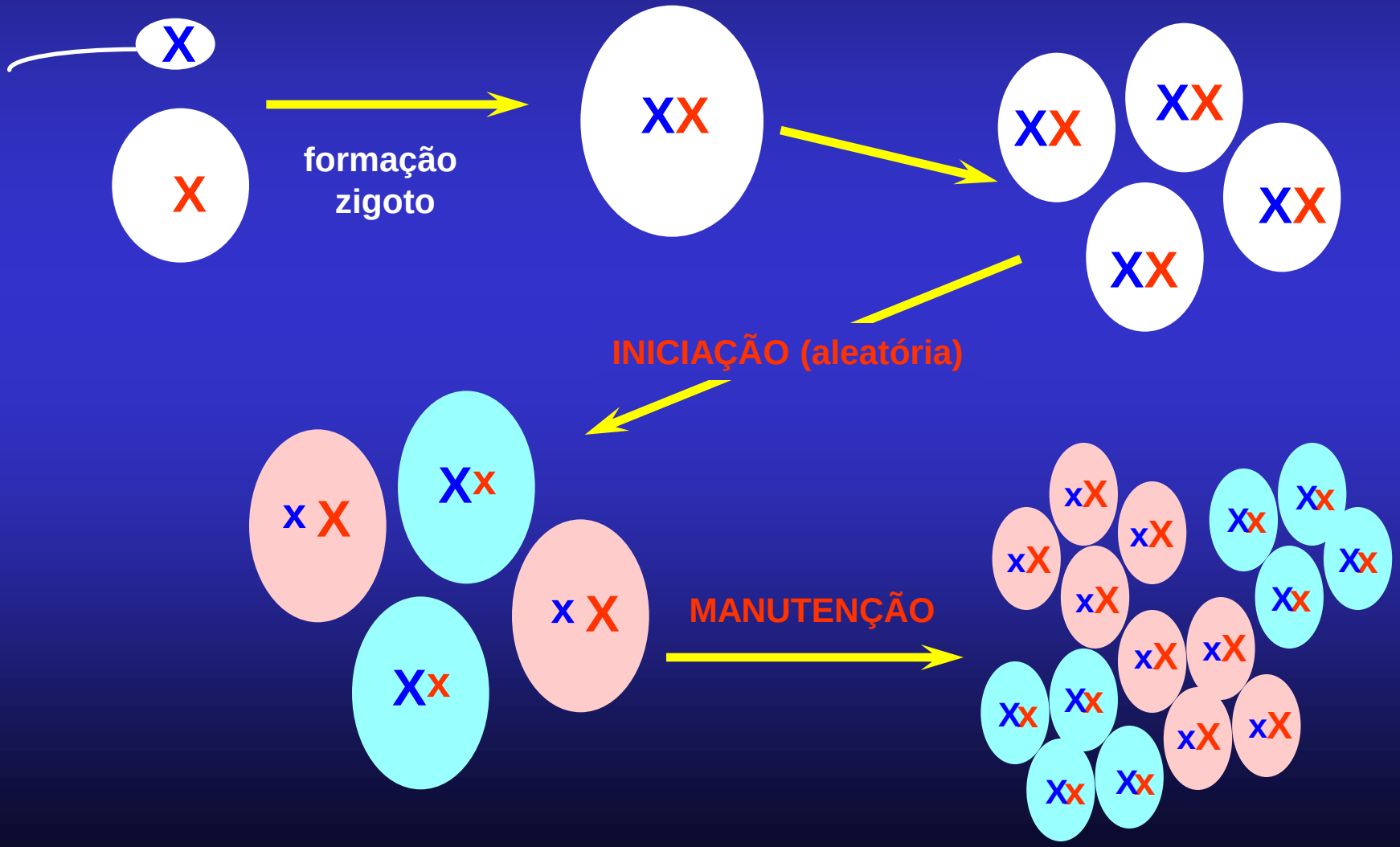




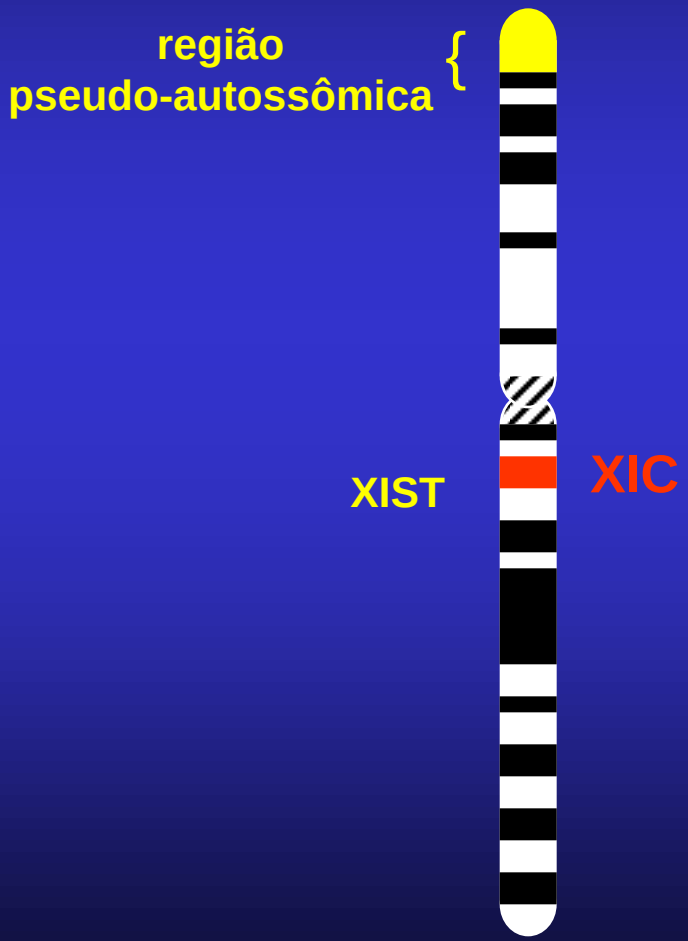


Inativação do Cromossomo X

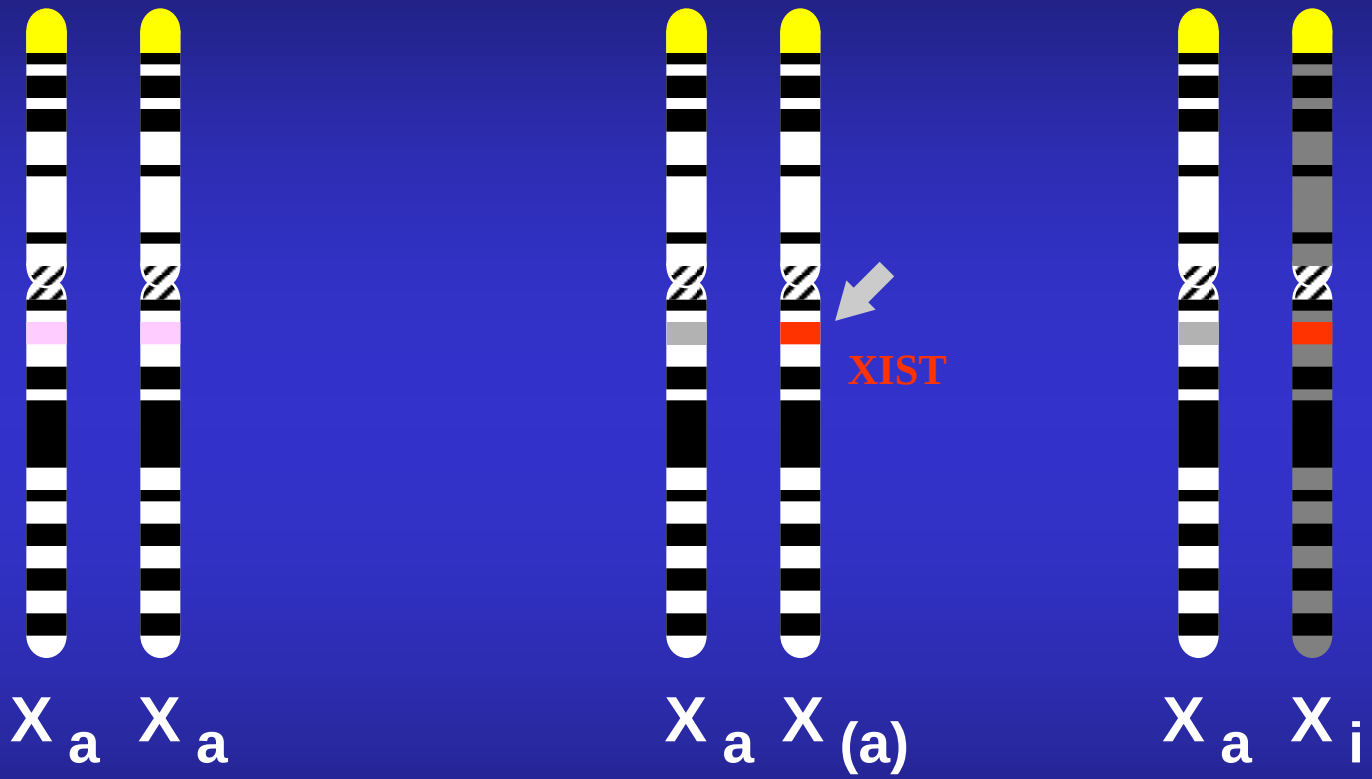
Hipótese de Lyon



Cromossomo X

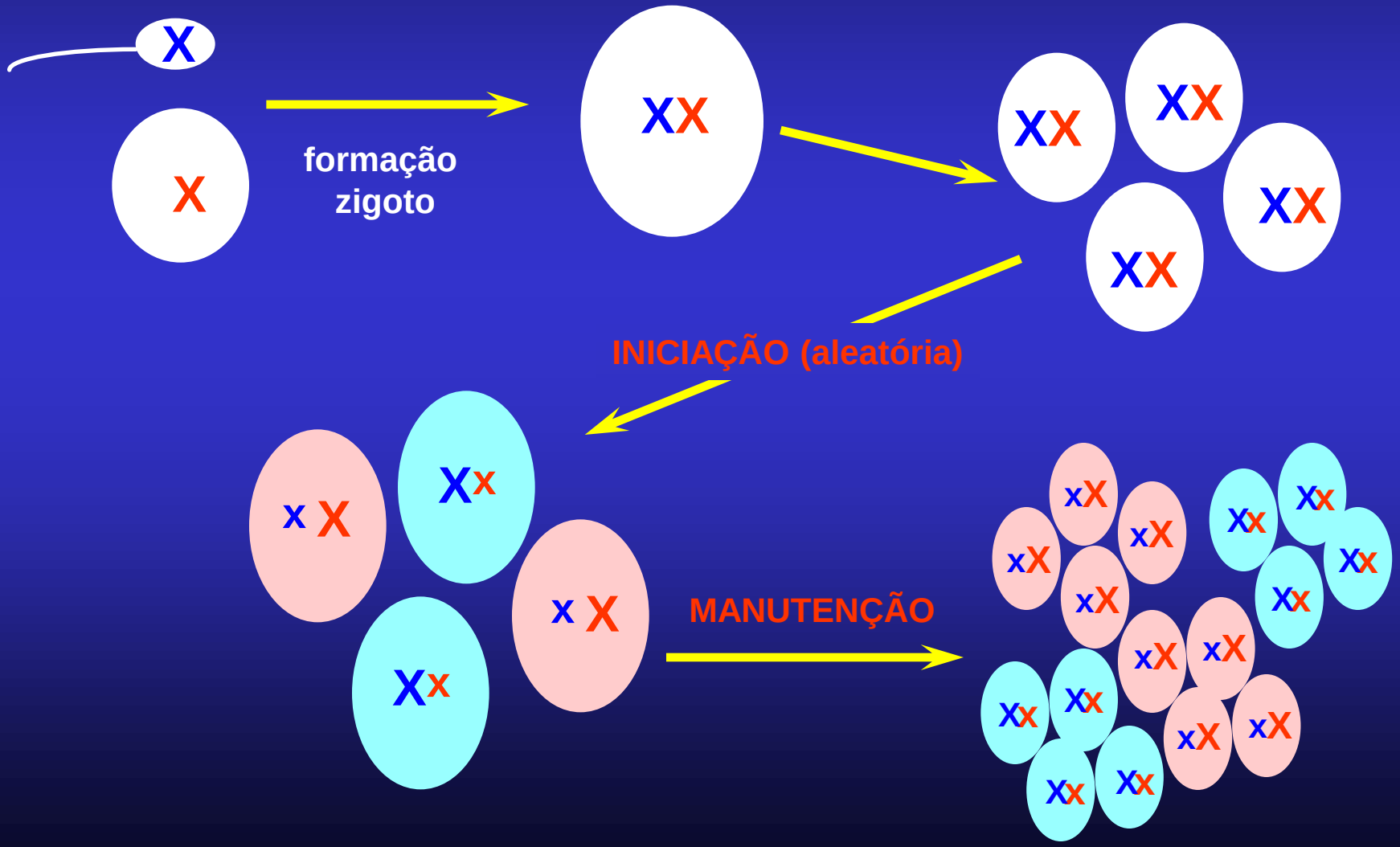


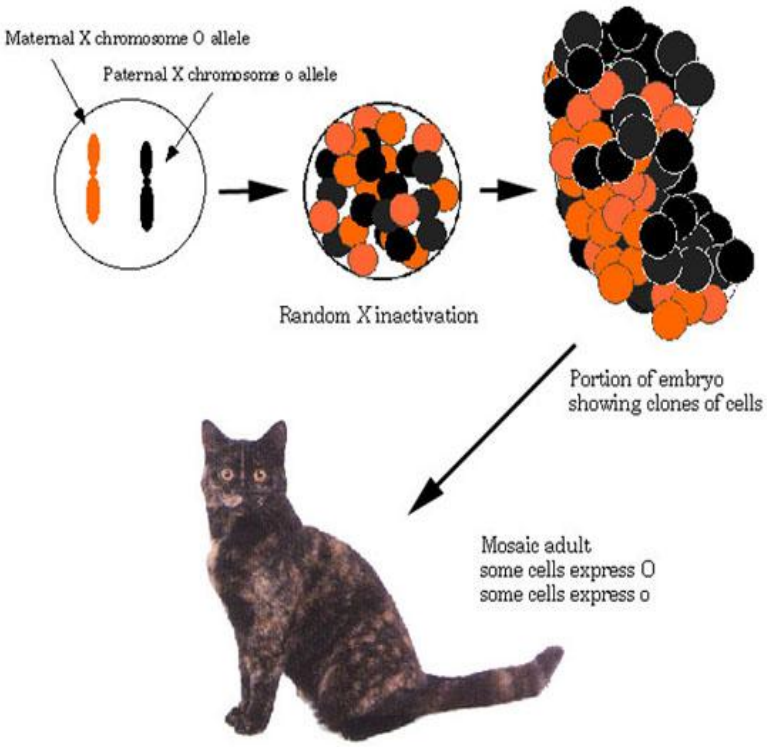
INICIAÇÃO

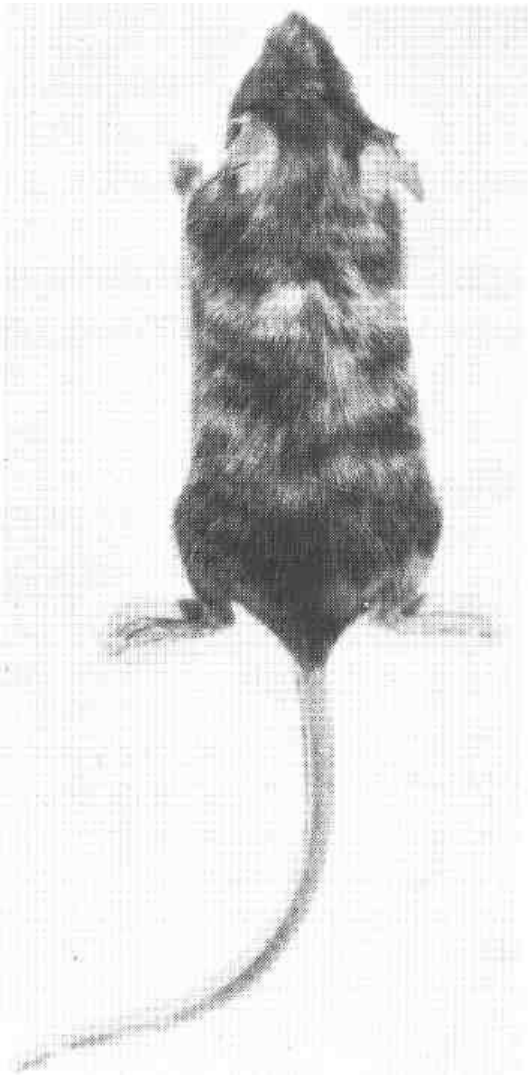


Inativação do Cromossomo X

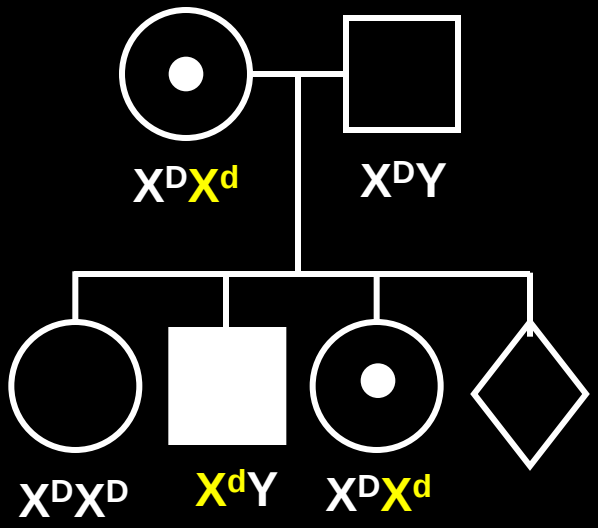
Hipótese de Lyon

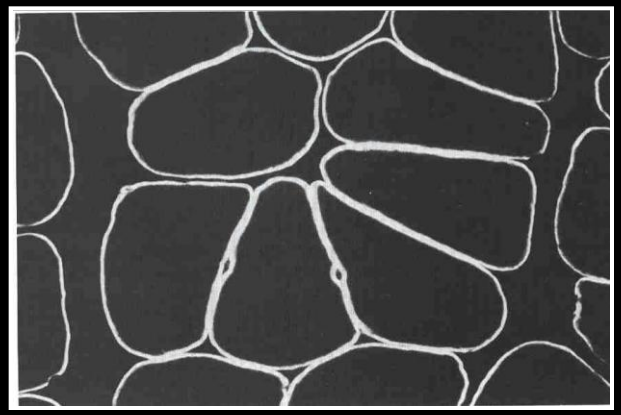


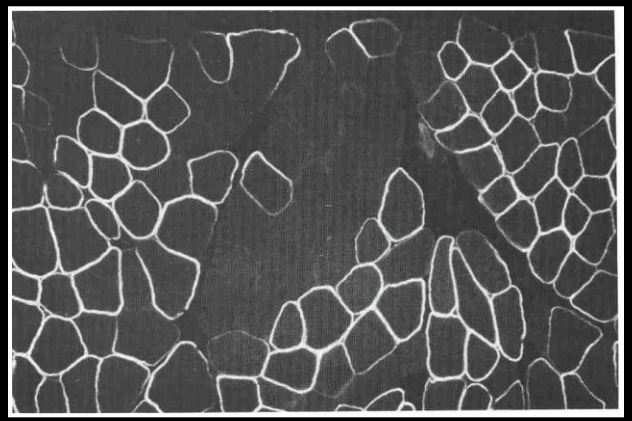

Maternal X chromosome O allele
Paternal X chromosome o allele
Random X inactivation
Portion of embryo
showing clones of cells
Mosaic adult
some cells express O
some cells express o

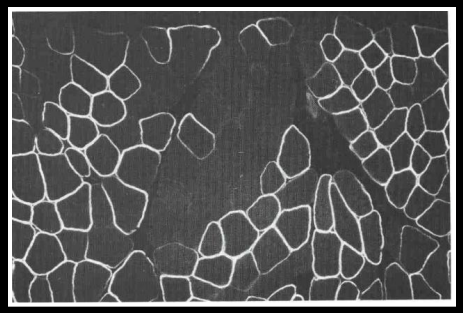


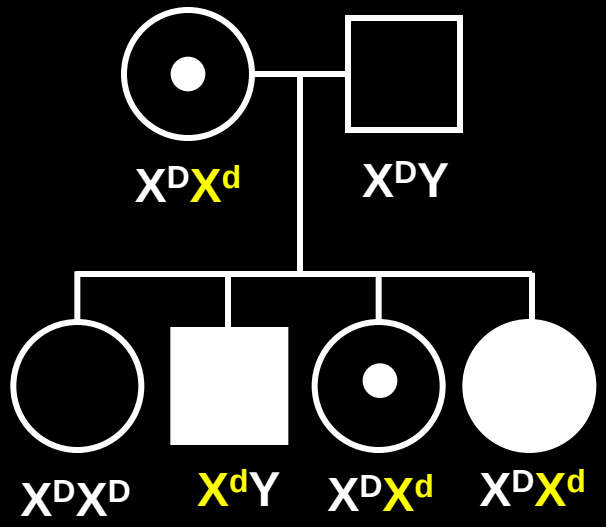
Herança recessiva ligada ao X: DMD

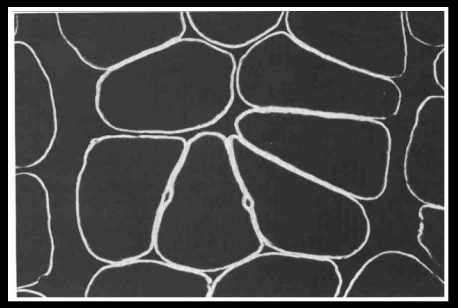


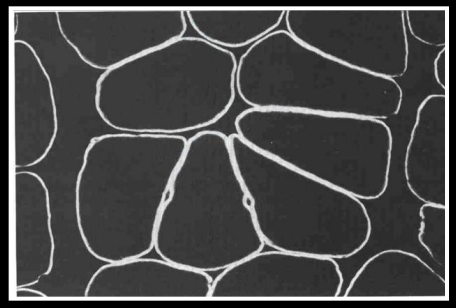


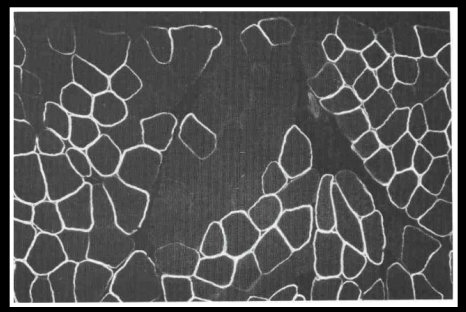




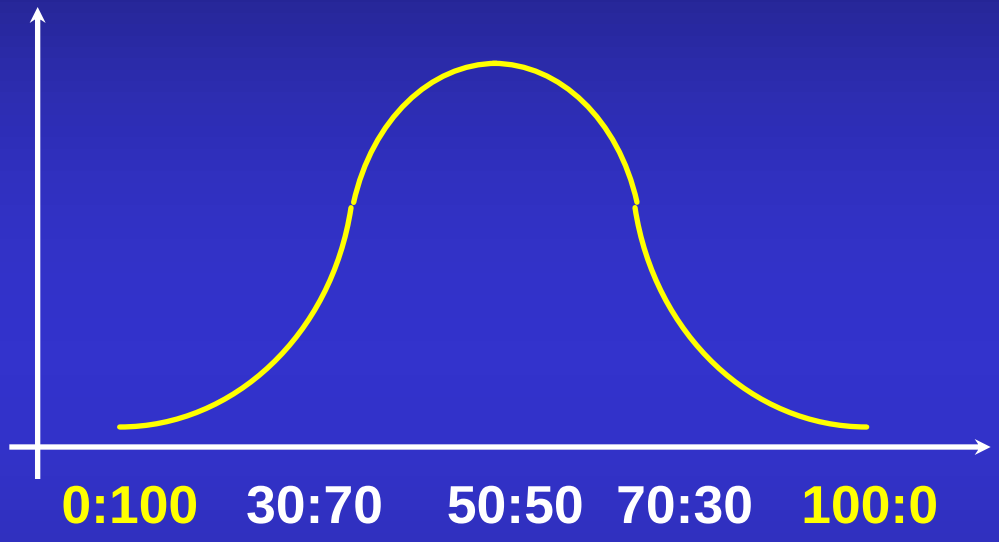

X^DX^d
X^DY
X^DX^D
X^dY
X^DX^d
X^DX^d







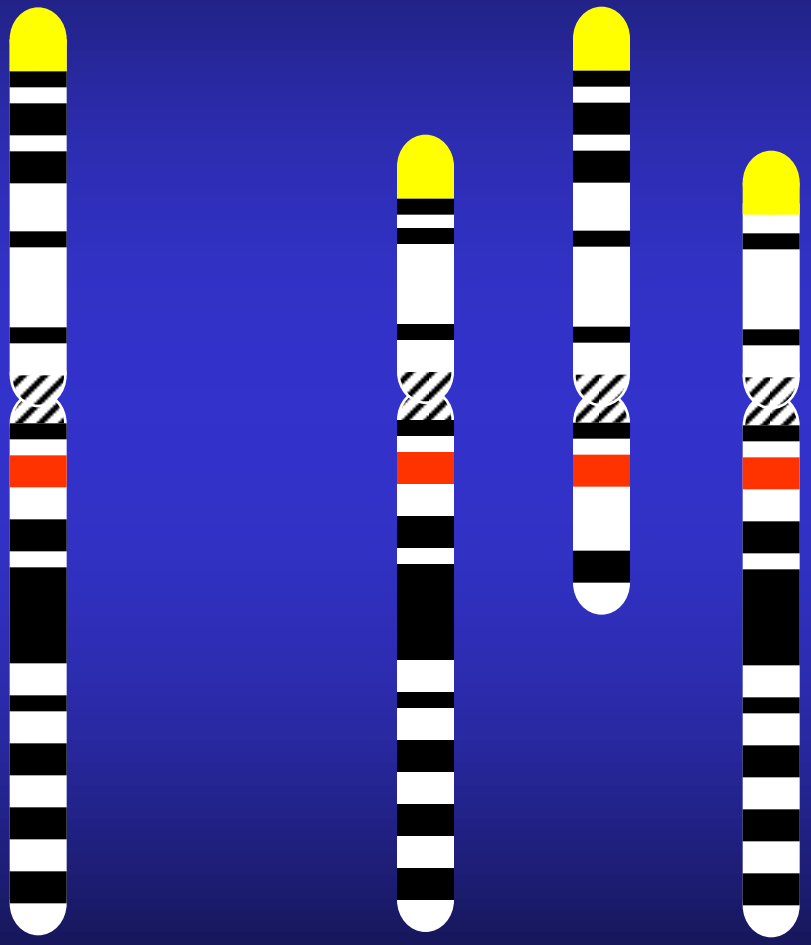
PADRÕES DE ICX – Distribuição Normal



DESVIO DE ICX (100:0 - 80:20)

Desvio de ICX

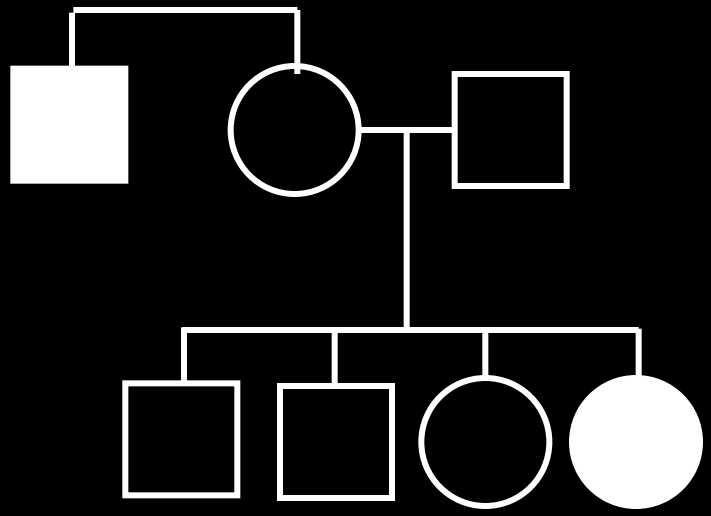
GRANDES DELEÇÕES



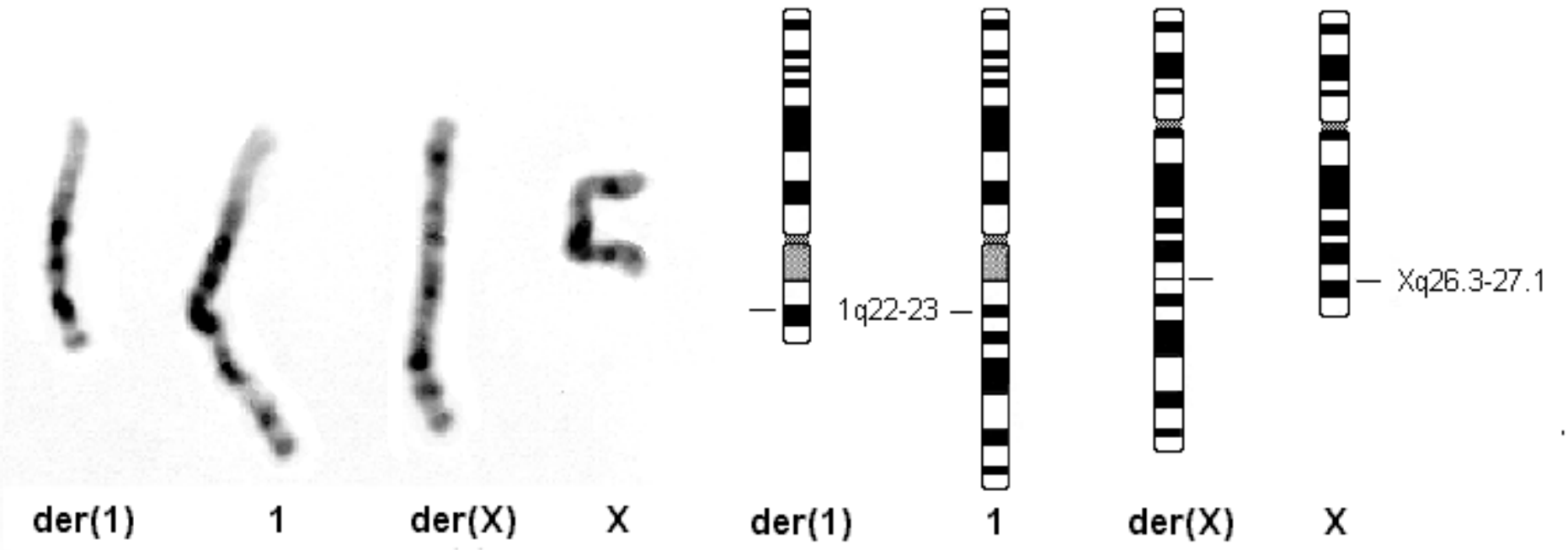
X

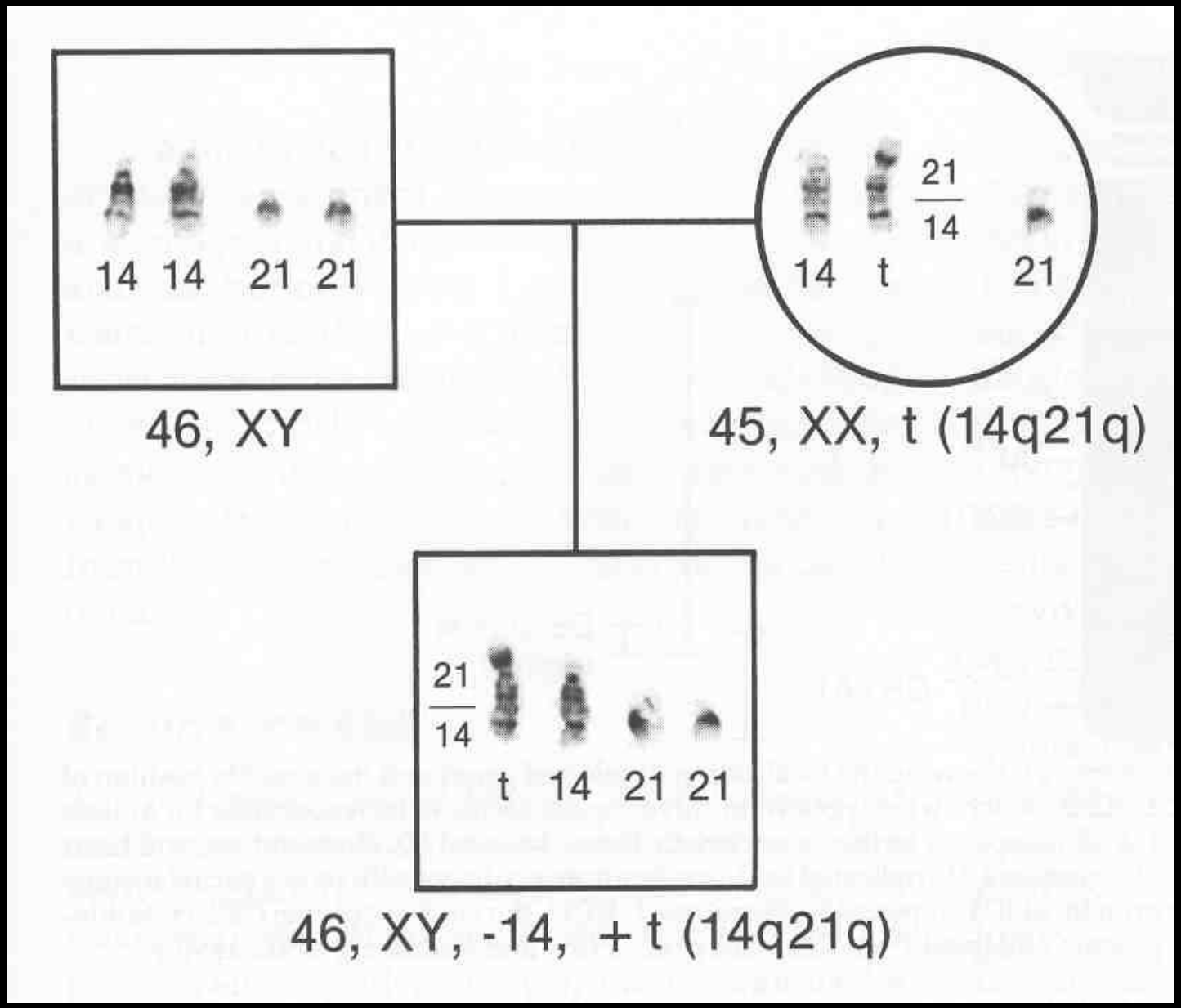
X-del

Hemofilia



Translocação Balanceada – 46,XX,t(1q,Xq)



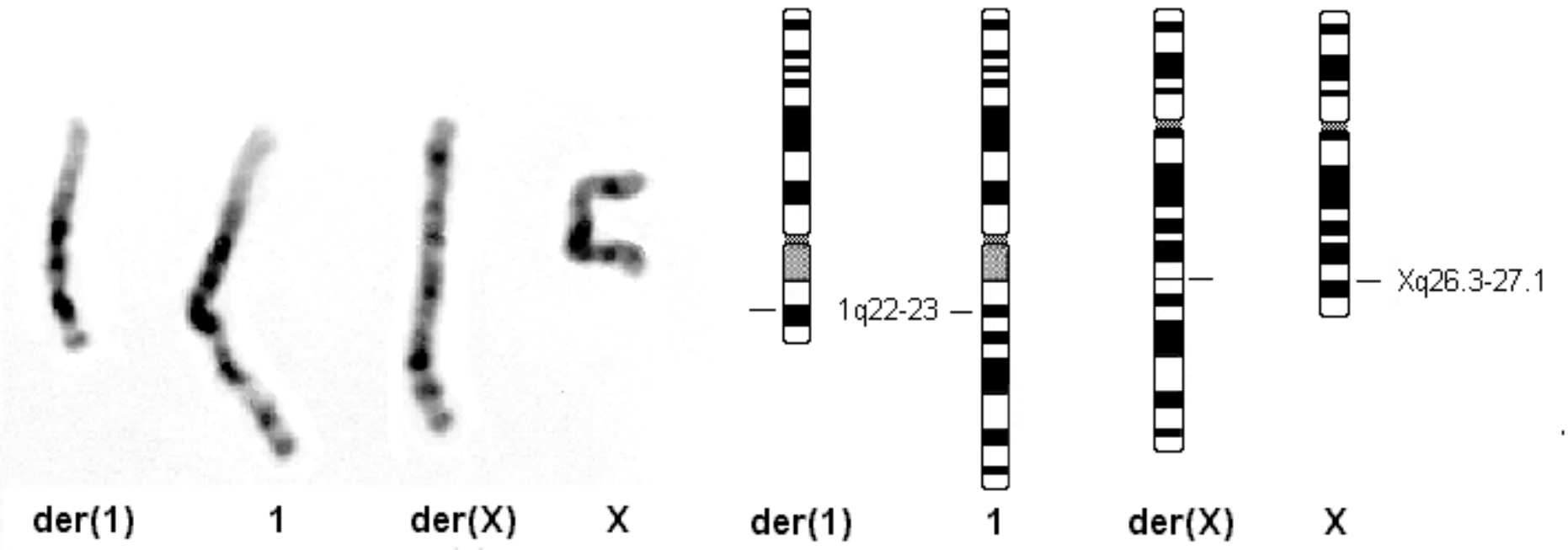

14 14 21 21
46, XY
21/14
14 t 21
45, XX, t (14q21q)
21/14
t 14 21 21
46, XY, -14, + t (14q21q)

ABERRAÇÕES CROMOSSÔMICAS ESTRUTURAIS BALANCEADAS

- **Sem efeito fenotípico;**
- **Gametas = ?**
- **Mais comum em :**retardo mental;
  >= 2 abortos expont.;
  homens estéreis.

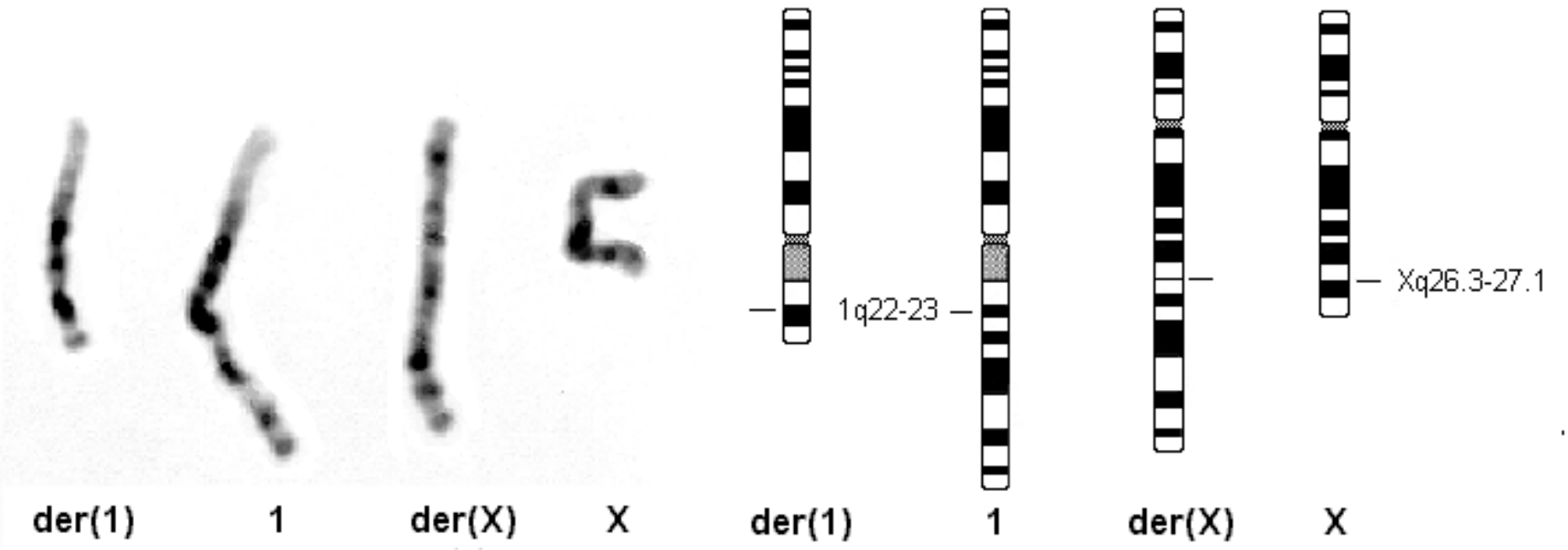
Translocação Balanceada

X:autossomo



Translocação Balanceada

X:autossomo



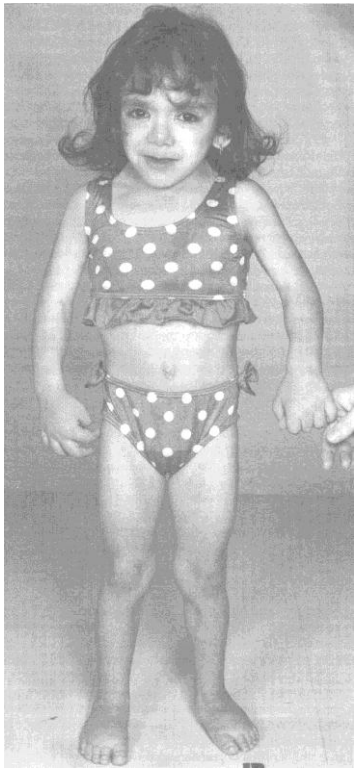
DESVIO DE ICX (100:0 - 80:20)

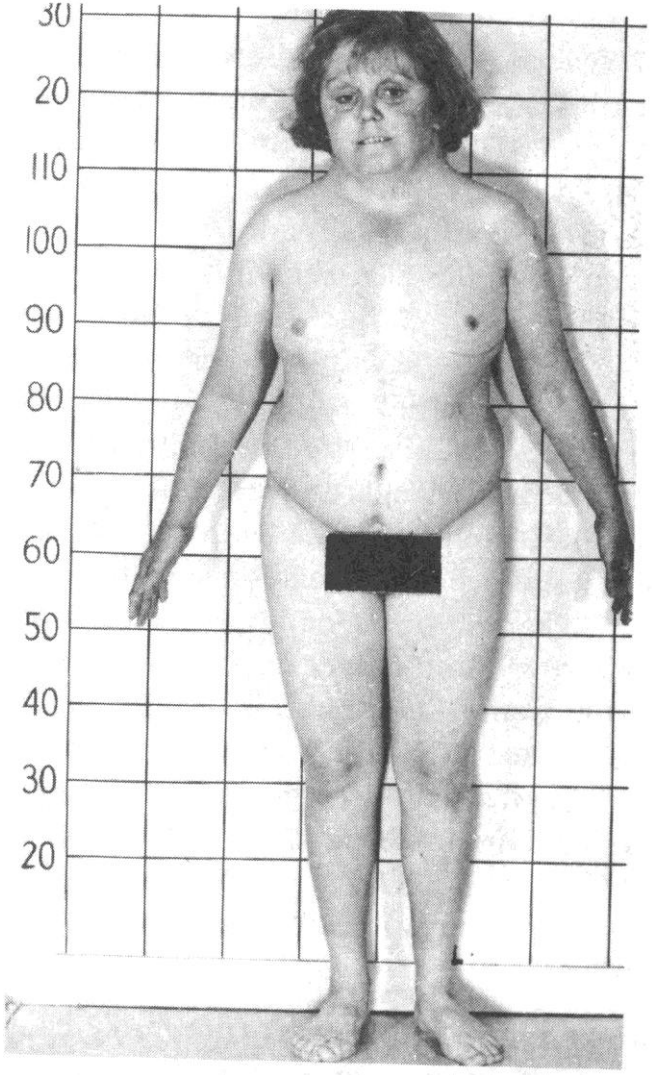
- Mulheres manifest. doença recess. ligada ao X ;
- Grandes deleções X ;
- Translocações balanceadas X:autosomo;
- População normal: 1-30% ???

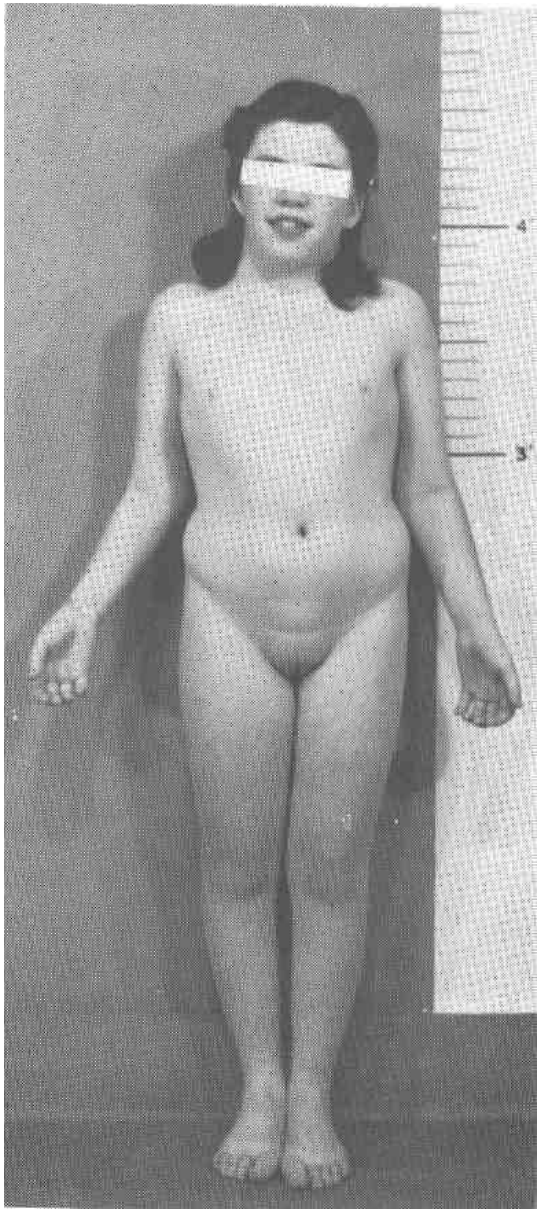
Translocações NÃO-balanceadas X:autosomo = ???

ABERRAÇÕES CROMOSSOMOS SEXUAIS NUMÉRICAS

1/400 – 1/650 nascimentos



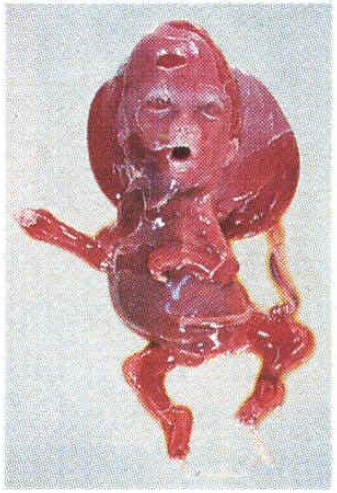

30
20
110
100
90
80
70
60
50
40
30
20

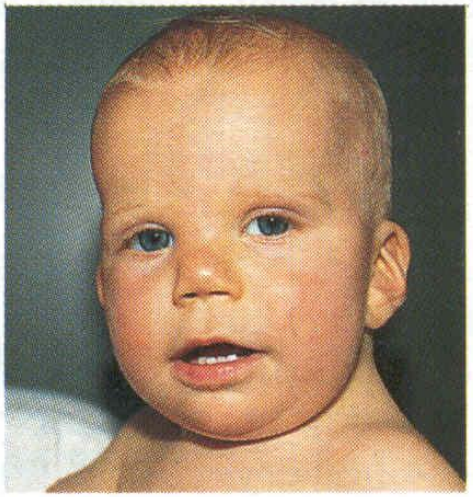


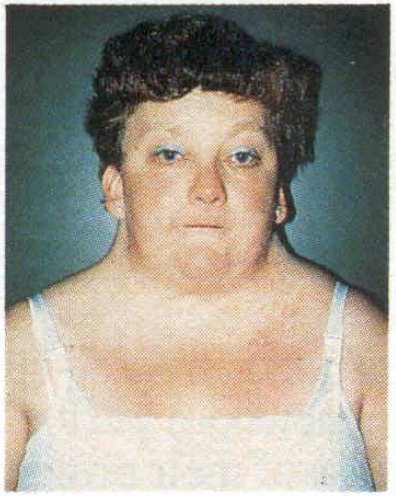
Síndrome de Turner (45,X0)

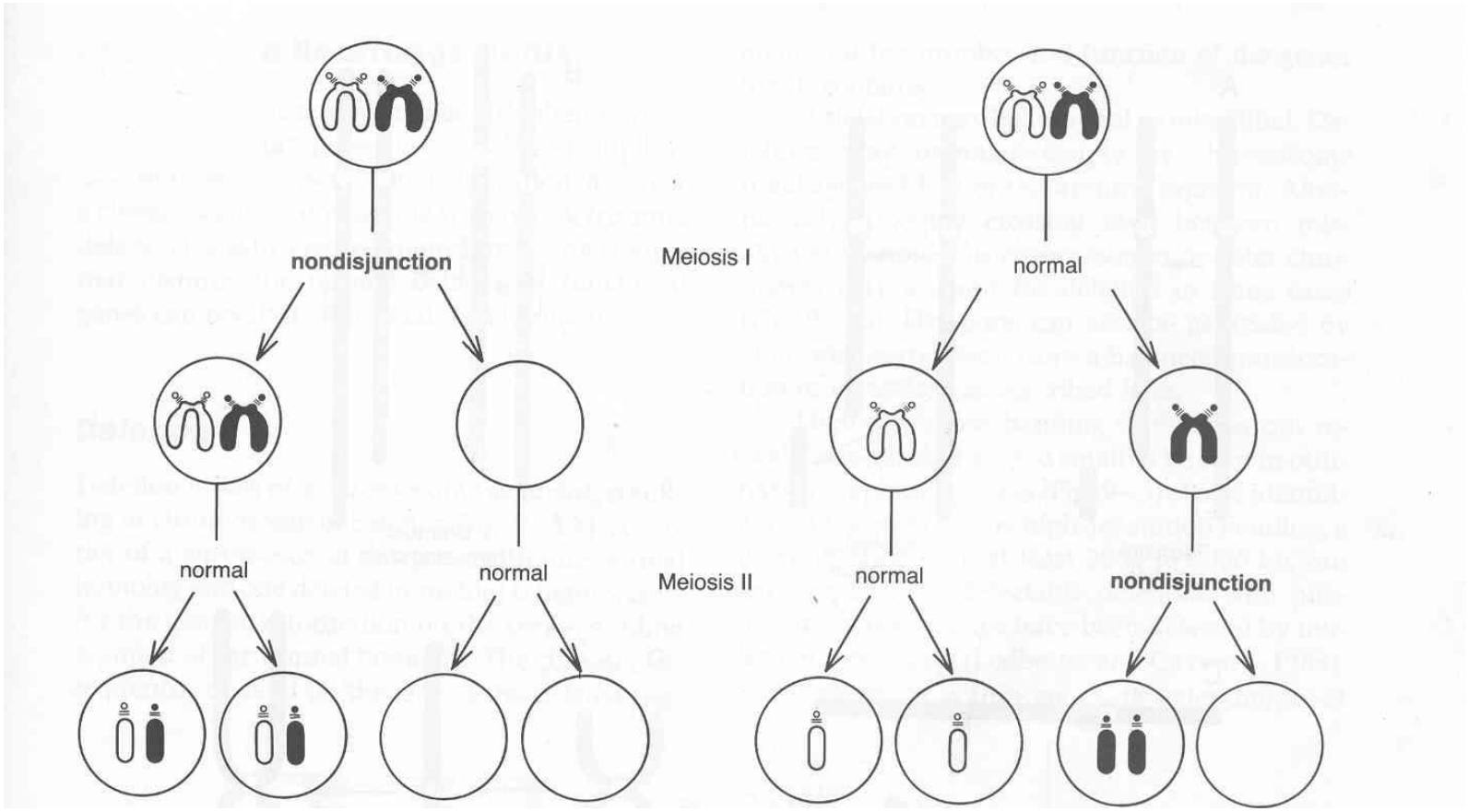
- **1/5.000 mulheres**
- **baixa estatura, infertilidade**
- **Mosaicos**
- **Xp^-**

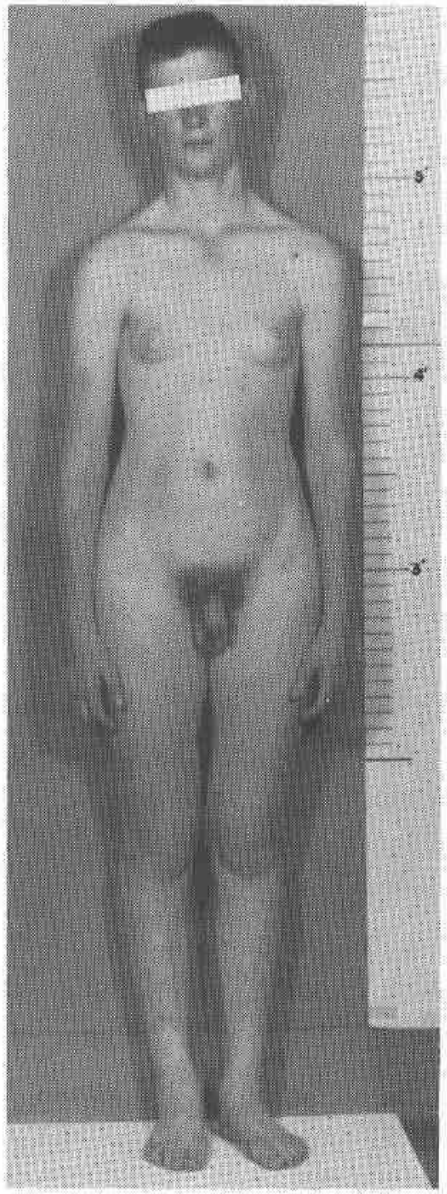
18% abortos expontâneos

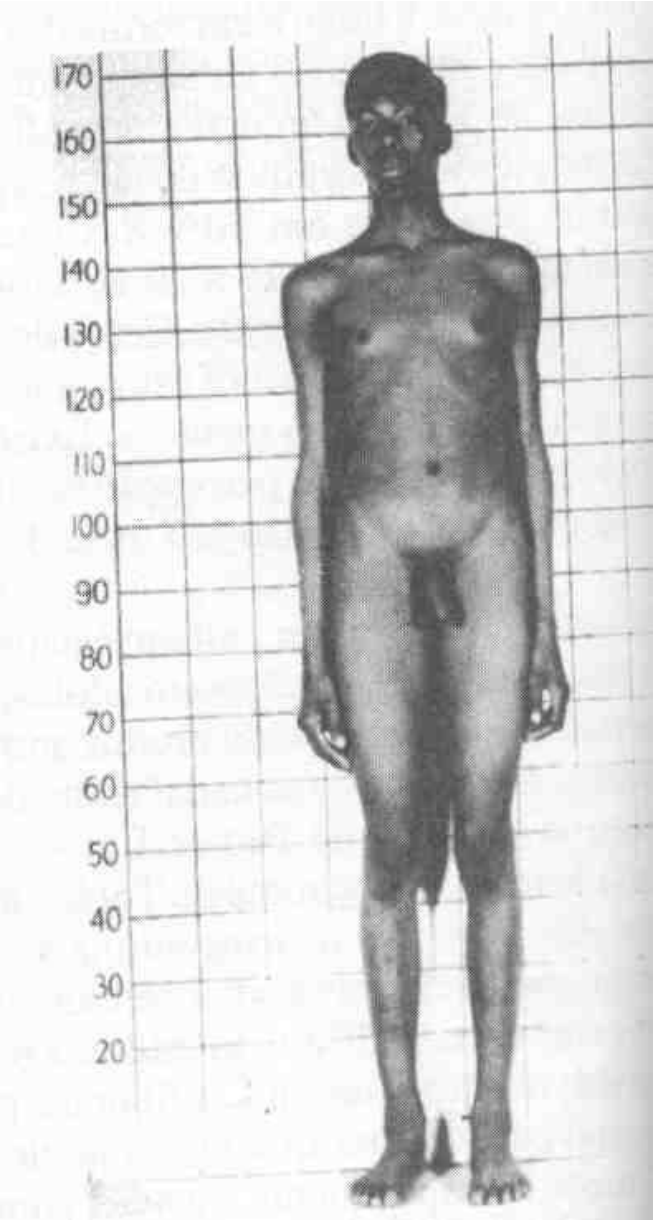
1. 

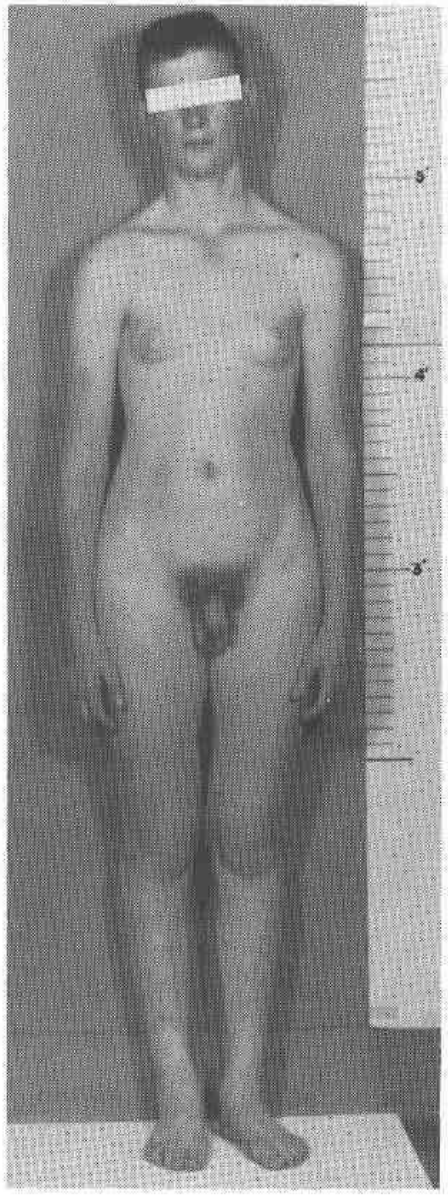
2. 

3. 


nondisjunction
normal
normal
Meiosis I
normal
Meiosis II
normal
nondisjunction



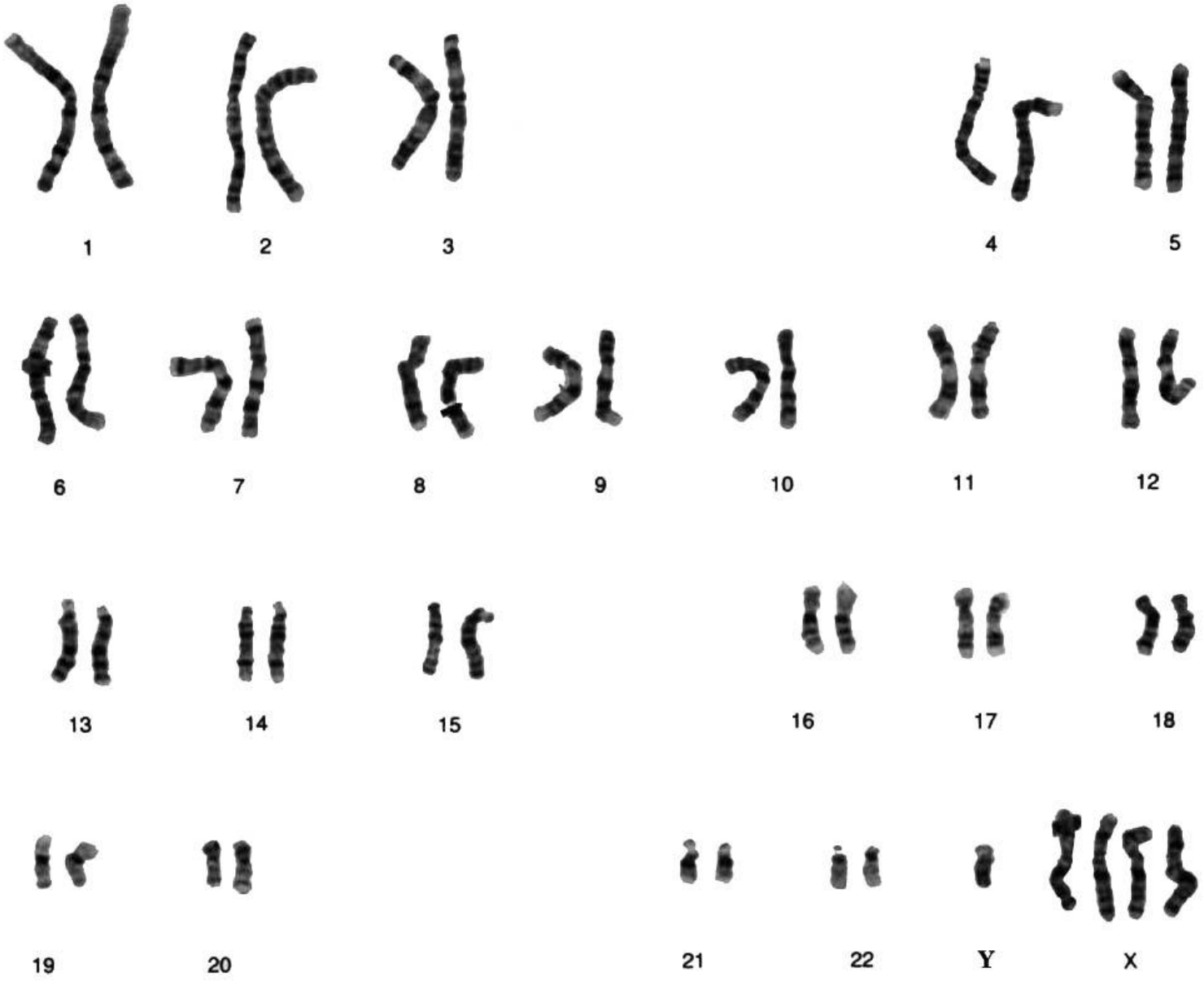

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

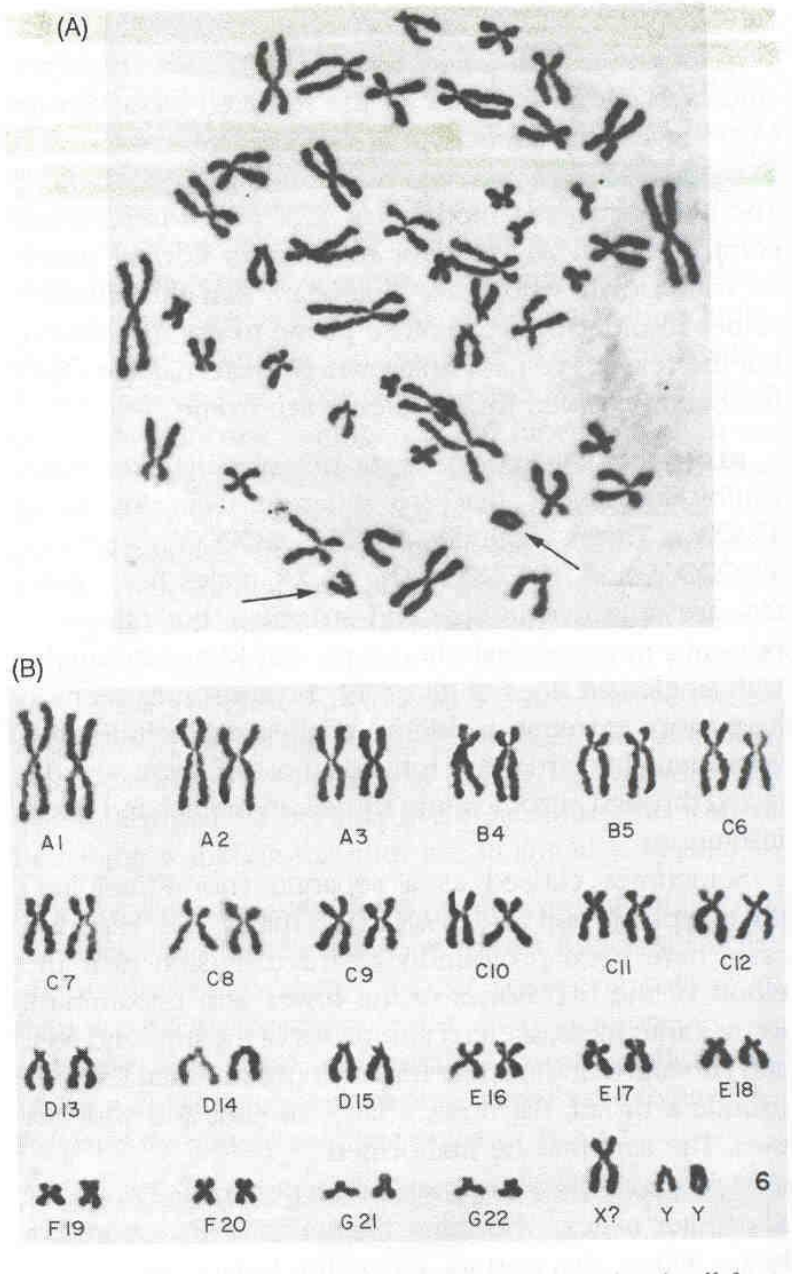


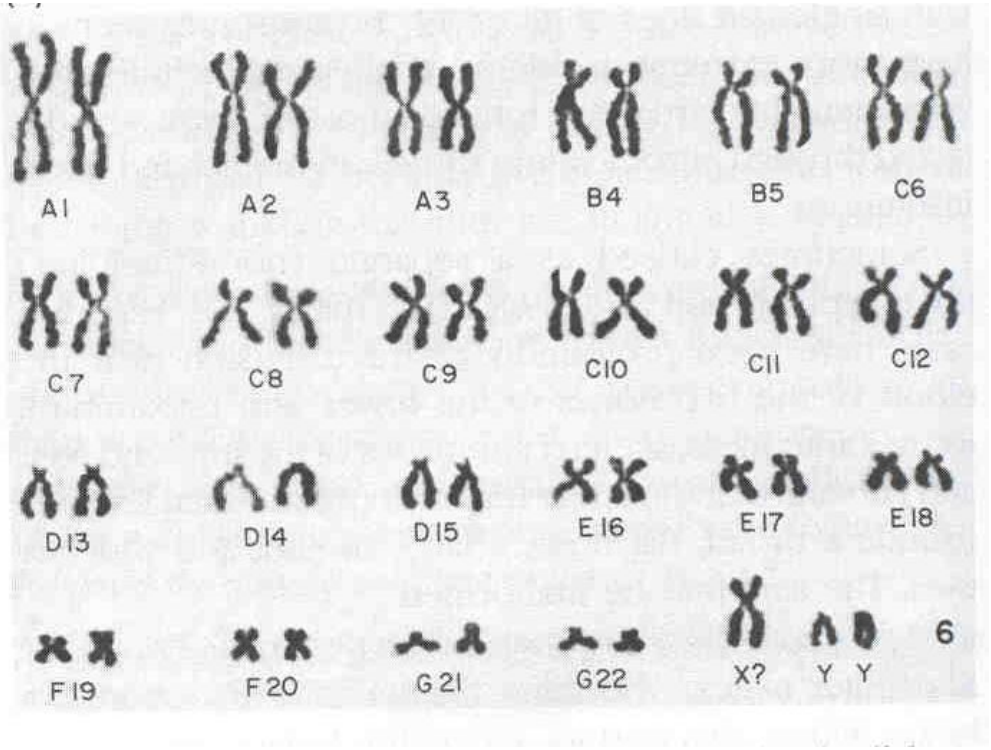
Síndrome de Klinefelter (47,XXY)

- 1/1.000 homens
- infertilidade, QI
- mulher 47,XXX

49,XXXXY
Klinefelter's
Syndrome

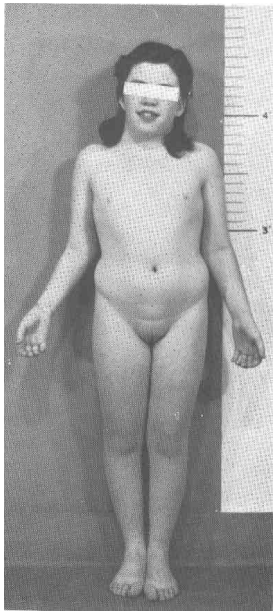



(A)
(B)
A1
A2
A3
B4
B5
C6
C7
C8
C9
C10
C11
C12
D13
D14
D15
E16
E17
E18
F19
F20
G21
G22
X?
Y Y
6

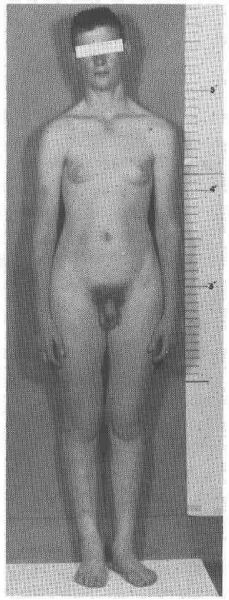


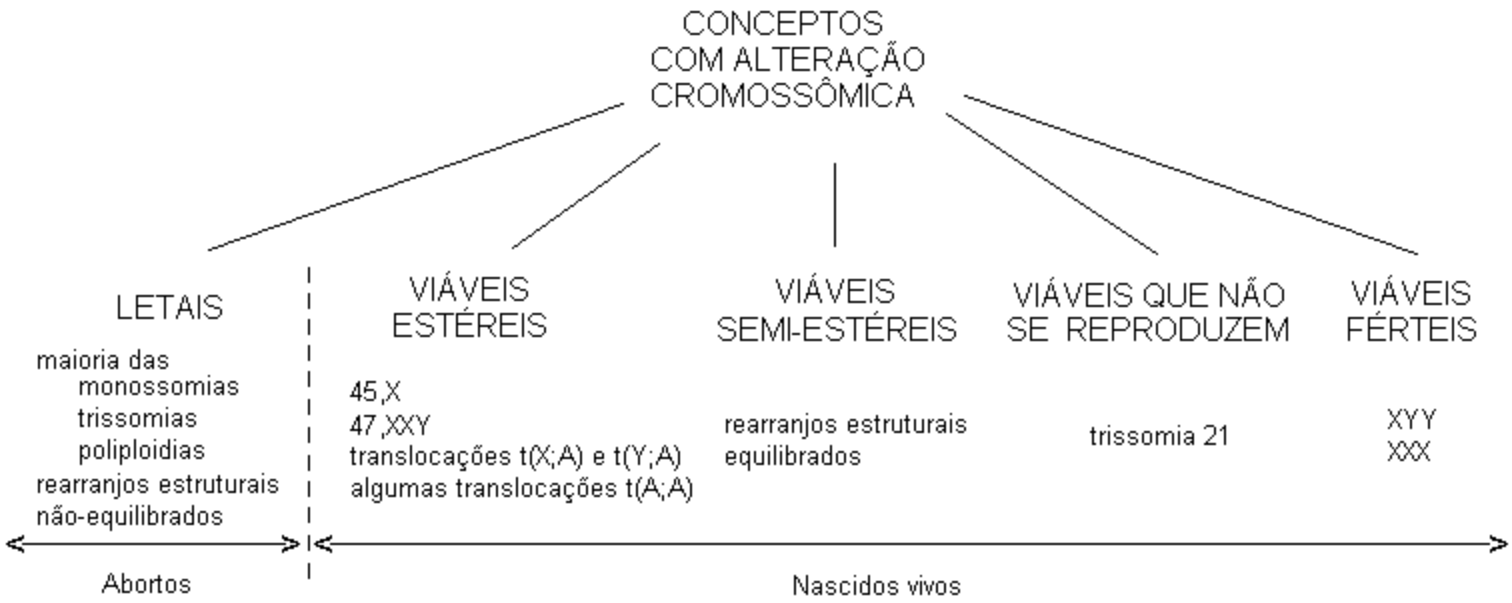
- **47, XYY**
- **1/1.000 homens**
- **QI**
- **hiper-atividade**

No Y chromosome present		Y chromosome present	
45, XO	46, XX	46, XY	47, XXY
One X chromosome only			Additional X chromosome
Turner syndrome female	Normal female	Normal male	Klinefelter syndrome male

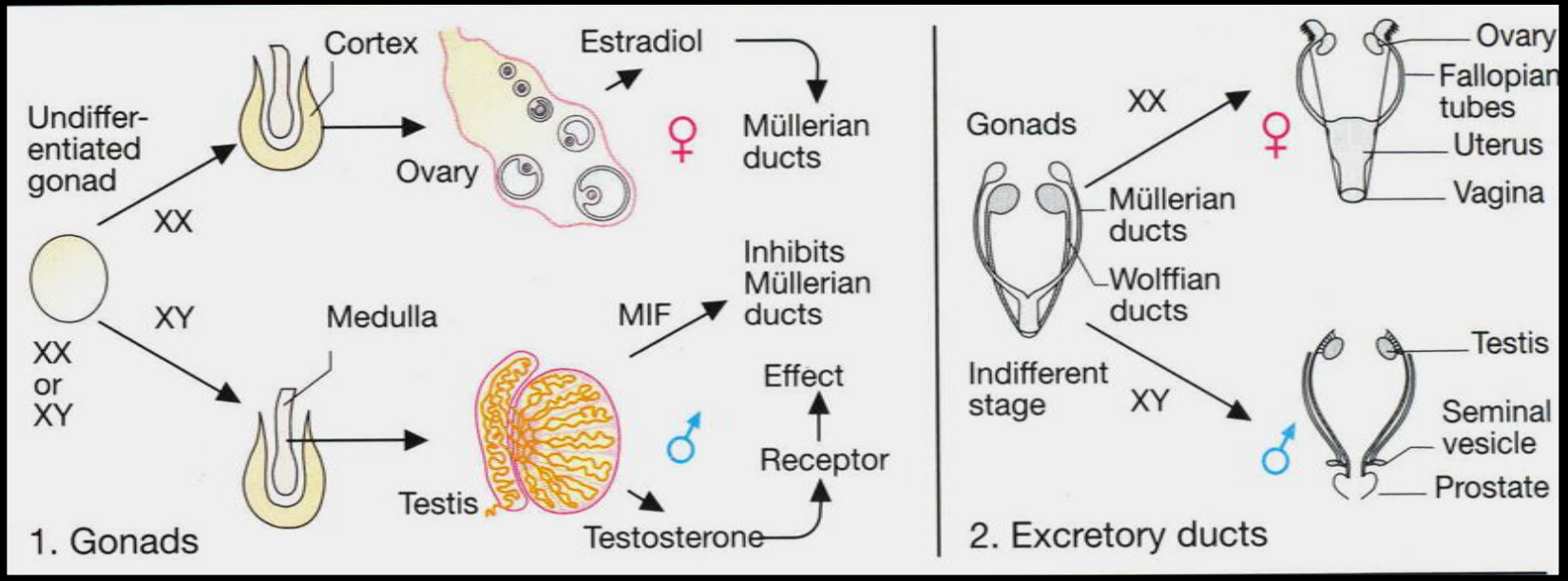


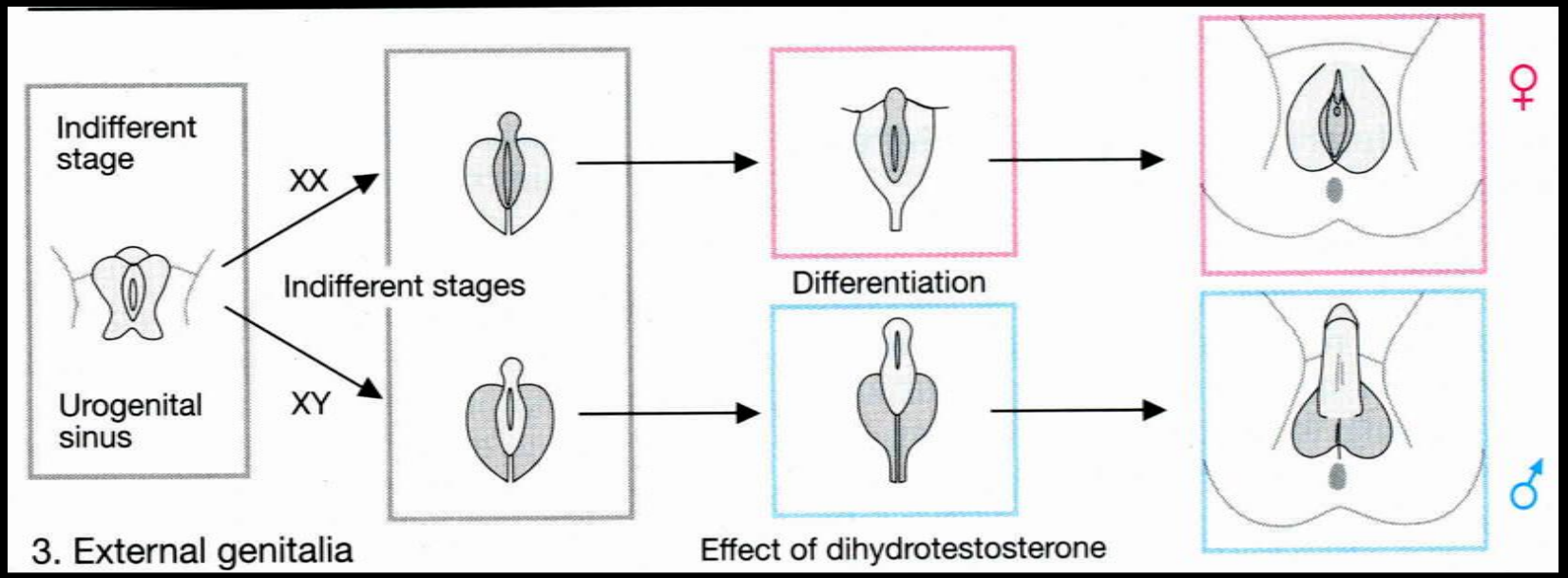
Menos graves do que autossomos -> ??

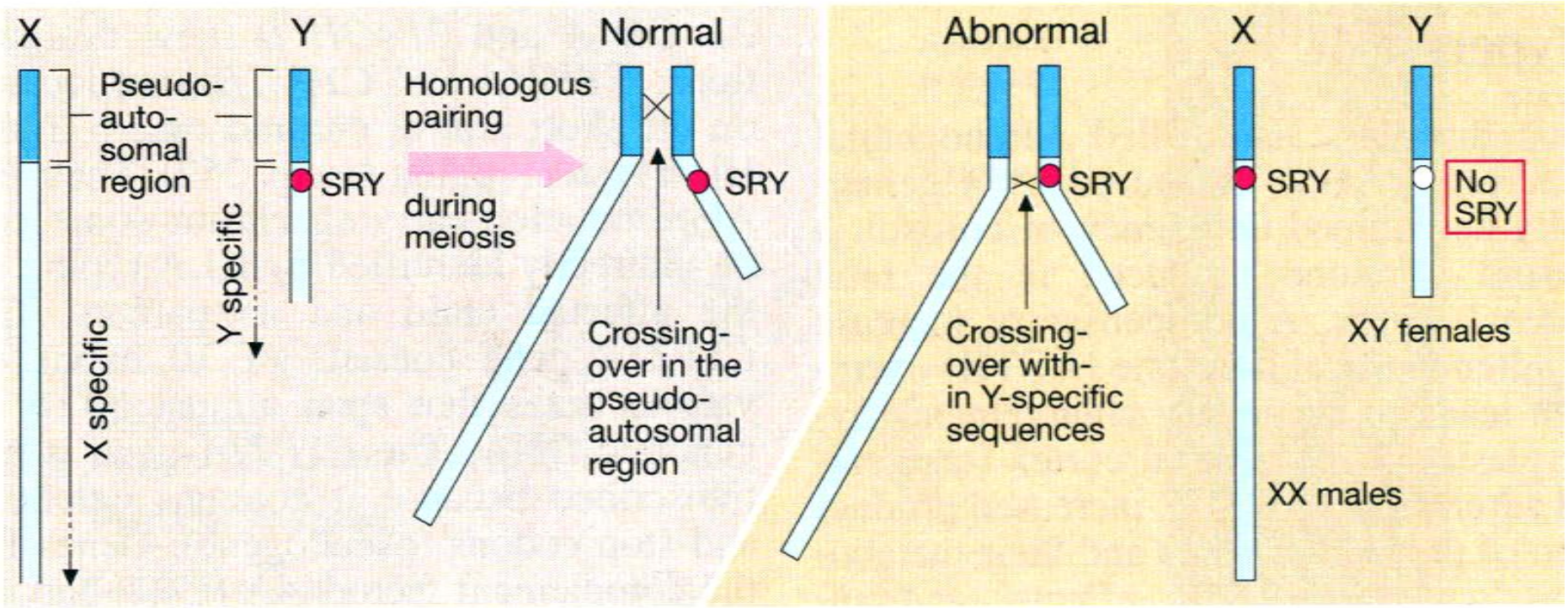


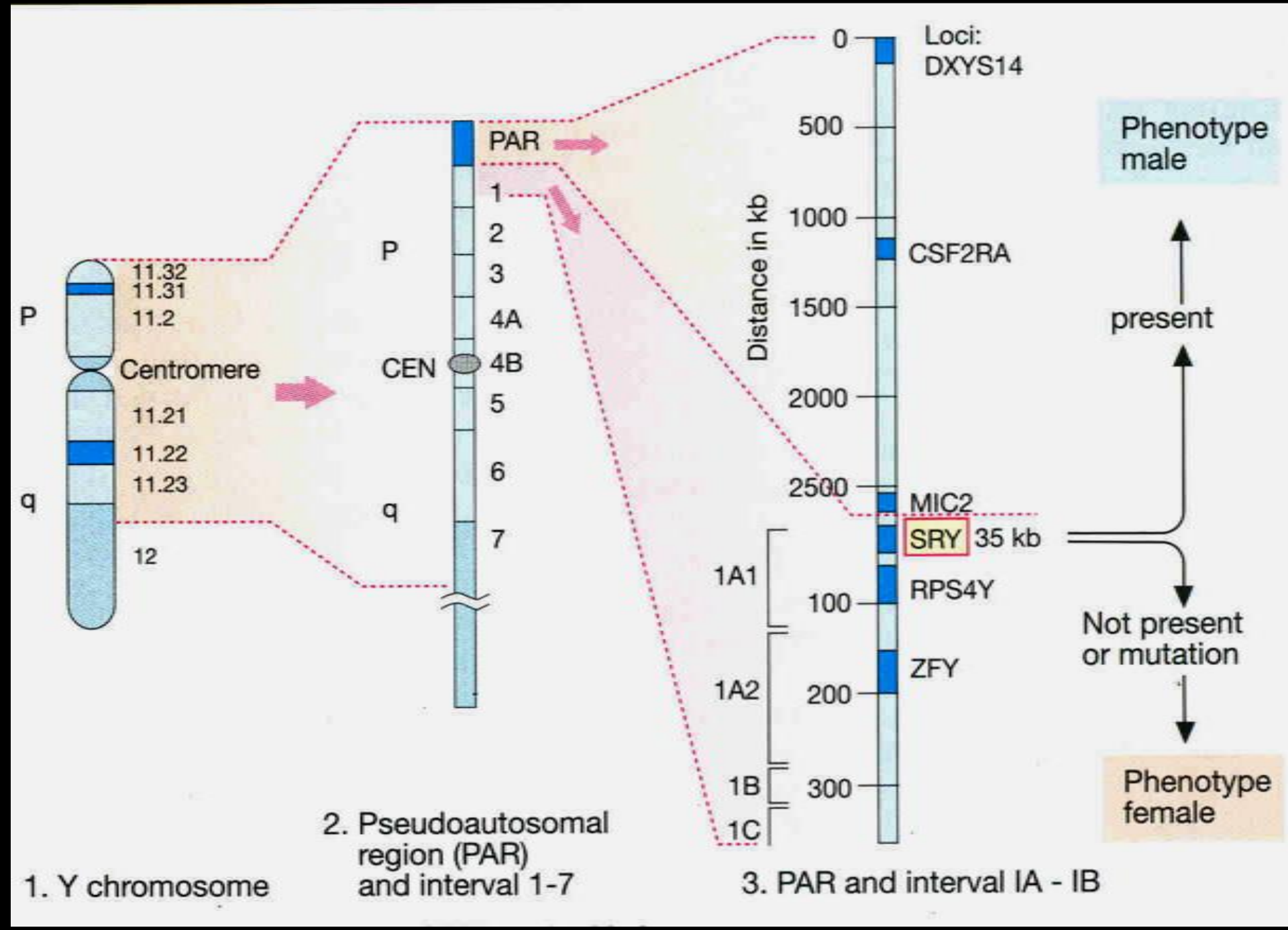

CONCEPTOS
COM ALTERAÇÃO
CROMOSSÔMICA
LETAIS
maioria das
monossomias
trissomias
poliploidias
rearranjos estruturais
não-equilibrados
VIÁVEIS
ESTÉREIS
45,X
47,XXY
translocações t(X;A) e t(Y;A)
algumas translocações t(A;A)
VIÁVEIS
SEMI-ESTÉREIS
rearranjos estruturais
equilibrados
VIÁVEIS QUE NÃO
SE REPRODUZEM
trissomia 21
VIÁVEIS
FÉRTEIS
XYY
XXX
Abortos
Nascidos vivos

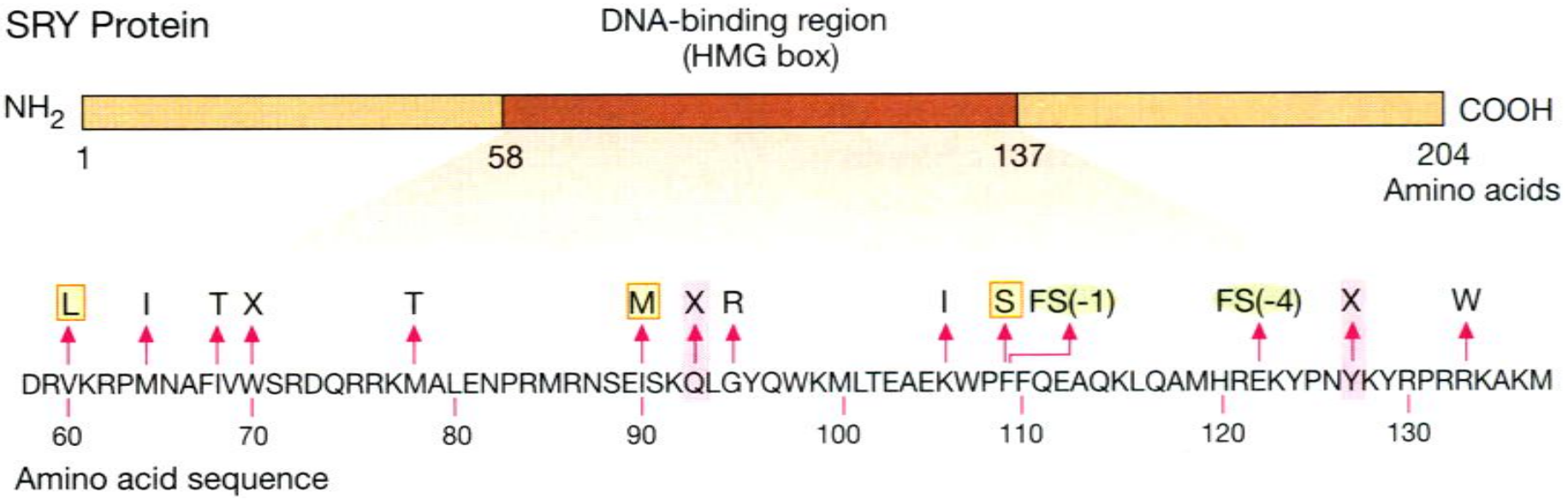
Diferenciação Sexual

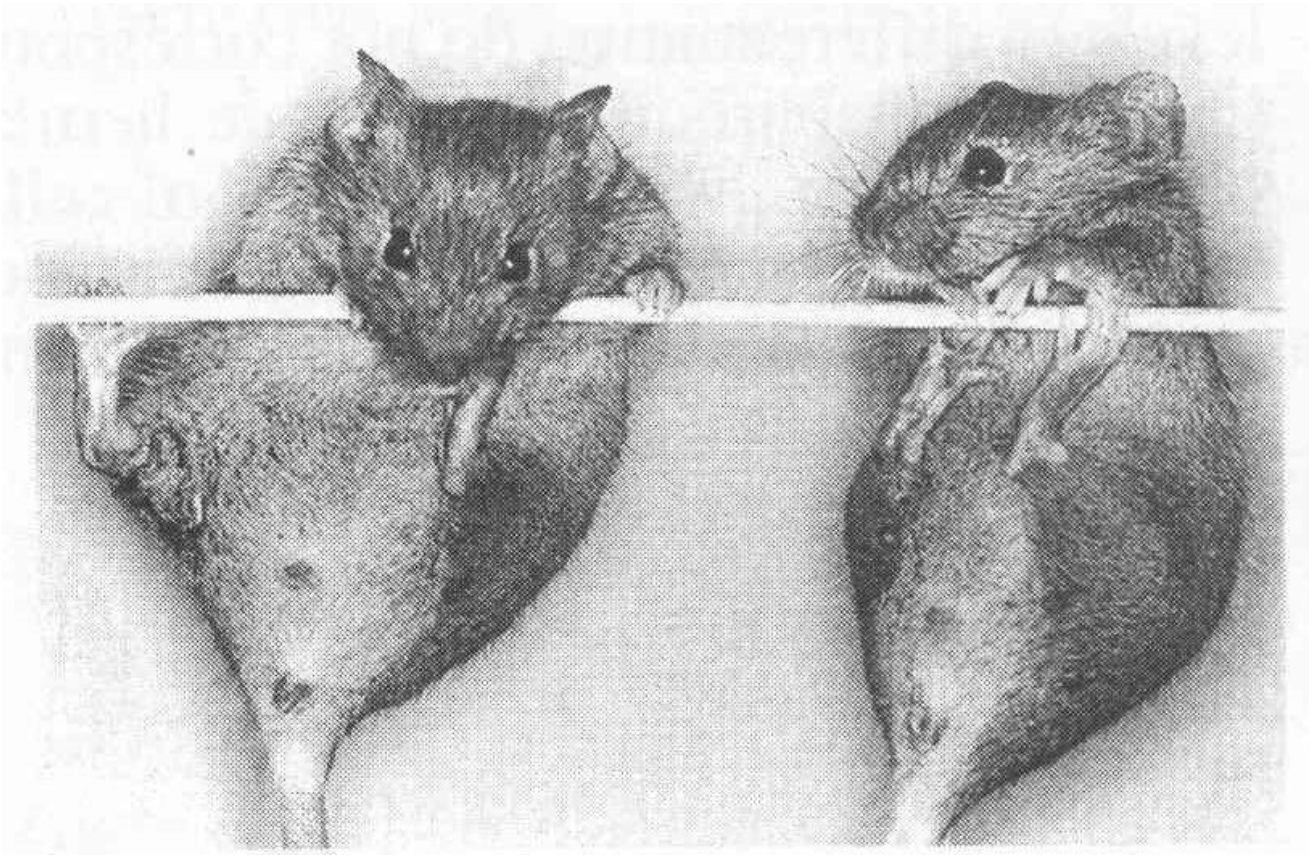





X
Y
Pseudo-
auto-
somal
region
SRY
Y specific
X specific
Normal
Homologous
pairing
during
meiosis
SRY
Crossing-
over in the
pseudo-
autosomal
region
Abnormal
SRY
Crossing-
over with-
in Y-specific
sequences
X
Y
SRY
No
SRY
XY females
XX males


P
11.32
11.31
11.2
Centromere
11.21
11.22
11.23
q
12
P
CEN
q
PAR
1
2
3
4A
4B
5
6
7
2. Pseudoautosomal region (PAR) and interval 1-7
1. Y chromosome
Distance in kb
0
500
1000
1500
2000
2500
100
200
300
Loci:
DXYS14
CSF2RA
MIC2
SRY
35 kb
RPS4Y
ZFY
1A1
1A2
1B
1C
3. PAR and interval IA - IB
Phenotype male
present
Not present or mutation
Phenotype female


SRY Protein
DNA-binding region
(HMG box)
NH2
COOH
1
58
137
204
Amino acids
L I T X T M X R I S FS(-1) FS(-4) X W
DRVKRPMNAFIVWSRDQRRKMALENPRMRNSEISKQLGYQWKMLTEAEKWPFFQEAQKLQAMHREKYPNYKYRPRRKAKM
60
70
80
90
100
110
120
130
Amino acid sequence



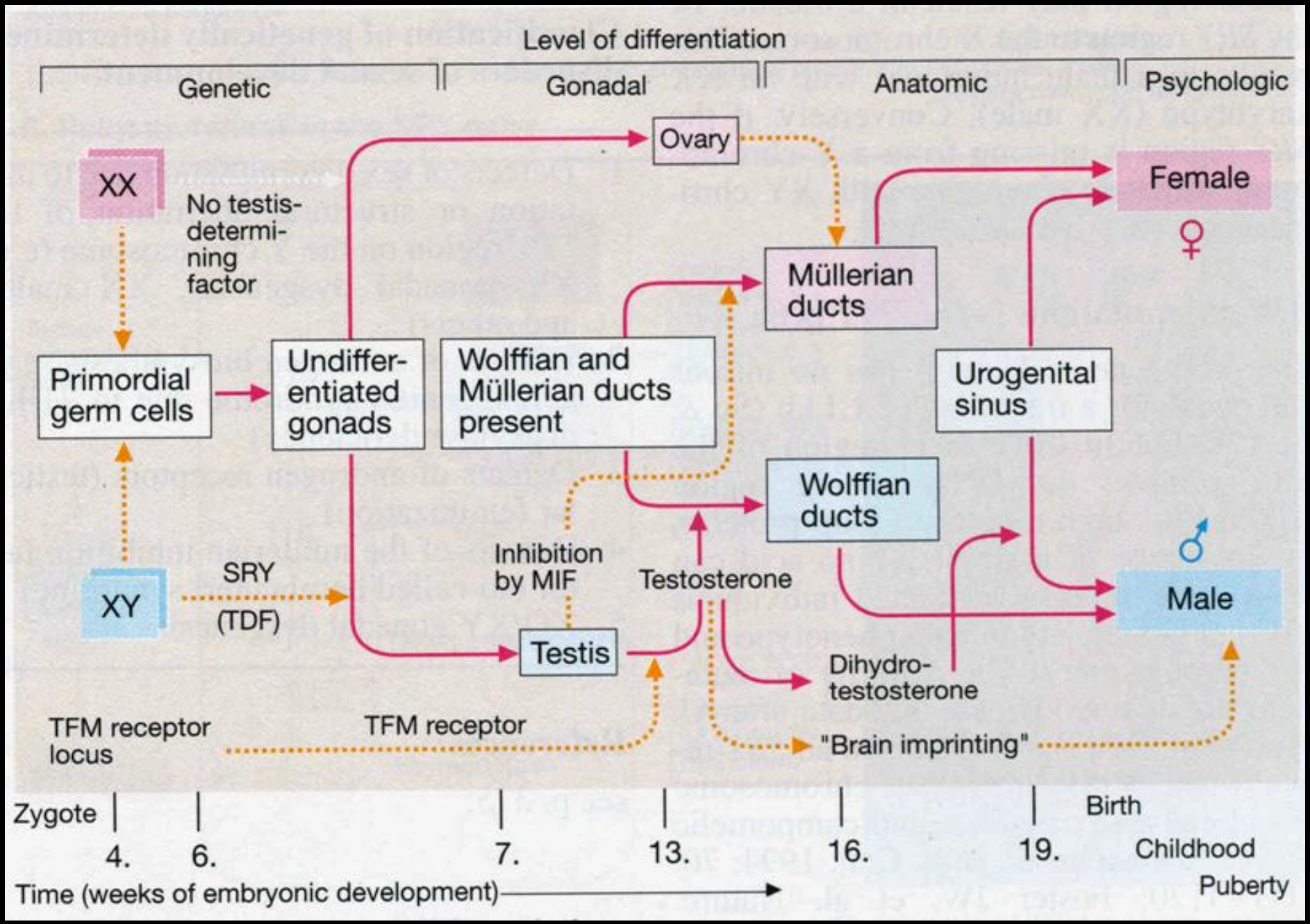
XY normal male

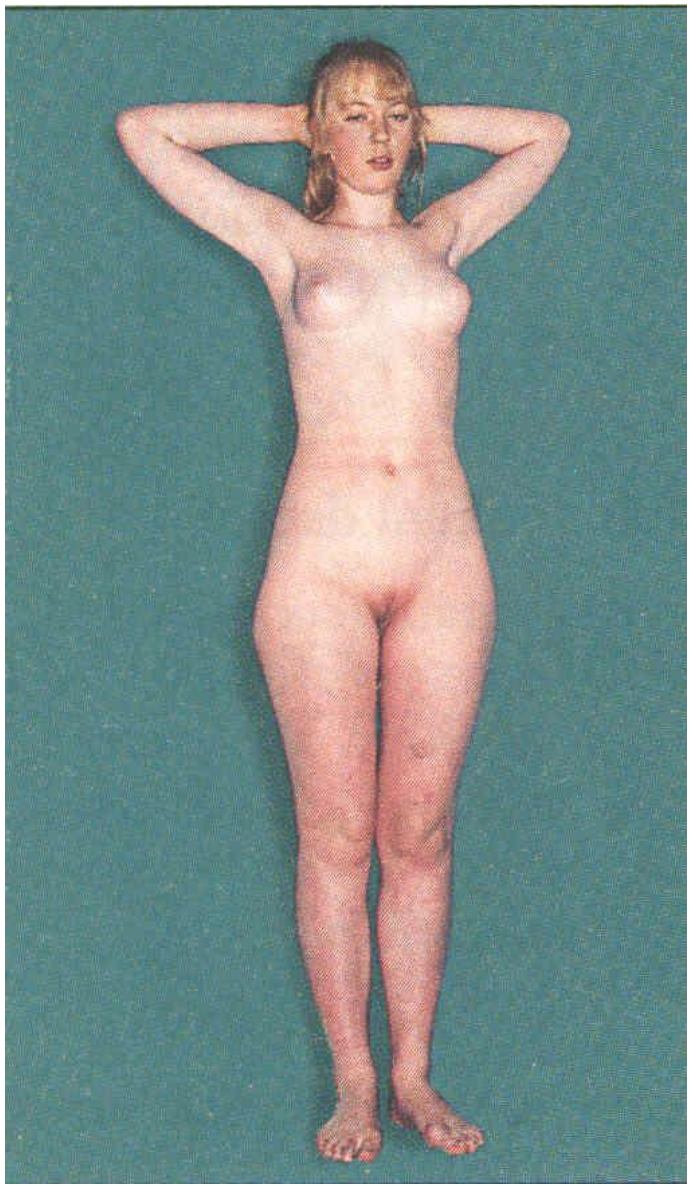
XX with Sry gene (male)

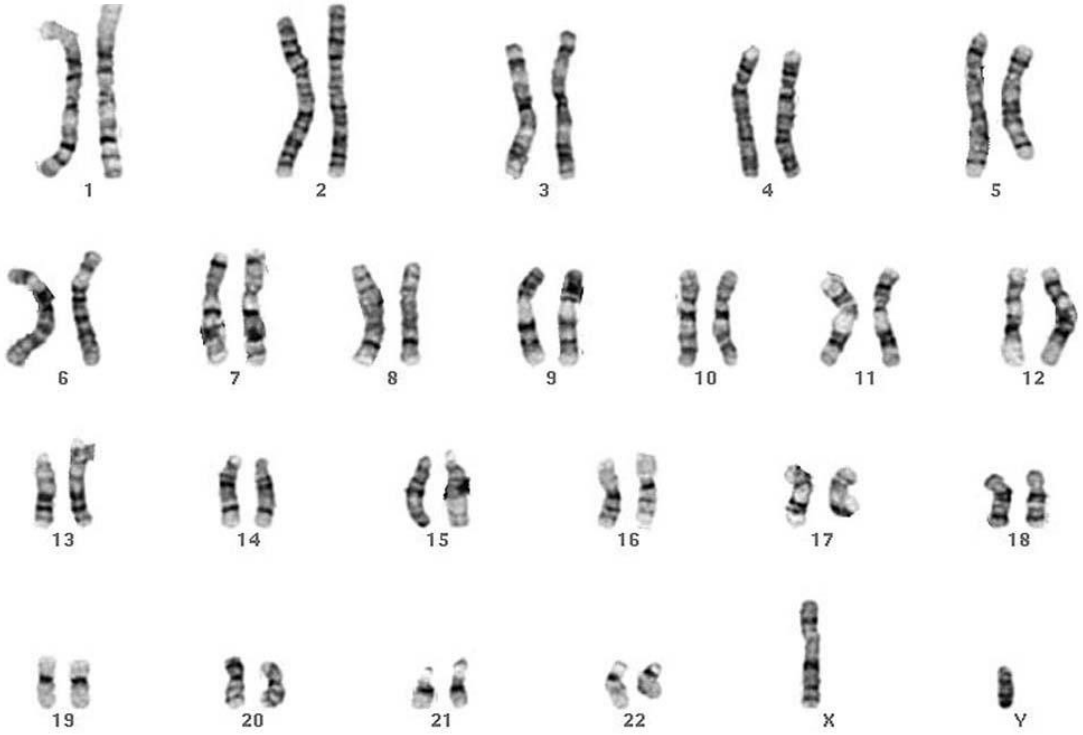
CARACTERIZAÇÃO DO SEXO

- Citogenética;
- Histologia – gônadas;
- Anatomia-dutos;
- Anatomia-genital;

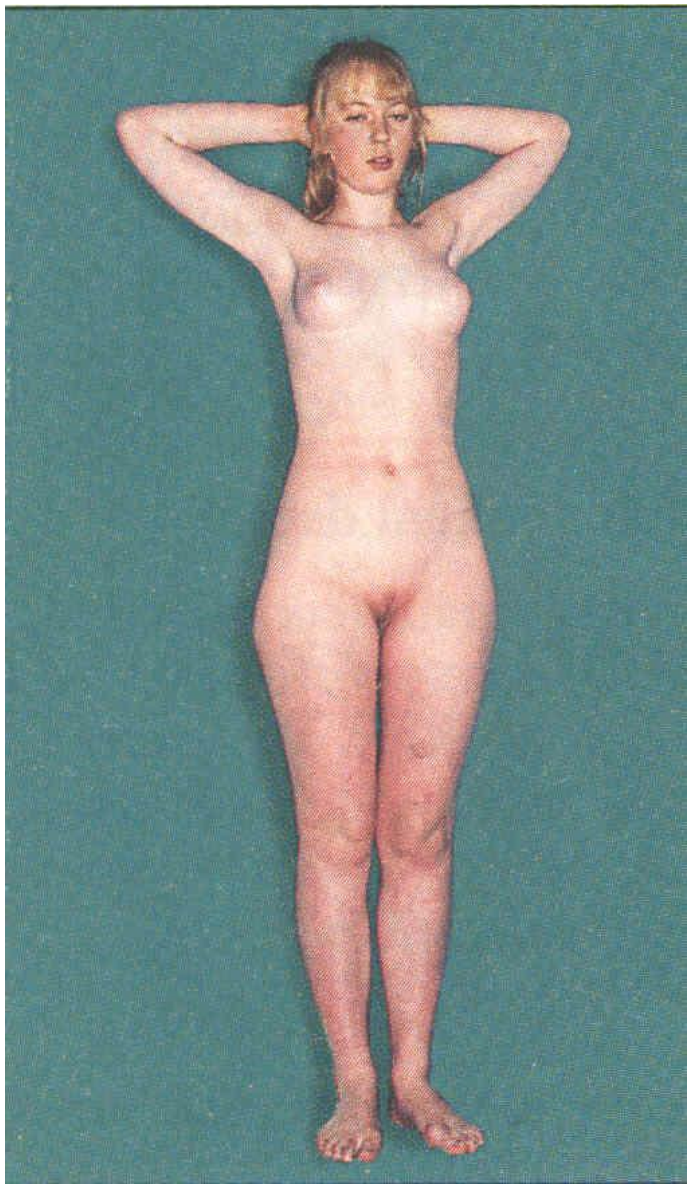
INTERSEXOS

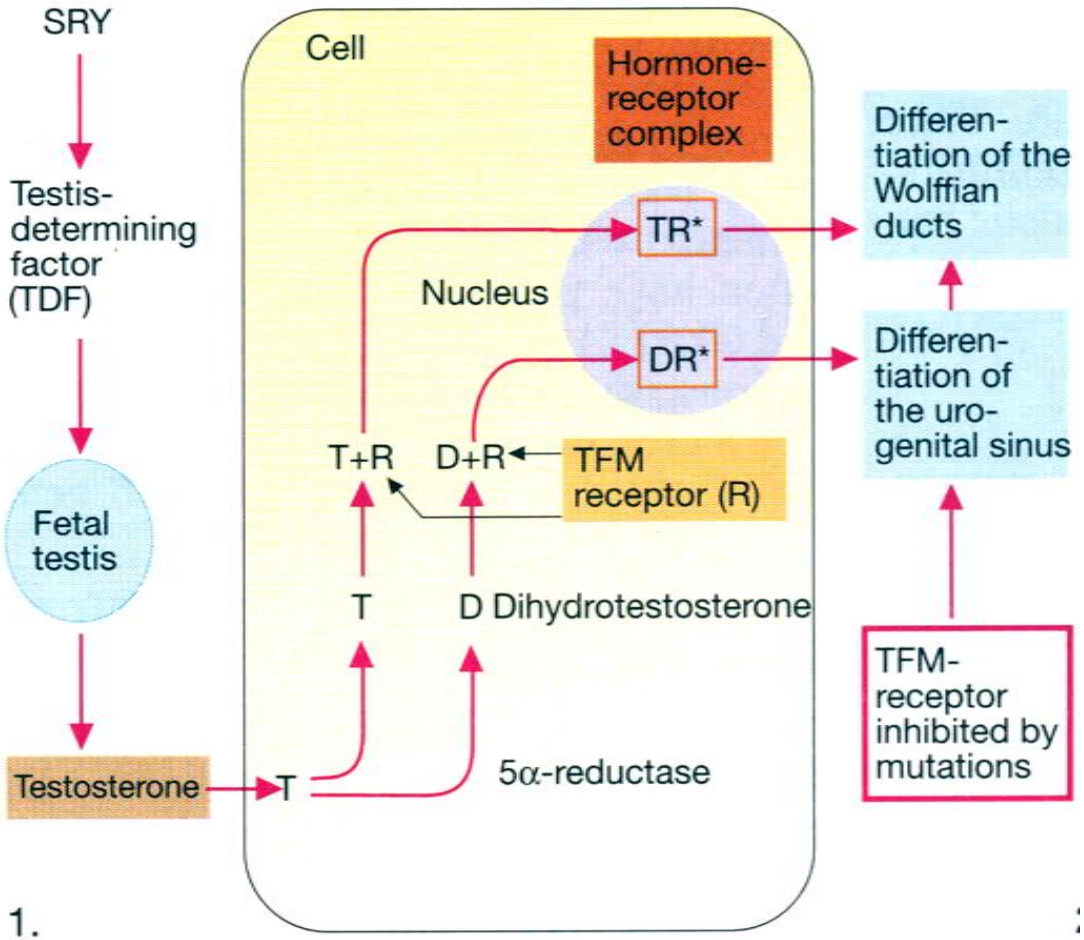

Level of differentiation
Genetic
Gonadal
Anatomic
Psychologic
XX
No testis-determining factor
Ovary
Female
Müllerian ducts
Primordial germ cells
Undifferentiated gonads
Wolffian and Müllerian ducts present
Urogenital sinus
Wolffian ducts
Inhibition by MIF
Testosterone
XY
SRY (TDF)
Male
Testis
Dihydrotestosterone
TFM receptor locus
TFM receptor
"Brain imprinting"
Zygote
4.
6.
7.
13.
16.
19.
Birth
Childhood
Puberty
Time (weeks of embryonic development)




1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y

Insensibilidade a andrógeno



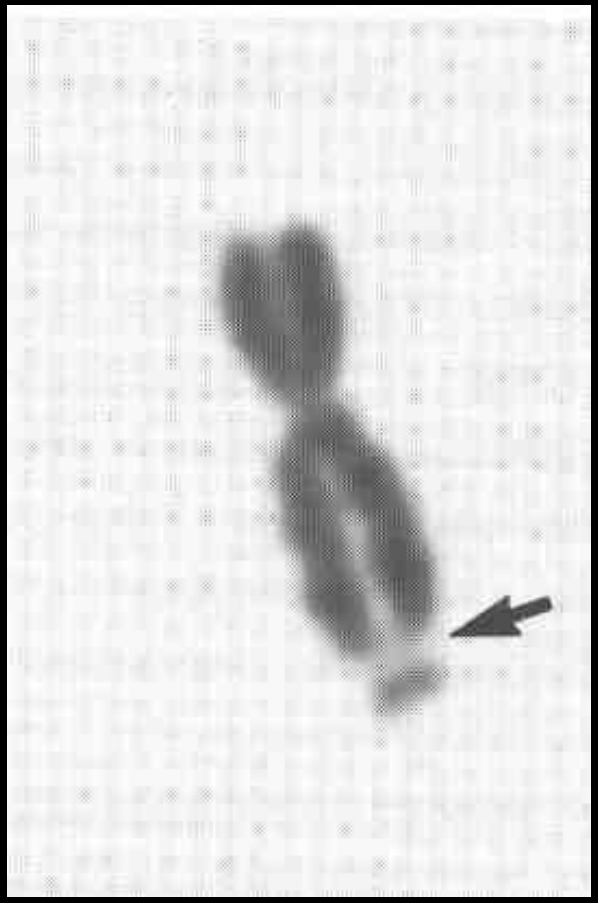


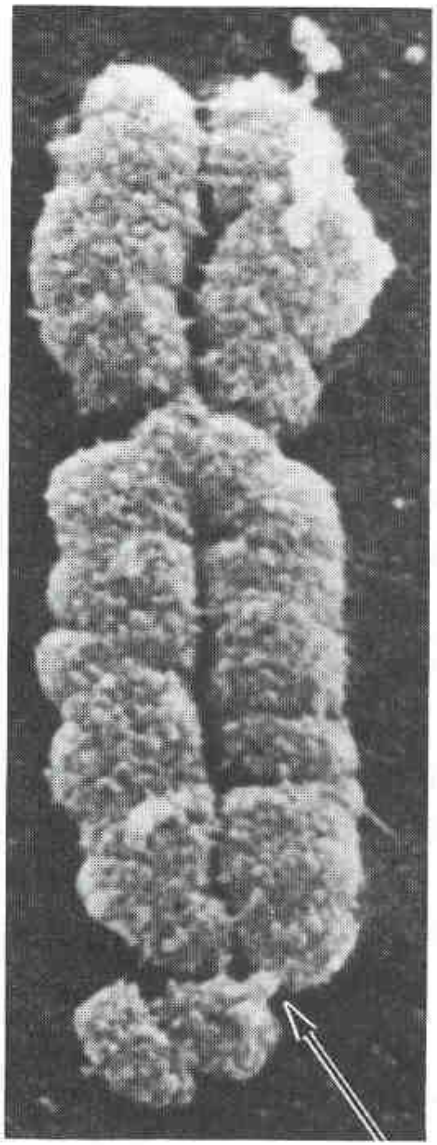
CARACTERIZAÇÃO DO SEXO

- Citogenética;
- Histologia – gônadas;
- Anatomia-dutos;
- Anatomia-genital;
- Psicologia ??

INTERSEXOS

Síndrome do X-frágil





(A)

fragile site

band region arm

band	region	arm
2	2	p
1		
1	1	
1	1	q
1	2	
2		
3		
4		
5		
6		
7		
8		

X

(B)

INDICAÇÕES CLÍNICAS

ANÁLISE CROMOSSÔMICA

Problemas início de crescimento & desenvolvimento:

- atraso desenvolvimento;
- face dismórfica
- malformação múltiplas;
- retardo mental;
- baixa estatura;
- genitália ambígua;

Nascimento morto/morte neo-natal;

Problemas de fertilidade:

- 3-6% abortos sucessivos & infertilidade;

Mulher manifest. doença recessiva ligada ao X;

História familiar:

- anomalia em parente de 1º grau;

Down: trissomia vs. translocação.