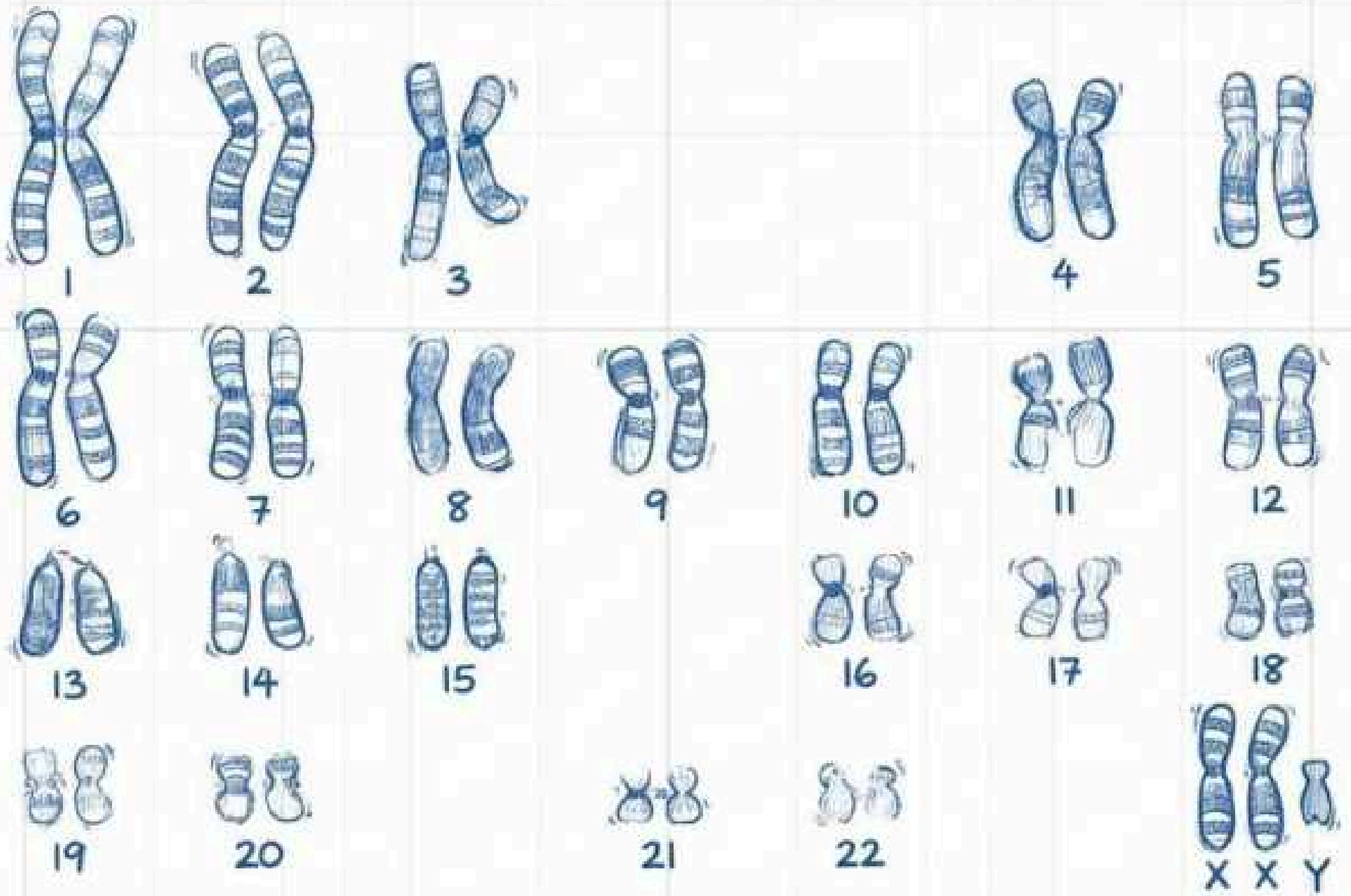
Lecture 4: Chromosomes and Their Disorders

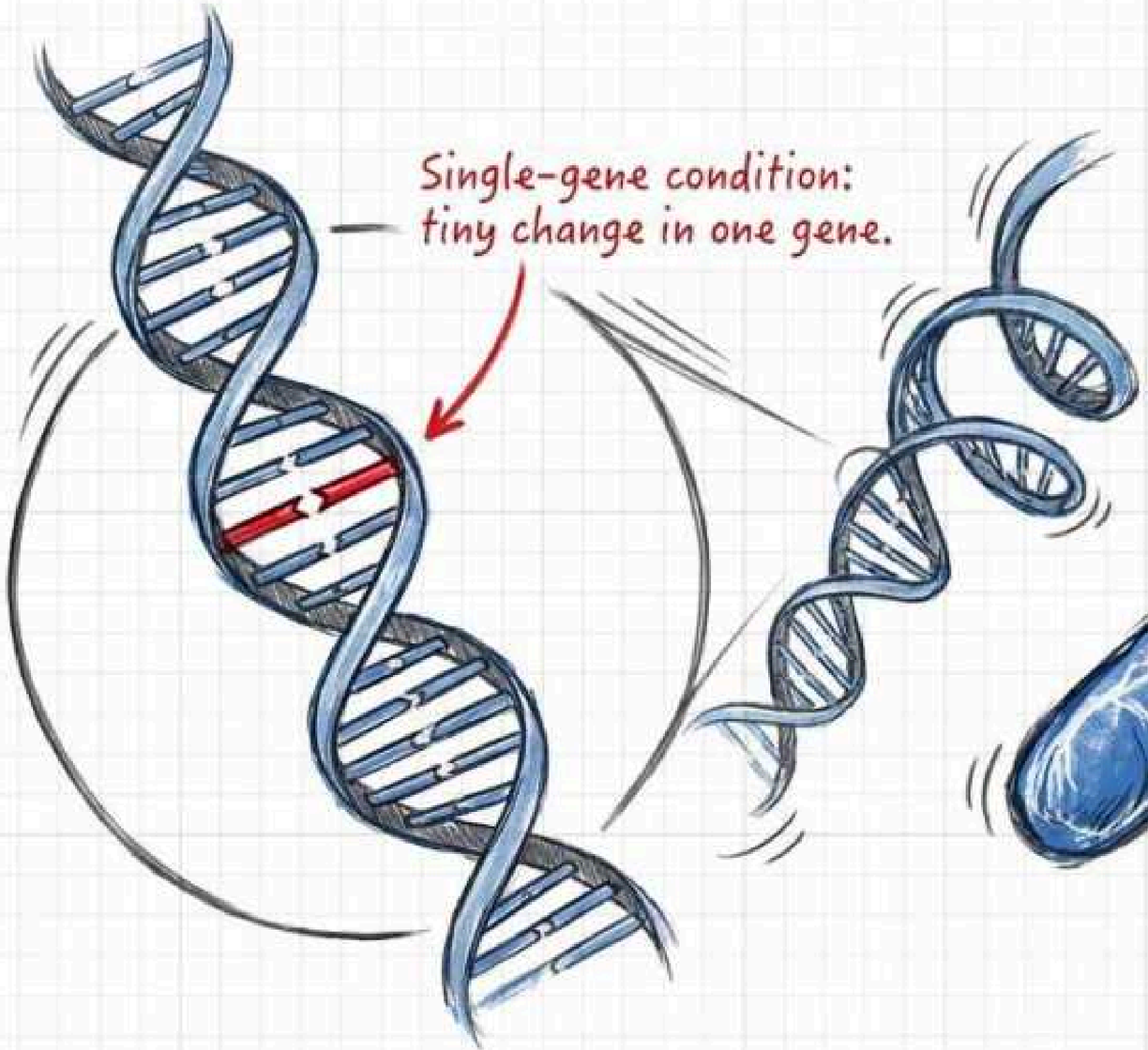
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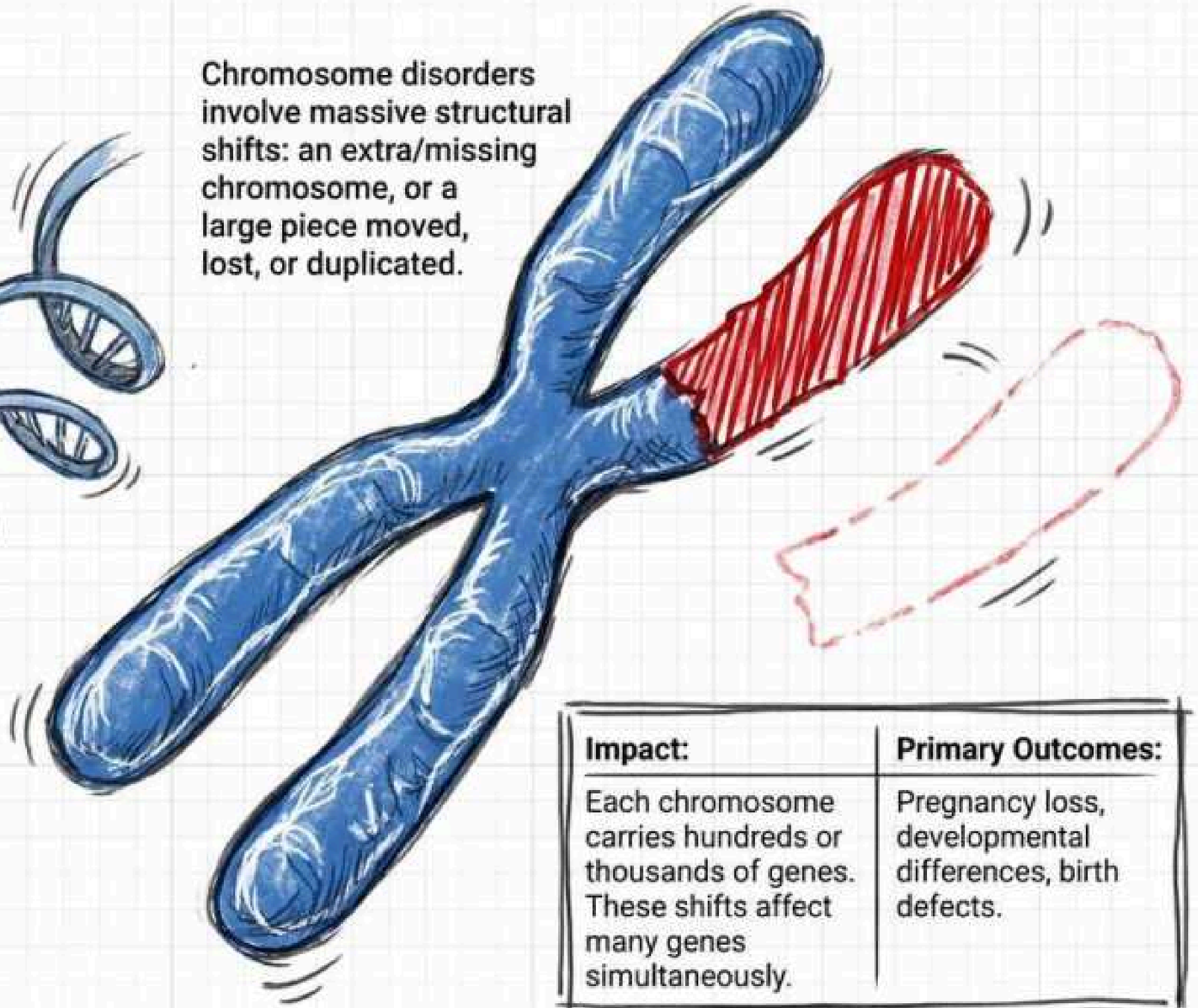
Questions or feedback: garyanderson@mail.grokbot.com · X: @garyanderson

The Scale of Genetic Disruption

¶ 4.1



Chromosome disorders involve massive structural shifts: an extra/missing chromosome, or a large piece moved, lost, or duplicated.



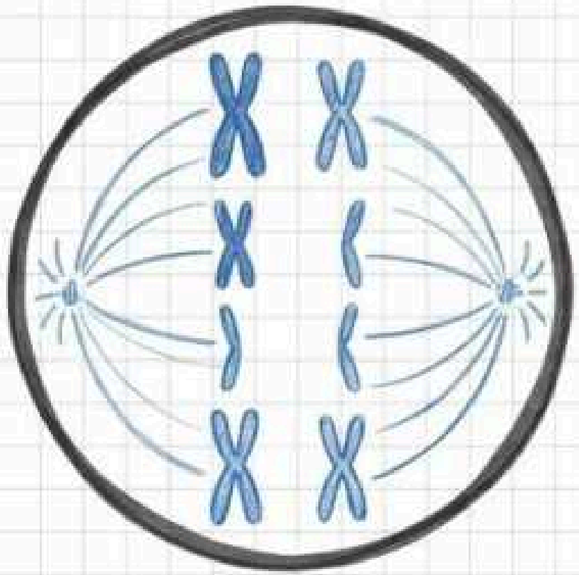
Impact:	Primary Outcomes:
Each chromosome carries hundreds or thousands of genes. These shifts affect many genes simultaneously.	Pregnancy loss, developmental differences, birth defects.

The Mechanics of Meiosis and Non-Disjunction

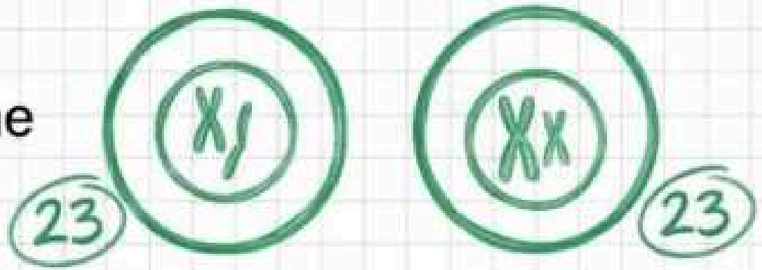
¶ 4.2

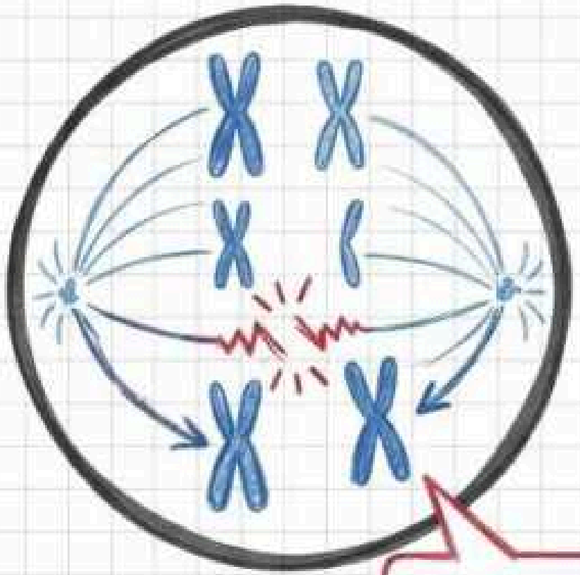
Meiosis halves the chromosome number (46 → 23) so the resulting embryo returns to 46.

Normal

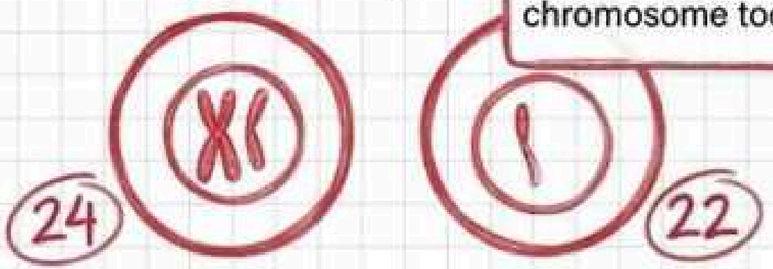


Outcome



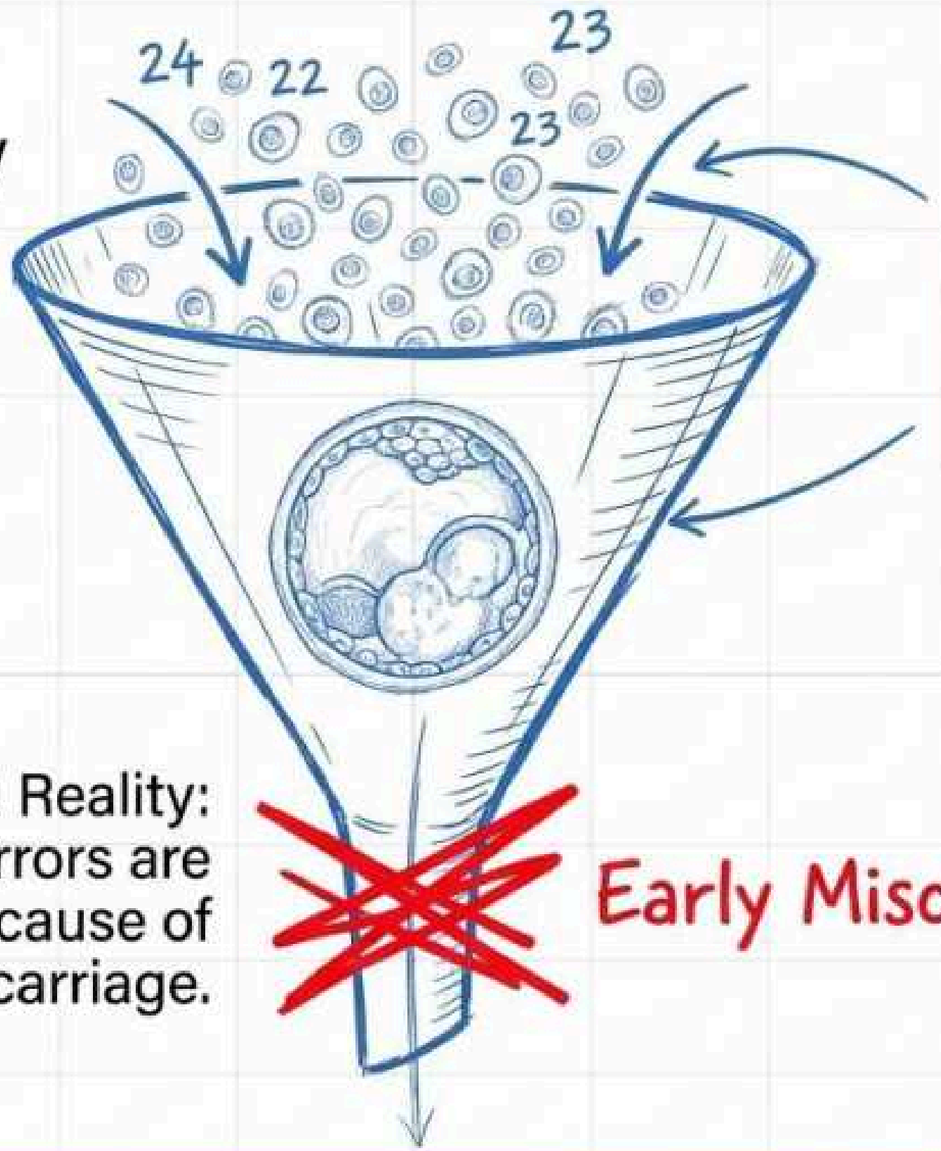


Non-disjunction:
The failure of a chromosome pair to separate correctly, resulting in an egg or sperm with one chromosome too many or too few.



The Survival Funnel: Trisomy and Monosomy

¶ 4.3



Trisomy: Embryo with an extra copy.

Monosomy: Embryo with a missing copy.

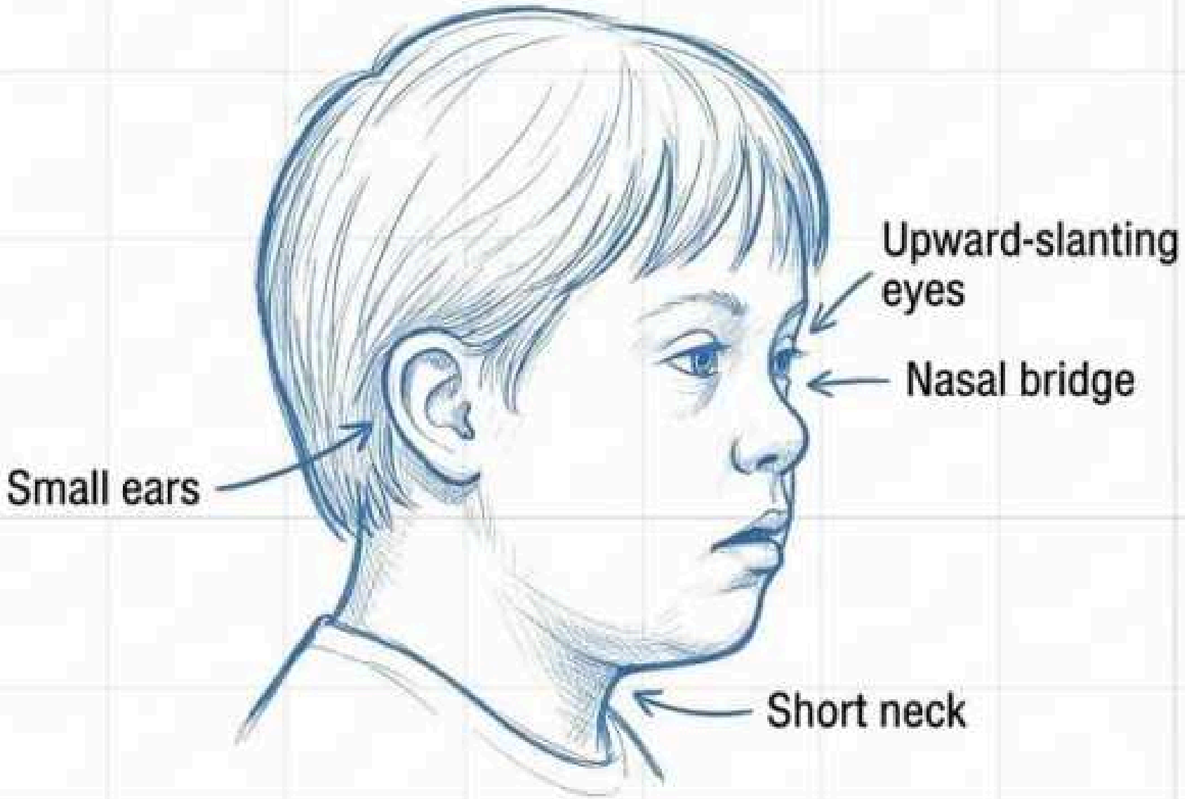
The Clinical Reality: Chromosome errors are the most common cause of early miscarriage.

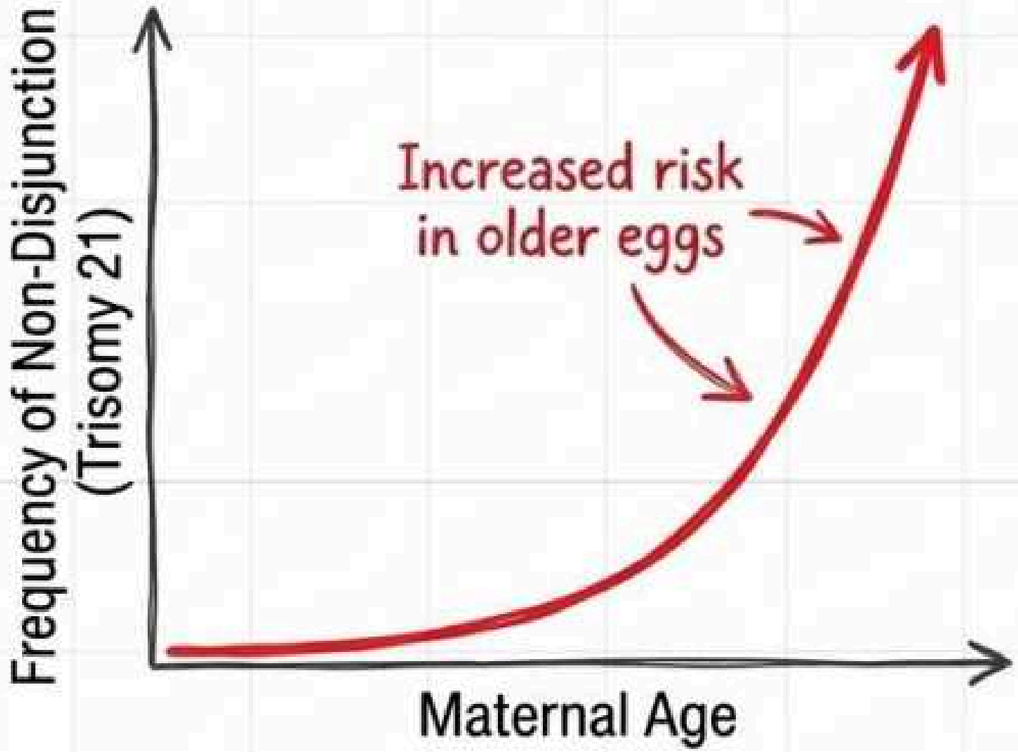
Early Miscarriage

Note to Families: Most early miscarriages are caused by chance chromosome errors that nobody could have prevented, not by anything a parent did.

Clinical Profile: Trisomy 21 (Down Syndrome)

¶ 4.4





Features: Characteristic facial features, varying degrees of intellectual disability, higher risks of certain heart defects and other health problems.

Trend: Risk rises with maternal age due to increased frequency of meiosis errors in older eggs.

Prognosis: With good care, wide variation exists, and many live long, active, and rewarding lives.

Sex Chromosome Variations

¶ 4.5

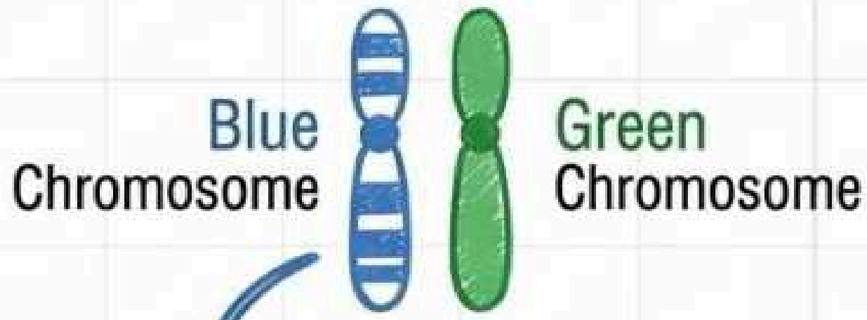
Usually milder because only one X chromosome is fully active in each cell.

	Turner Syndrome	Klinefelter Syndrome
Karyotype	45,X	47,XXY
Active X Count	1	1
Phenotypic Sex	Female	Male
Primary Physical Impacts	Short stature, reduced ovary function	Reduced fertility
Clinical Visibility	Often immediate	May go unrecognised for years

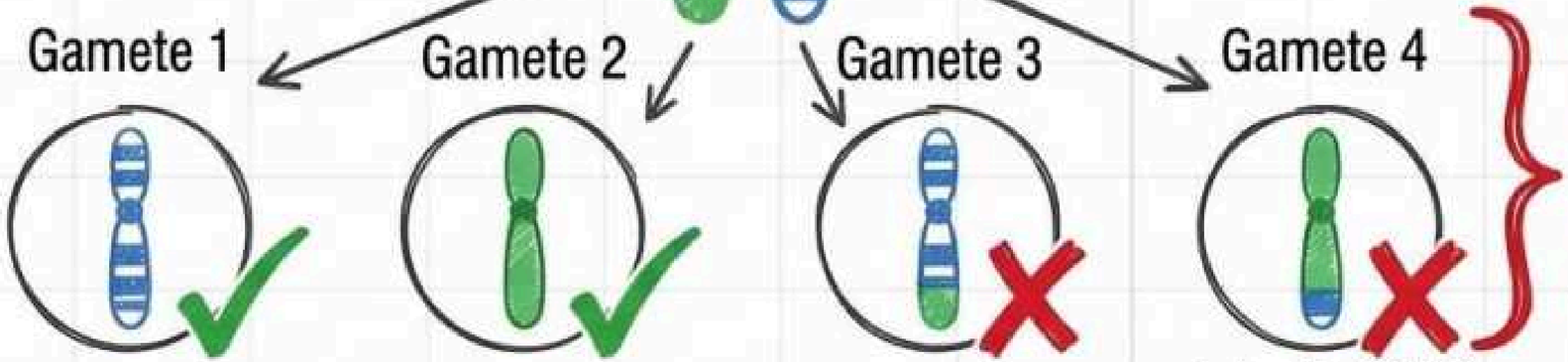
Management: Both supported with appropriate medical care

Structural Rearrangements: Translocations

¶ 4.6



Balanced Carrier: No genetic material lost/gained. Person is usually healthy.



Inherits normal Blue chromosome

Inherits normal Green chromosome

Inherits ONLY the Blue chromosome with the Green tip

Inherits ONLY the Green chromosome with the Blue tip

Unbalanced Set: Leads to miscarriages or a child with a chromosome condition.

Microdeletions: A tiny deletion of part of a chromosome that removes several neighboring genes, causing a recognizable syndrome.

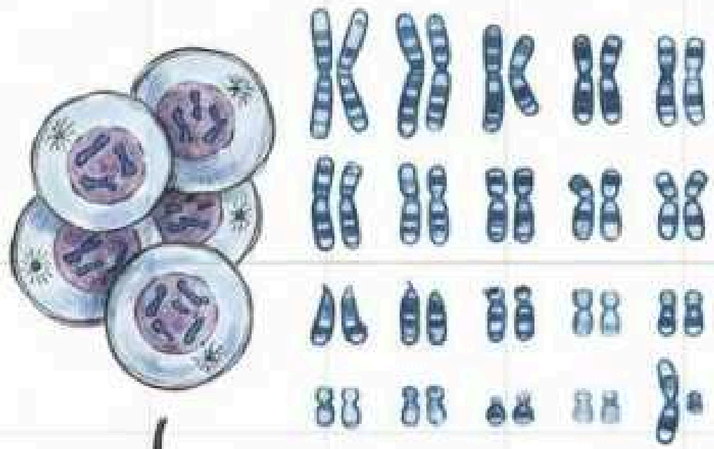
The Diagnostic Resolution Scale

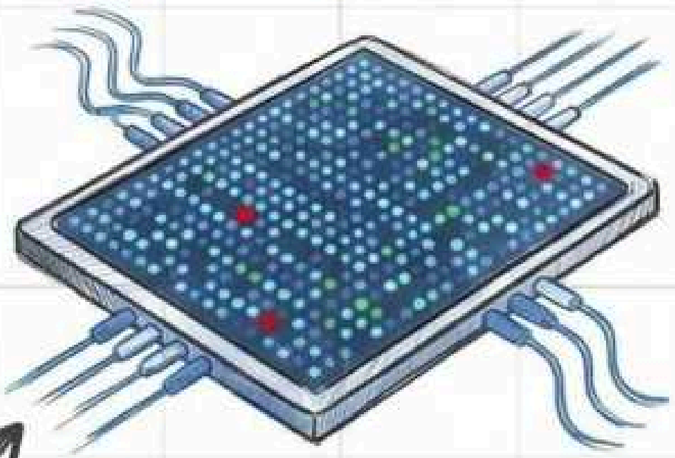
¶ 4.7

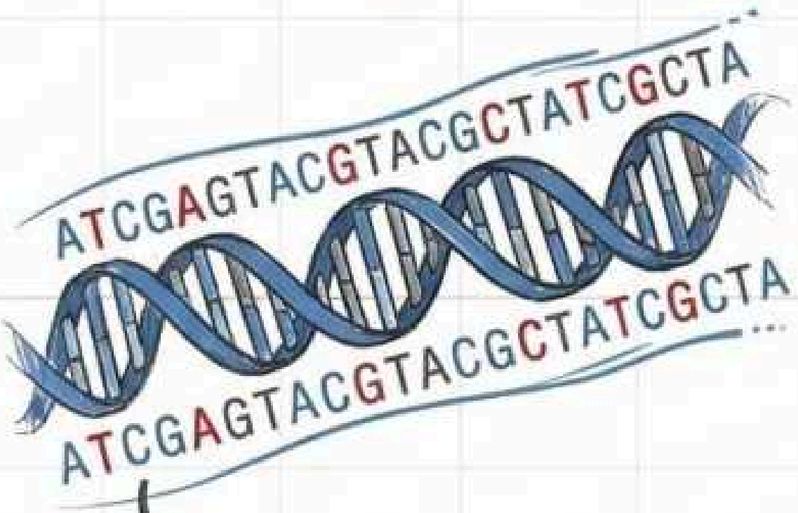
Macro Scale

Micro Scale

Molecular Scale







Karyotype

Classic method. Arranged by size/banding pattern. Reveals large, whole-chromosome changes.

Chromosomal Microarray

First-line test for developmental differences. Detects much smaller microdeletions and duplications across the whole genome.

Sequencing

Detects changes of every size (covered in Lecture 6).

INCREASING RESOLUTION

Prenatal Assessment Pathways

¶ 4.8

Screening Tests

Tools: Ultrasound, Maternal Blood, cfDNA (fragments of placental DNA circulating in mother's blood)

Goal: Estimate the chance of certain conditions (highly accurate for common trisomies)

Sample Origin: Maternal circulation

Miscarriage Risk: Zero

Diagnostic Tests

Tools: Amniocentesis, Placental Tissue Sampling

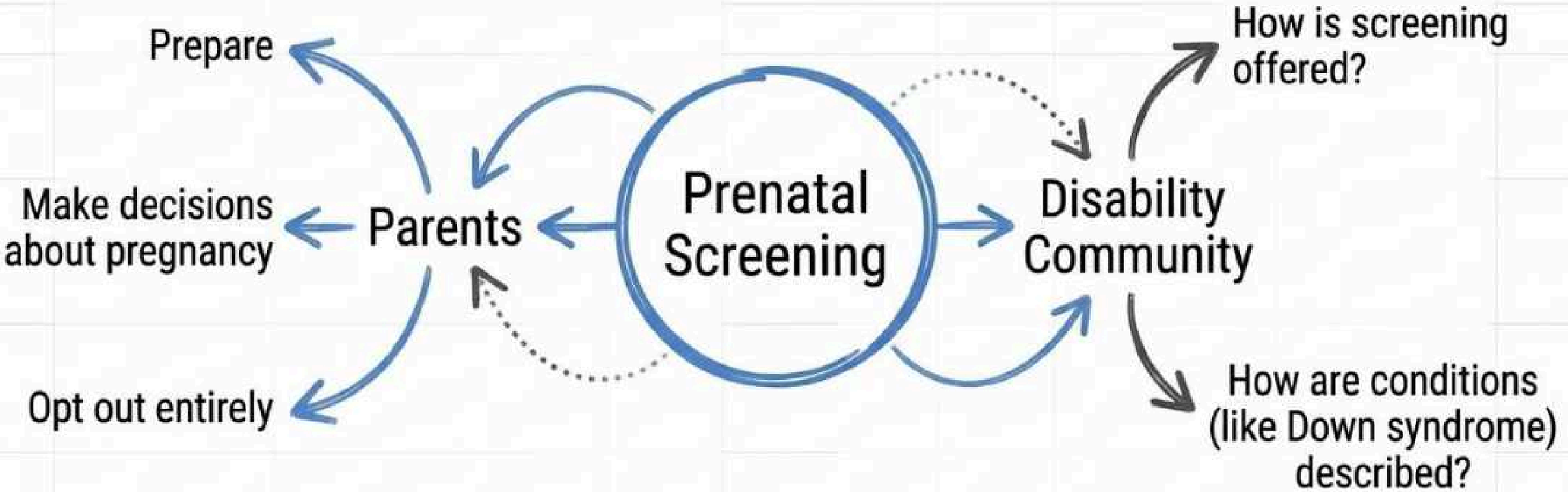
Goal: Confirm a result / definitive diagnosis

Sample Origin: Direct fetal or placental tissue

Miscarriage Risk: Carries a small risk

The Personal Dimensions of Screening

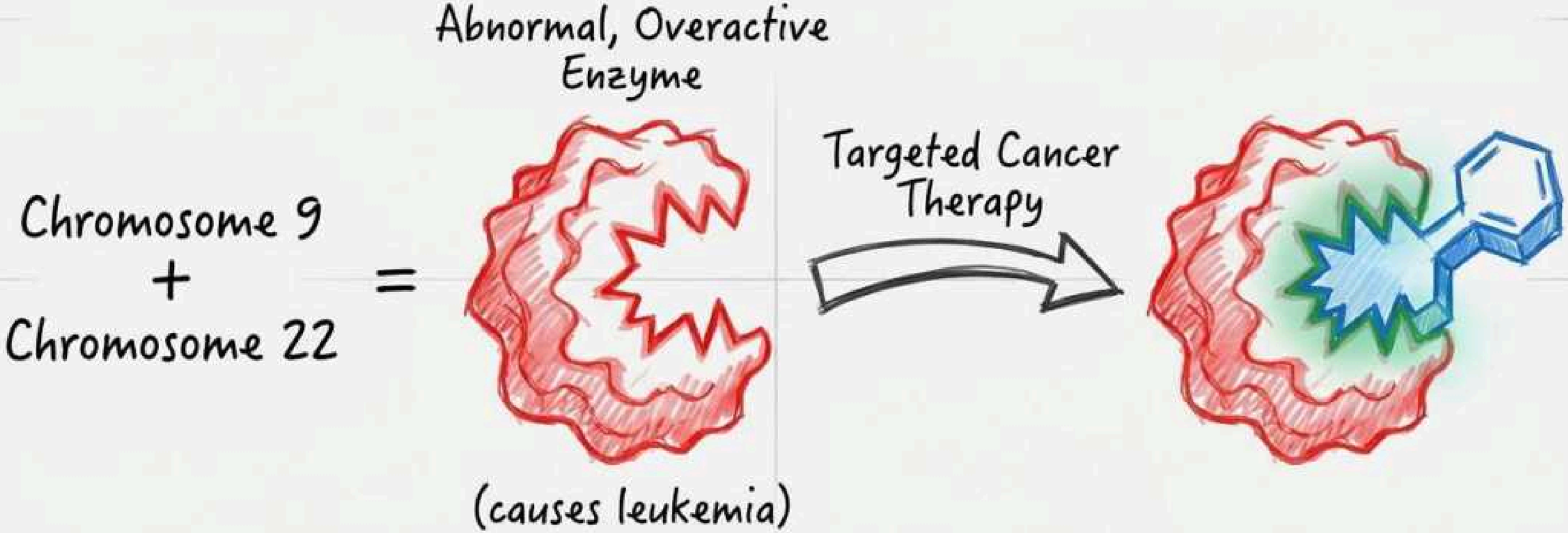
¶ 4.9



Good Medical Practice: Give clear information and support whatever choice parents make.

Somatic Changes: The Philadelphia Chromosome

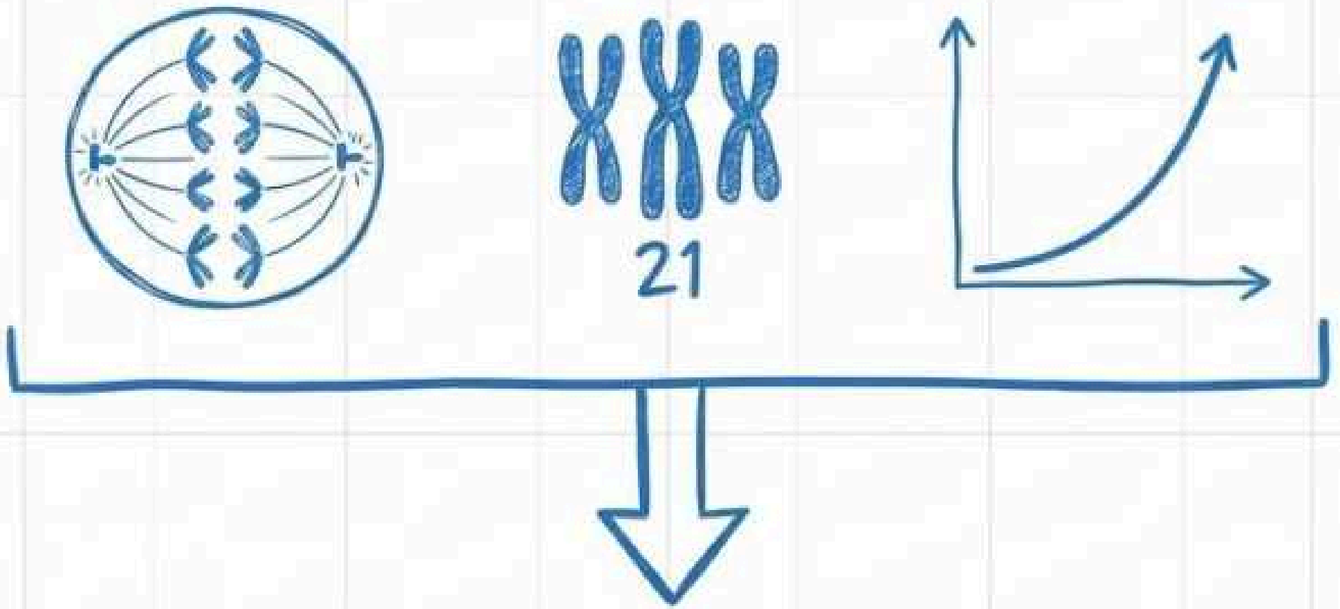
¶ 4.10



Somatic chromosome changes transform the disease outlook. Blocking this fused enzyme helped launch the era of targeted cancer therapy.

Synthesis Assessment

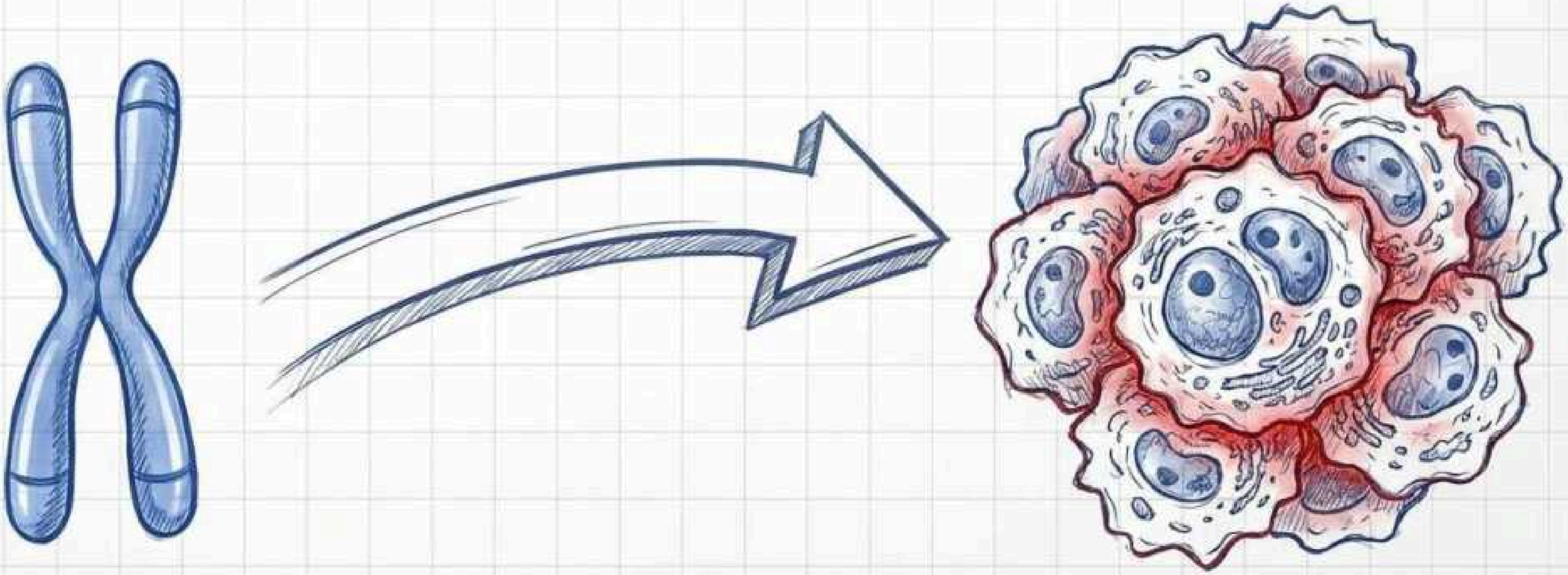
¶ 4.11



Explain how an error in meiosis can lead to a child with trisomy 21, and why the chance of this rises with the mother's age.

Looking Ahead

¶ 4.12



Next: Lecture 5. Moving from single genes and chromosomes to common diseases and cancer genetics.