Anemia falciforme

Doença de Gaucher

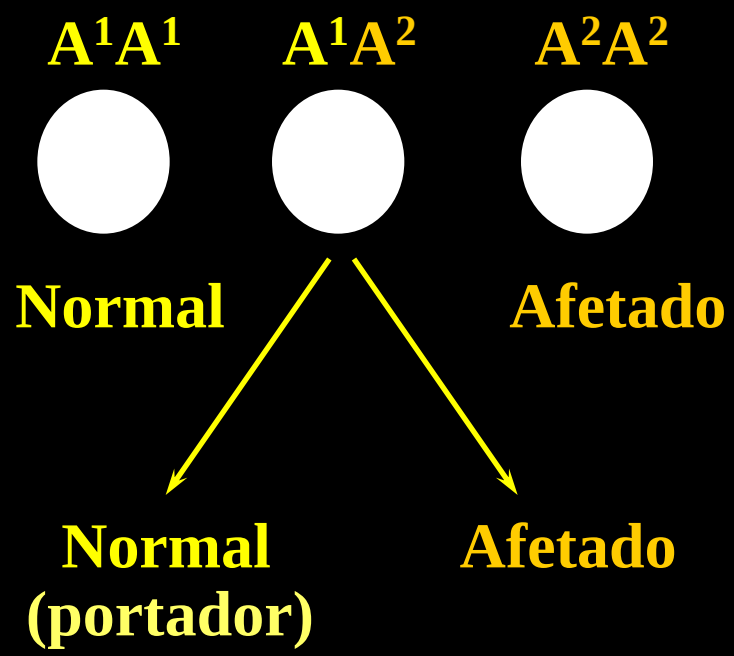
Fibrose cística

Distrofia de Duchenne

Síndrome de Marfan

A^1 = gene normal

A^2 = gene mutado



CARACTERÍSTICAS DETERMINADAS PELA INTERAÇÃO DE VÁRIOS GENES

Cor de olho

Altura

Hipertensão arterial

Doença de Alzheimer

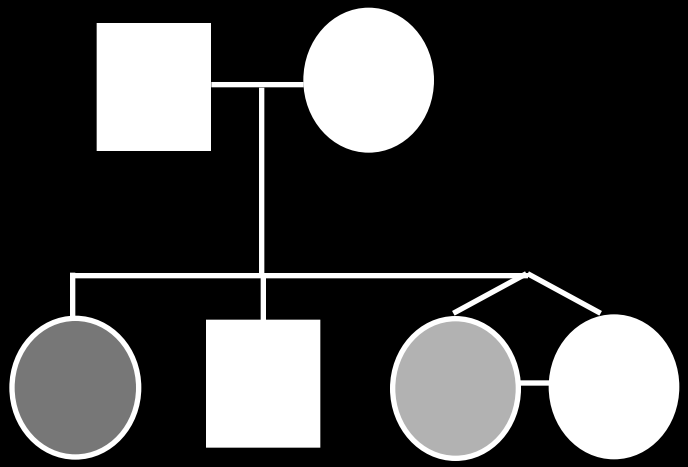
Esquizofrenia

Diabetes mellitus

A + B + C + ... + K

TRAÇOS MULTIFATORIAIS

A^1A^2 A^3A^4
B^1B^2 B^3B^4
C^1C^2 C^3C^4
D^1D^2 D^3D^4



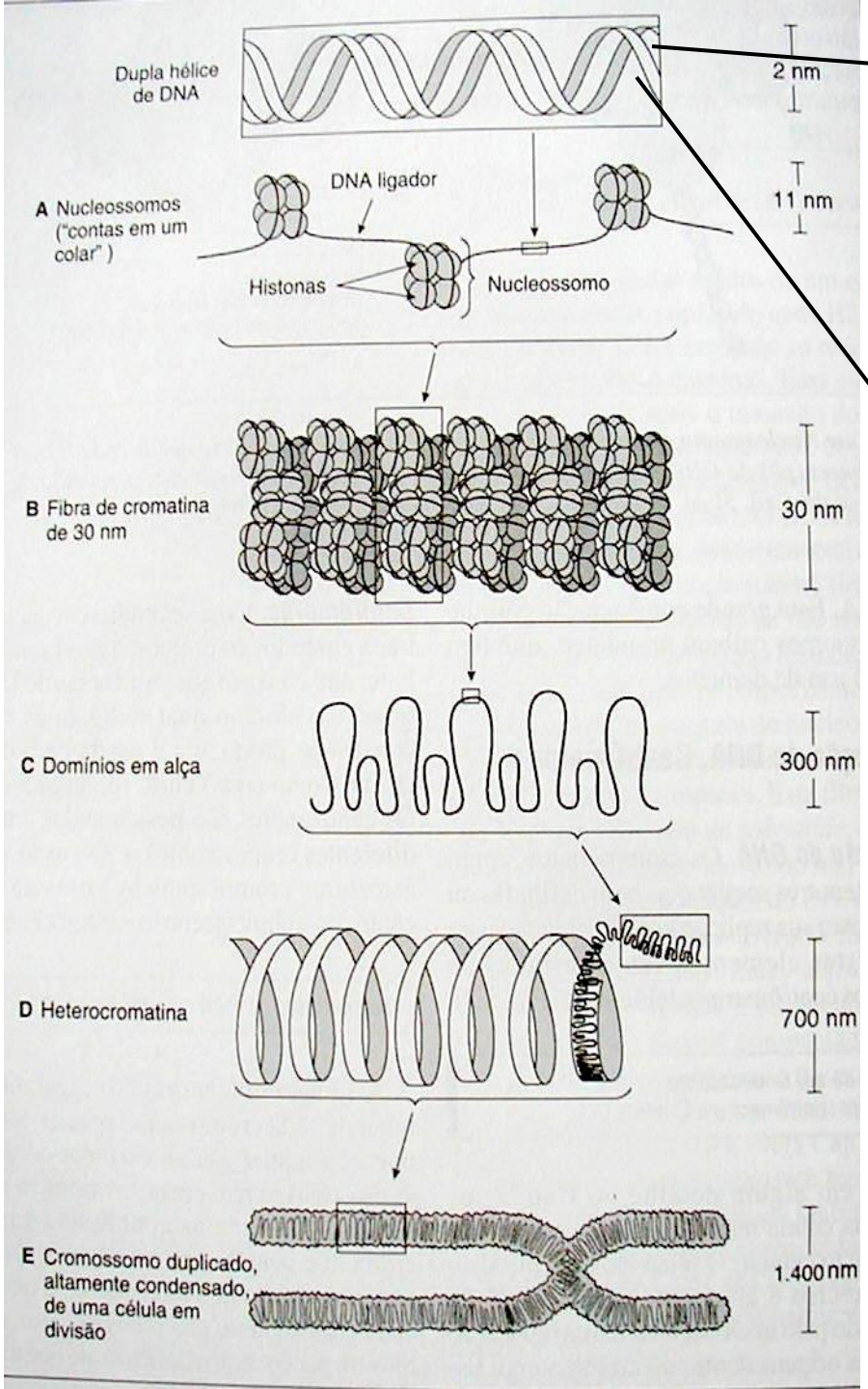
A^2A^4 A^1A^4 A^2A^4 A^2A^4
B^1B^4 B^1B^3 B^2B^3 B^2B^3
C^1C^3 C^2C^4 C^1C^4 C^1C^4
D^2D^4 D^2D^4 D^2D^4 D^2D^4

FENÓTIPO =

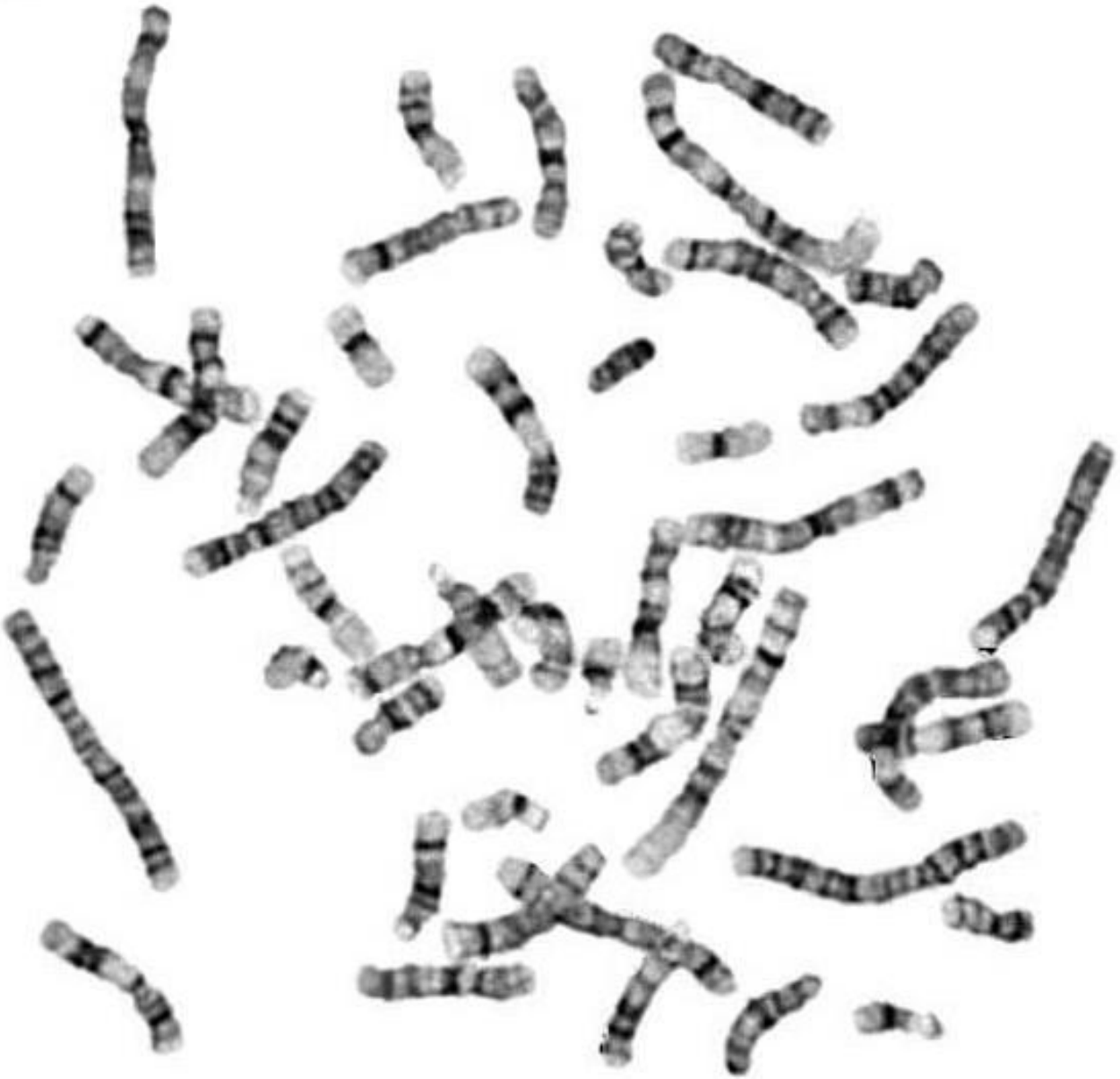
Σ (genes)

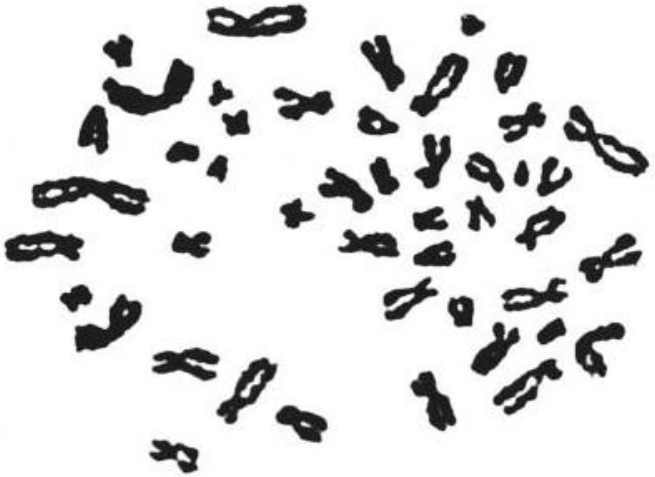
+

MEIO AMBIENTE!!!



actgcatgcatcgatgcatcga





1956

2000's

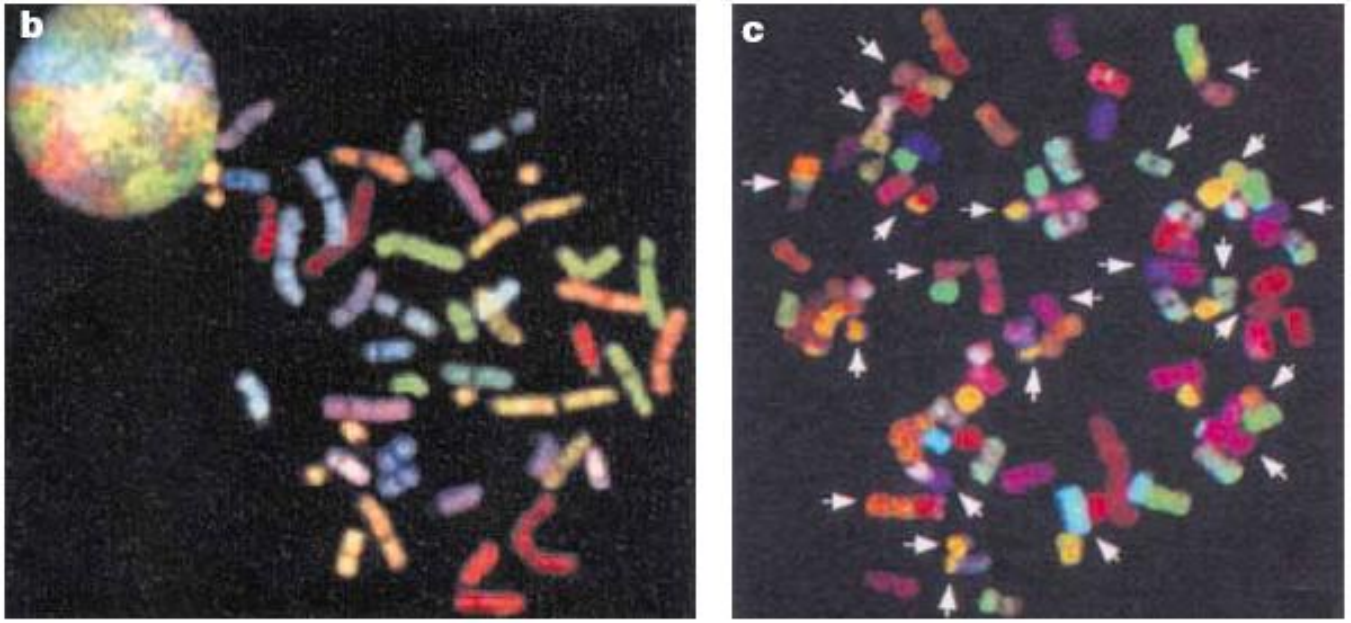
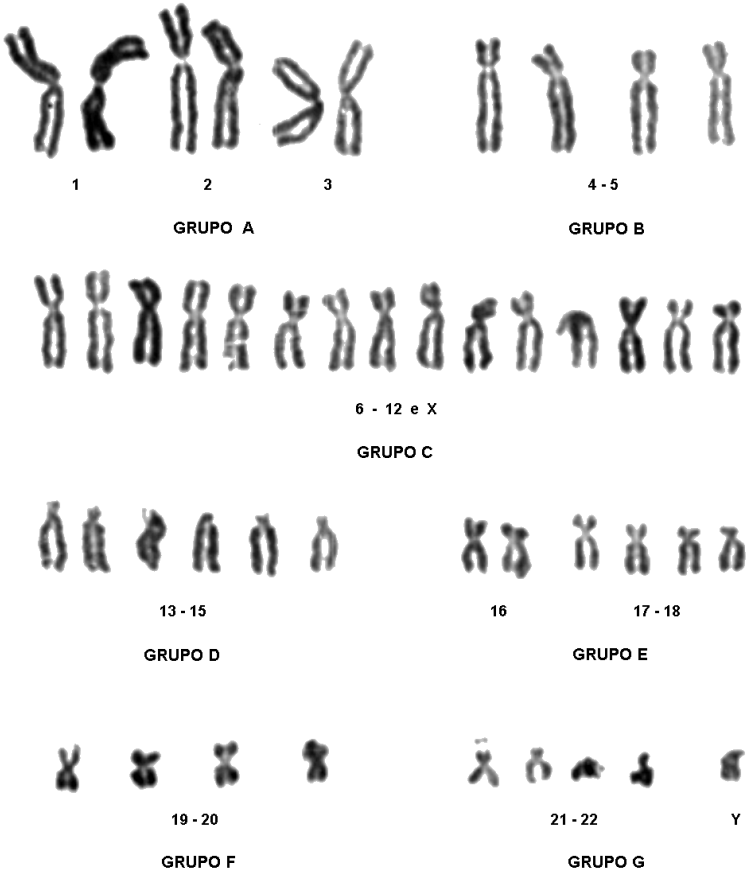


Figure 6 | **Spectral karyotyping and multicolour-FISH paint each human chromosome in one of 24 colours. a** | Outline of the spectral karyotyping (SKY) protocol. SKY and multicolour


10 µm


1
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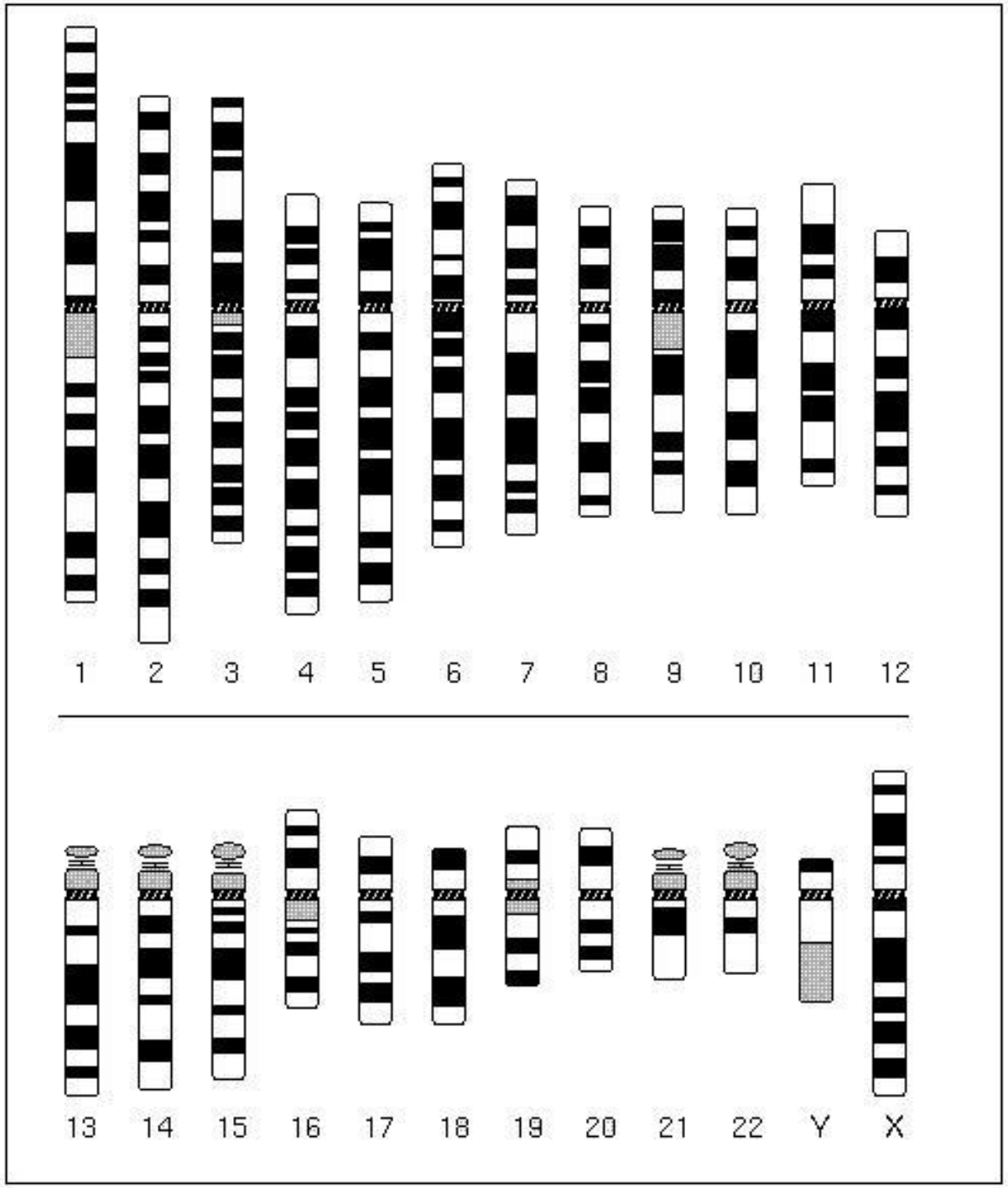
GRUPO A
4 - 5
GRUPO B
6 - 12 e X
GRUPO C
13 - 15
GRUPO D
16
17 - 18
GRUPO E
19 - 20
GRUPO F
21 - 22
Y
GRUPO G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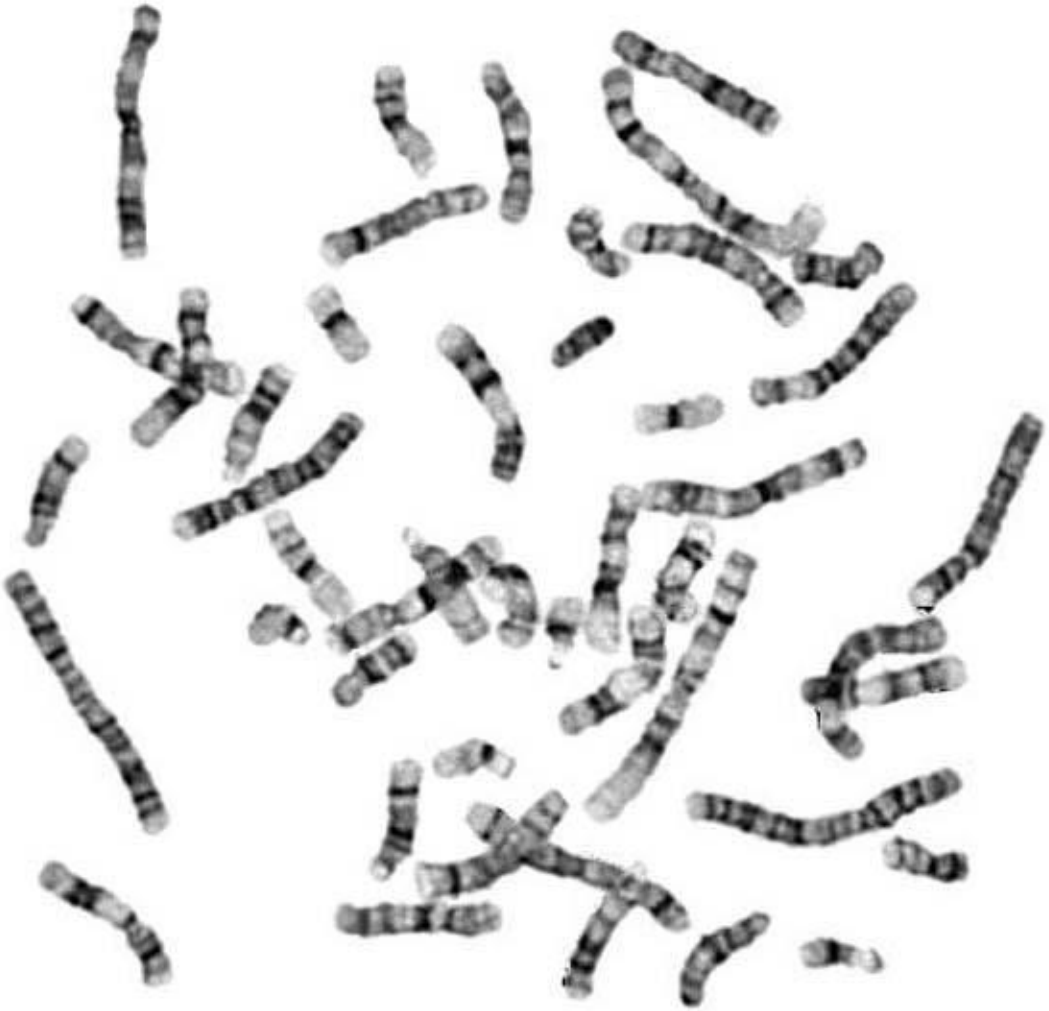
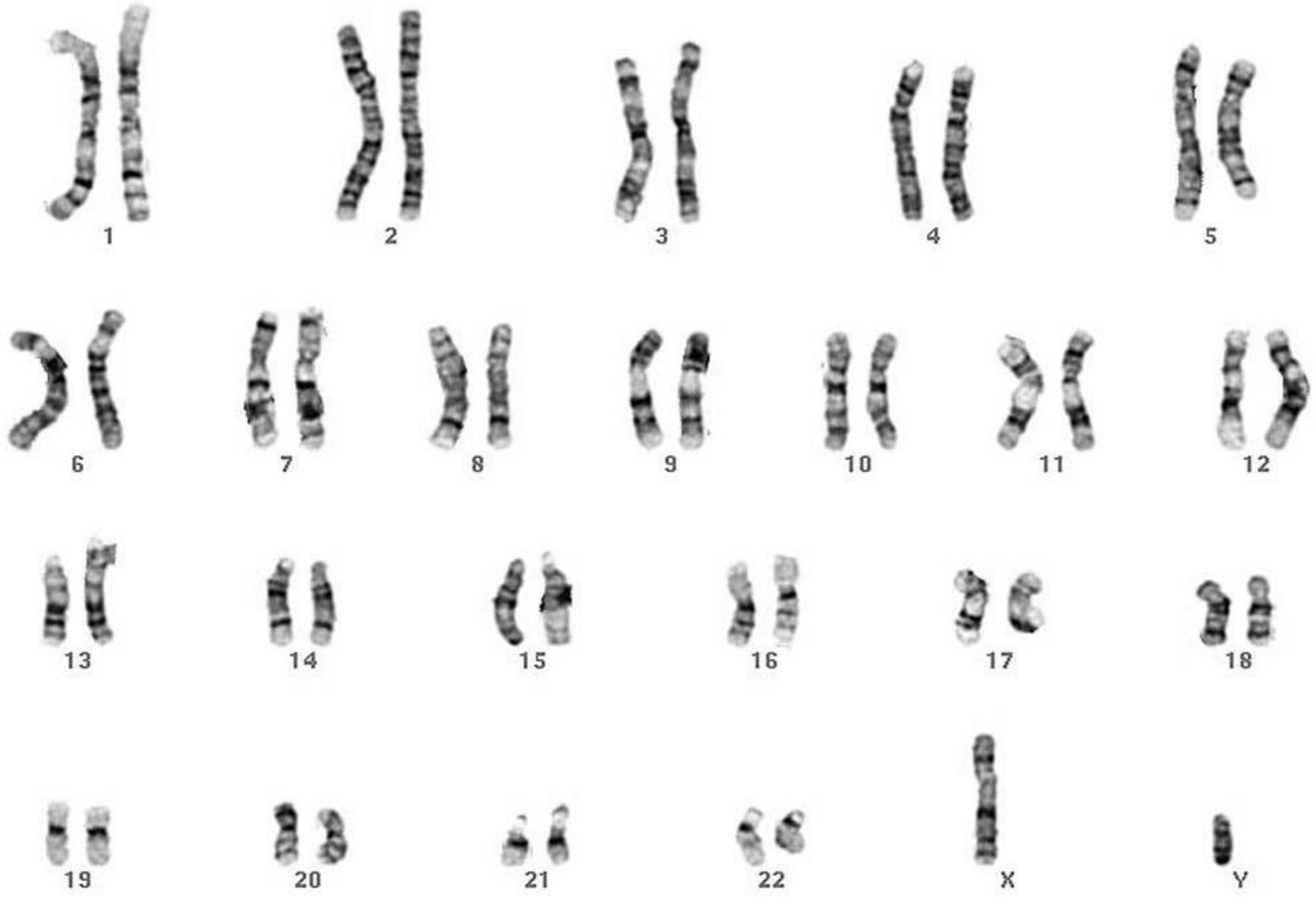
Y
X



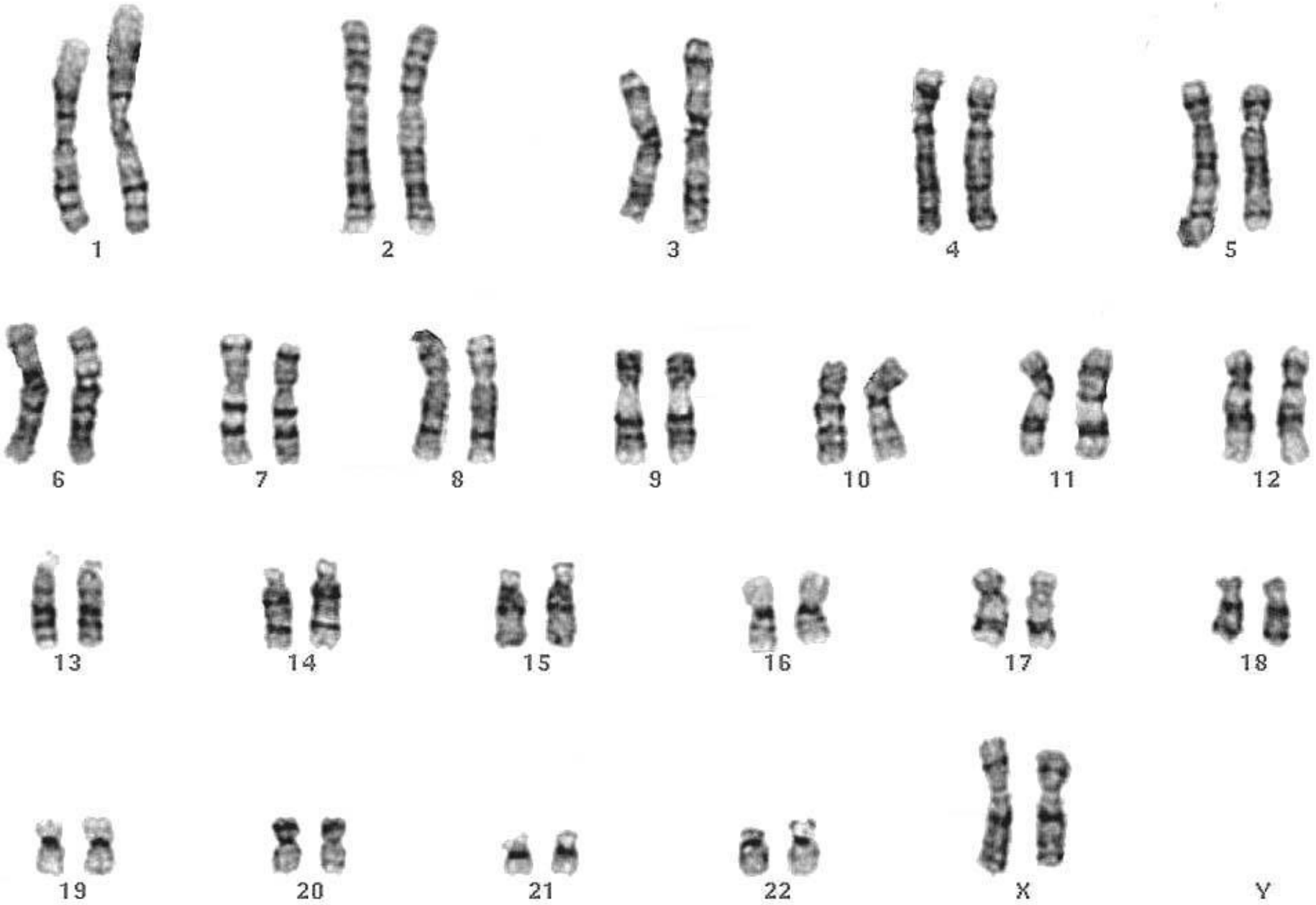
Human male
G-bands

46,XY



Human female
G-bands

46,XX



ABERRAÇÕES CROMOSSÔMICAS

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

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

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

Freqüência de doenças genéticas

Tipo	1.000 nascimentos
Monogênicas	4,5 – 14,0
Multifatoriais	26,0 – 32,0
Cromossômicas	4,0 – 6,8
Total	34,5 – 52,8

Cromossômicas ~12,5%

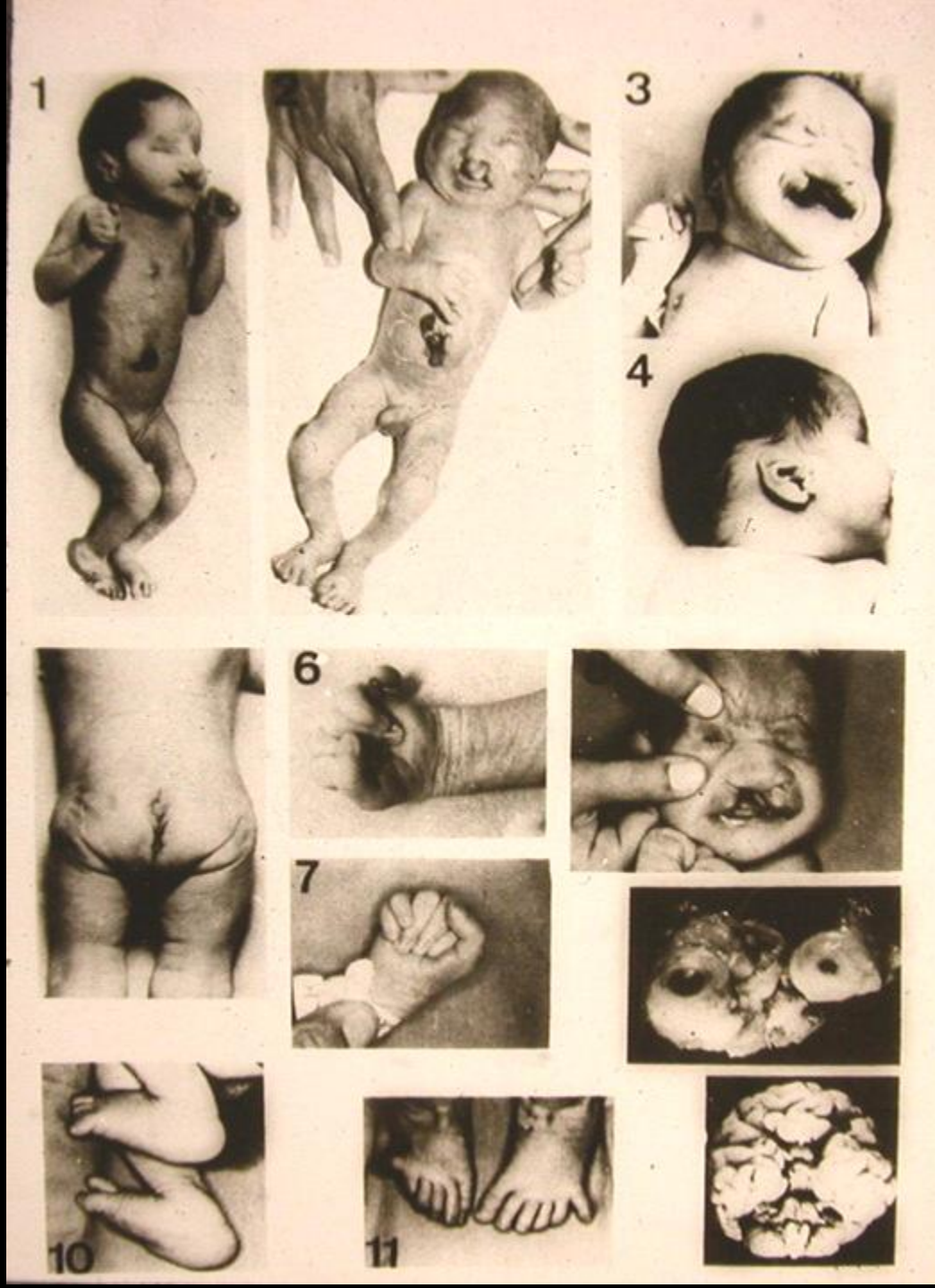
ABERRAÇÕES CROMOSSÔMICAS NUMÉRICAS

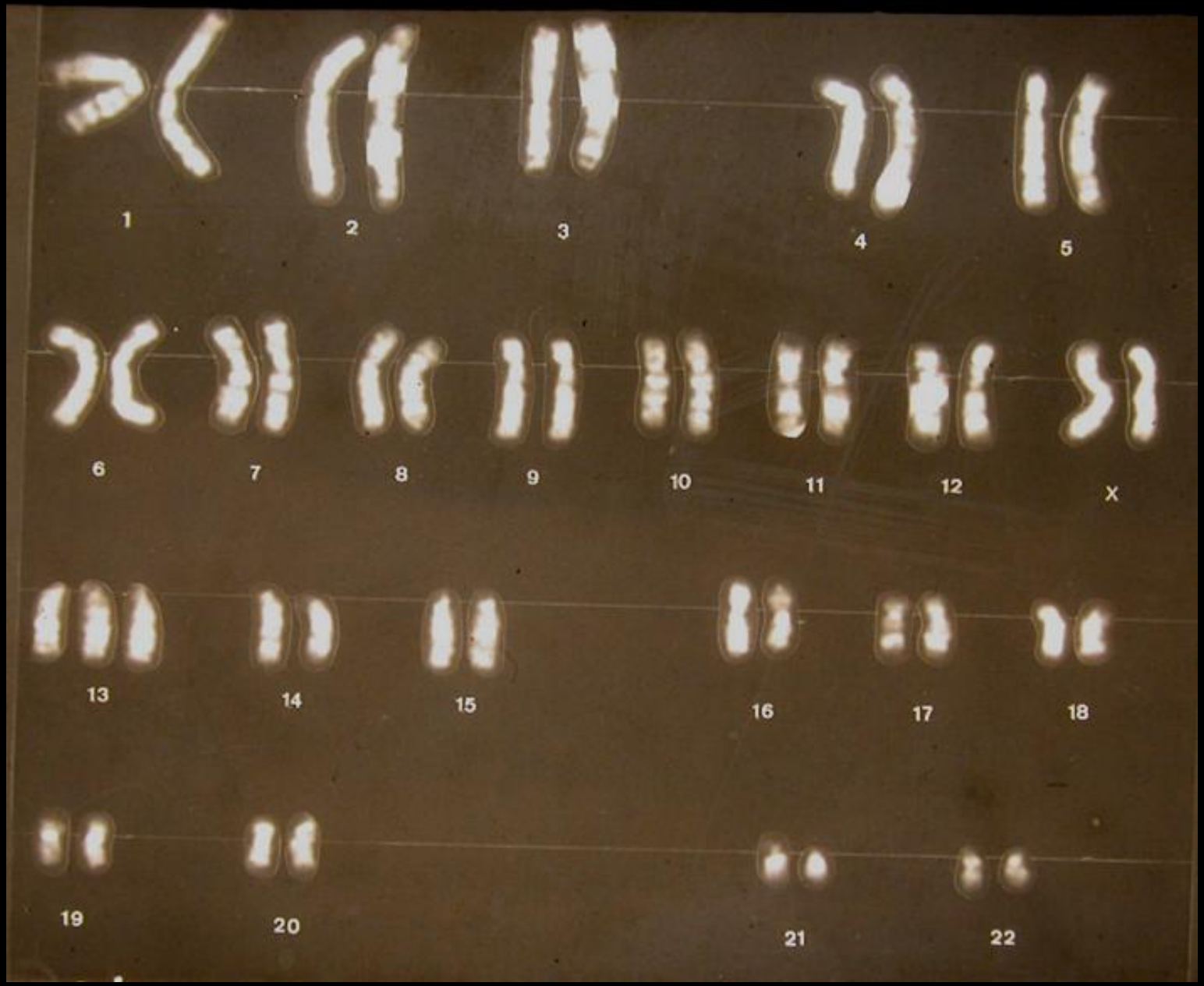
0.7% (60%) nascimentos

2% (85%) gravidezes (>35 anos);

50% (96%) abortos espontâneos 1º trimestre;

microcefalia
anomalias bulbo olho
hipertelorismo
labio leporino
palato fendido
polidactilia

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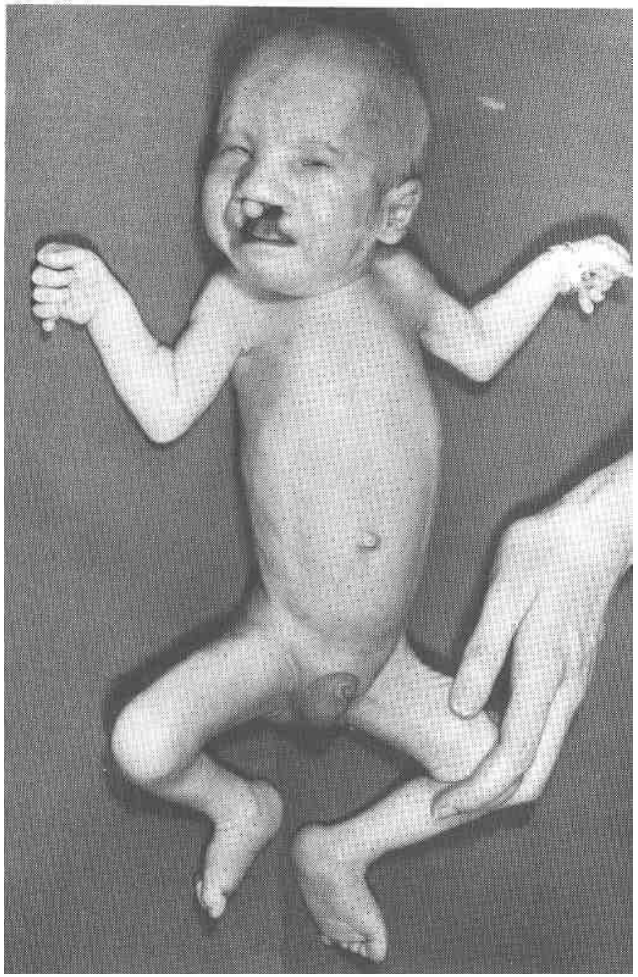
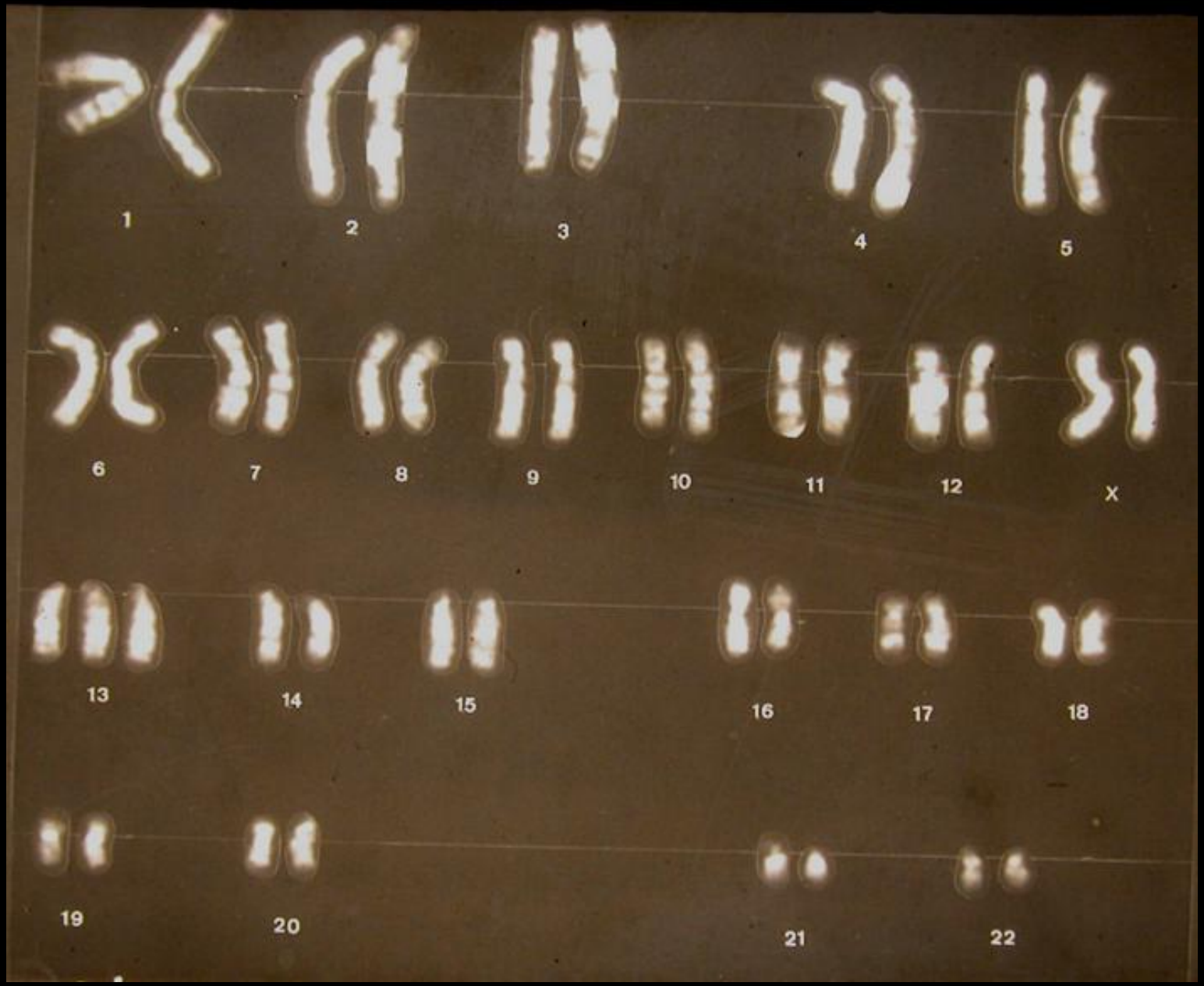
Síndrome de Patau (trissomia 13): 47,XY,+13



1/10.000;

Letal < 6 meses;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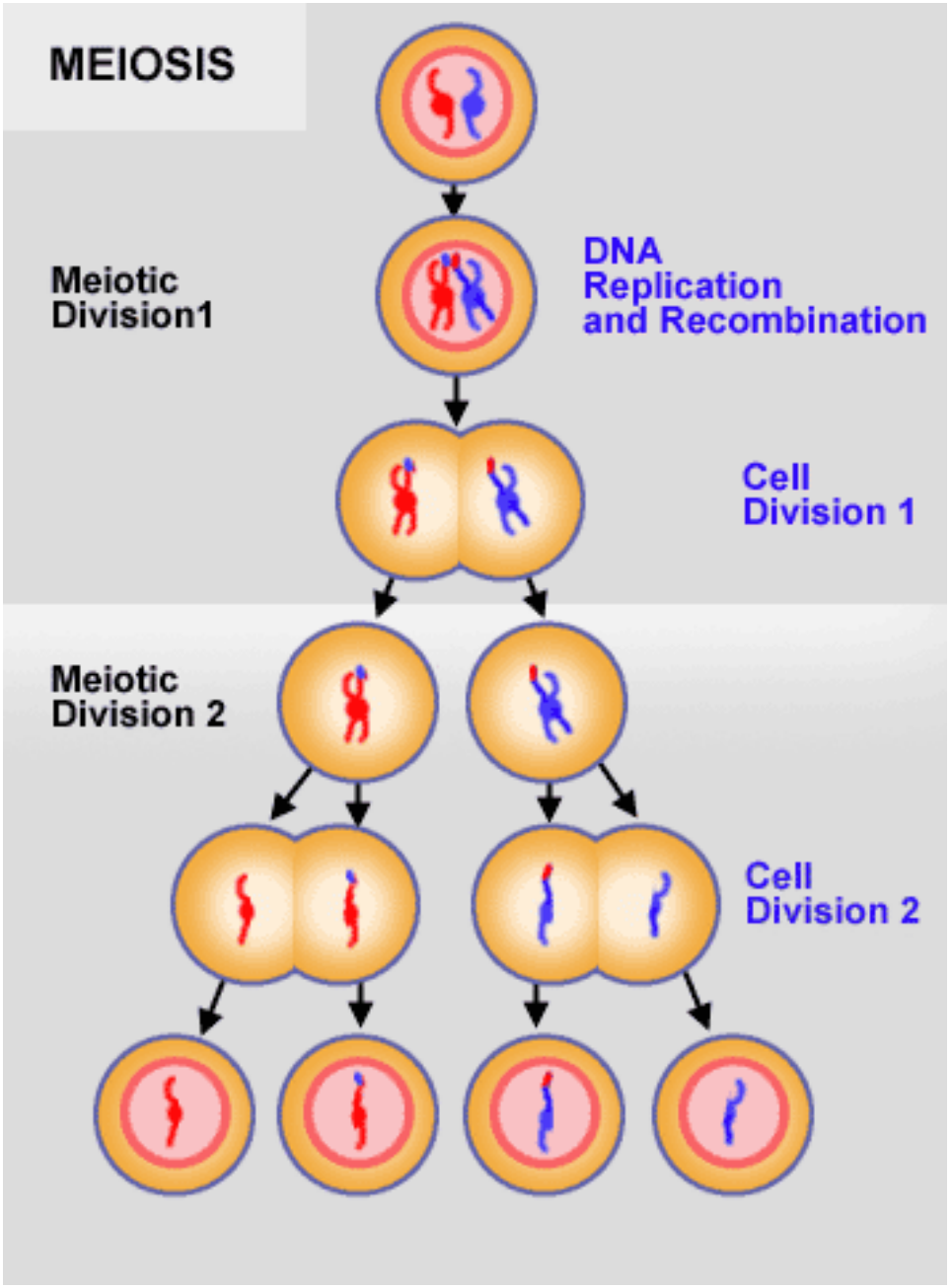
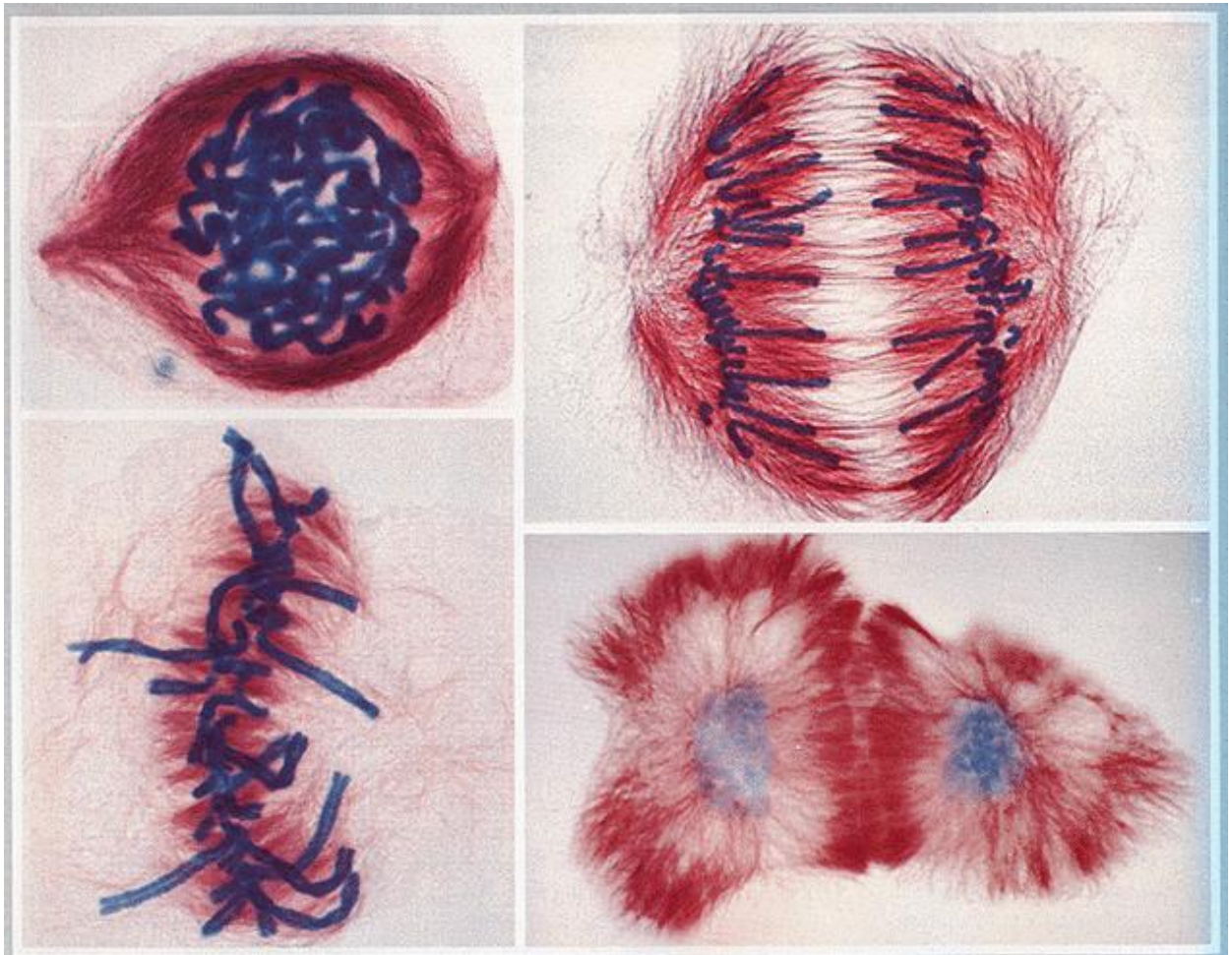
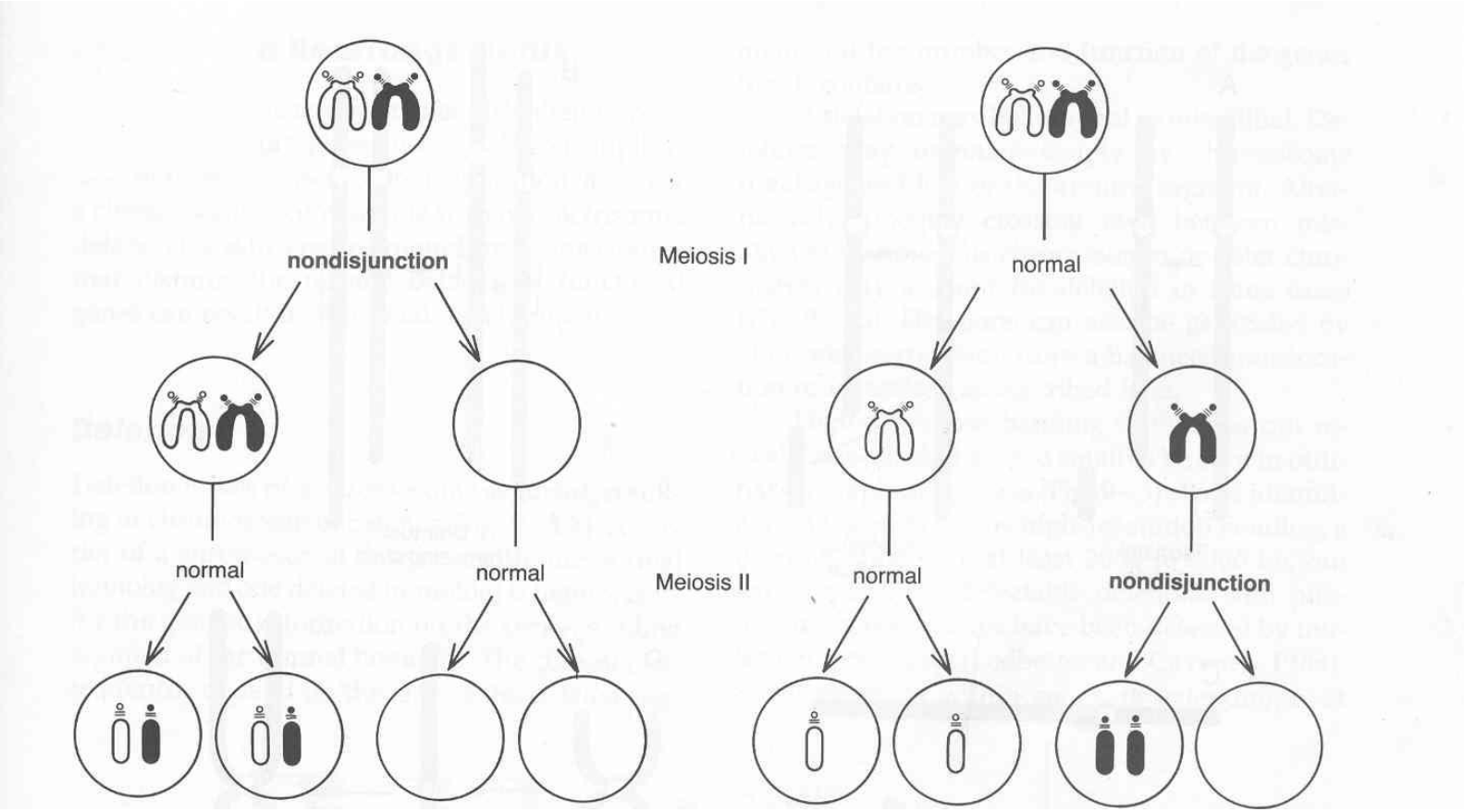
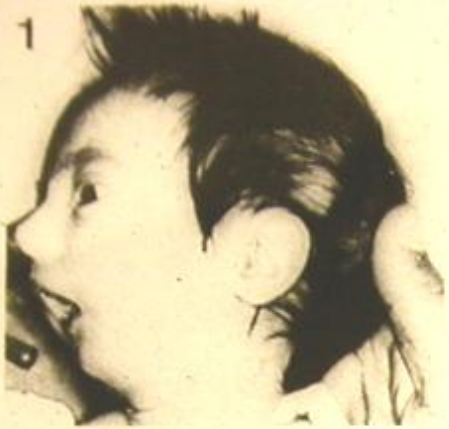

MEIOSIS
Meiotic Division1
DNA Replication and Recombination
Cell Division 1
Meiotic Division 2
Cell Division 2

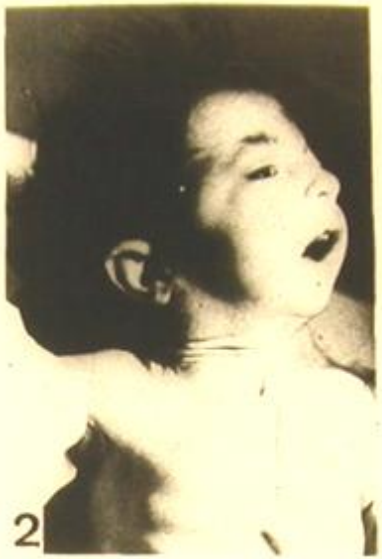


Plant cells in various stages of mitosis: (a) prophase; (b) metaphase; (c) anaphase; (d) telophase (all magnified about 2,700 times).

NÃO DISJUNÇÃO




1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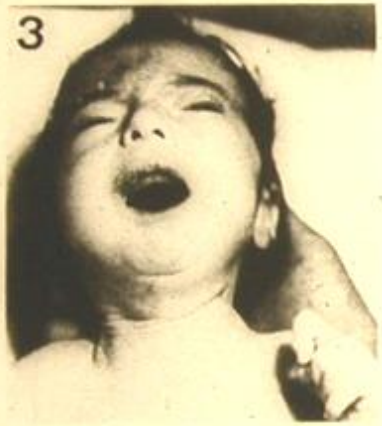
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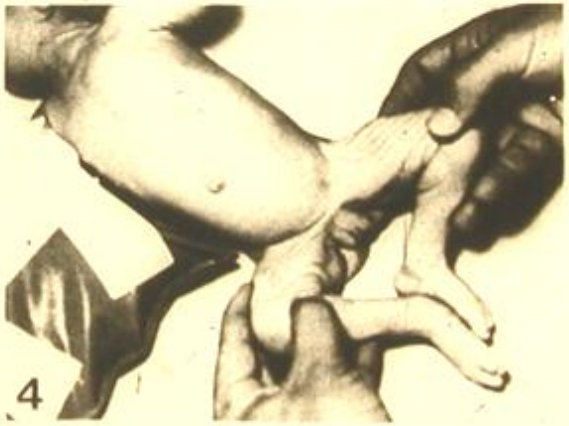
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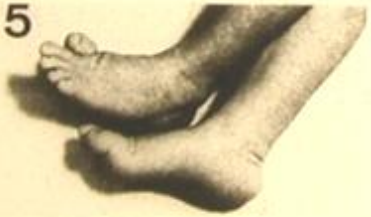
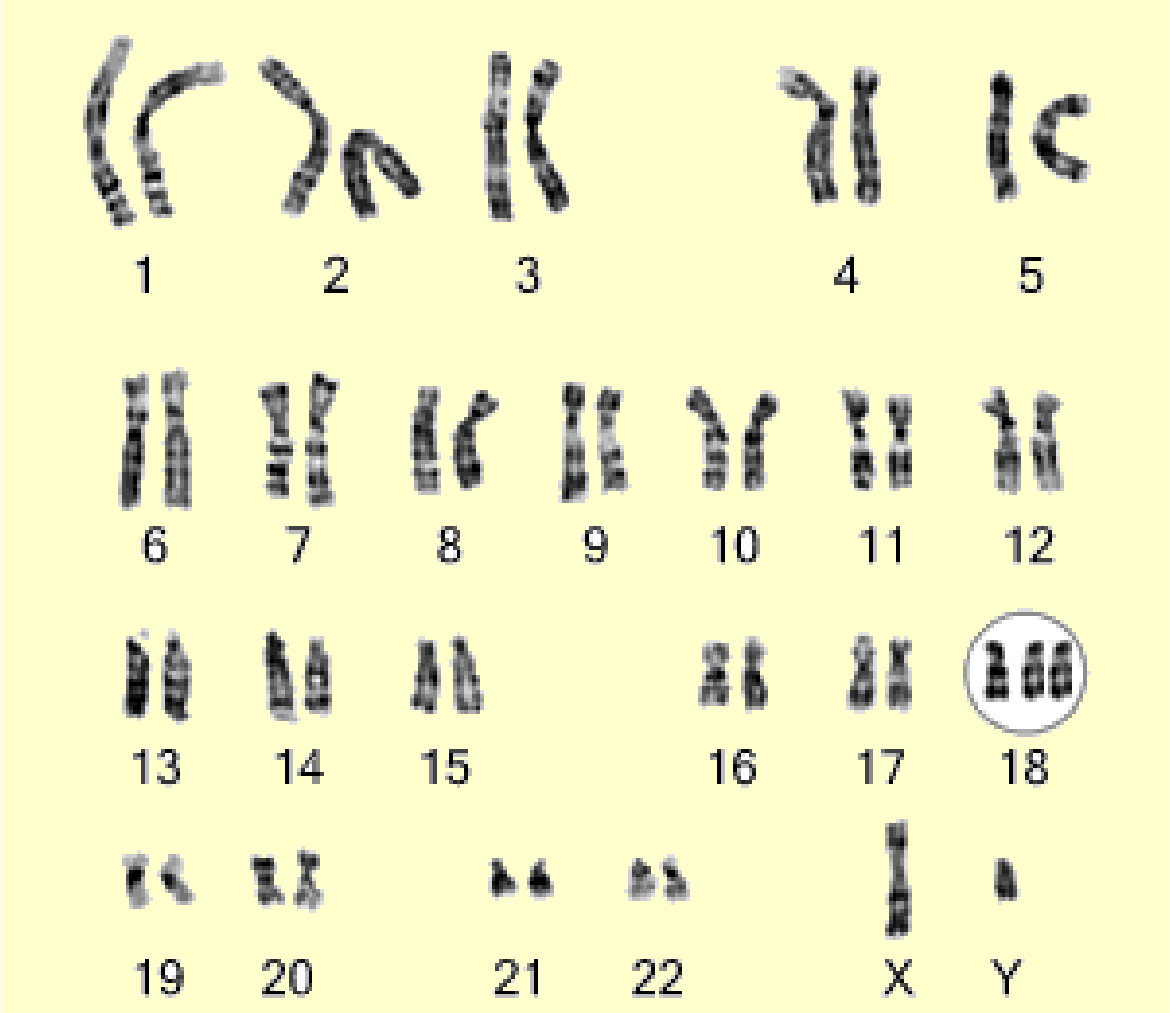

5


6

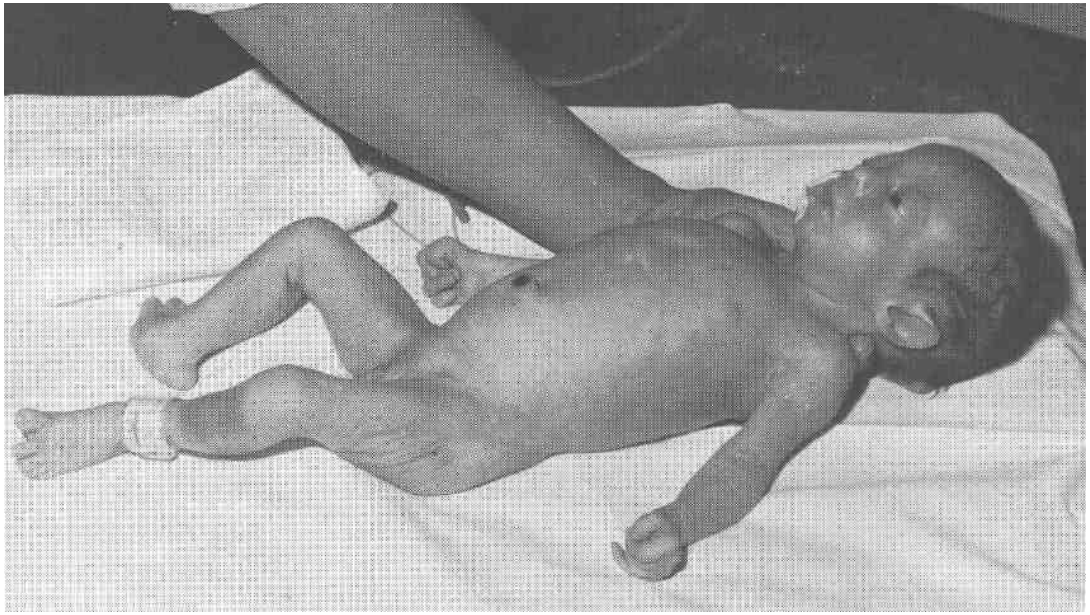

7

Trissomia do cromossomo 18



47,XY,+18

Síndrome de Edwards (trissomia 18): 47,XY,+18

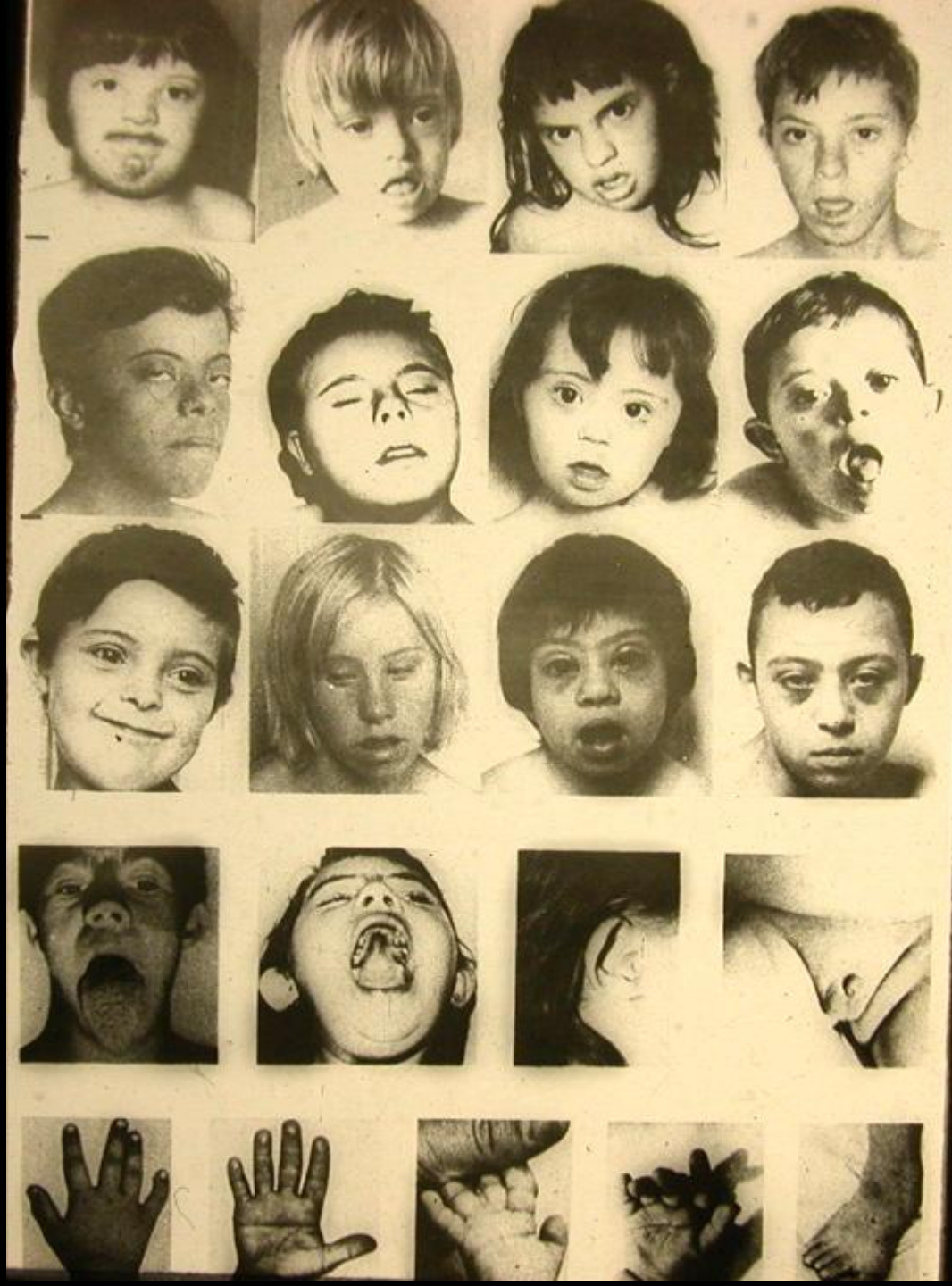


1/8.000;

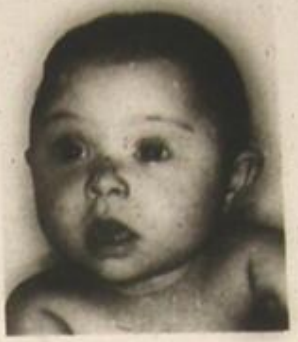
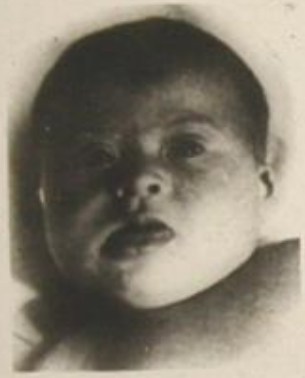
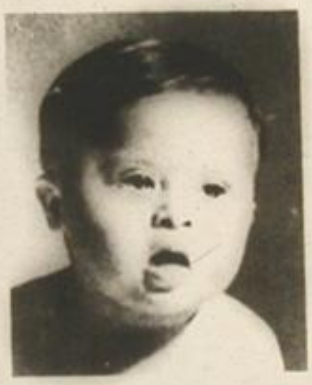
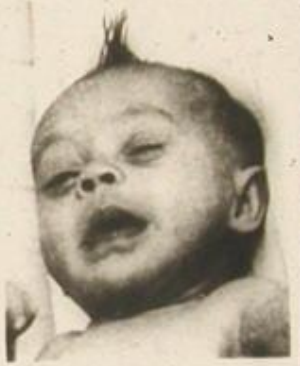
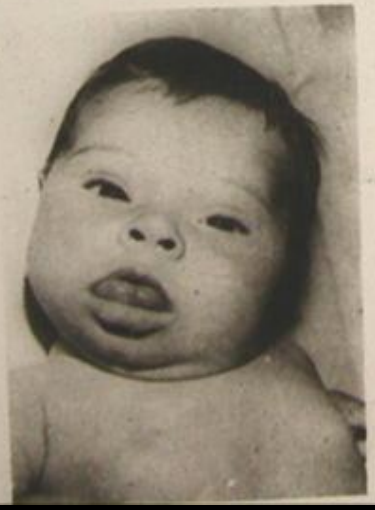
Letal < 1 mês;

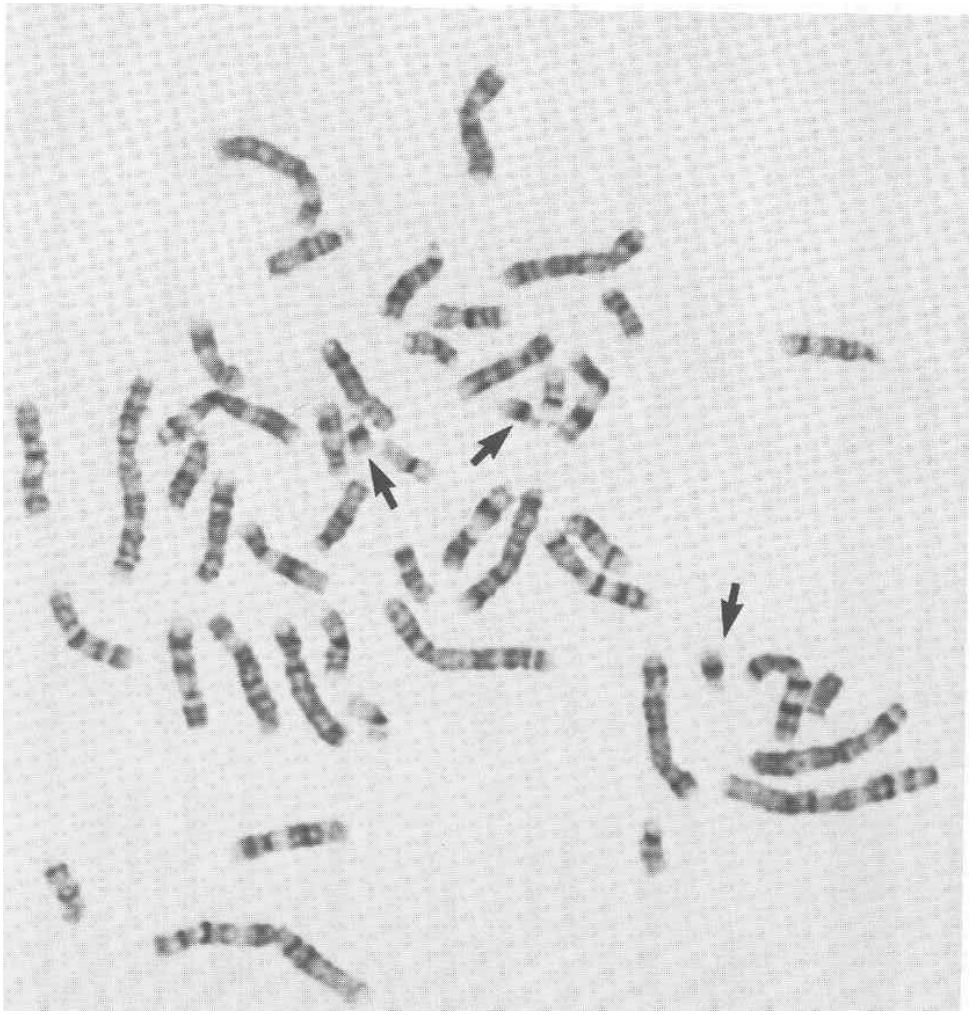
95% aborto espontâneo.

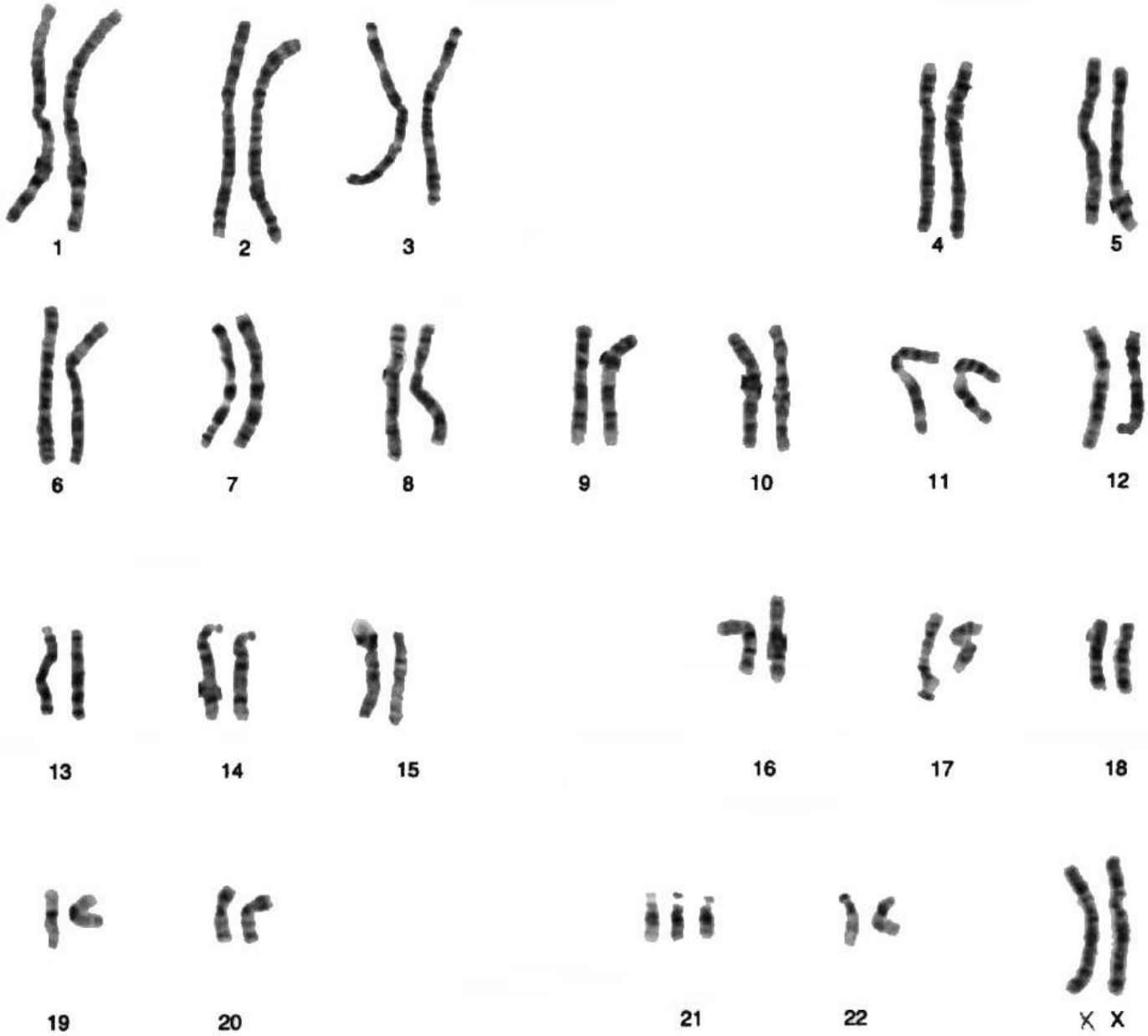
hipotonia
face típica
ponte nasal achatada
pescoço curto/pele nuca
prega única na mão
retardo mental



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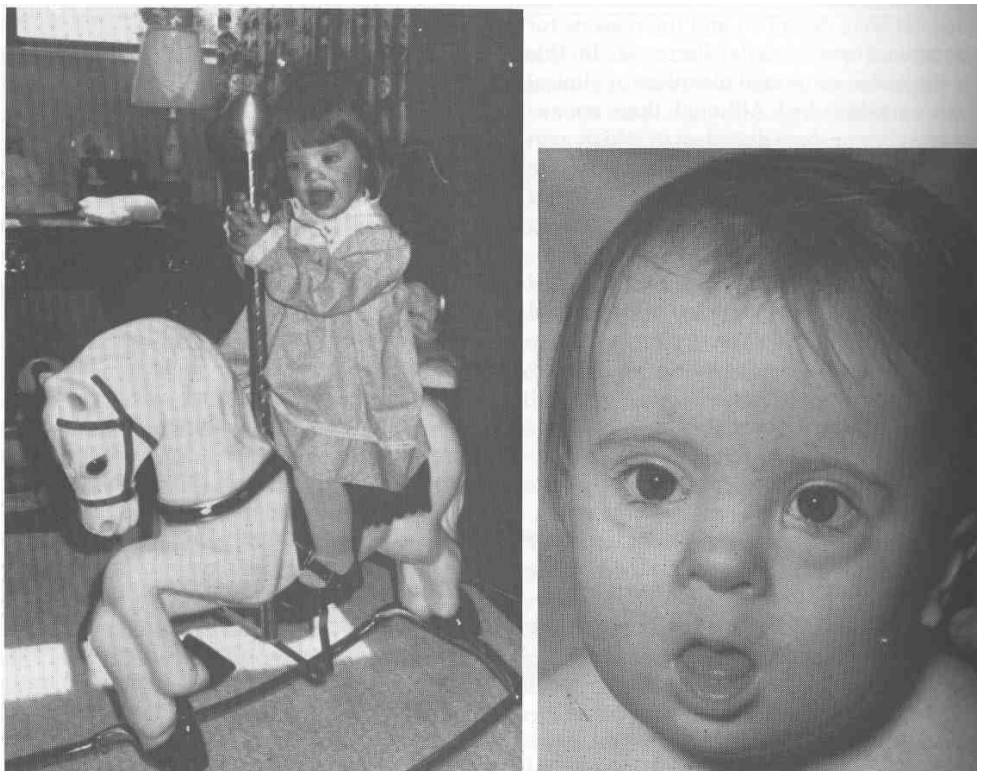
X X

Síndrome de Down

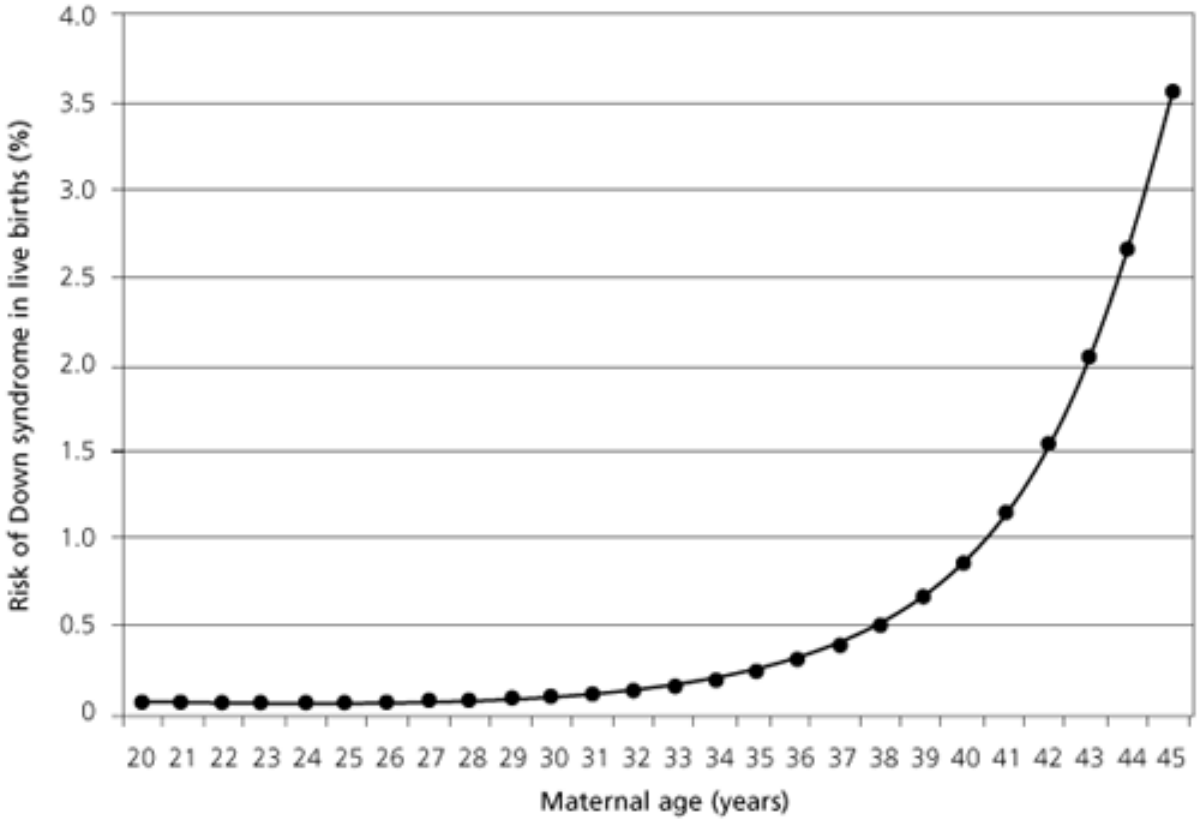


- **mais comum;**
- **maior causa genética de retardo mental;**
- **1/800 nascimentos;**

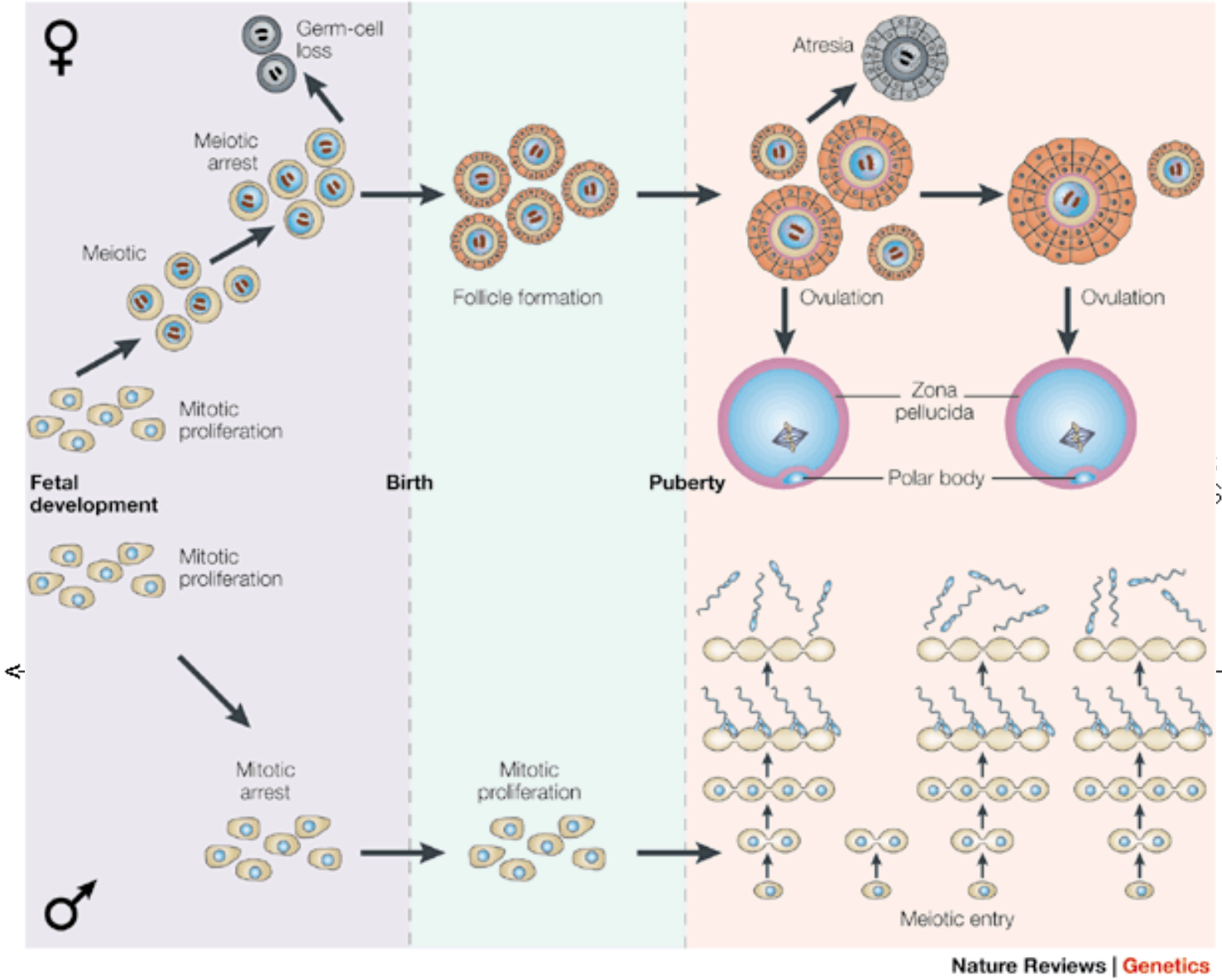
Origem da não-disjunção do cromossomo 21

Materna	89%		
		MI	75%
		MII	25%
Paterna	9%		
		MI	46%
		MII	54%
Mitótica	2%		

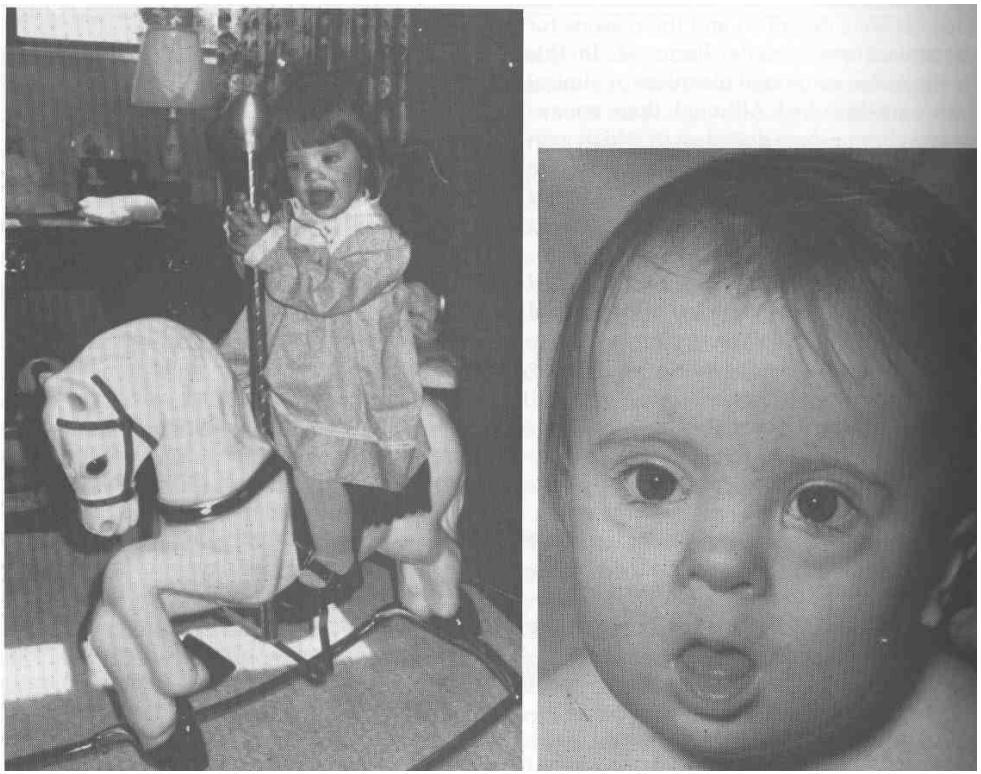
Síndrome de Down e Idade Materna



A formação de gametas no homem e na mulher



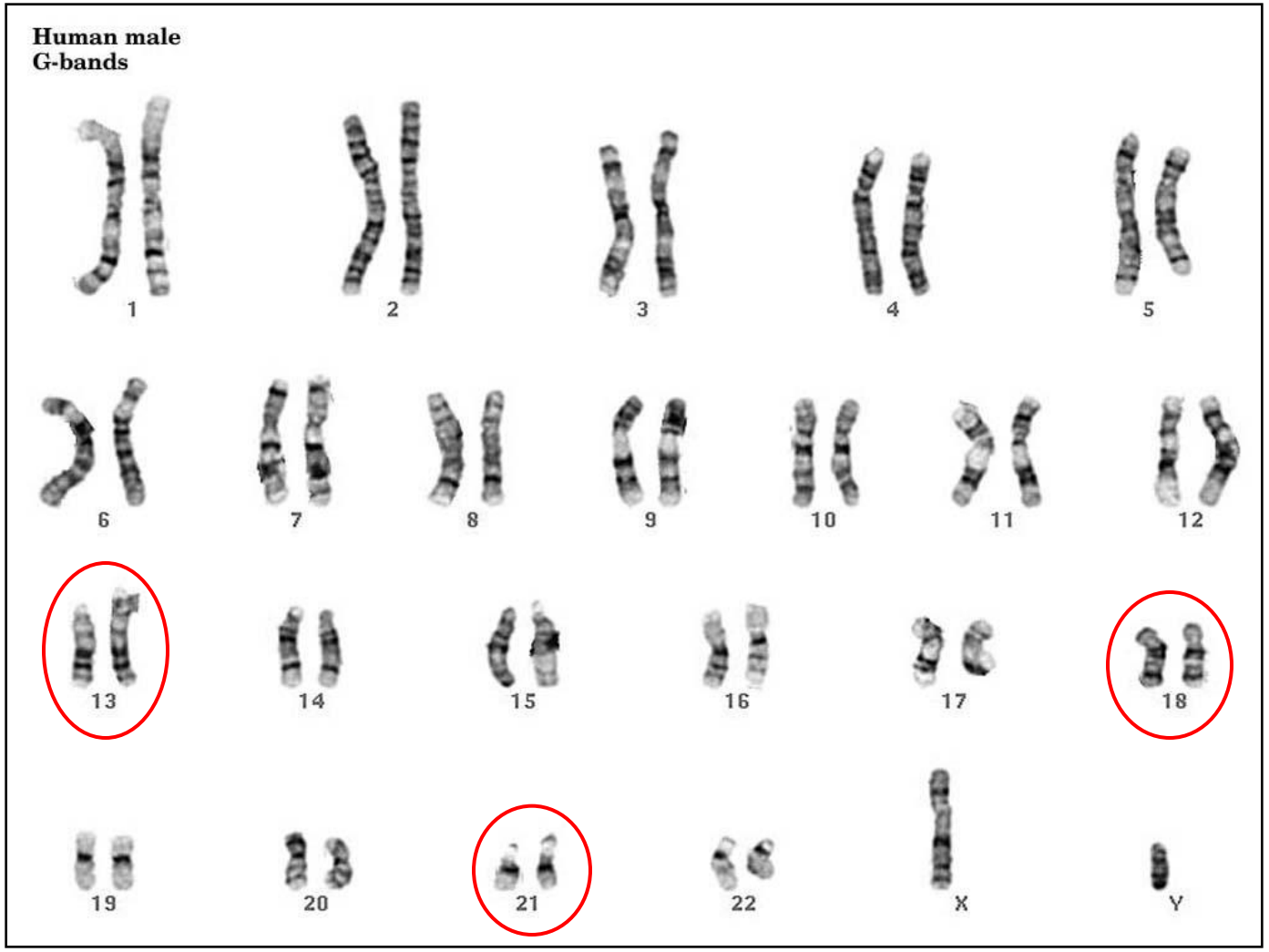
Síndrome de Down



- **mais comum;**
- **maior causa genética de retardo mental;**
- **1/800 nascimentos;**

Formação de embrião com mosaiscismo

GRAVIDADE ≡ ?


Human male
G-bands
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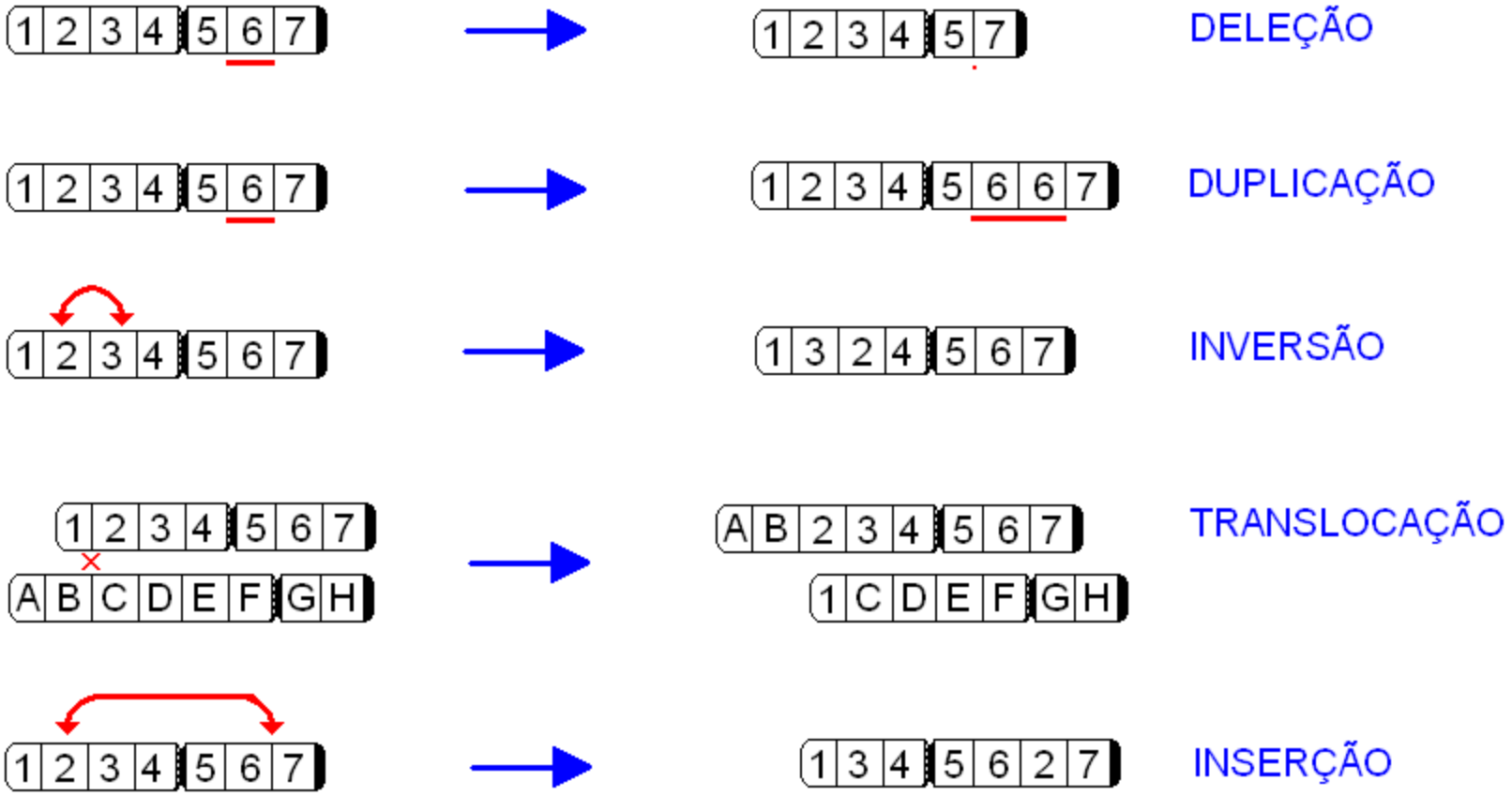
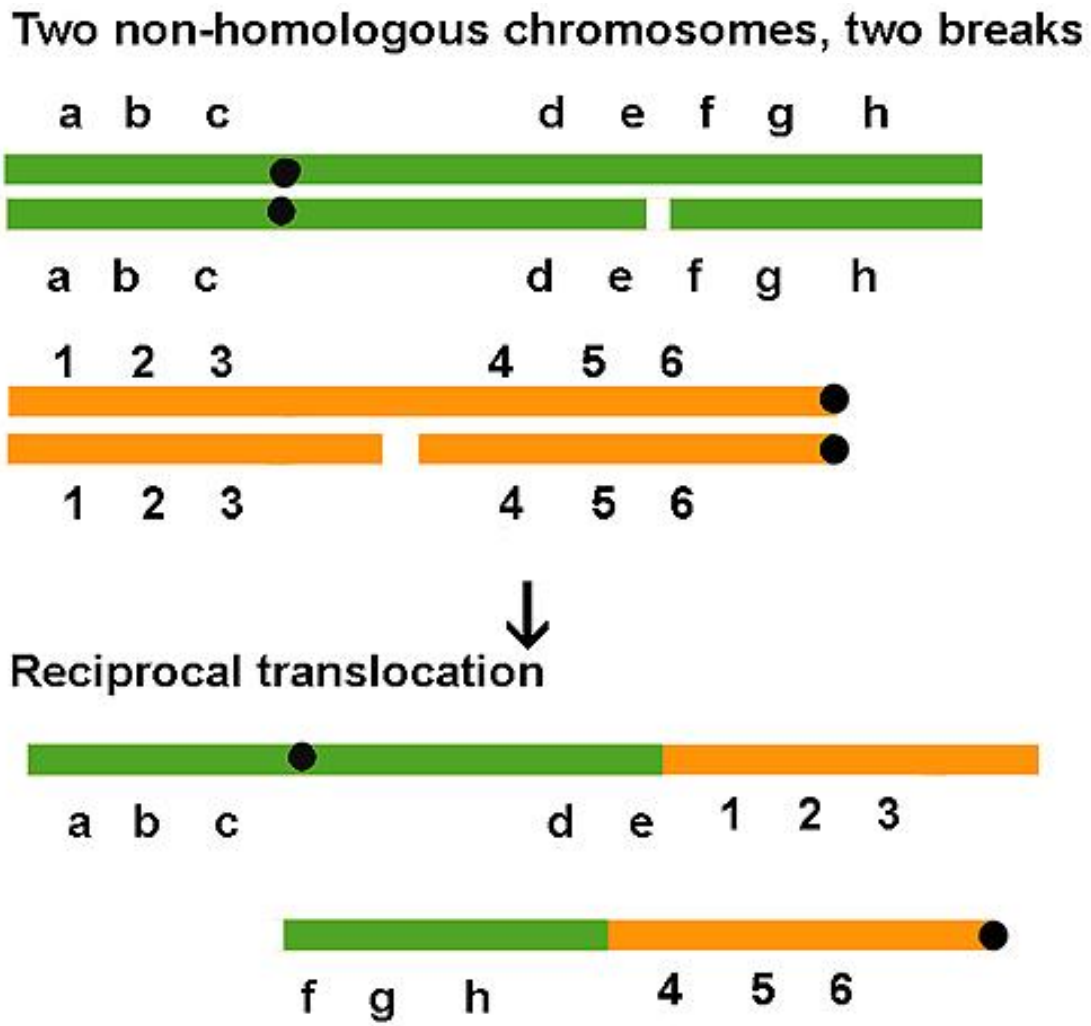
Y

ALTERAÇÕES CROMOSSÔMICAS ESTRUTURAIS



Formação de rearranjos cromossômicos
Translocação recíproca

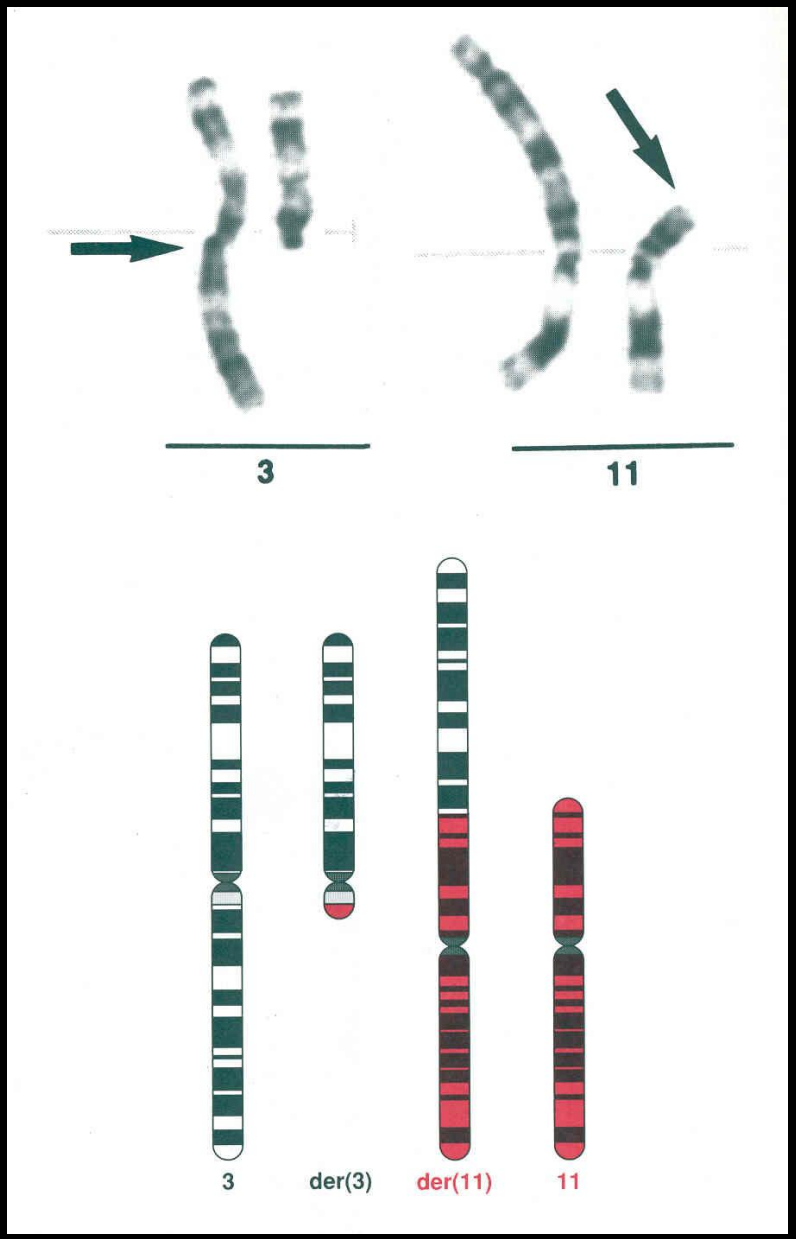


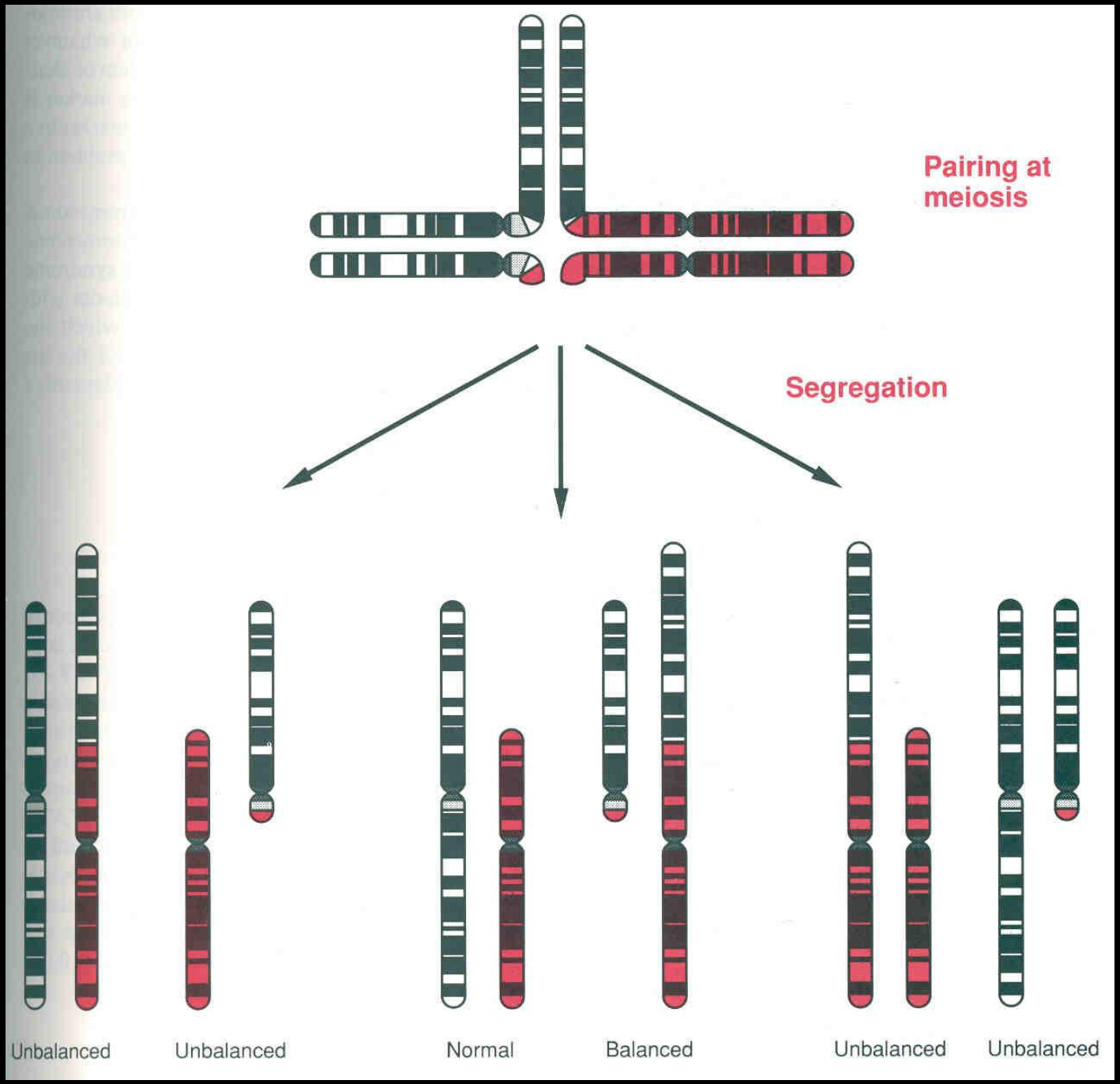
ABERRAÇÃO CROMOSSÔMICA

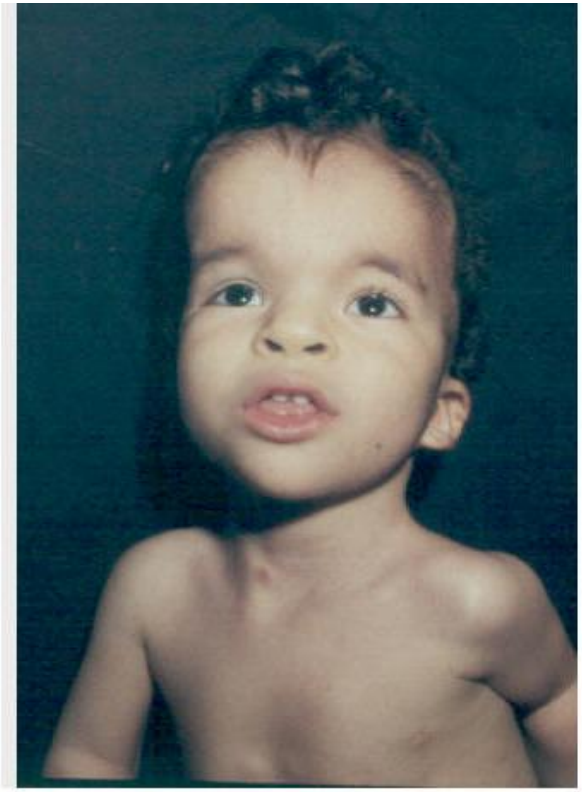
ESTRUTURAL

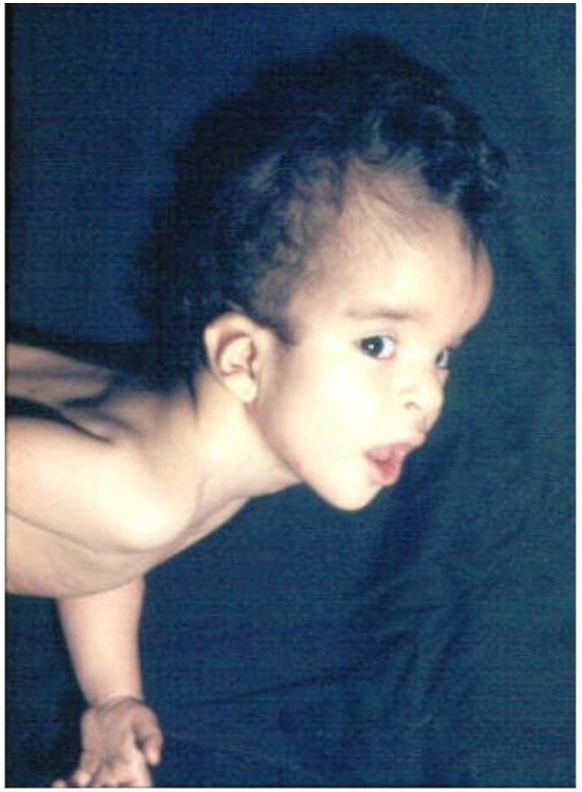
TRANSLOCAÇÃO

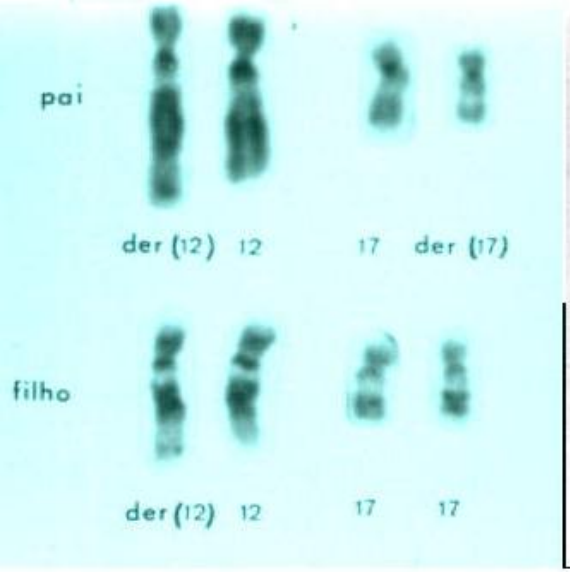
46,XX,t(3q11p)




Pairing at meiosis
Segregation
Unbalanced
Unbalanced
Normal
Balanced
Unbalanced
Unbalanced






pai
der (12)
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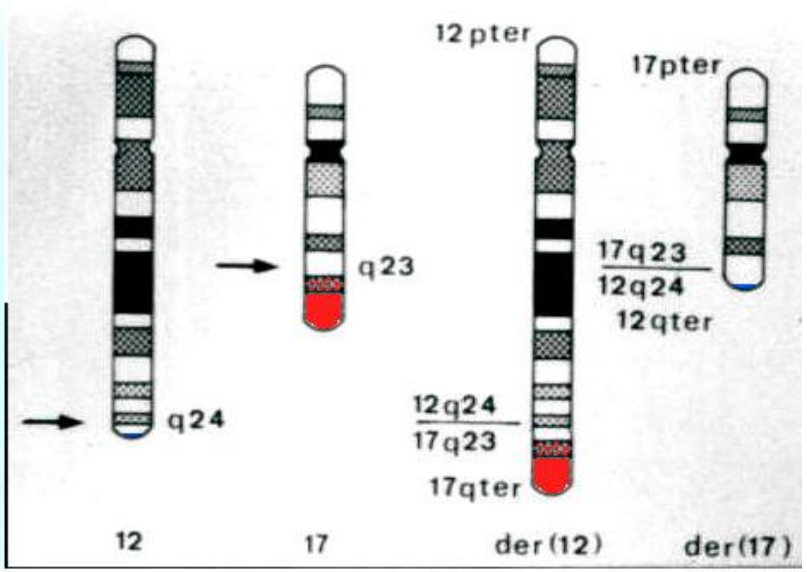
der (17)
filho
der (12)
12
17
17


12 pter
17pter
q23
17q23
12q24
12qter
q24
12q24
17q23
17qter
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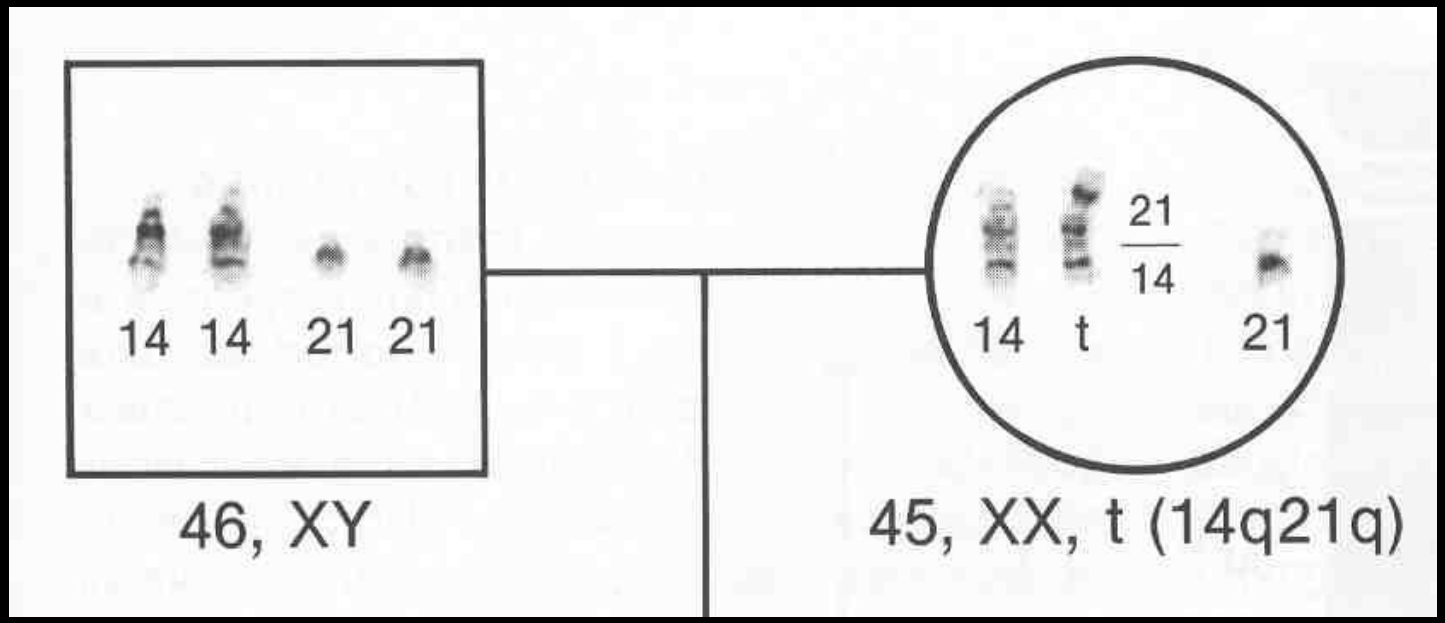
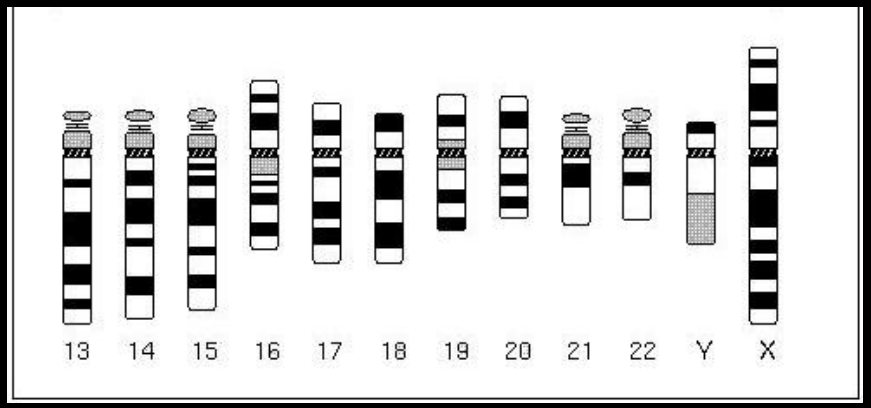
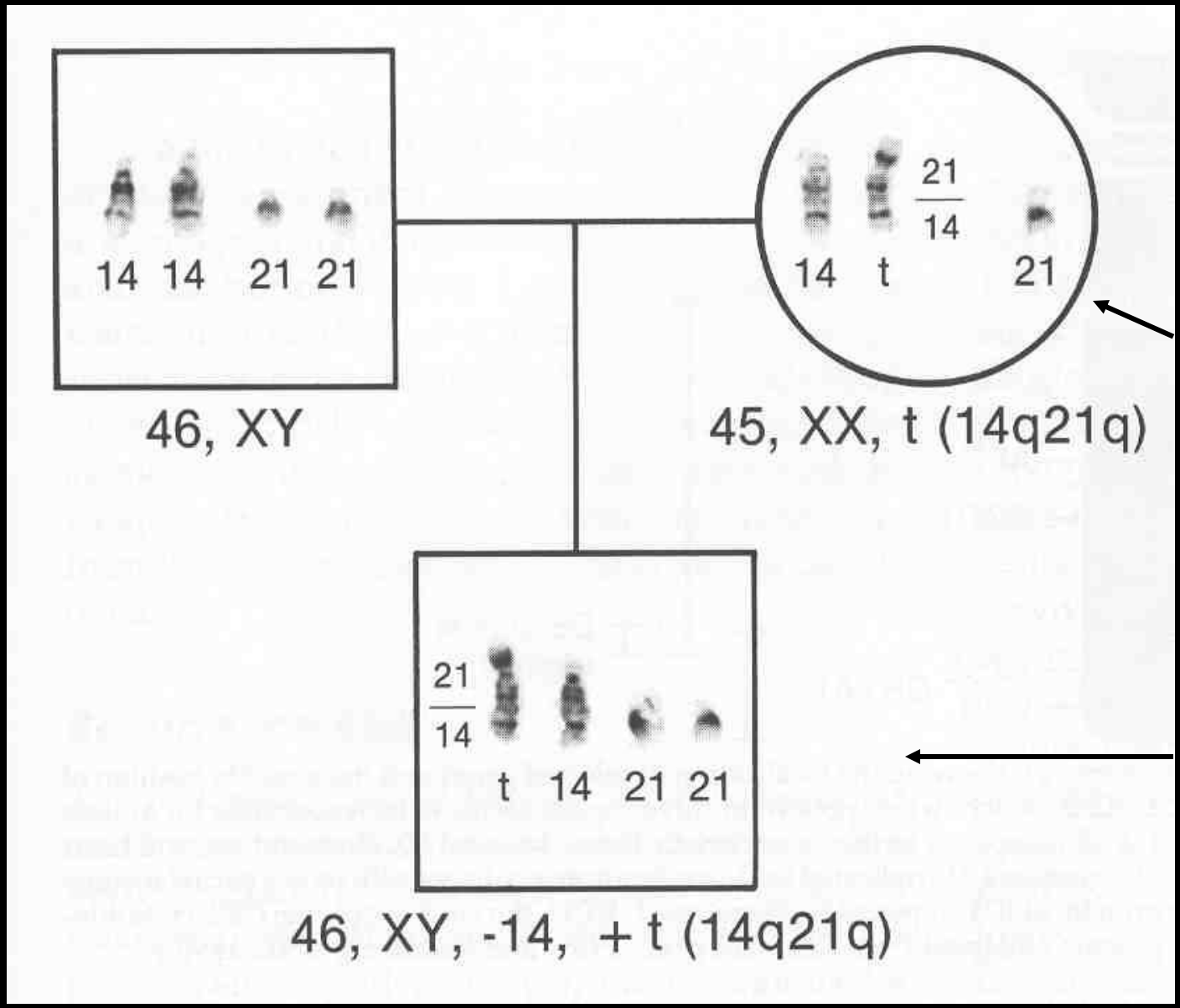
17
der(12)
der(17)

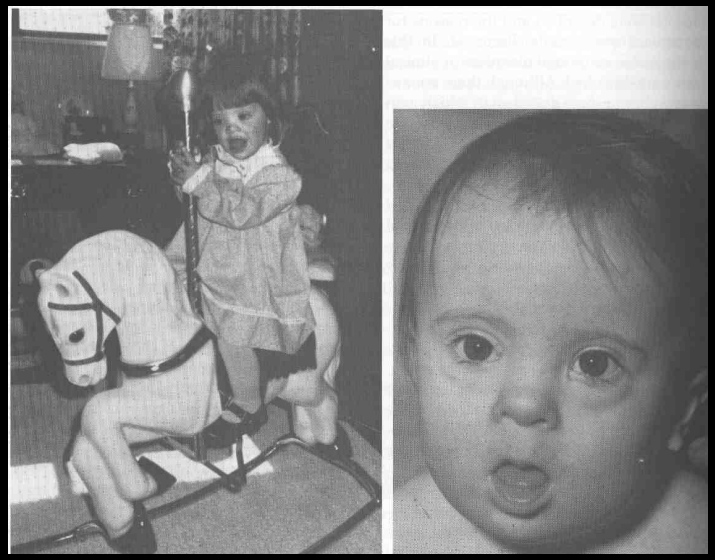


TRANSLOCAÇÃO Robertsoniana



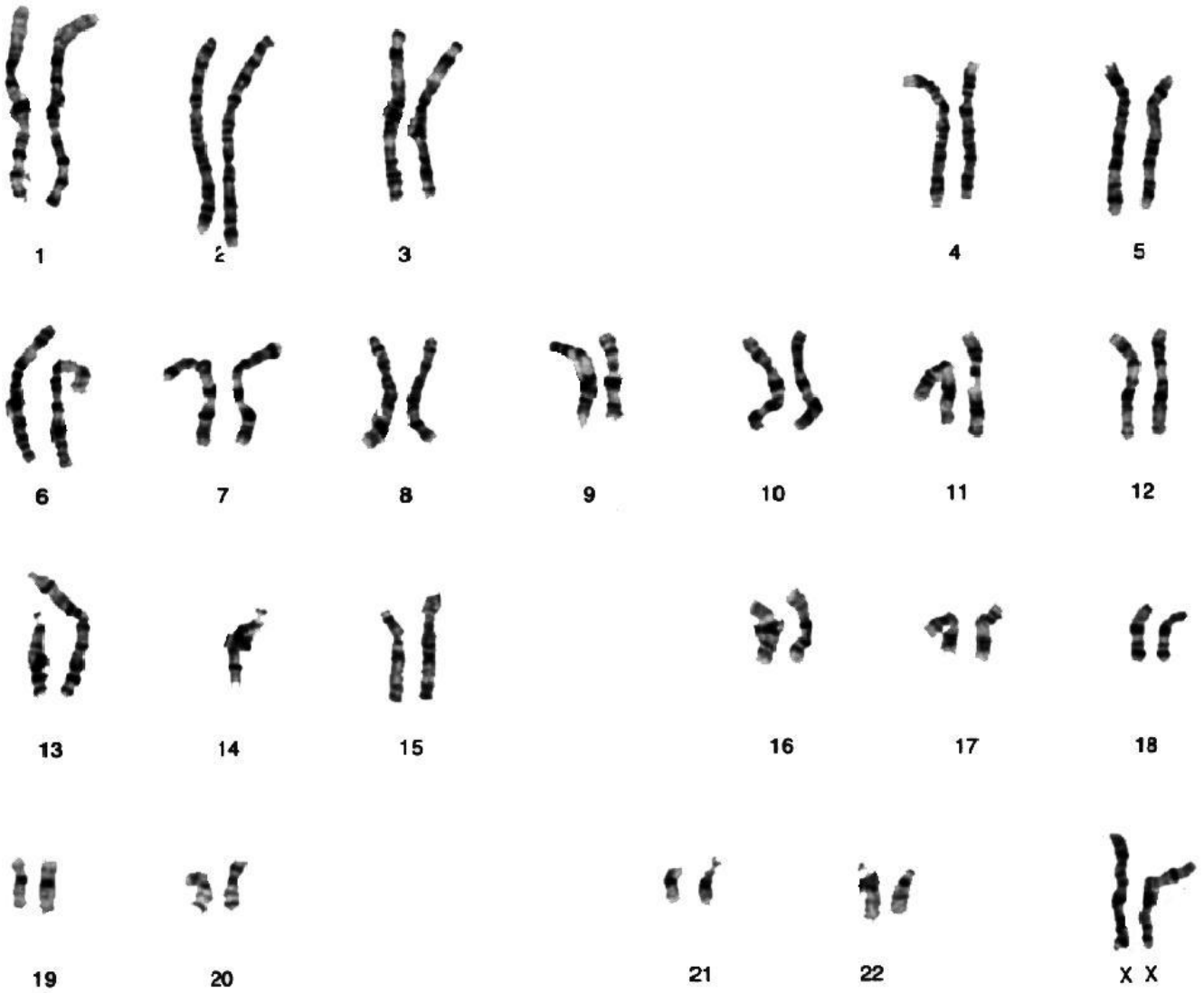

14 14 21 21
46, XY
14 t 21/14 21
45, XX, t (14q21q)
21/14 t 14 21 21
46, XY, -14, + t (14q21q)
balanceada
não balanceada

Síndrome de Down



Trissomia livre 21:	**95%**	**(1%)**
Translocação:	**4%**	**(15%)**
Mosaicismo:	**1%**	**(???)**

Robertsonian
translocation
45,XX,t(13;14)



ABERRAÇÕES CROMOSSÔMICAS

ESTRUTURAIS

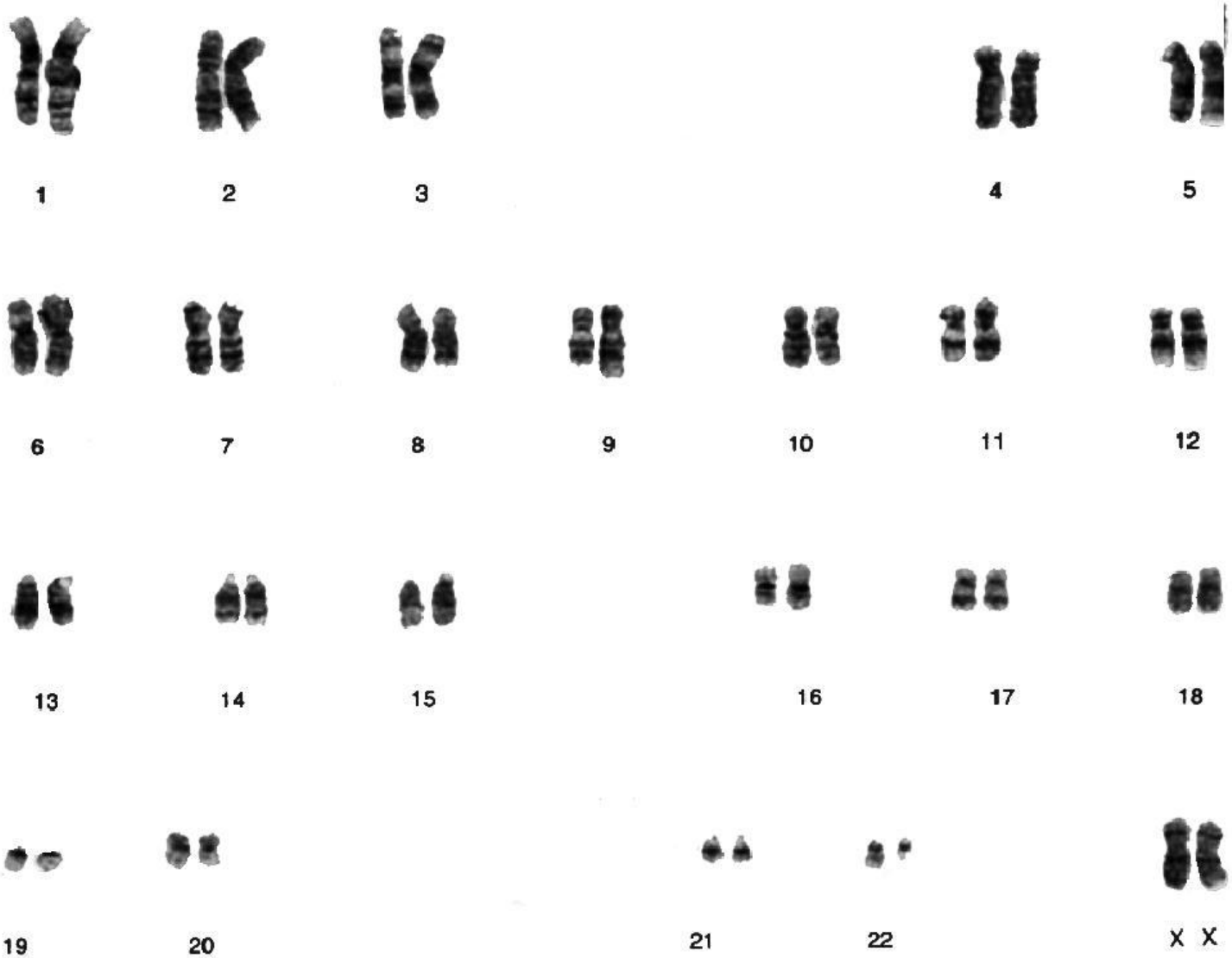
BALANCEADAS

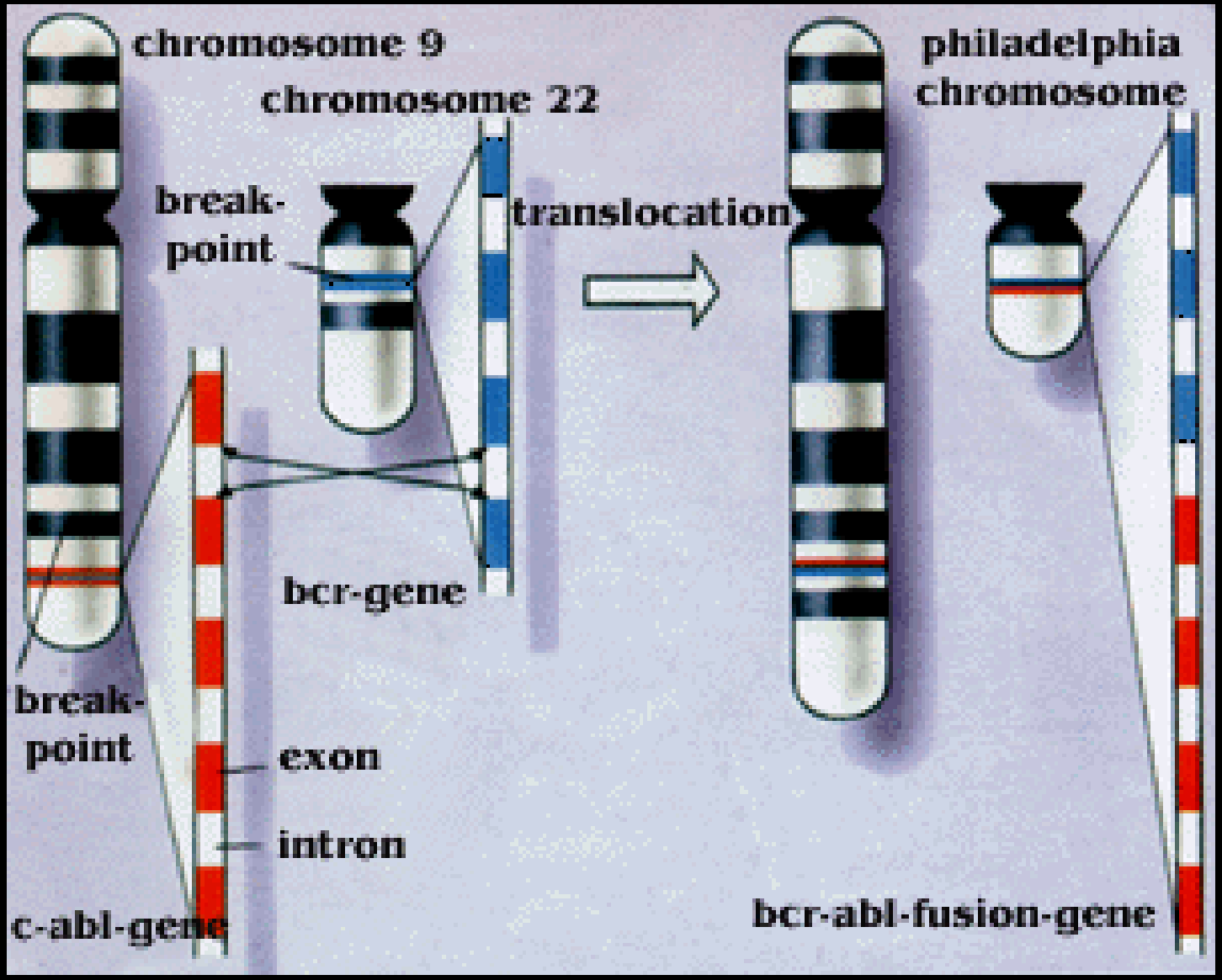
- **Sem efeito fenotípico;**
- **Gametas = ?**
- **Mais comum em :** retardo mental;

  >= 2 abortos expont.;

  homens estéreis.

Philadelphia
chromosome
t(9,22)



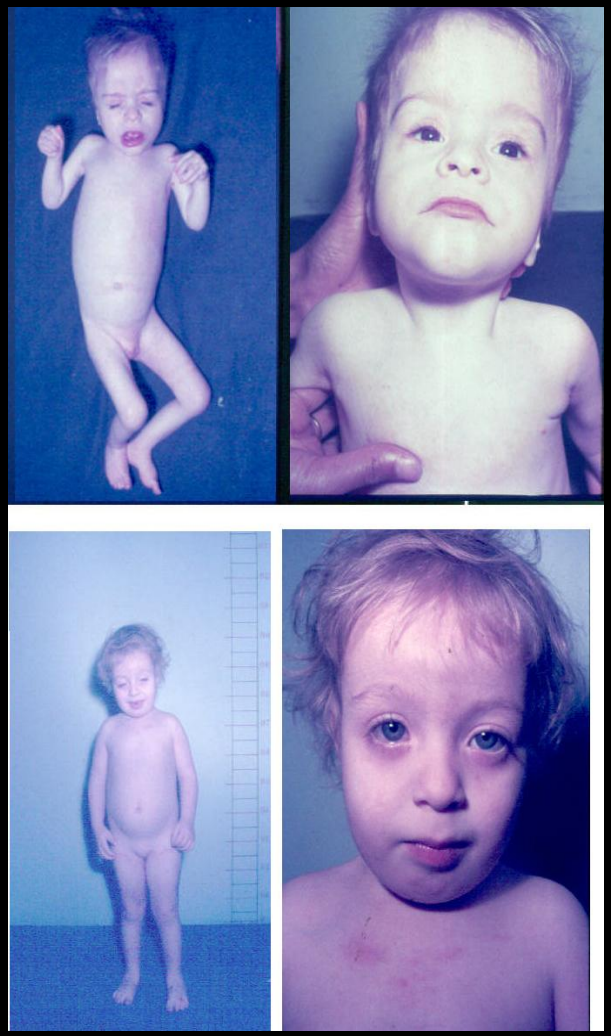

chromosome 9
chromosome 22
break-
point
translocation
philadelphia
chromosome
bcr-gene
break-
point
exon
intron
c-abl-gene
bcr-abl-fusion-gene

ABERRAÇÃO CROMOSSÔMICA

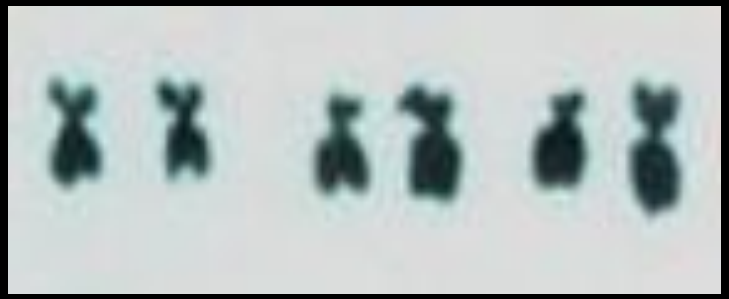
ESTRUTURAL

INVERSÃO

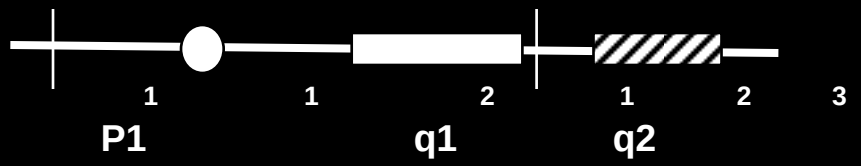
INVERSÃO PERICENTRICA DO 18



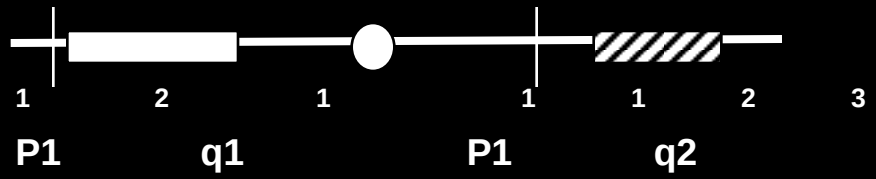
16 17 18



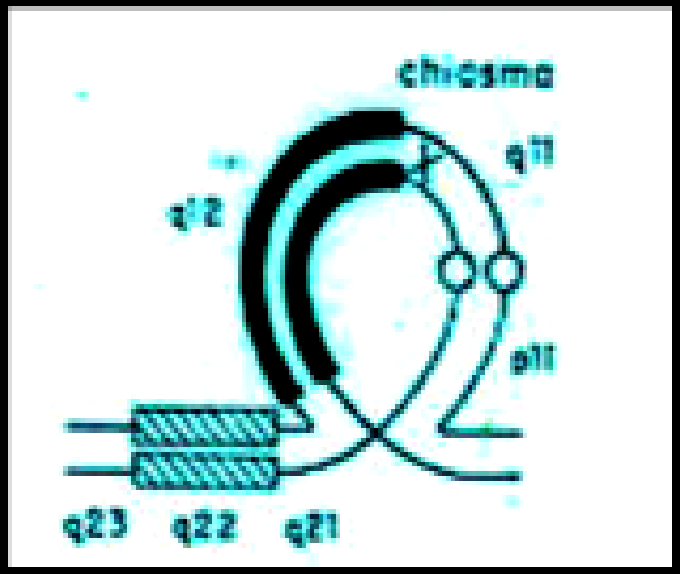
mãe

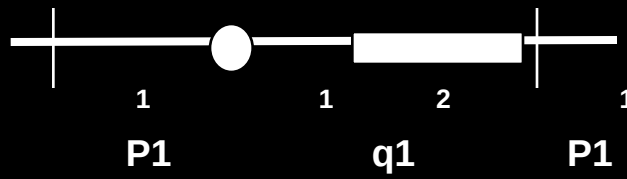


normal

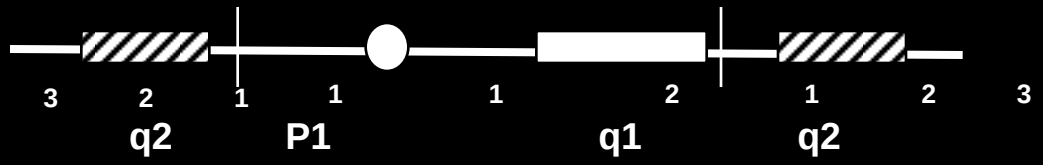


mãe

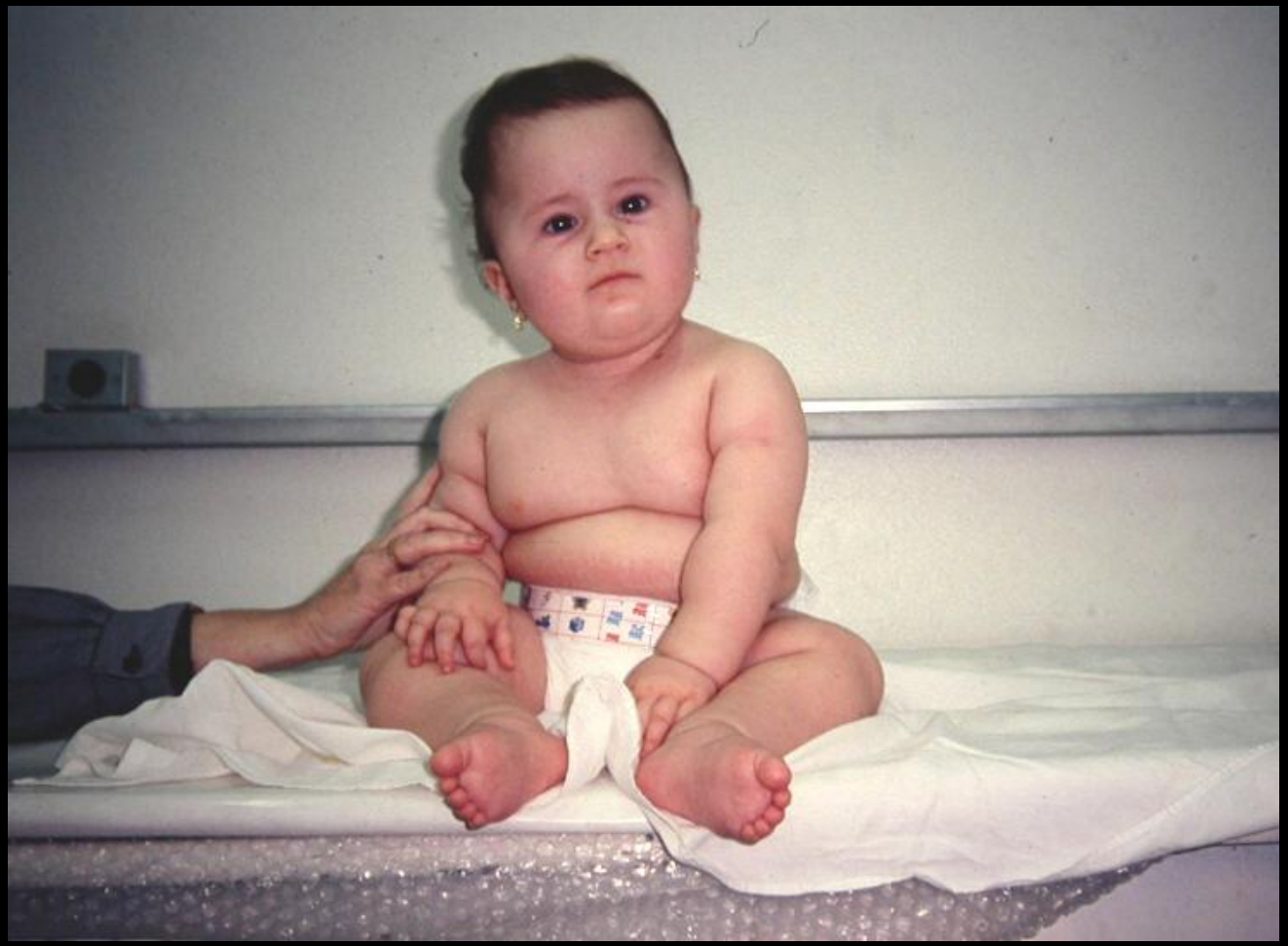


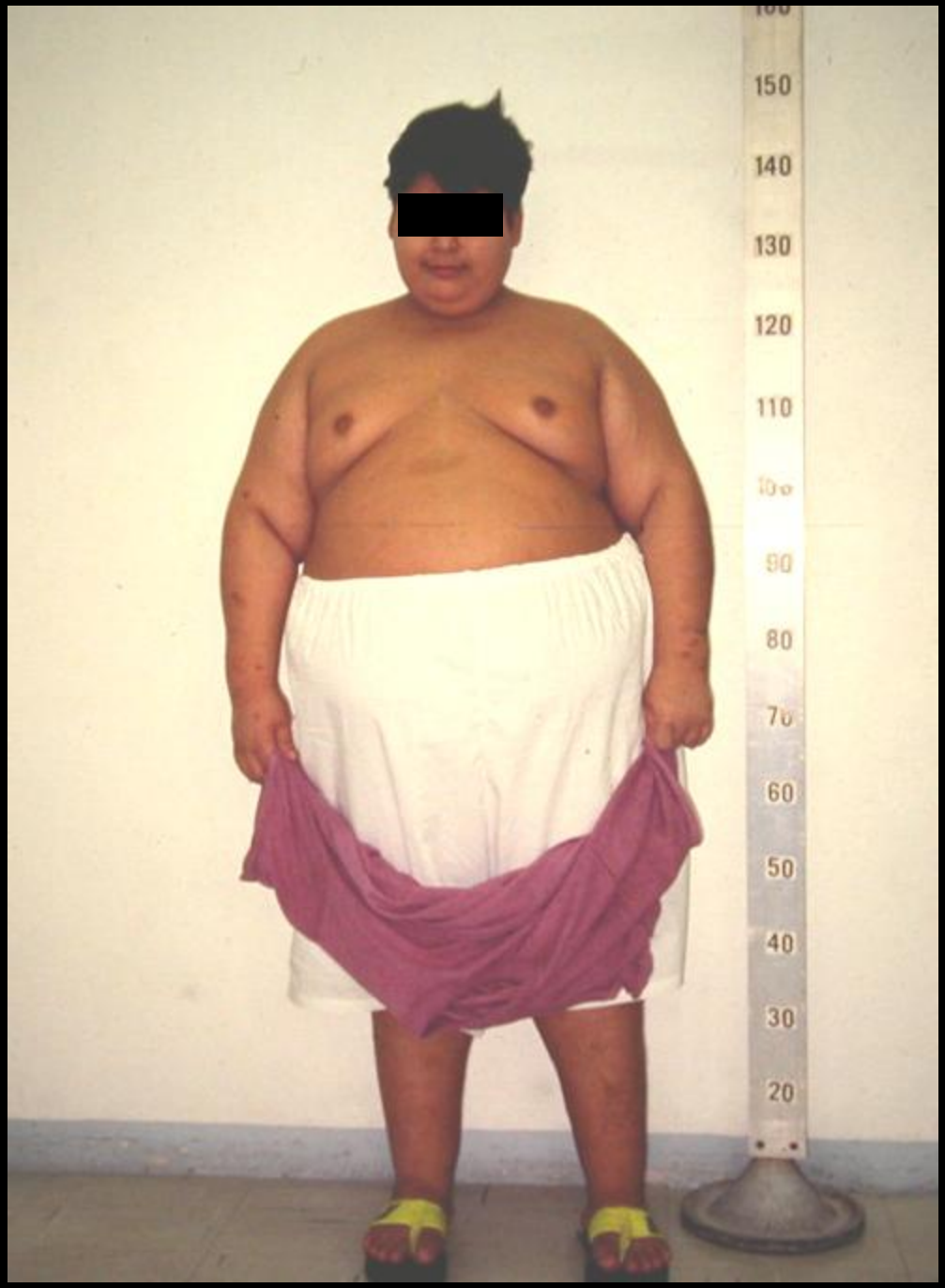


deleção



duplicação

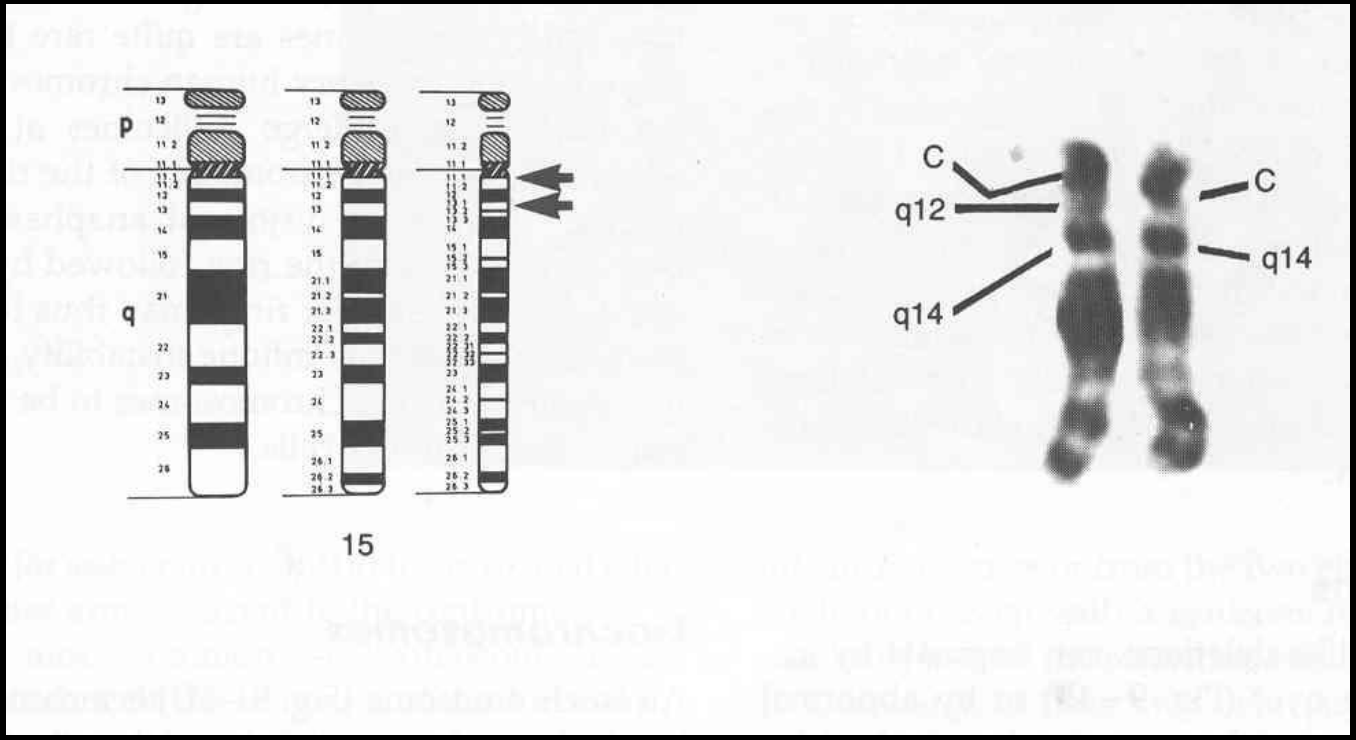



150
140
130
120
110
90
80
60
50
40
30
20

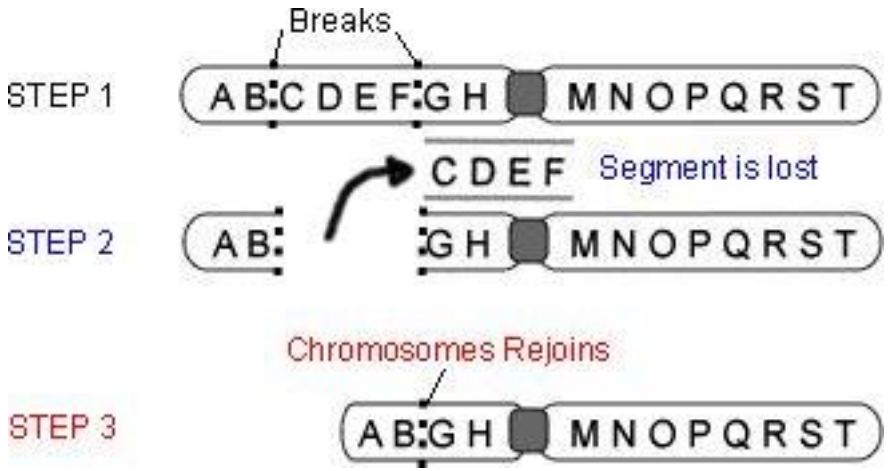
ABERRAÇÃO CROMOSSÔMICA

ESTRUTURAL

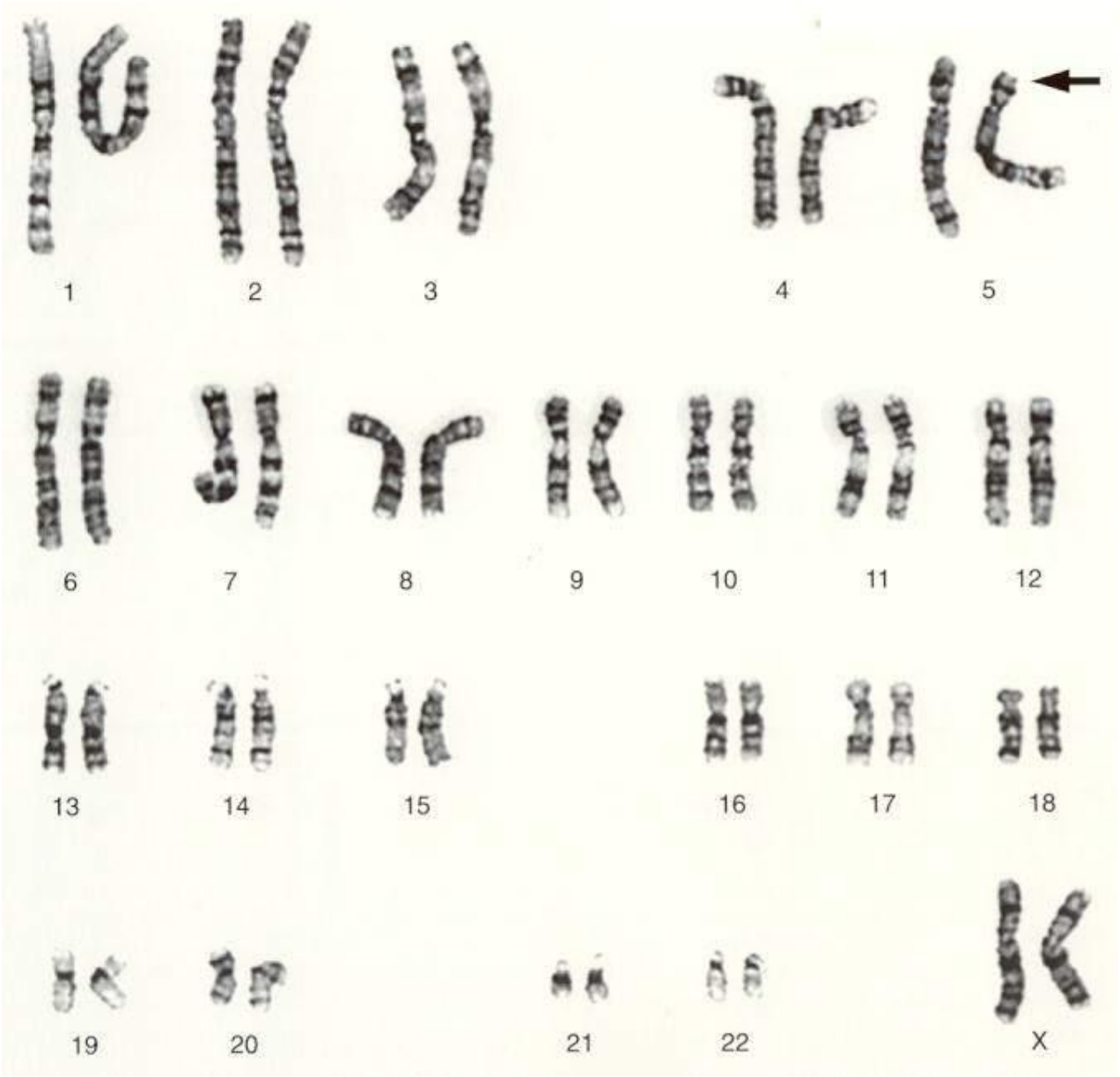
DELEÇÃO



Deleção cromossômica



Deleção do braço curto do cromossomo 5



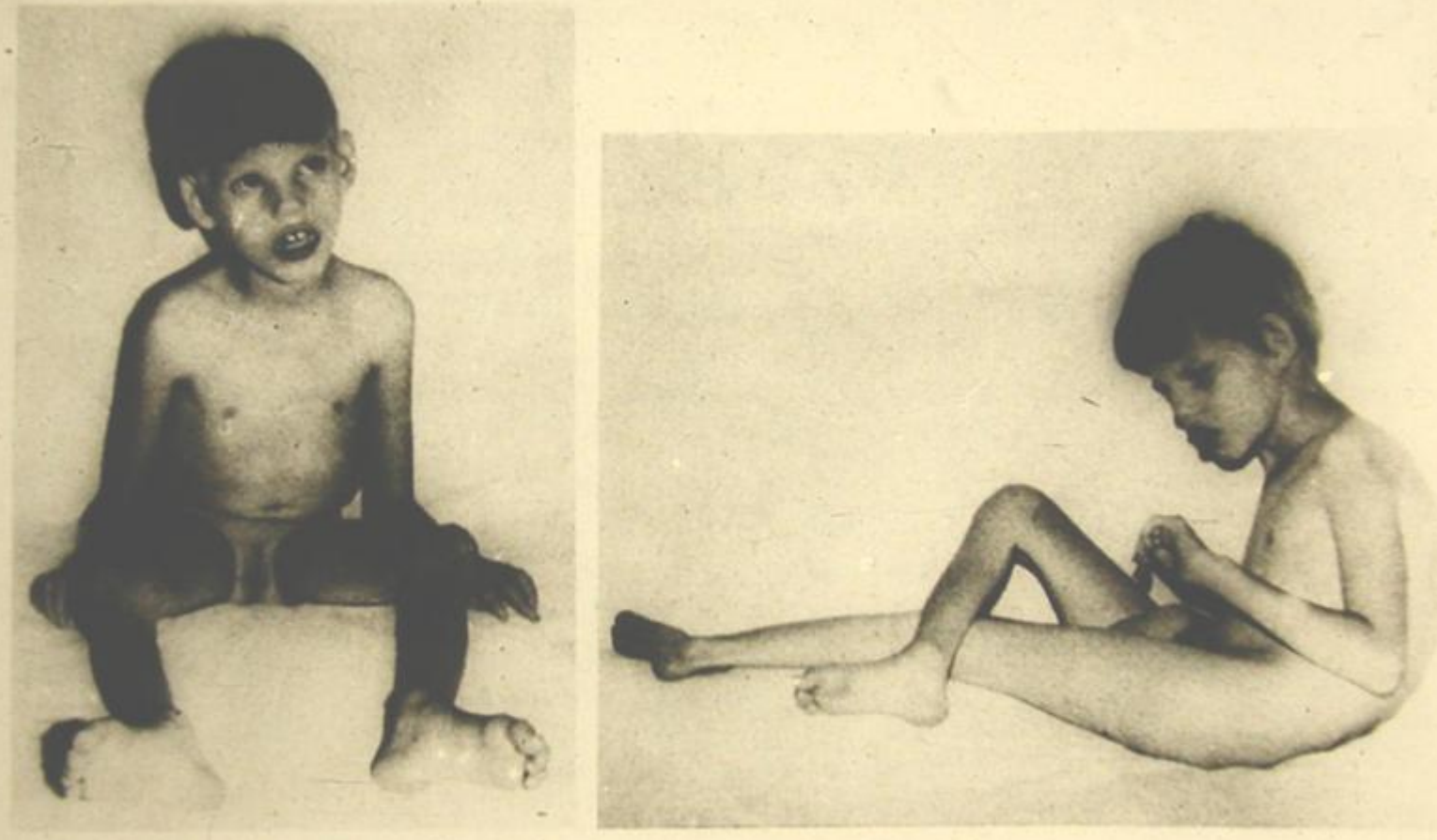
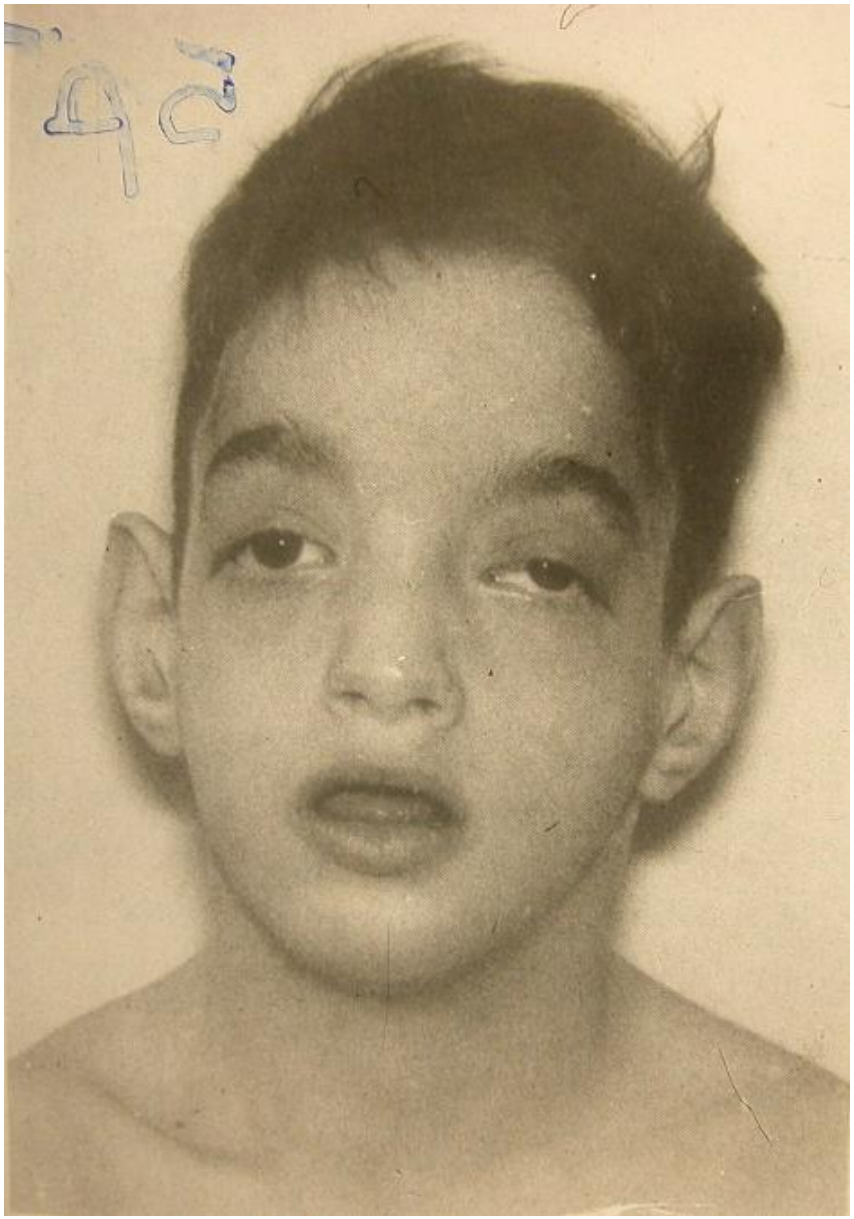


Fig. V.14 – Fotos de uma paciente com síndrome do *cri du chat* e cariótipo 46, XX, 5p– mat aos 10 anos de idade. Notar a fácies de retardada mental, o hipertelorismo e a hipotrofia dos membros. (Cortesia do Dr. Walter Pinto Junior, do Departamento de Genética Médica da UNICAMP).



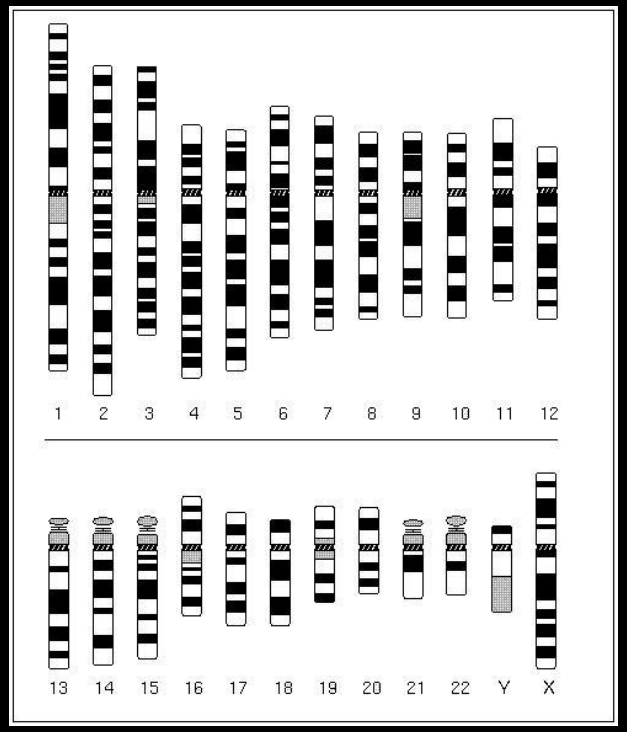
ABERRAÇÕES CROMOSSÔMICAS ESTRUTURAIS

NÃO - BALANCEADAS

- **Dismorfismos;**
- **Atraso de desenvolvimento físico/mental;**

INDICAÇÕES CLÍNICAS

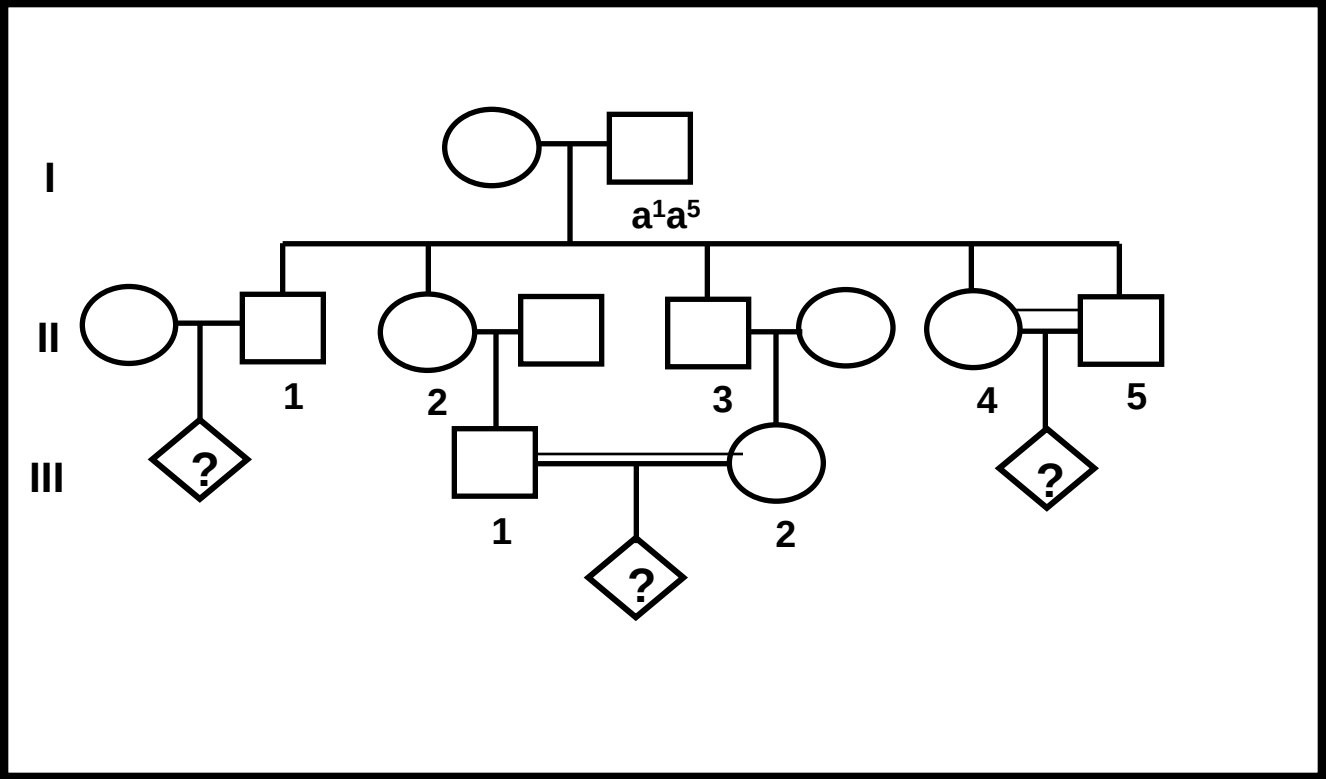
ANÁLISE CROMOSSÔMICA



INDICAÇÕES CLÍNICAS

ANÁLISE CROMOSSÔMICA

CONSANGUINIDADE!



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;

História familiar:

- anomalia em parente de 1o grau;

Down: trissomia vs. translocação.