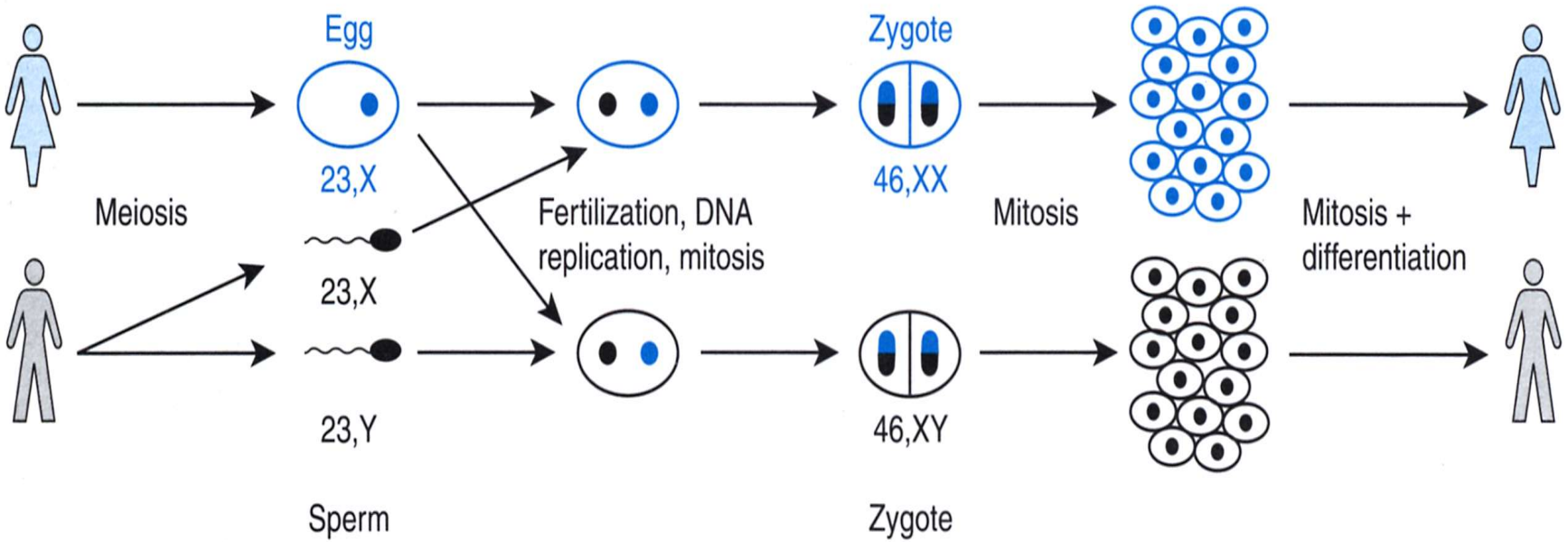
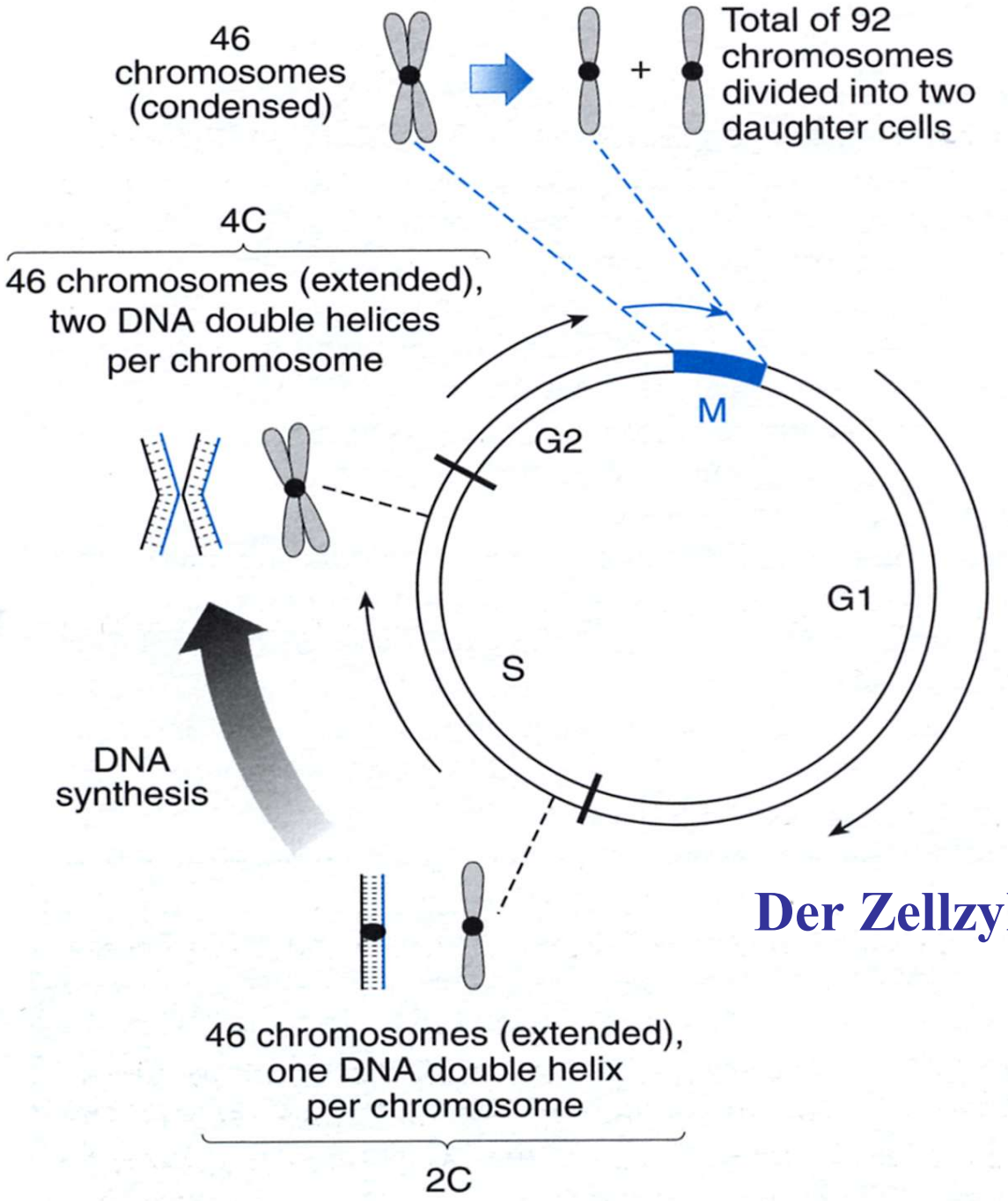


Figure 2.3: Human life, from a chromosomal viewpoint.



Der Zellzyklus

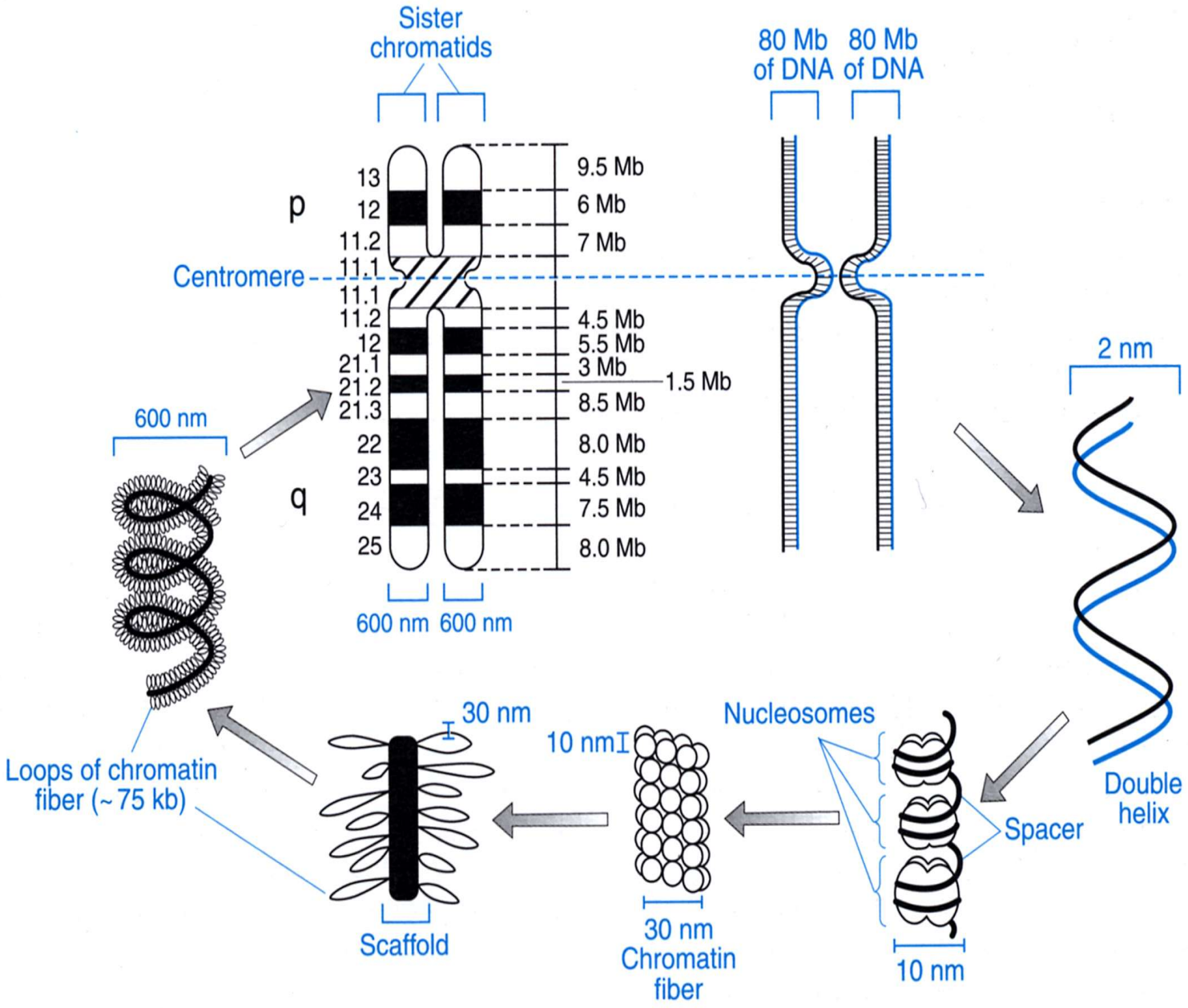
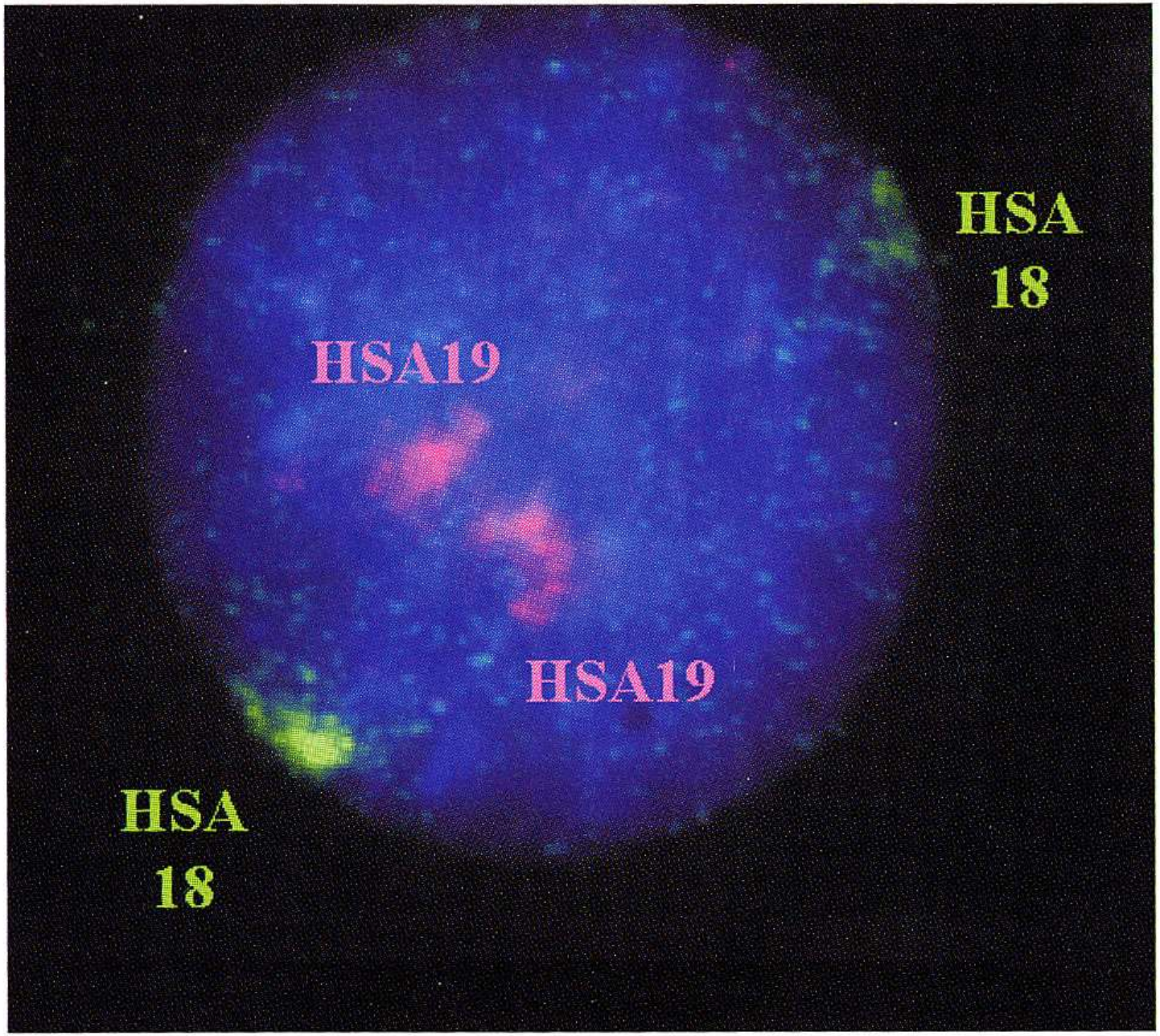


Figure 2.7: From DNA duplex to metaphase chromosome.


HSA
18
HSA19
HSA19
HSA
18

Centromere

TCACATGAT AGTGTACTA	80–90 bp > 90% (A+T)	TGATTTCCGAA ACTAAAGGCTT
I	II	III

Telomere

Tandem repeats based on the general formula

$(TG)_{1-3}\,TG_{2-3}/C_{2-3}\,A(CA)_{1-3}$

e.g.

5′....TGTGTGGGTGTGGTGTGTGTGG....3′
3′....ACACACCCACACCACACACACC....5′

Autonomous replicating sequence

Contains an 11-bp core consensus that is AT-rich, plus some imperfect copies of this sequence spanning an approximately 50-bp region of DNA

Imperfect copies

Core consensus =

ATTTAT(A/G)TTTA
TAAATA(T/C)AAAT

Figure 2.8: The functional elements of a yeast chromosome.

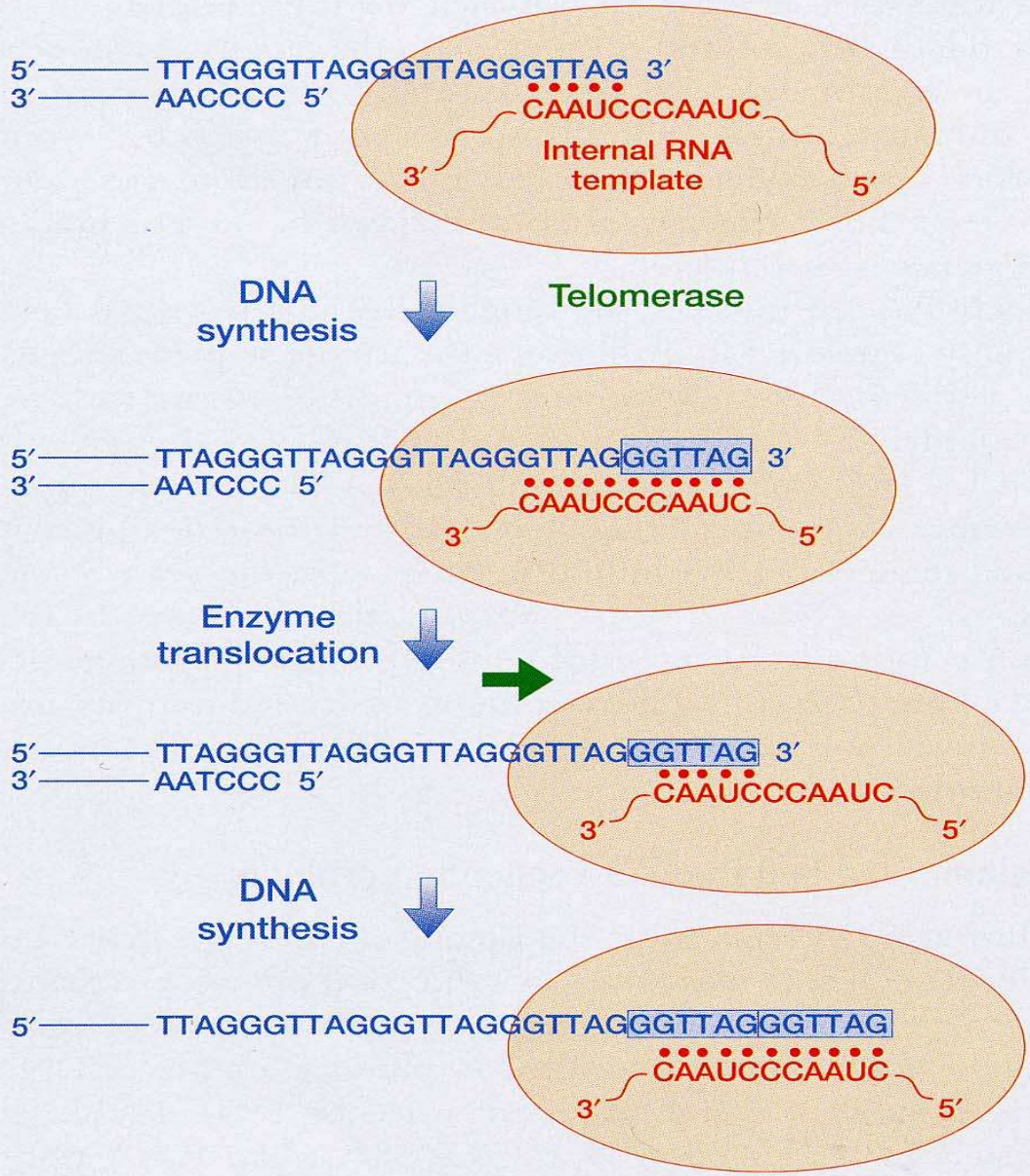


Figure 2.6: Telomerase extends the TG-rich strand of telomeres by DNA synthesis using an internal RNA template.

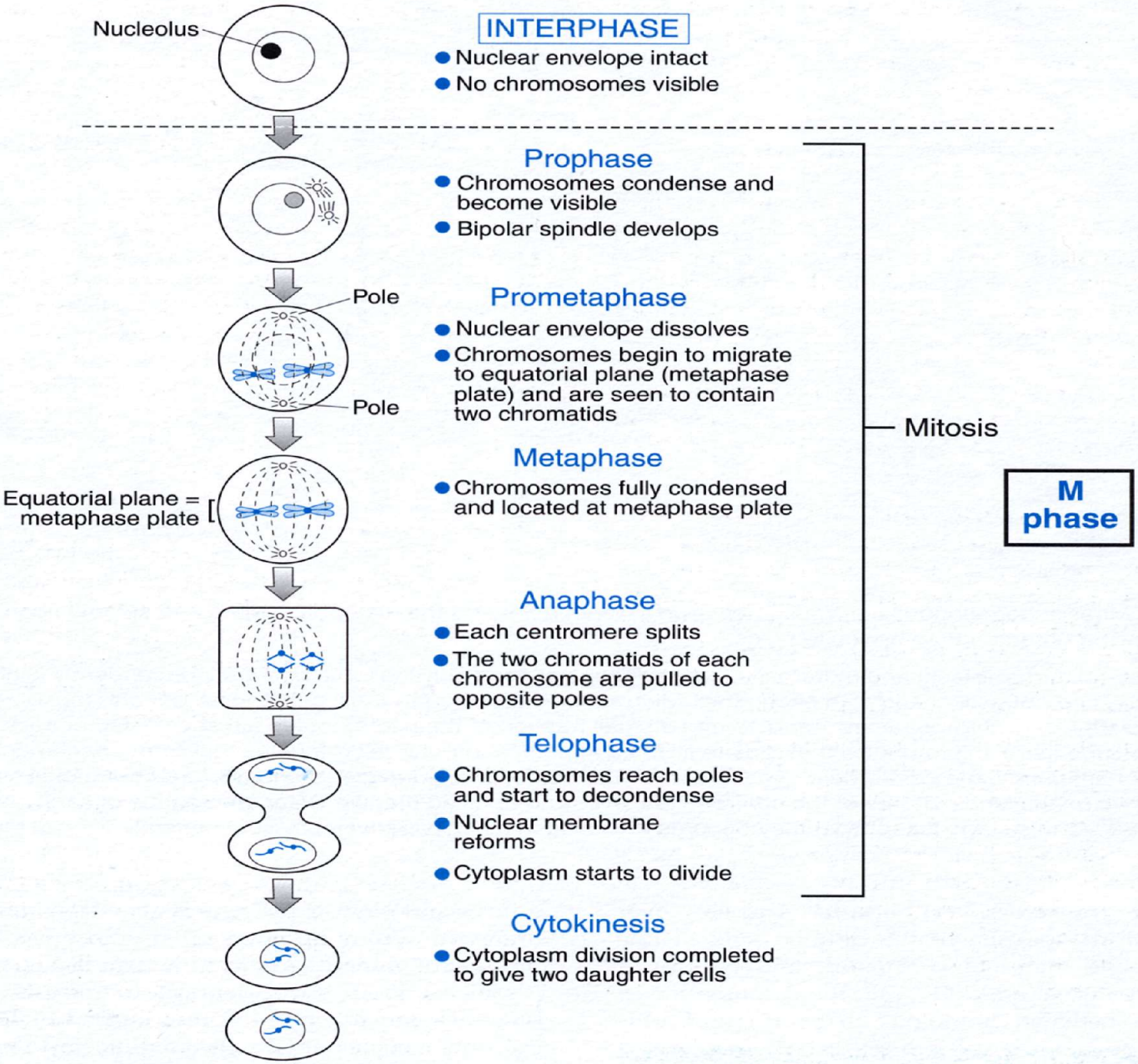


Figure 2.10: Cell division by mitosis.

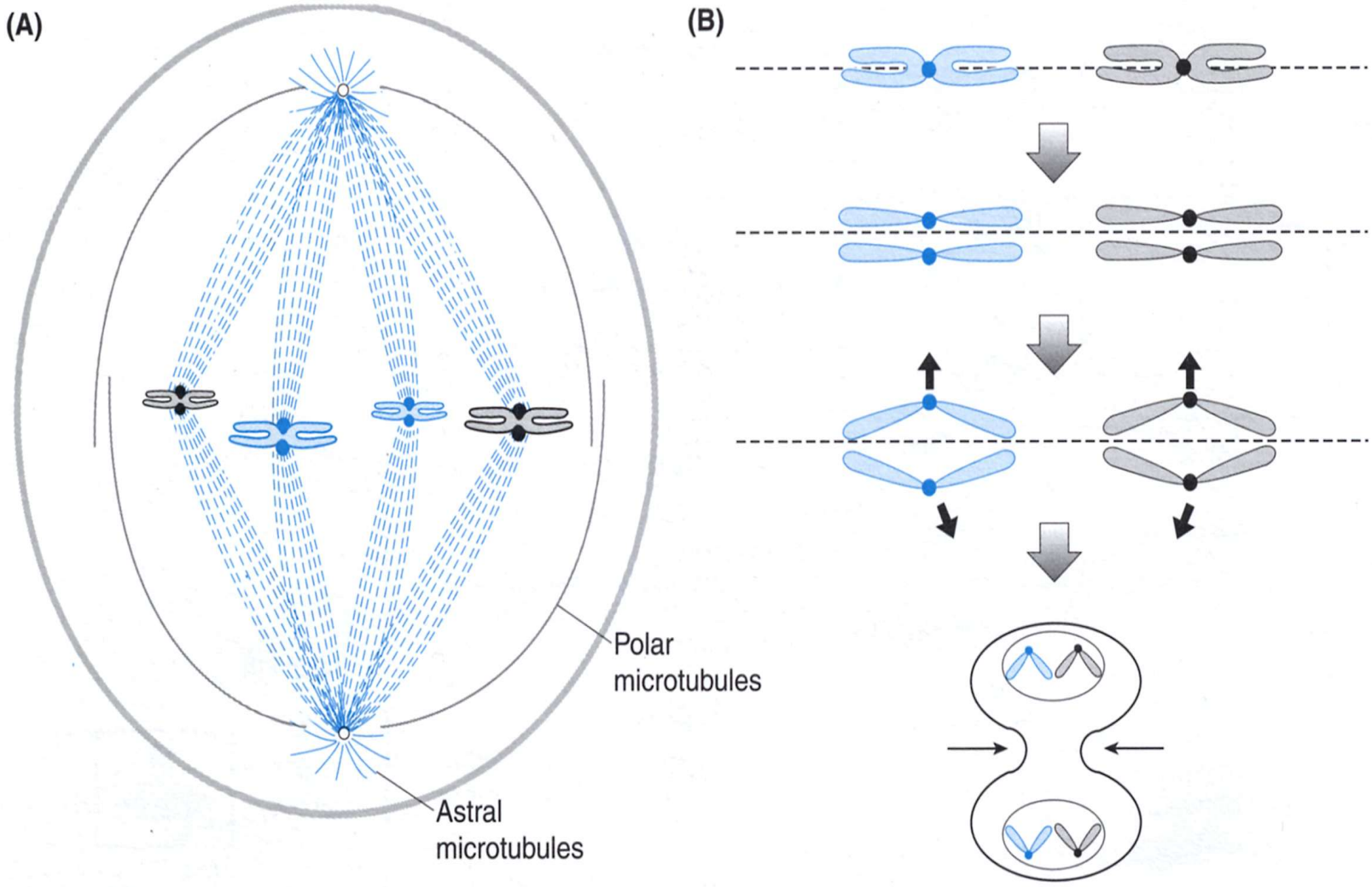
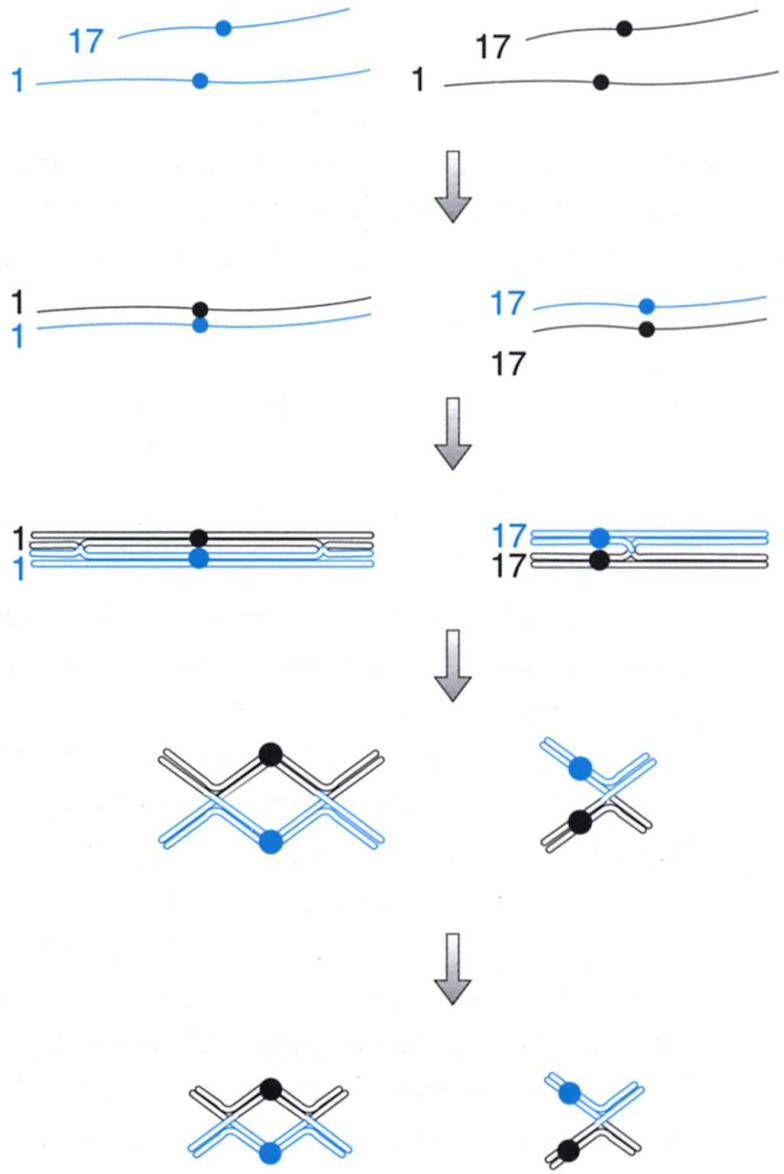


Figure 2.11: Mitosis: homologous chromosomes align independently on the metaphase plate and spindle fibers then pull the separated sister chromatids to opposite poles.



Leptotene

Chromosomes are unpaired fine threads consisting of two tightly bound sister chromatids

Zygotene

Maternal and paternal homologs pair together to form bivalents

Pachytene

Chromosomes thicken
Crossing-over occurs

Diplotene

Homologs separate but are held together by chiasmata

Crossovers can be counted and positions recorded

Diakinesis

Bivalents more contracted

Figure 2.14: Meiosis: the five stages of prophase in meiosis I.

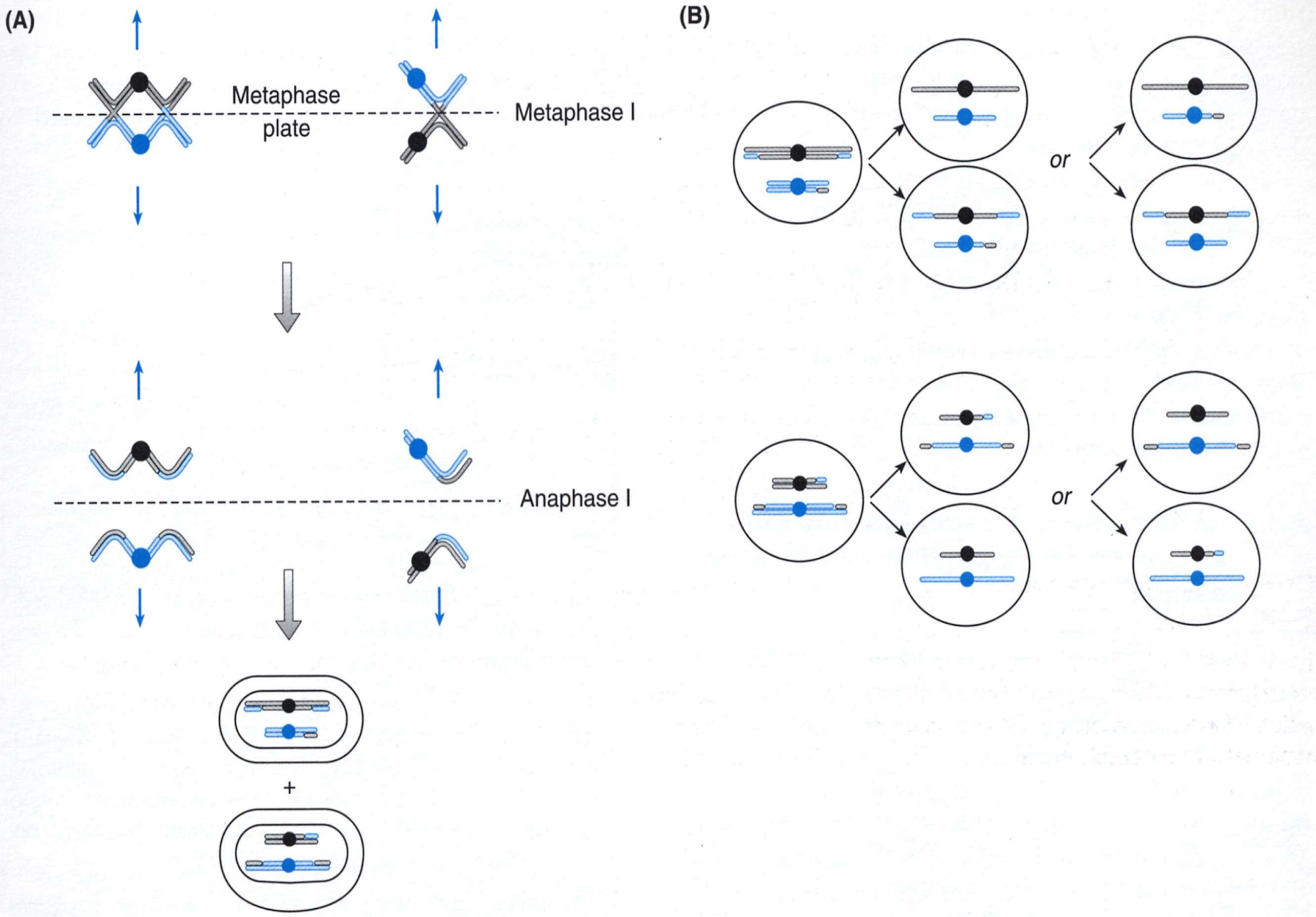


Figure 2.15: Meiosis: from metaphase I to the gametes.

Table 2.2: Mitosis and meiosis compared

	Mitosis	Meiosis
Location	All tissues	Only in testis and ovary
Products	Diploid somatic cells	Haploid sperm and egg cells
DNA replication and cell division	Normally one round of replication per cell division	Only one round of replication but two cell divisions
Extent of prophase	Short (~30 min in human cells)	Meiosis I is long and complex; can take years to complete
Pairing of homologs	None	Yes (in meiosis I)
Recombination	Rare and abnormal	Normally at least once in each chromosome arm
Relationship between daughter cells	Genetically identical	Different (recombination and independent assortment of homologs)

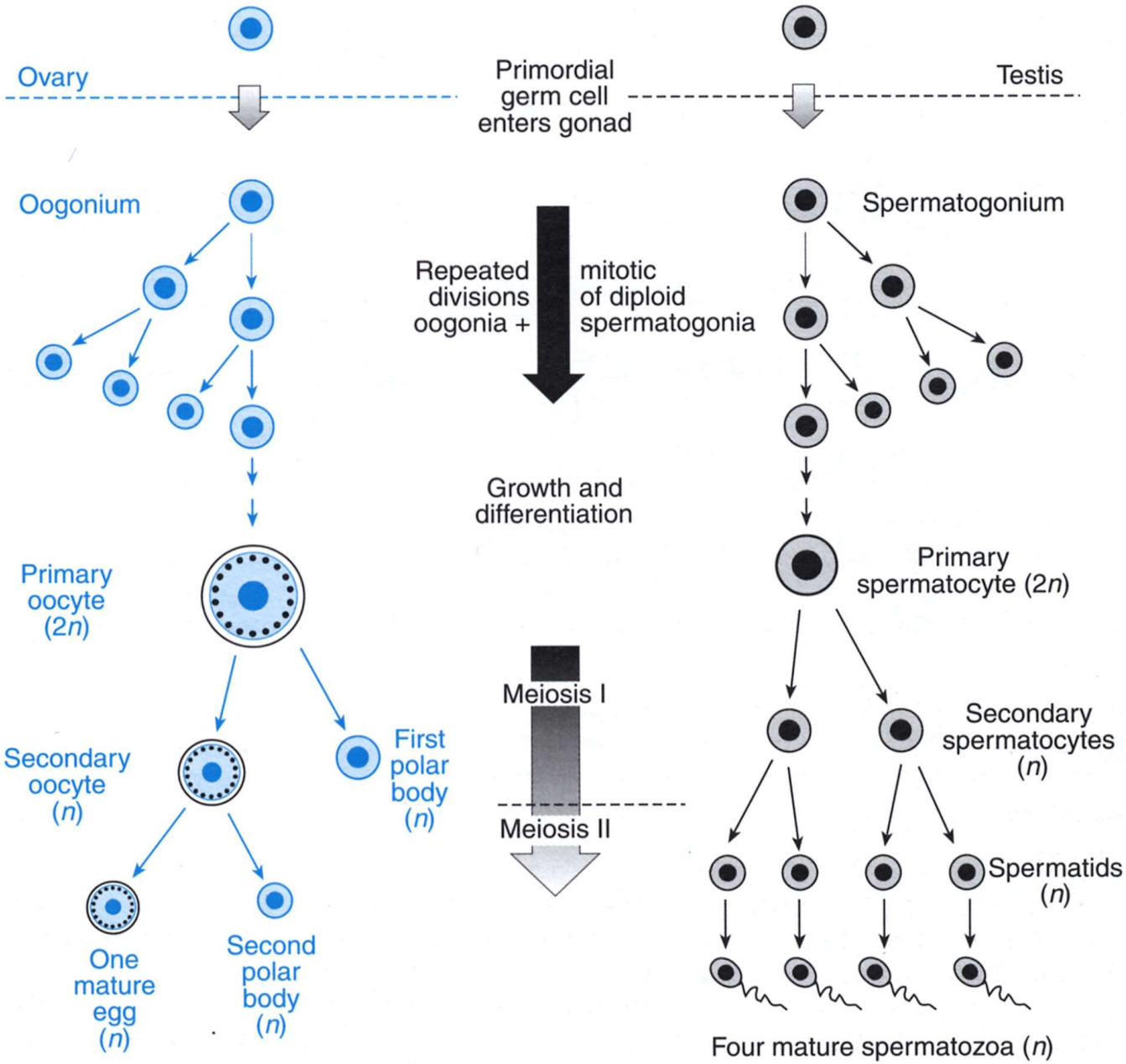


Figure 2.12: Development of the germ line.

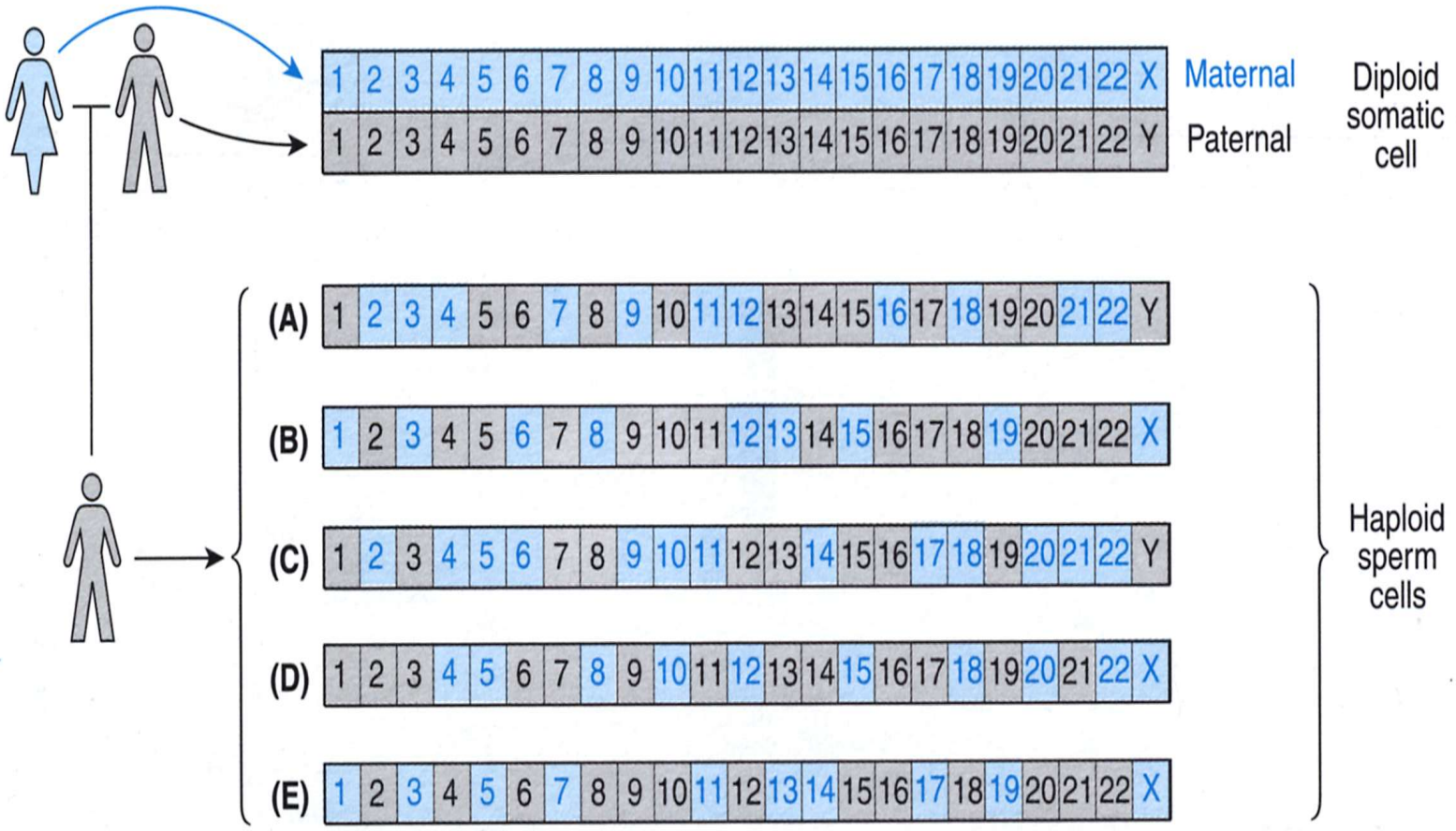
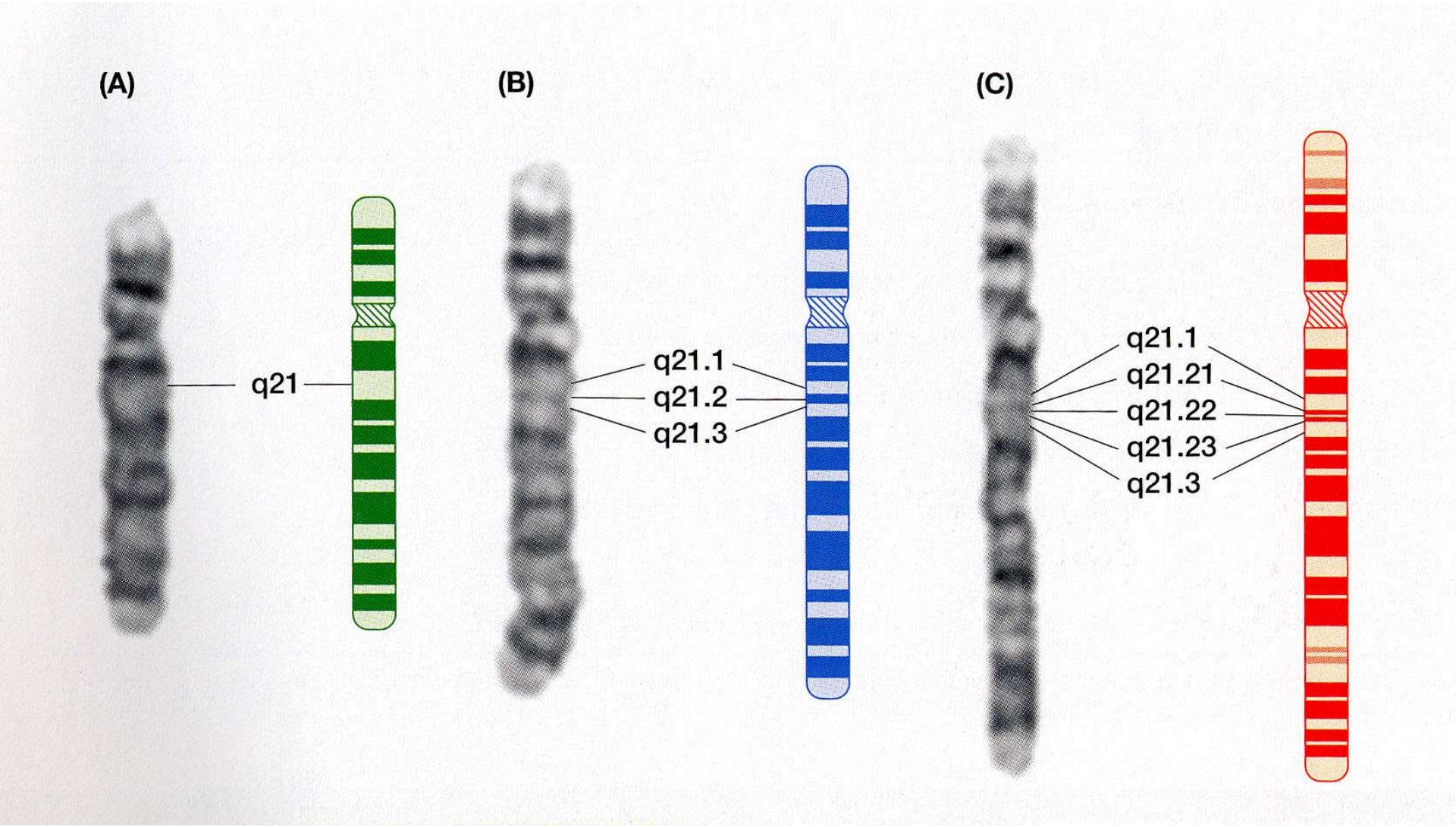


Figure 2.13: Meiosis: independent assortment of maternal and paternal homologs at meiosis I produces the first level of genetic diversity.


(A)
q21
(B)
q21.1
q21.2
q21.3
(C)
q21.1
q21.21
q21.22
q21.23
q21.3

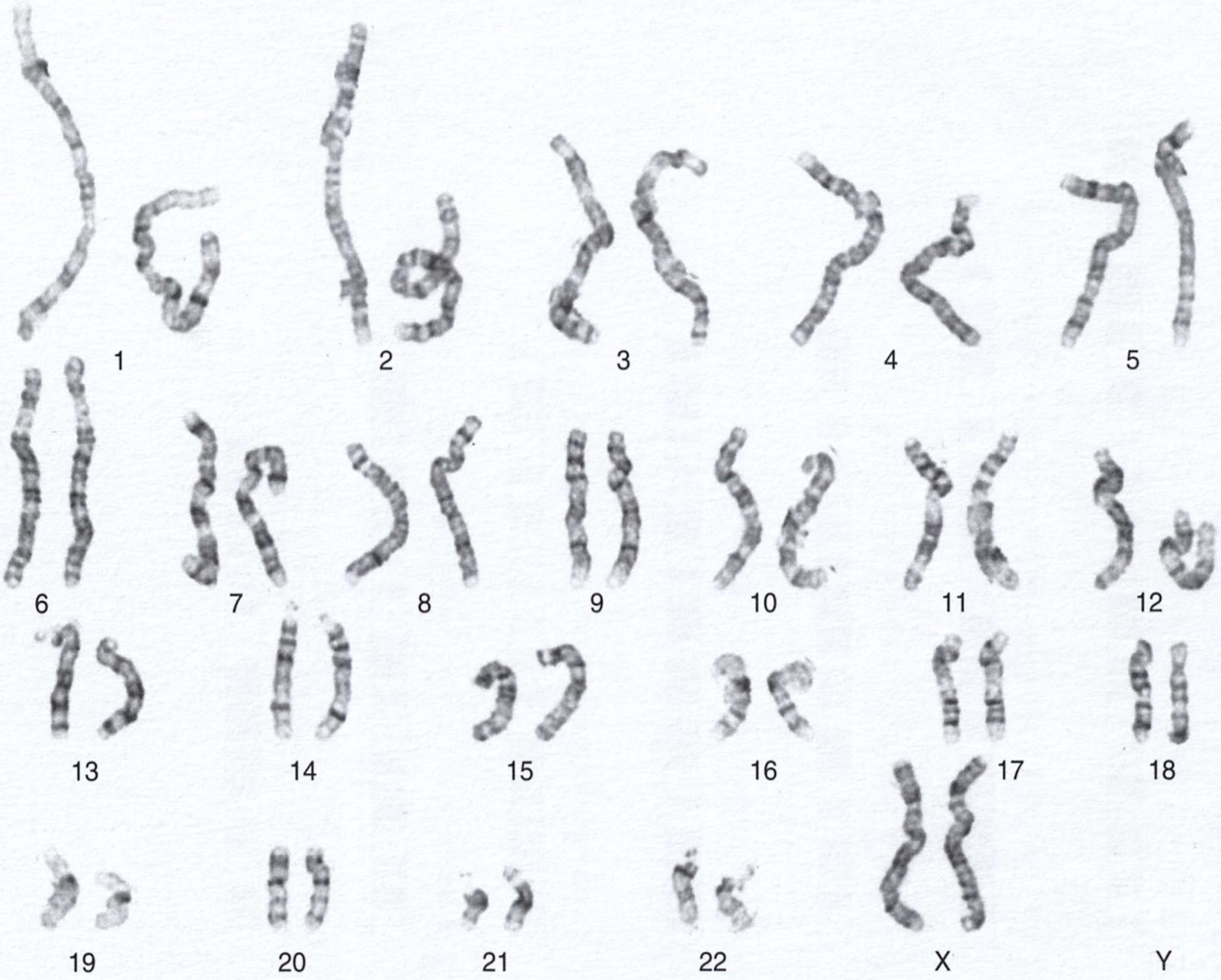


Figure 2.17: G-banded prometaphase karyogram of mitotic chromosomes from lymphocytes of a normal female.

Table 2.3: Human chromosome groups

Group	Chromosomes	Description
A	1–3	Largest; 1 and 3 are metacentric but 2 is submetacentric
B	4,5	Large; submetacentric with two arms very different in size
C	6–12,X	Medium size; submetacentric
D	13–15	Medium size; acrocentric with satellites
E	16–18	Small; 16 is metacentric but 17 and 18 are submetacentric
F	19,20	Small; metacentric
G	21,22,Y	Small; acrocentric, with satellites on 21 and 22 but not on the Y

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

STANDARD FISH *or* CHROMOSOME PAINTING

PURIFIED DNA CLONE

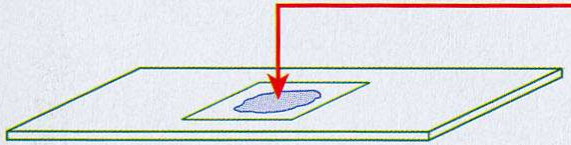
Heterogeneous collection of many DNA clones with inserts derived from many different regions of a *single* chromosome

Chromosome preparation on microscope slide

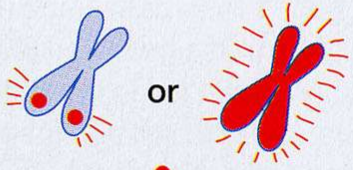
Denature DNA *in situ*

Label by incorporating nucleotides with attached fluorophore; denature

Label single probe ● *or* Chromosome paint



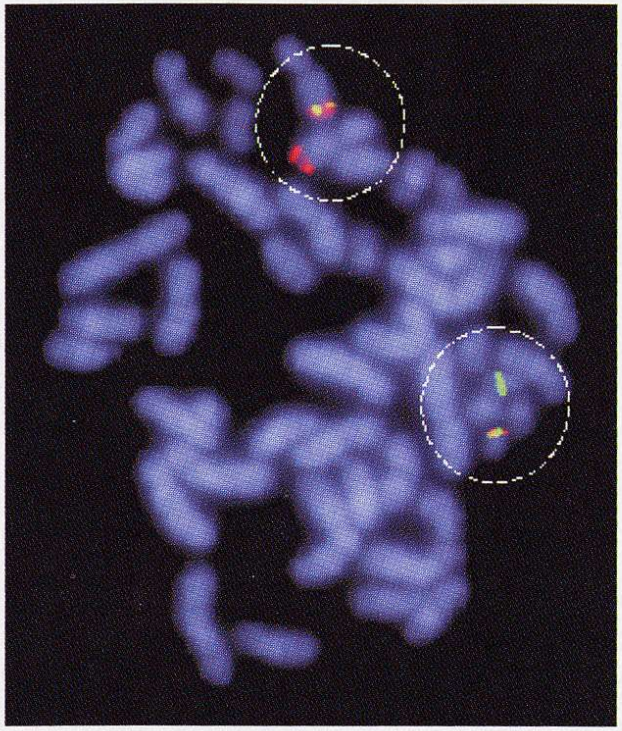
Allow to anneal, expose to UV and visualize fluorescence *in situ*

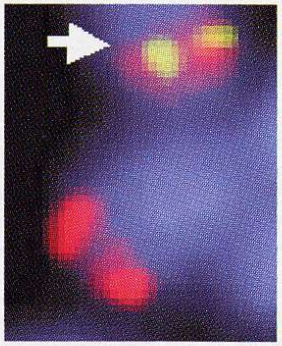


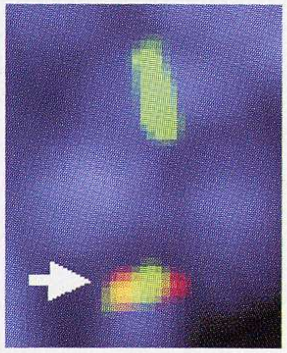
or

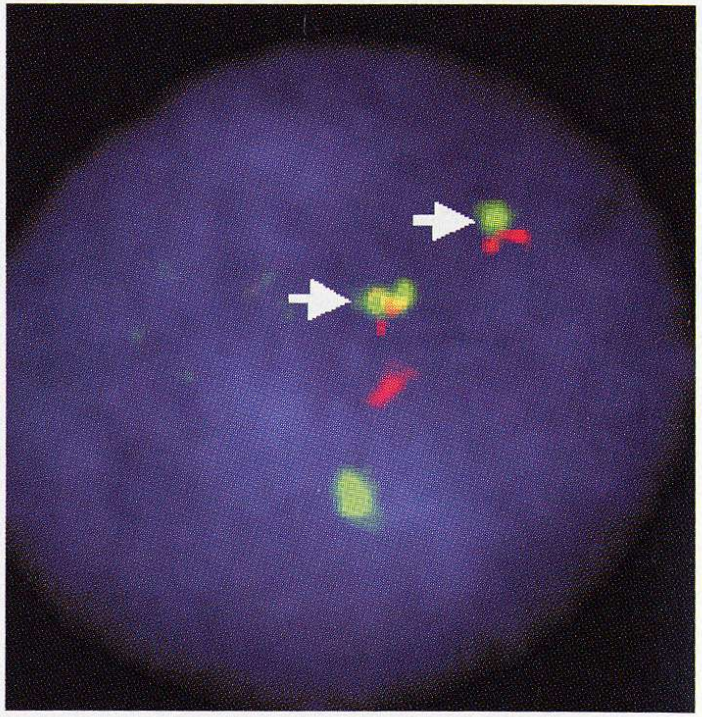
Single probe ● bound

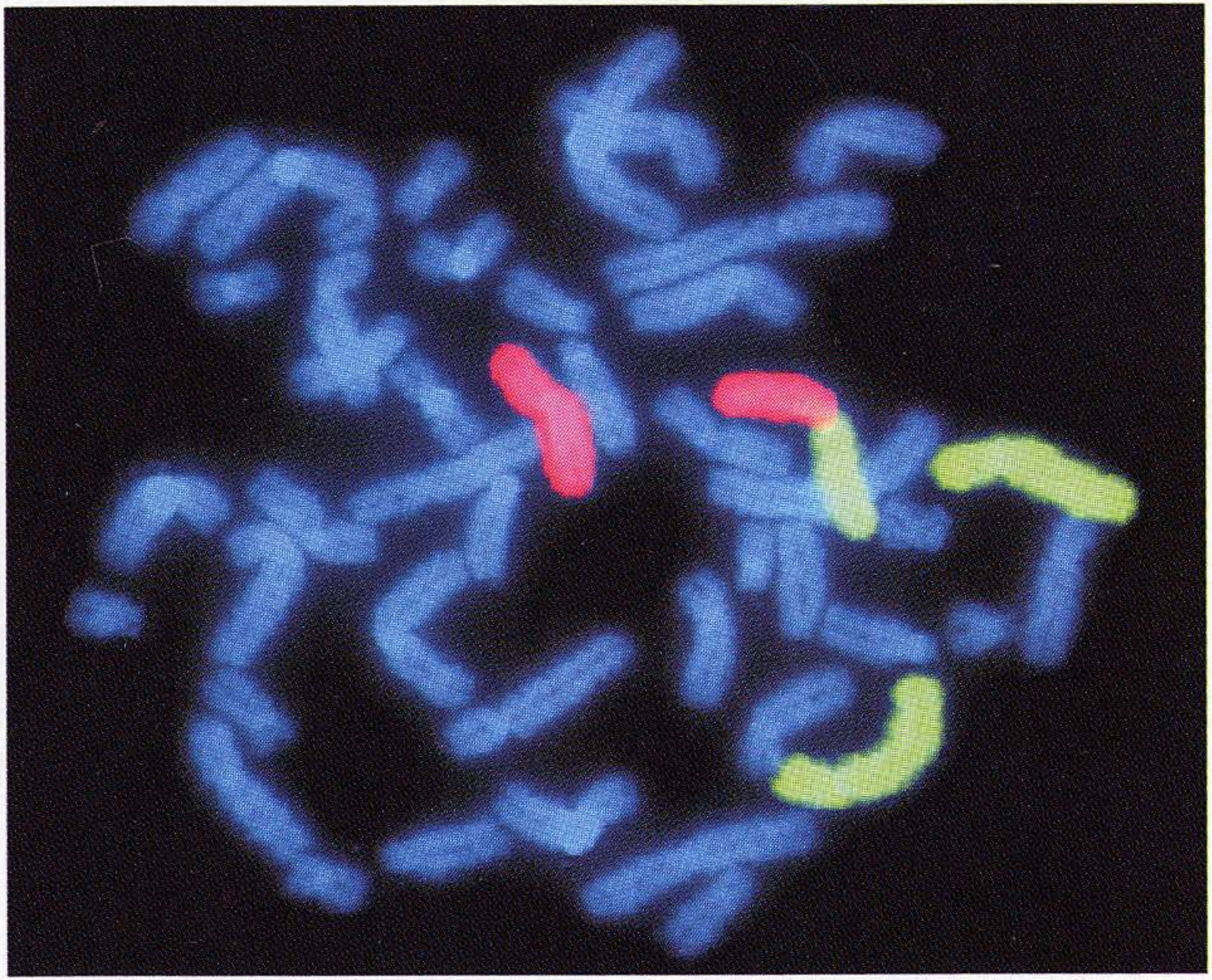
Chromosome paint bound











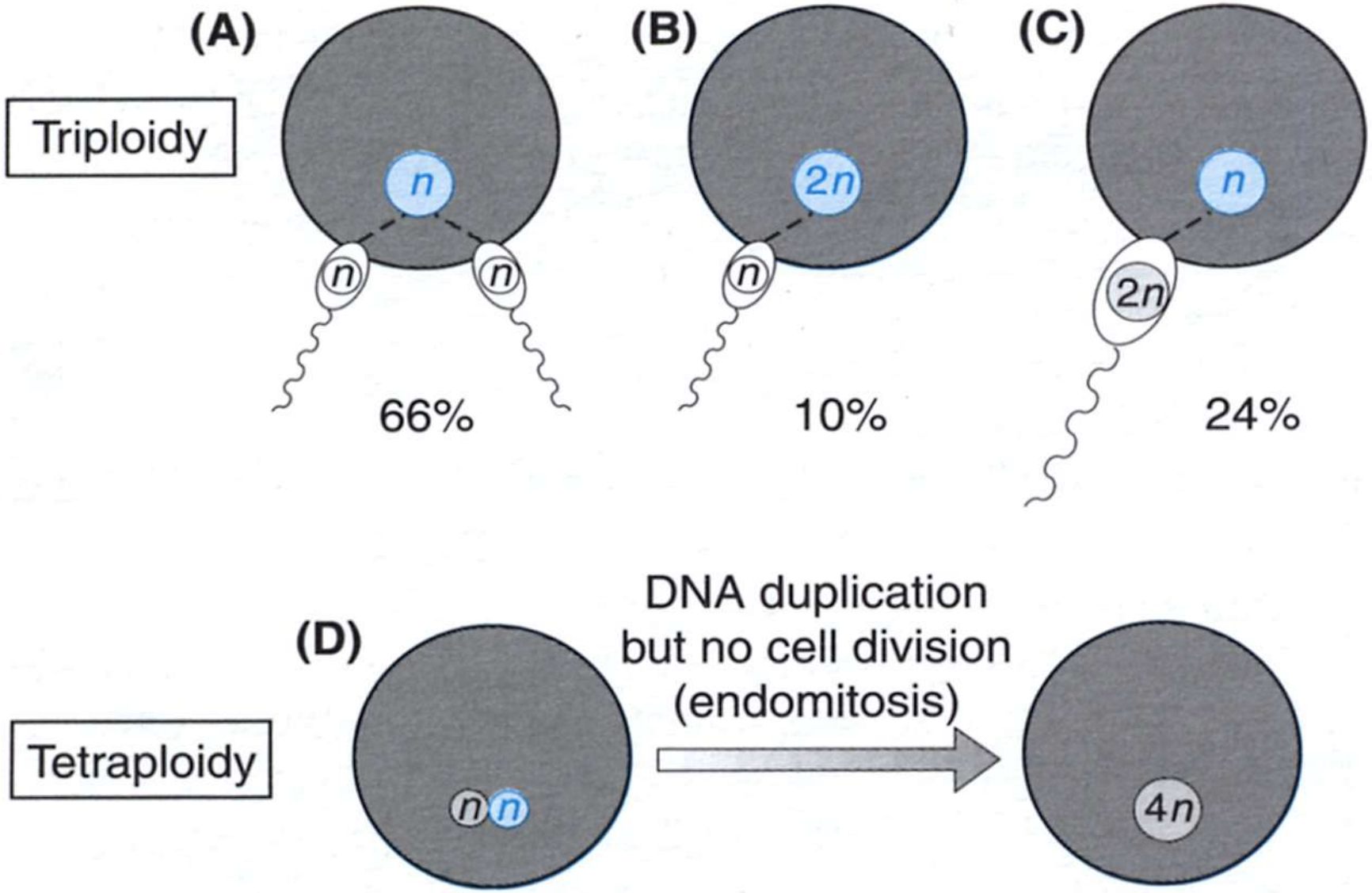


Figure 2.19: Origins of triploidy and tetraploidy.

Entstehung von Trisomien und Monosomien:

Chromosomenfehlverteilung während der Meiose
(--> Keimzellen mit einem Chromosom zu viel oder zu wenig)

Ursache von Mosaiken (z.B. 46,XX/45, X0 = Turner-Mosaik):
- Mitotische Chromosomenfehlverteilung während der frühen Keimesentwicklung ('somatic nondisjunction')
- oder 'Reparaturversuch' eines meiotischen Fehlers (Verlust eines überzähligen Chromosoms in einem Teil der Körperzellen bei Trisomie)

Sonderfall 'uniparentale Disomie': euploider Karyotyp (z.B. 46,XX), beide Chromosomen eines Chromosomenpaares stammen jedoch vom gleichen Elternteil (z.B. beide Chromosomen 15 von der Mutter --> Prader-Willi-Syndrom). Ursache meist wie oben (hier: Verlust des einzigen väterlichen #15 nach (letaler) Trisomie 15)

Table 2.4: Consequences of numerical chromosomal abnormalities.

Polyploidy	
Triploidy (69,XXX, XXY or XYY)	1–3% of all conceptions; almost never live born; do not survive
Aneuploidy (autosomes)	
Nullisomy (missing a pair of homologs)	Pre-implantation lethal
Monosomy (one chromosome missing)	Embryonic lethal
Trisomy (one extra chromosome)	Usually lethal at embryonic or fetal stages, but trisomy 13 (Patau syndrome) and trisomy 18 (Edwards syndrome) may survive to term and trisomy 21 (Down syndrome) may survive to age 40 or longer
Aneuploidy (sex chromosomes)	
Additional sex chromosomes	(47, XXX; 47, XXY; 47, XYY) present relatively minor problems, with normal lifespan
Lacking a sex chromosome	45,X = Turner syndrome. About 99% of cases abort spontaneously; survivors are of normal intelligence but infertile and show minor physical signs. 45,Y = not viable

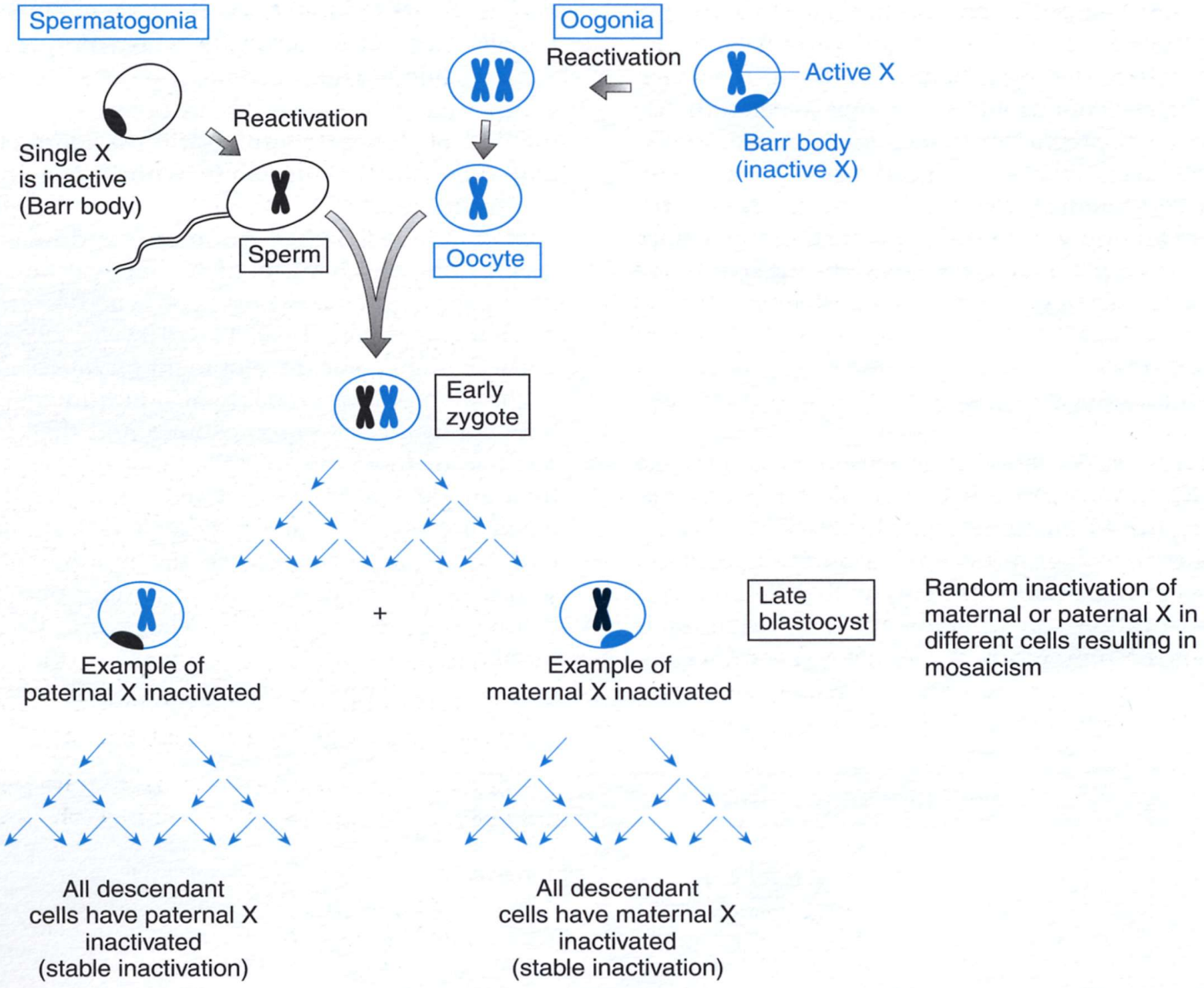


Figure 2.6: The process of X chromosome inactivation in mammals.

Nomenclature of chromosome abnormalities

Numerical abnormalities:

Triploidy 69,XXX; 69,XXY; 69,XYY
Trisomy e.g. 47,XX, +21
Monosomy e.g. 45,X
Mosaicism e.g. 47,XXX/46, XX

Structural abnormalities:

Deletion e.g. 46,XY, del(4)(p16.3); 46, XX, del(5)(q13q33)
Inversion e.g. 46,XY, inv(11)(p11p15)
Duplication e.g. 46,XX, dup(2)(q22q25)
Insertion e.g. 46,XX, ins(2)(p13q21q31)
Ring e.g. 46,XY, r(7)(p22q36)
Marker e.g. 47,XX, +mar
Translocation, reciprocal e.g. 46, XX, t(2;6)(q35;p21.3)
Translocation, Robertsonian e.g. 45,XY, der(14;21)(q10;q10)
(may give rise to 46,XX, der(14;21)(q10;q10),+21)

Table 2.5: Structural abnormalities resulting from misrepair of chromosome breaks or recombination between nonhomologous chromosomes

	One chromosome involved	Two chromosomes involved
One break	Terminal deletion (healed by adding telomere)	–
Two breaks	Interstitial deletion; Inversion; Ring chromosome (*Figure 2.20*) Duplication or deletion by unequal sister-chromatid exchange (*Figure 9.7*)	Reciprocal translocation (*Figure 2.21*) Robertsonian translocation (*Figure 2.21*) Duplication or deletion by unequal recombination (*Figure 9.7*)
Three breaks	Various rearrangements, e.g. inversion with deletion, intrachromosomal insertion	Interchromosomal insertion (direct or inverted)

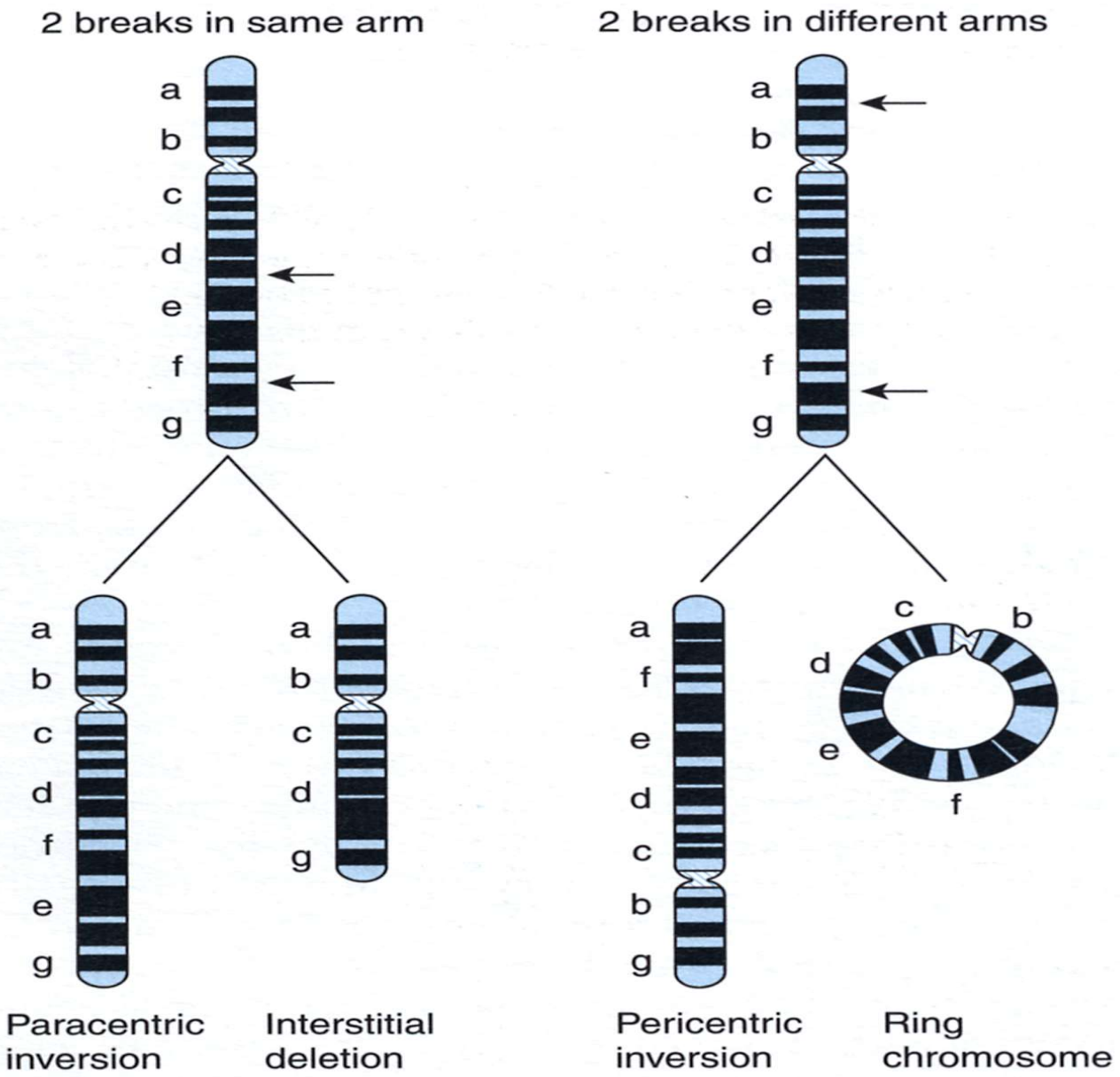


Figure 2.20: Possible stable results of two breaks on a single chromosome.

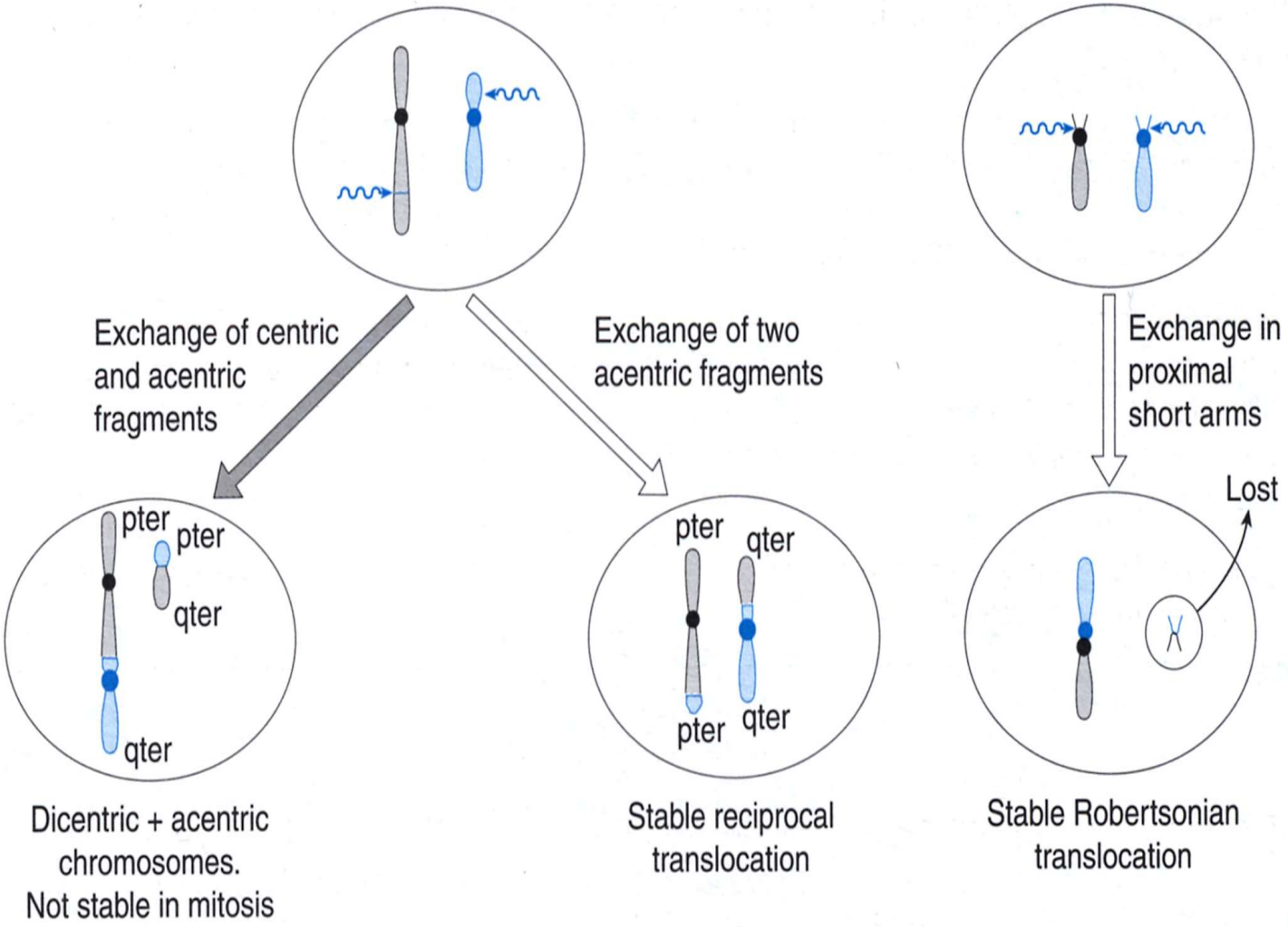


Figure 2.21: Origins of translocations.

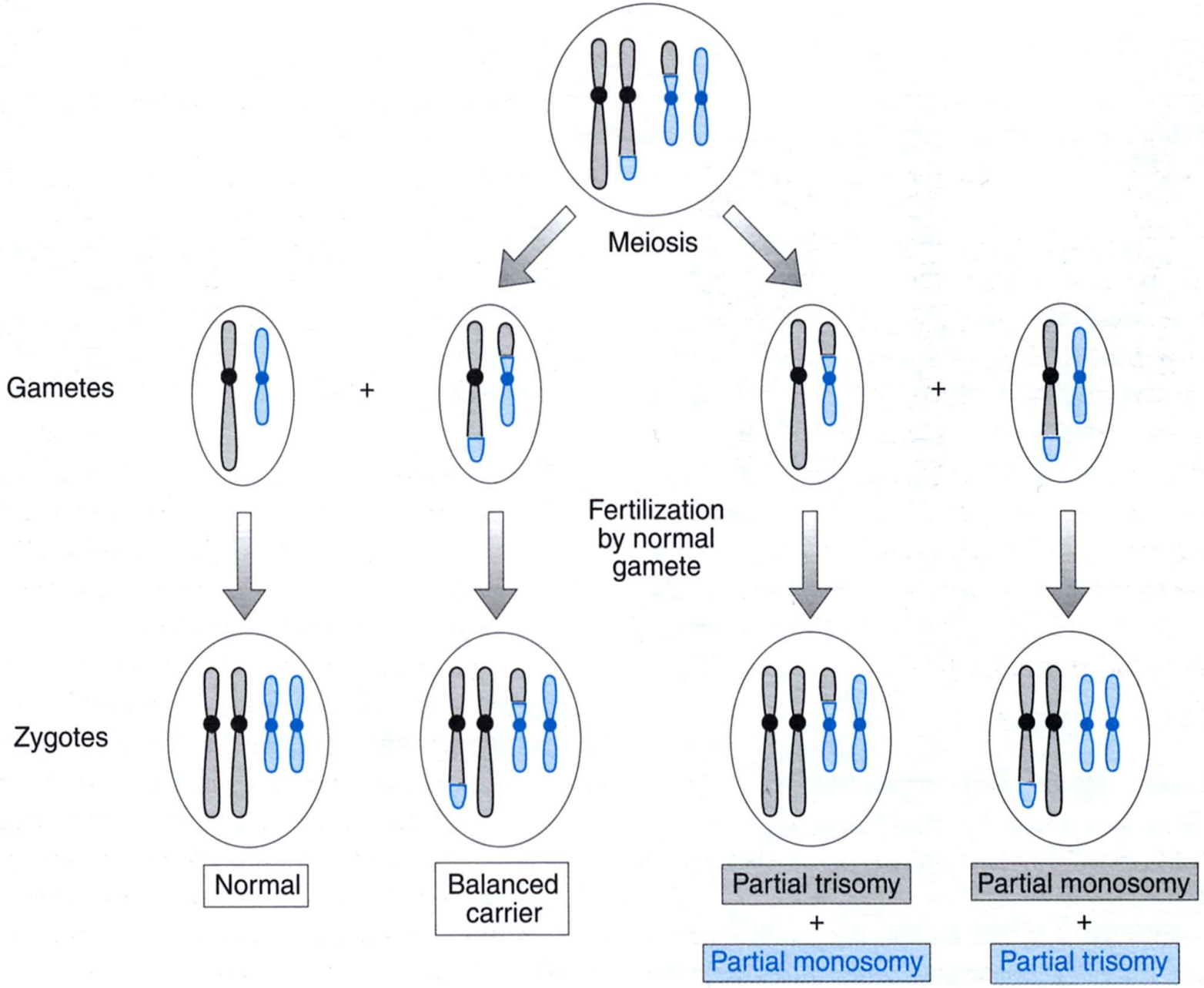


Figure 2.22: Results of meiosis in a carrier of a balanced reciprocal translocation.

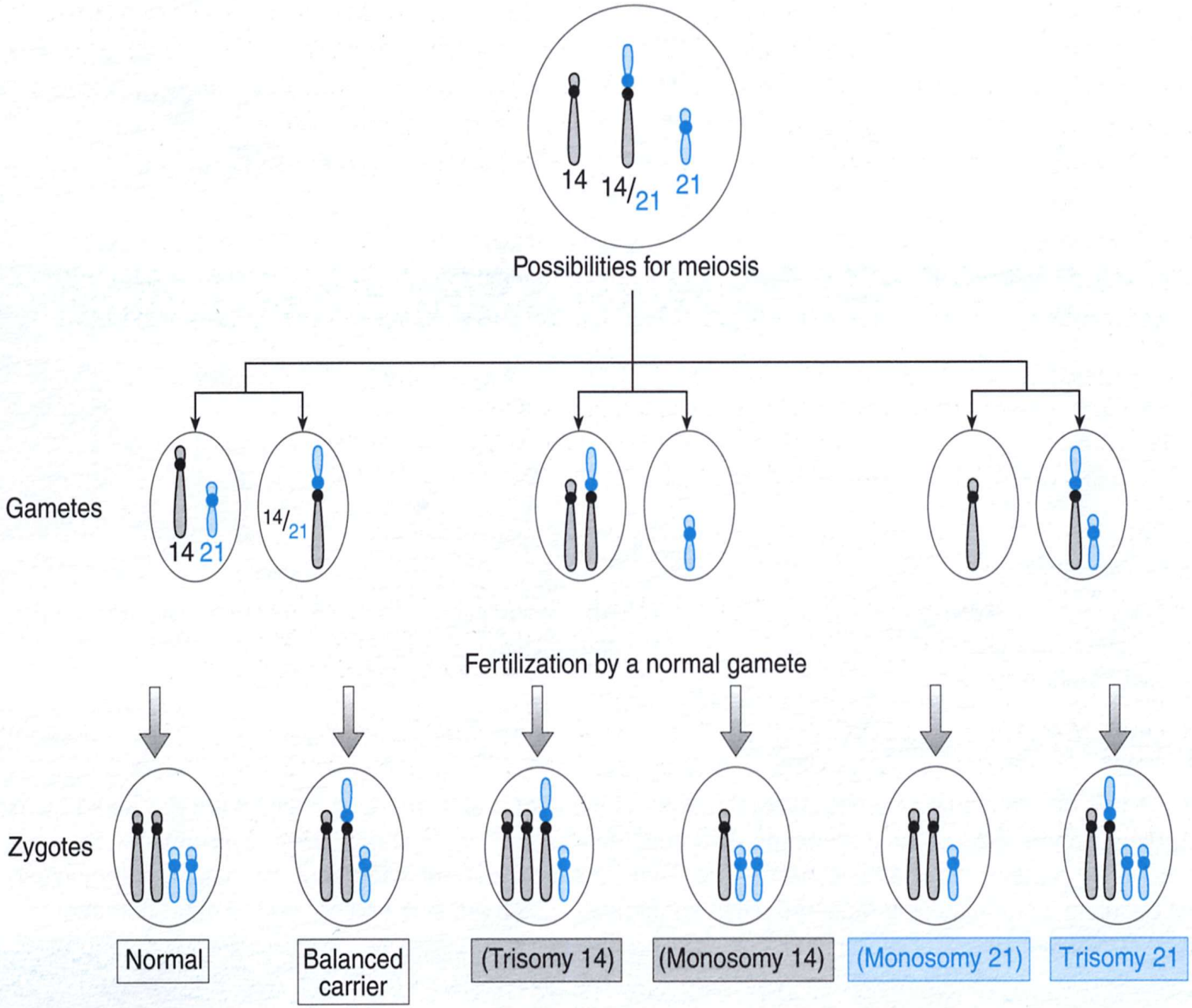


Figure 2.23: Results of meiosis in a carrier of a Robertsonian translocation.

Table 2.1: Variation in chromosome number and genome size

Species	Haploid chromosome number	Haploid genome size (Mb)
Saccharomyces cerevisiae (yeast)	16	14
Dictyostelium discoideum (slime mold)	7	70
Caenorhabditis elegans (nematode)	11/12	100
Drosophila melanogaster (fruit fly)	4	170
Gallus domesticus (chicken)	39	1200
Mus musculus (mouse)	20	3000
Xenopus laevis (toad)	18	3000
Homo sapiens (human)	23	3000
Zea mays (maize)	10	5000
Allium cepa (onion)	8	15000

Box 2.4: Nomenclature of chromosome abnormalities.

Numerical abnormalities:

Triploidy	69,XXX, 69,XXY, 69,XYY
Trisomy	e.g. 47,XX,+21[a]
Monosomy	e.g. 45,X
Mosaicism	e.g. 47,XXX/ 46,XX

Structural abnormalities:

Deletion	e.g. 46,XY,**del**(4)(p16.3)[b]; 46,XX,**del**(5)(q13q33)[b]
Inversion	e.g. 46,XY,**inv**(11)(p11p15)
Duplication	e.g. 46,XX,**dup**(1)(q22q25)
Insertion	e.g. 46,XX,**ins**(2)(p13q21q31)[c]
Ring	e.g. 46,XY,**r**(7)(p22q36)
Marker	e.g. 47,XX,+**mar**[d]
Translocation, reciprocal	e.g. 46,XX,**t**(2;6)(q35;p21.3)[e]
Translocation, Robertsonian (gives rise to one **der**ivative chromosome)	e.g.45,XY,**der**(14;21)(q10;q10)[f] 46,XX,**der**(14;21)(q10;q10),+21[g]

Notes:

[a]Gain of a chromosome is indicated by +; loss of a chromosome by –.

[b]Terminal deletion (breakpoint at 4p16.3) and interstitial deletion (5q13–q33).

[c]A rearrangement of one copy of chromosome 2 by insertion of segment 2q21–q31 into a breakpoint at 2p13.

[d]Karyotype of a cell that contains a **marker chromosome** (an extra unidentified chromosome).

[e]A balanced reciprocal translocation with breakpoints in 2q35 and 6p21.3.

[f]A balanced carrier of a 14;21 Robertsonian translocation. q10 is not really a chromosome band, but indicates the centromere; **der** means **derivative chromosome** (used when one chromosome from a translocation is present).

[g]Translocation Down syndrome; a patient with one normal chromosome 14, a Robertsonian translocation 14;21 chromosome and two normal copies of chromosome 21.

This is a short nomenclature; a more complicated nomenclature is defined by the ISCN that allows complete description of any chromosome abnormality – see Further reading.