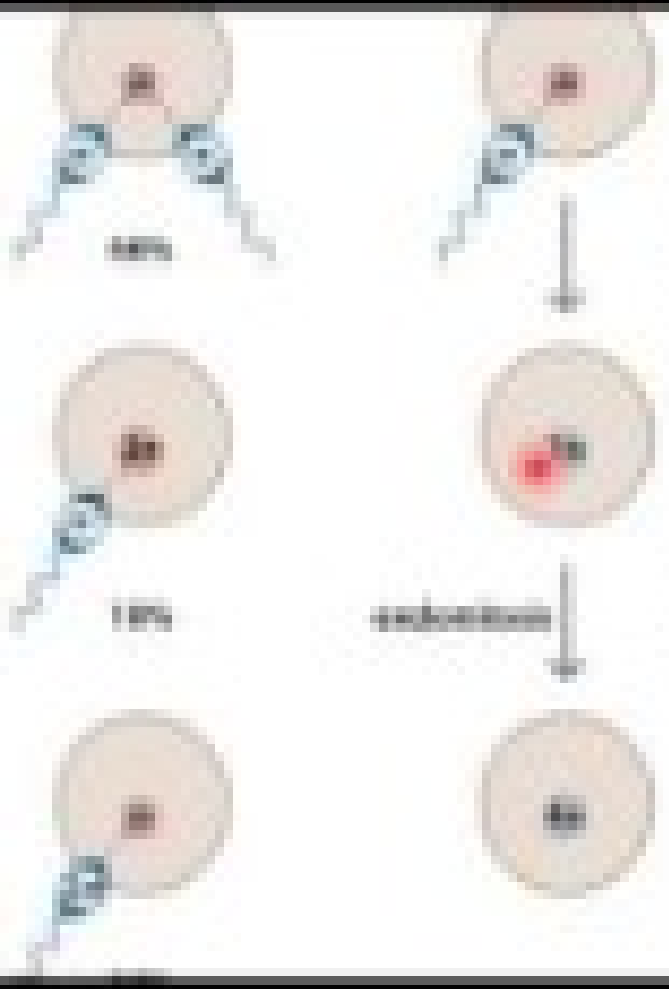


Origins of triploidy and tetraploidy.

(A) Origins of human triploidy. **Dispermy** is the principal cause, accounting for 80% of cases. Triploidy is also caused by **diploid gametes** that arise by occasional faults in meiosis. Fertilization of a diploid ovum and fertilization by a diploid sperm account for 15% and 20% of cases, respectively.

(B) **Tetraploidy** involves normal fertilization and fusion of gametes to give a normal zygote. Subsequently, however, tetraploidy arises by **endoreduplication** when DNA replication without subsequent cell division.

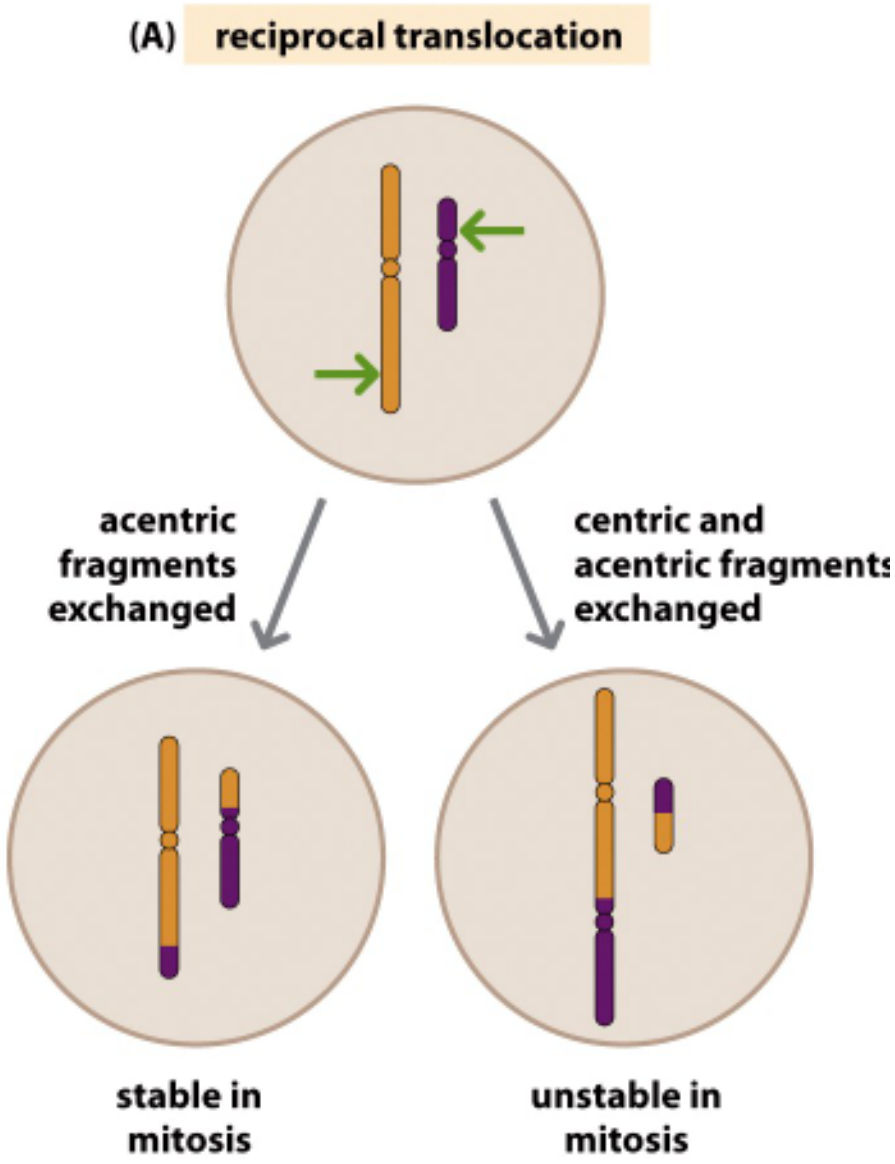
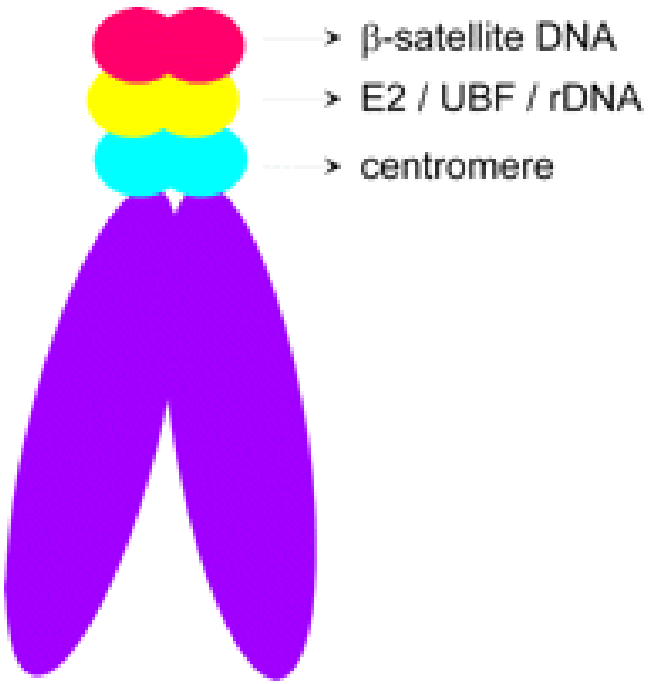


Figure 2.23 Human Molecular Genetics, 4ed. (© Garland Science)

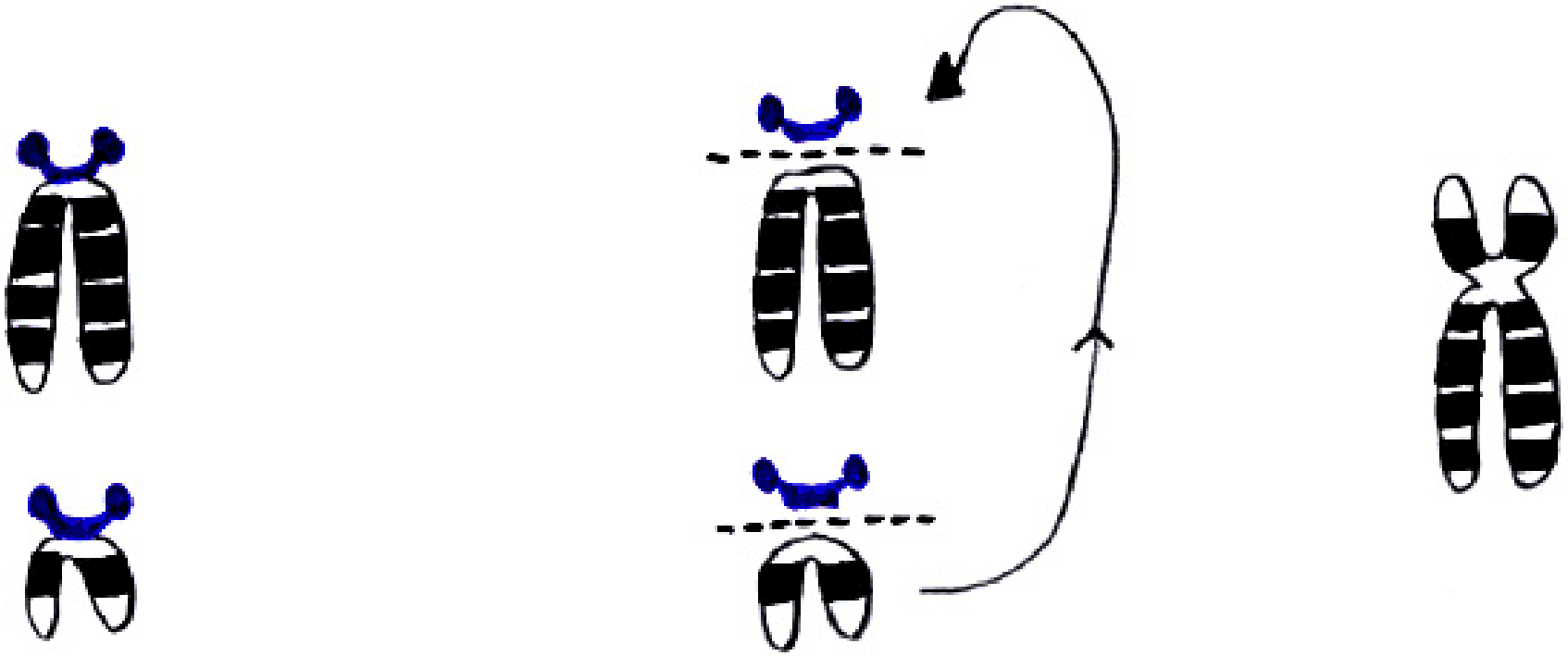
(A) Reciprocal translocation. The derivative chromosomes are stable in mitosis when one acentric fragment is exchanged for another; when a centric fragment is exchanged for an acentric fragment, unstable acentric and dicentric chromosomes are produced.

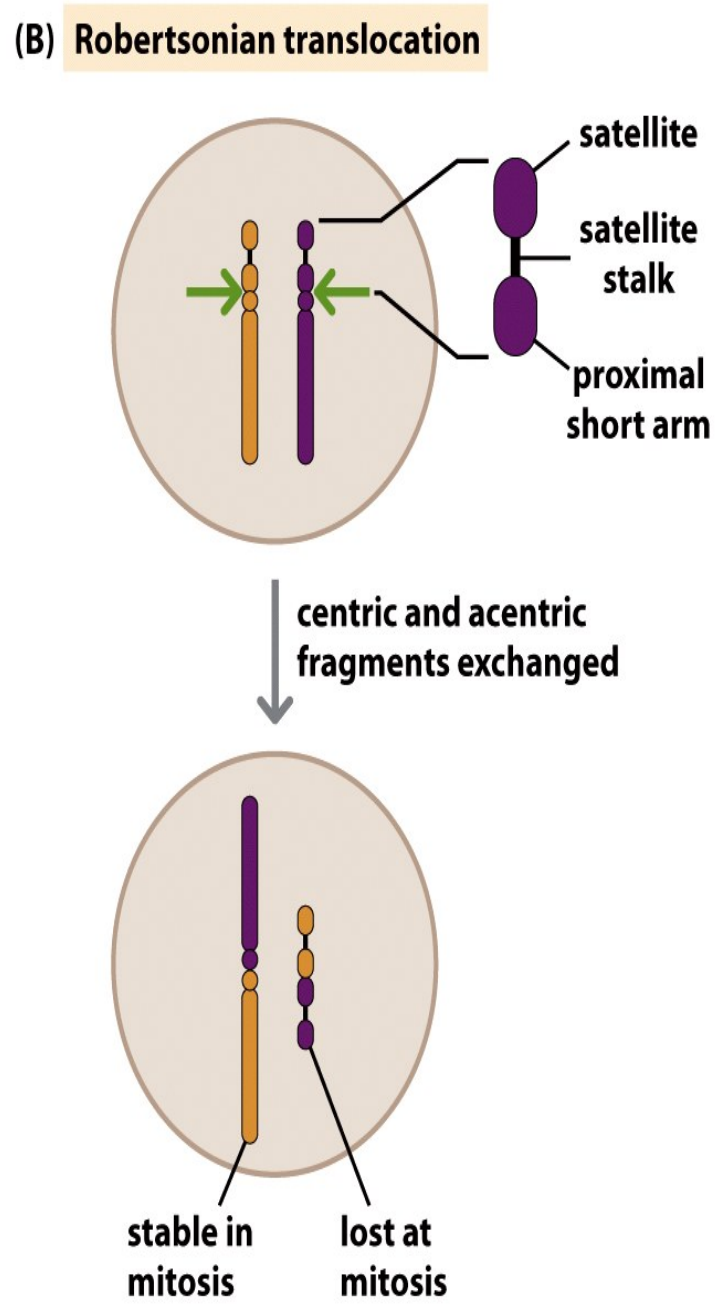
If an acentric fragment from one chromosome is exchanged for an acentric fragment from another, the products are stable in mitosis, however exchange of an acentric fragment for a centric fragment results in acentric and dicentric chromosomes that are unstable in mitosis.

- **A robertsonian translocation** is a specialized type of translocation between two of the five types of **acrocentric** chromosome in human (13,14,15,21,and 22) the short arm is very small and very similar in DNA content ,each contains **1-2Mb** of tandemly repeated rRNA genes sandwiched between two blocks of heterochromatic DNA



Robertsonian translocation
(with chromosome #14 and chromosome #21)





(B) Robertsonian translocation. This is a highly specialized reciprocal translocation in which exchange of centric and acentric fragments produces a **dicentric chromosome** that is nevertheless stable in mitosis, plus an acentric chromosome that is lost in mitosis without any effect on the phenotype. It occurs exclusively after breaks in the short arms of the human acrocentric chromosomes 13, 14, 15, 21, and 22.

The short arm of the acrocentric chromosomes consists of three regions: a proximal heterochromatic region (composed of highly repetitive noncoding DNA), a distal heterochromatic region (called a chromosome satellite), and a thin connecting region of euchromatin (the satellite stalk) composed of tandem rRNA genes. Breaks that occur close to the centromere can result in a dicentric chromosome in which the **two centromeres** are so **close** that they can function as a **single centromere**. The loss of the small acentric fragment has no phenotypic consequences because the only genes lost are rRNA genes that are also present in large copy number on the other acrocentric chromosomes

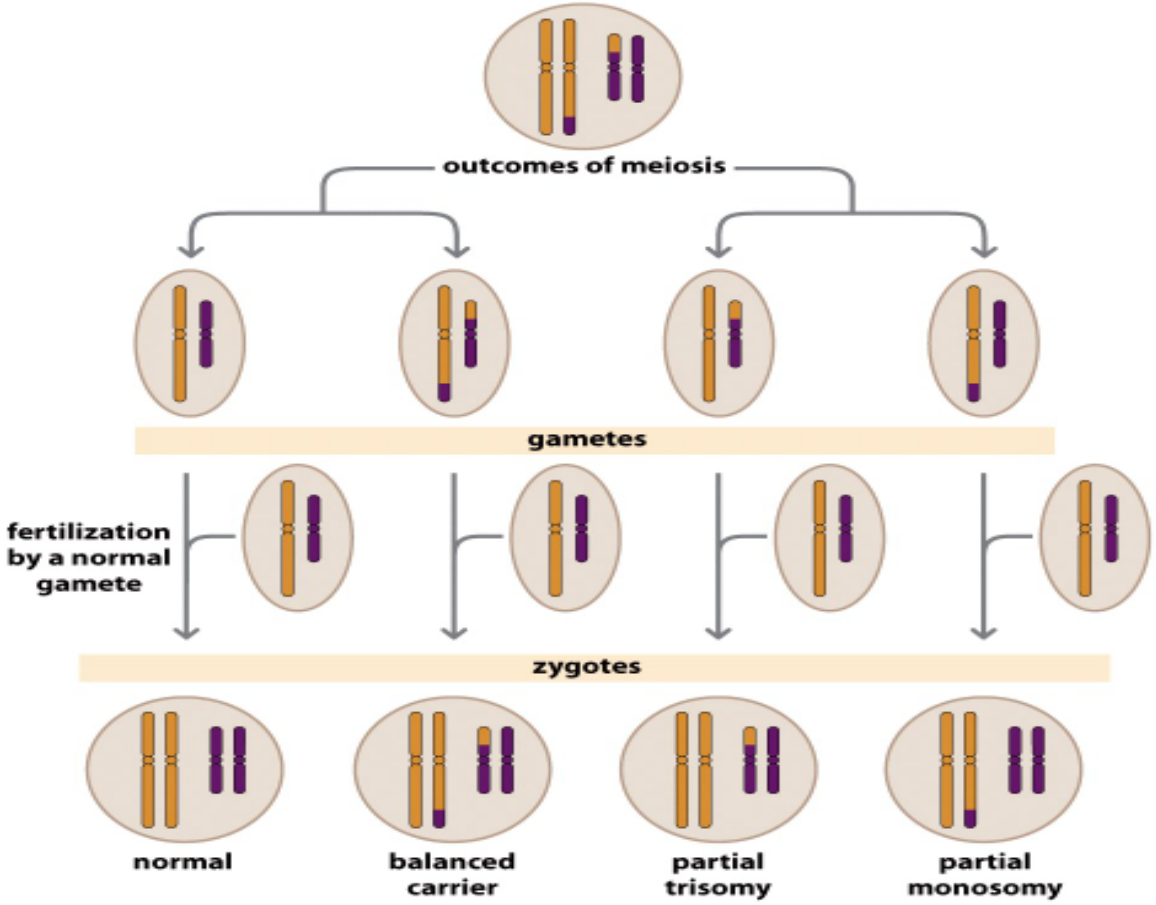


Figure 2.24 Human Molecular Genetics, 4ed. (© Garland Science)

Figure 2.24 Possible outcomes of meiosis in a carrier of a balanced reciprocal translocation. Other modes of segregation are also possible, for example 3:1 segregation.

The relative frequency of each possible gamete is not readily predicted.

The risk of a carrier having a child with each of the possible outcomes depends on its frequency in the gametes and also on the likelihood of a conceptus with that abnormality developing to term.

- A carrier of a balanced Robertsonian translocation can produce gametes that after fertilization give rise to an entirely normal child ,a phenotypically normal balanced carrier , or a conceptus with full trisomy or full monosomy for one of the chromosomes involved

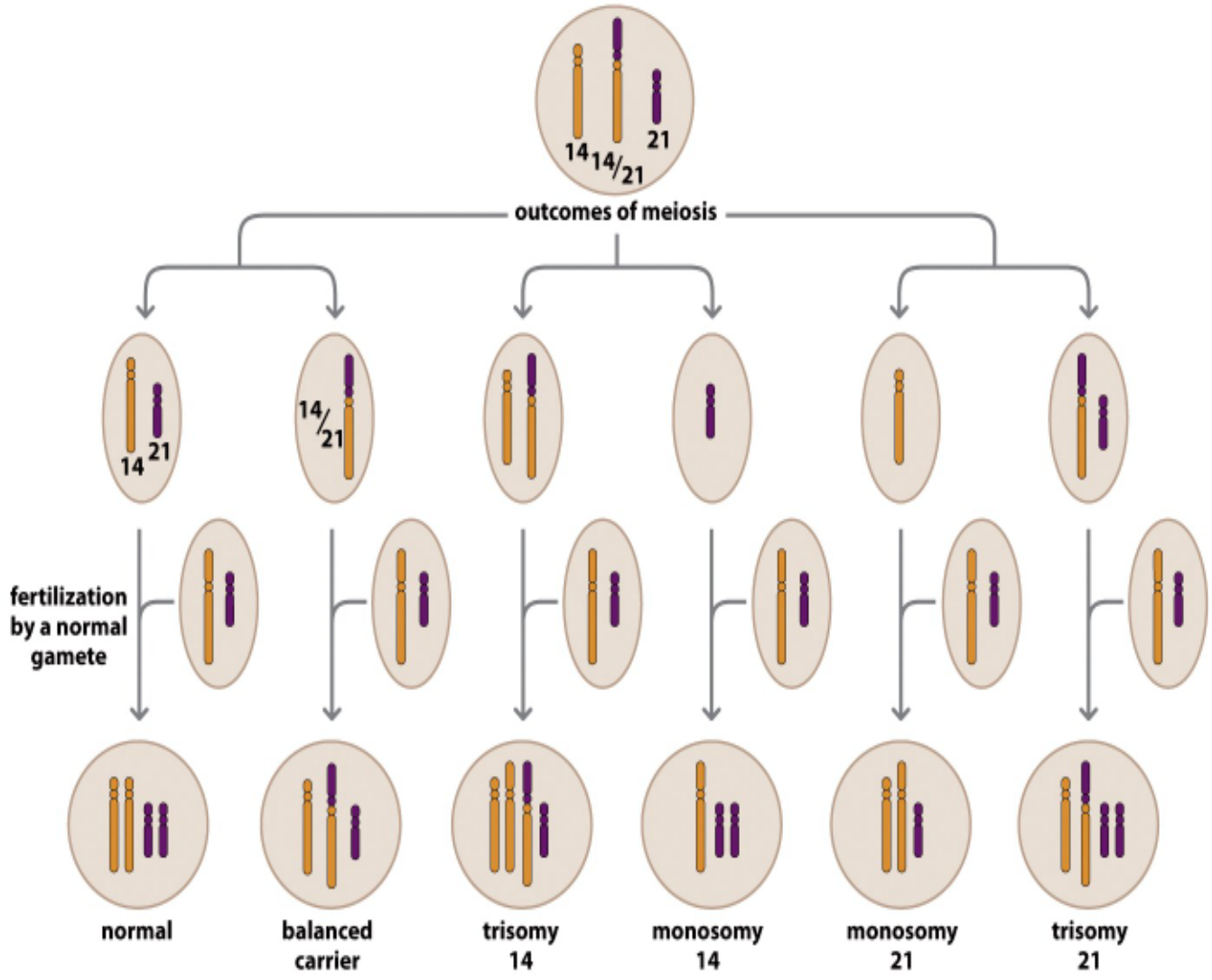


Figure 2.25 Possible outcomes of meiosis in a carrier of a Robertsonian translocation.
Carriers are asymptomatic but often produce unbalanced gametes that can result in a monosomic or trisomic zygote. The two monosomic zygotes and the trisomy 14 zygote in this example would not be expected to develop to term.

Figure 2.25 Human Molecular Genetics, 4ed. (© Garland Science)

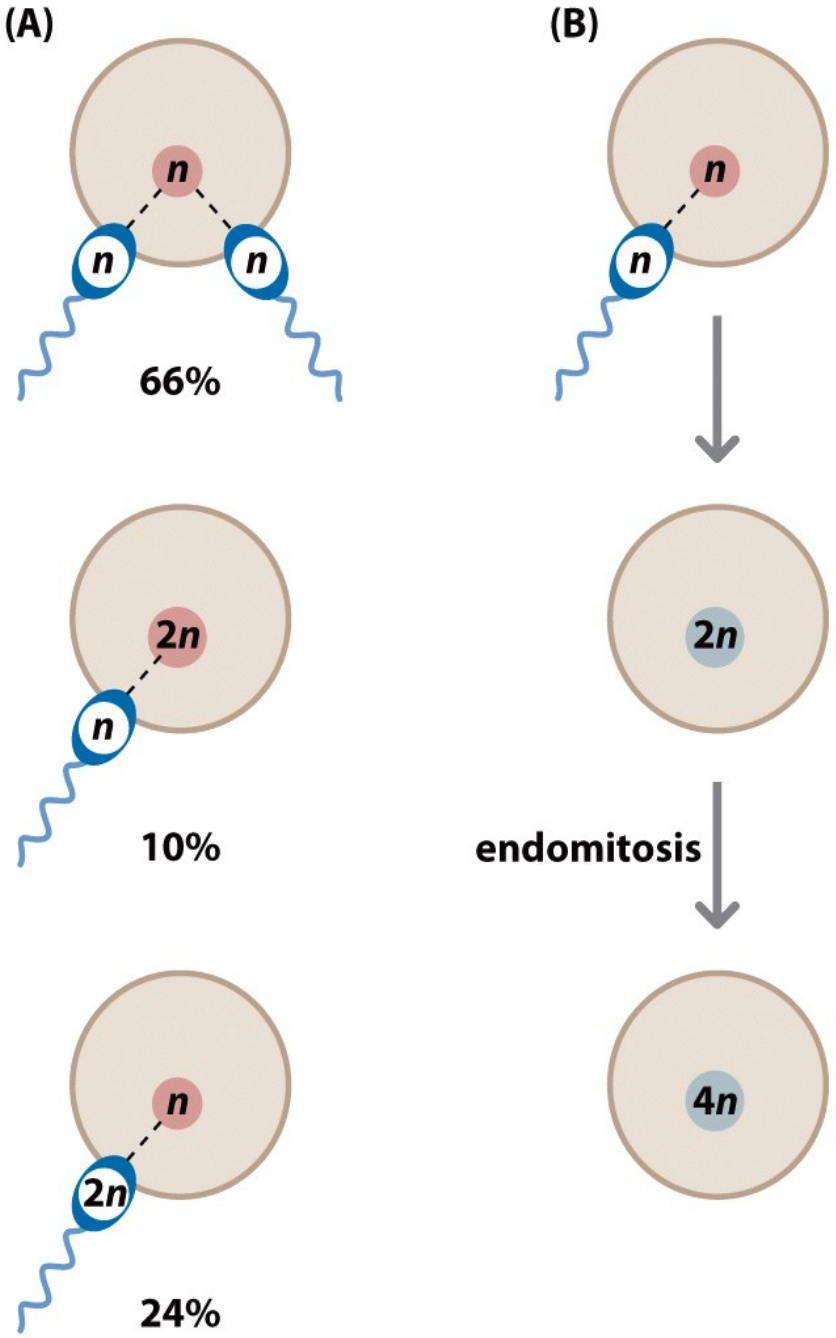


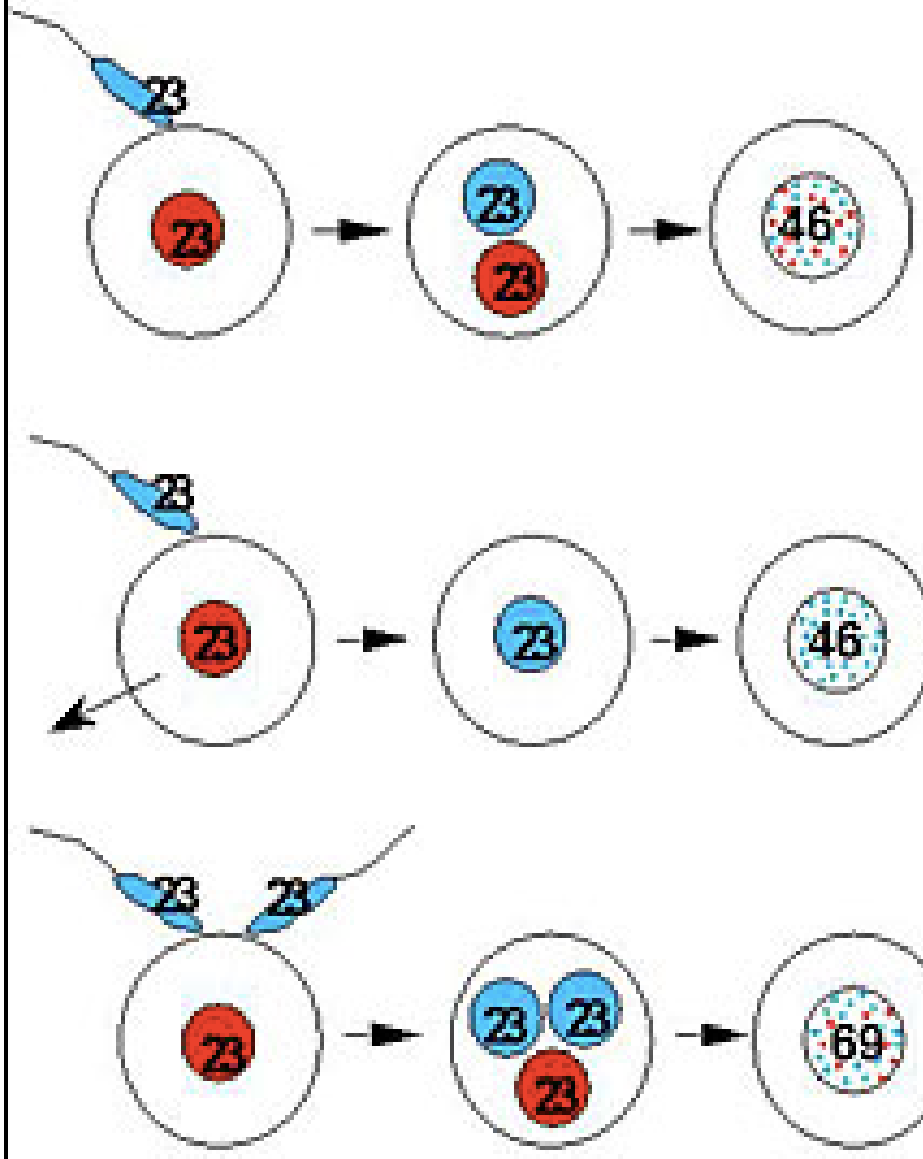
Figure 2.21 Human Molecular Genetics, 4ed. (© Garland Science)

Origins of triploidy and tetraploidy.

(A) Origins of human triploidy. **Dispermy** is the principal cause, accounting for 66% of cases. Triploidy is also caused by **diploid gametes** that arise by occasional faults in meiosis; fertilization of a diploid ovum and fertilization by a diploid sperm account for 10% and 24% of cases, respectively.

(B) **Tetraploidy** involves normal fertilization and fusion of gametes to give a normal zygote. Subsequently, however, tetraploidy arises by endomitosis when DNA replicates without subsequent cell division.

Genetic status in normal conception and molar pregnancy



- **Normal conception**
- 2 sets of genes
- 1 paternal
- 1 maternal
- Viable foetus

- **Complete Mole**
- 2 sets of paternal genes
- no maternal genes
- No foetus

- **Partial mole**
- 3 sets of genes
- 1 maternal
- 2 paternal
- non-viable foetus

Triploidy is the presence of an additional haploid set of chromosomes, is the cause of 20% of spontaneous abortions, premature births and perinatal deaths.

Triploidy syndrome is a rare syndrome and is estimated to occur in about 2 per cent of conceptuses. Triploidy occurs when there is double fertilization of an ovum (dispermy). The result may be 69, XXX or 69, XXY or 69, XYY. The extra set of paternal chromosomes predisposes to formation of a partial mole, features of which may or may not be grossly or microscopically apparent.

- 69,XXX triploidy
- 69,XXY triploidy
- 69,XYY triploidy

Triploidy - stillbirth at 39 weeks (69,XXX) - note the appearance of the hands

Physiopathology

Triploidy is constituted by an extra haploid set of chromosomes for a total of 69 chromosomes in humans. A "parent-of-origin" effect has been demonstrated by analysis of cytogenetic polymorphisms of triploidy pregnancies. Two distinct phenotypes of human triploid fetuses have been recognized according to the parental origin of the extra haploid set.

The first one or triploidy of diandric type occurs when the extra haploid set of chromosomes arises from the father, the second one or triploidy of digynic type occurs when the extra haploid set of chromosomes arises from the mother. Diandric fetuses appear relatively well grown with a large placenta, while digynic fetuses show intrauterine growth retardation with a small placenta.

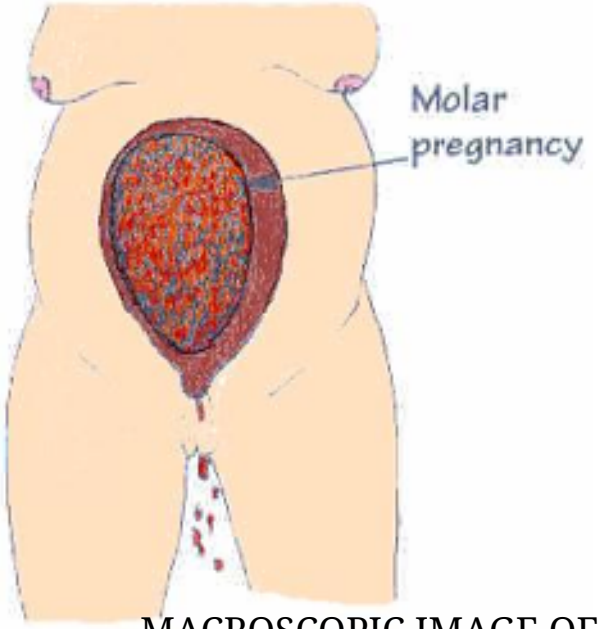
Types

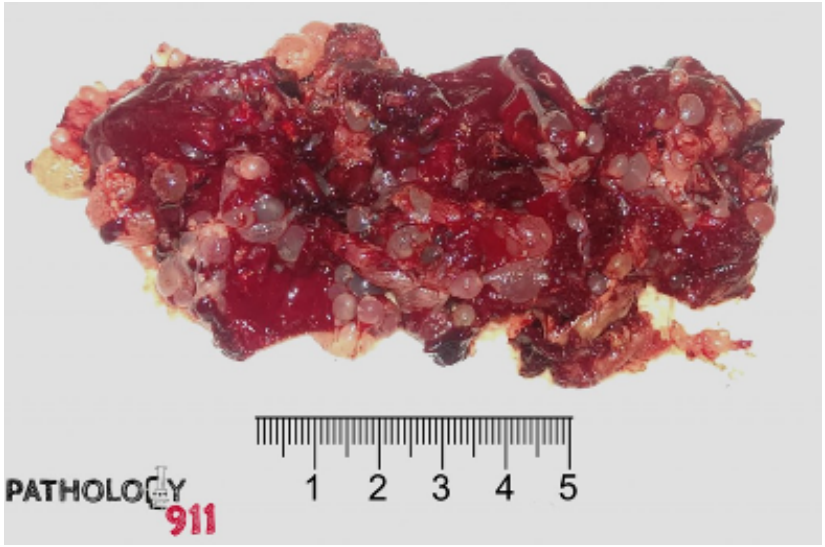
- maternal triploidy (triploidy by digyny)
- paternal triploidy (diandry or dispermy)

Synopsis

The most common clinical signs of triploidy are: severe intrauterine growth retardation, macrocephaly, total syndactyly of third and fourth fingers and CNS, heart and renal defects.

Hydatidiform mole, one of the characteristic features of pure triploidy, is found in more than 90% of cases.





MACROSCOPIC IMAGE OF A COMPLETE HYDATIDIFORM MOLE, SHOWING THE CHARACTERISTIC VESICULAR, OR 'BUNCHES OF GRAPES' APPEARANCE OF THE CHORIONIC VILLI.

PARTIAL MOLE

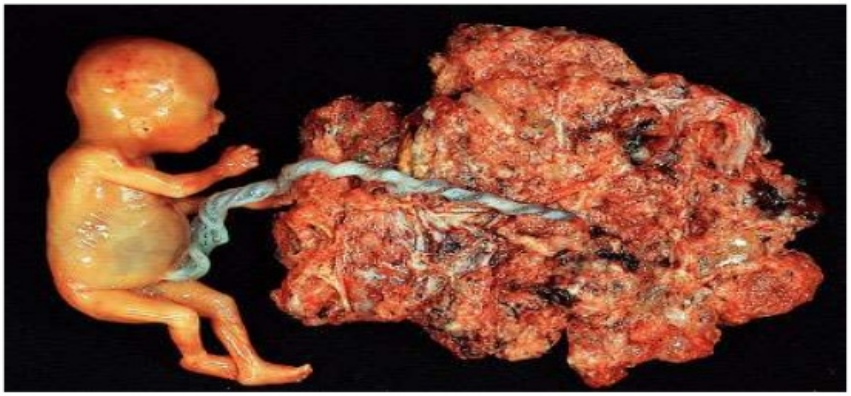
- The oocyte has an intact set of maternal DNA
- Option A: Fertilised by one sperm – reduplicates its own DNA
- Option B: Fertilised by two sperm
- Karyotype: Triploid – 69 chromosomes (69 XXY – an extra set of paternal DNA)

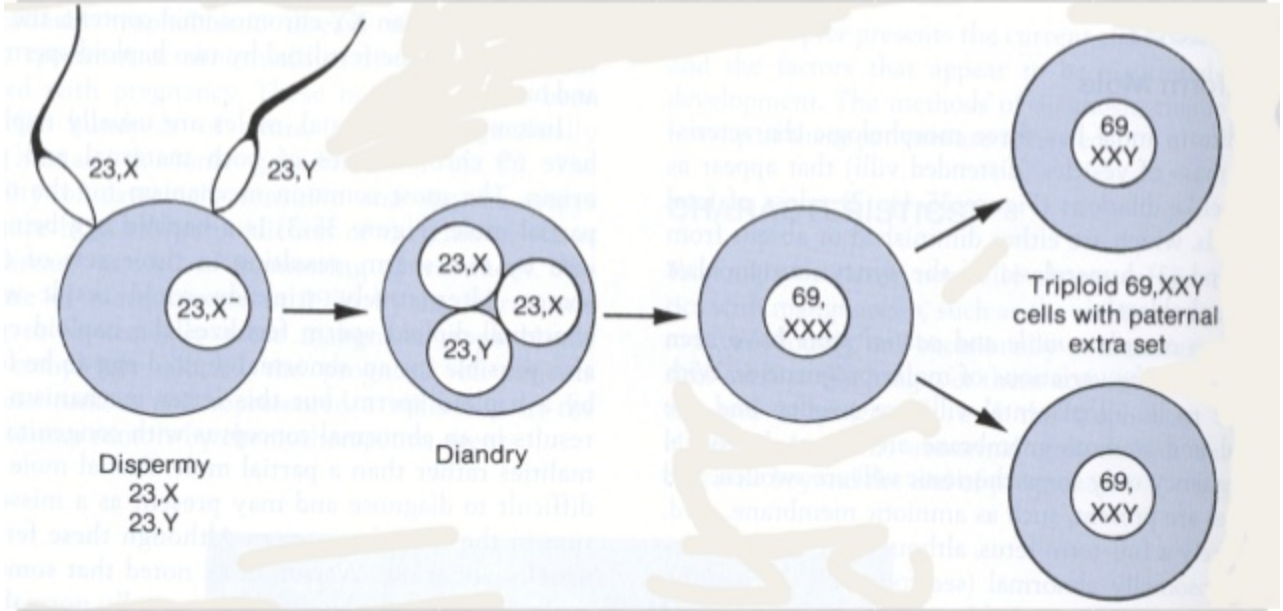
COMPLETE MOLE

- The oocyte has somehow lost its DNA – it is 'empty' of DNA
- Option A: Fertilised by one sperm – reduplicates its own DNA = *homozygous*
- Option B: Fertilised by two sperm = *heterozygous*
- Karyotype: Diploid – 46 chromosomes (46XX or 46XY – the 46YYs are not viable)

Note: (*all paternal DNA* – no maternal DNA – i.e. androgenetic)

Partial mole



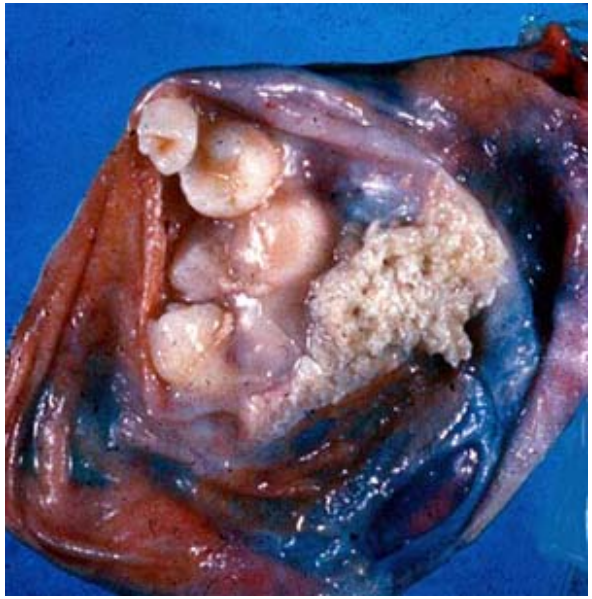


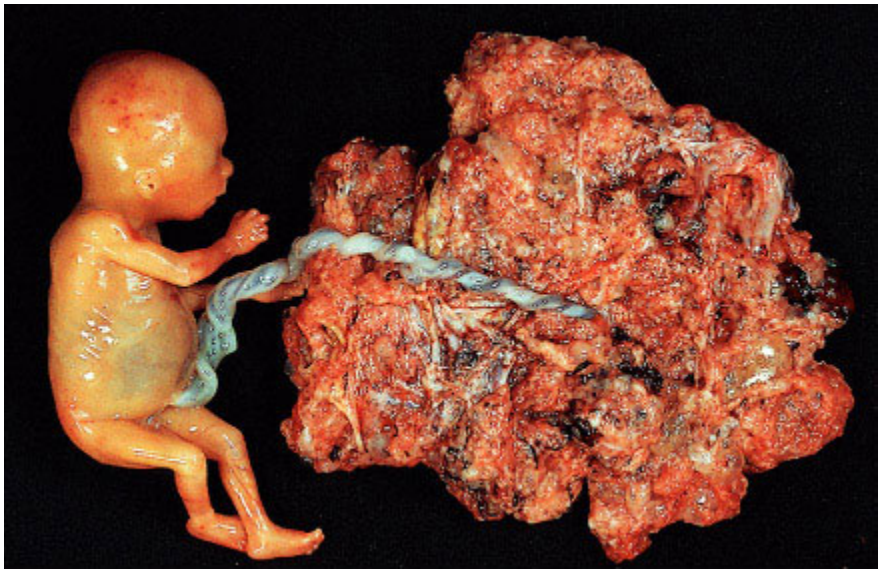
Diandric triploidy

Uniparental diploidy changes the balance between the embryo or fetus and its supporting membranes

- **Paternal uniparental diploidy** produces hydatidiform moles, abnormal conspectuses that develop to show widespread hyperplasia (overgrowth)of the trophoblast but no fetal parts, they may transform into choriocarcinoma.

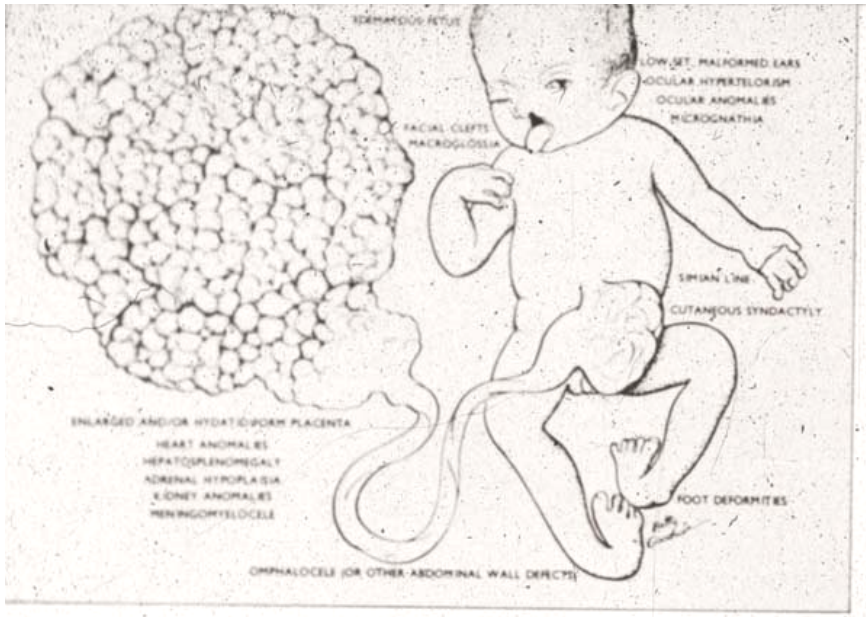
- **Maternal uniparental diploidy** results in ovarian teratomas , rare benign tumors of the ovary which consist of disorganized embryonic tissue but are lacking in vital extra-embryonic membranes.





Triploidy

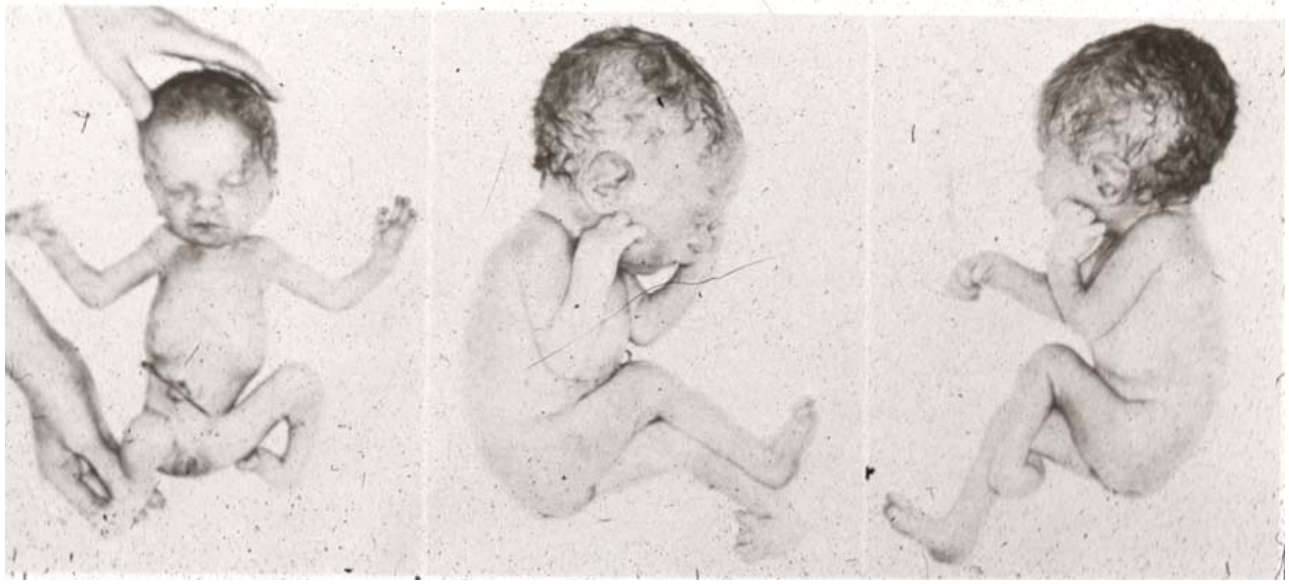
Findings:
CHD
Kidney anomalies
Low-set, malformed ears
Hypertelorism
Foot deformities
Abdominal wall defects



24.1

24.2

24.3



<u>Diandric</u>
Enlarged placenta
Cyst-like placenta
Well-formed fetus with or without microcephaly

<u>Digynic</u>
Macrocephaly
Severe intrauterine