Foreword

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Quality
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We wish you lots of success with your studies and your exams!

Team Slim Academy

P.S. This summary has been written based on the author's own interpretation. It remains a summary and should be seen as a supplement to the required study materials — not a replacement

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Chromosomal Abnormalities

ILOs (directly sourced from the course manual by the University of Manchester)

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3. Explain mitosis and meiosis during gamete formation and the effect of ageing on these processes.
4. Describe the principles of genetic screening during pregnancy and relate this to Down syndrome.
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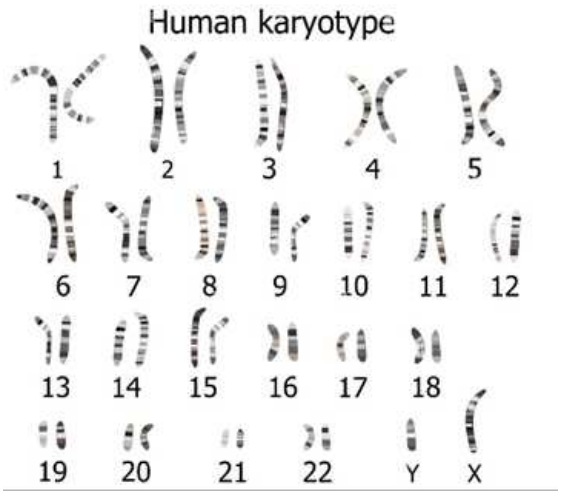
Chapter 1 - Normal chromosome structure

Introduction
This chapter describes the normal number, structure and arrangement of chromosomes.

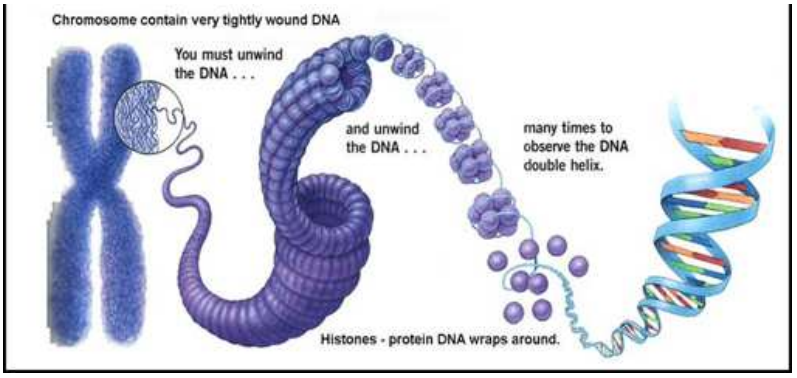
Number of Chromosomes
In a normal diploid cell, there are 46 chromosomes in total which can be arranged in 23 pairs. There are 22 pairs of autosomes, which are non-sex chromosomes, and 1 pair of sex chromosomes.

Karyotyping is a method used to create a visual representation of an individual's complete set of chromosomes. It involves collecting a cell sample and growing them in a lab to arrest them at the metaphase stage of mitosis when the chromosomes are condensed and visible. A normal karyotype would be 46XX or 46XY.



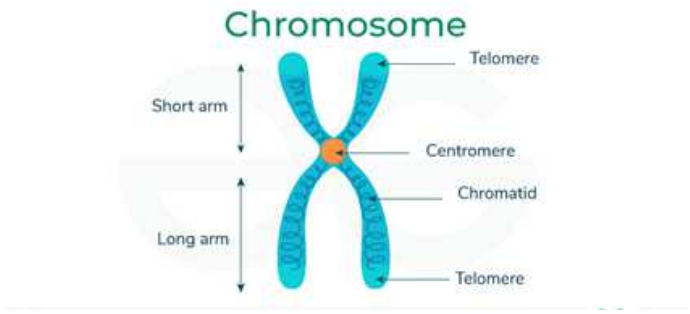
Normal human karyotype. *Source: animalia-life.club*

To form a chromosome, a DNA strand first wraps around histone proteins. It then winds around itself very tightly to form a chromosome shape.



Chromosome structure. *Source: golifescience.com*

Each individual chromosome has a short arm, a long arm, and a centromere connecting the two arms. In notation of karyotypes, the short arm is referred to as “p”, and the long arm is referred to as “q”. When a chromosome duplicates itself, it has two of each arm and the chromosome consists of two sister chromatids. At the very end of each arm is a telomere. A telomere is a protective cap made of repetitive DNA sequences that protect the chromosome from breaking down or fusing with others. However, every time the cell divides the telomeres get shorter and eventually, they are too short for further division so the cell dies.



Features of a chromosome. *Source: geeksforgeeks.org*

Several genes are found on each chromosome at specific loci. Genes are also paired like the chromosomes so the same pair of genes will be found at the same loci on a pair of chromosomes. Separate genes are often shown as separate horizontal bands on a chromosome.

Slim Summary!

- There are 46 chromosomes in a normal somatic diploid cell which includes 22 pairs of autosomes and 1 pair of sex chromosomes;
- Karyotyping can be used to create a visual representation of the chromosomes in the nucleus of a cell and a normal karyotype would be 46XX or 46XY;
- Chromosomes consist of tightly wound DNA around histone proteins. They have a long arm, a short arm and a centromere and have a telomere cap at the ends;
- Genes are found at specific loci on chromosomes and are often depicted as separate bands.

Chapter 2 - Chromosomal abnormalities

Introduction
This chapter explains how numerical and structural chromosomal abnormalities occur and their consequences for the embryo.

Numerical chromosomal abnormalities
Numerical abnormalities occur when there are a different number of chromosomes to the usual 46 chromosomes in a normal diploid cell.

A normal somatic cell with 23 pairs of chromosomes is diploid and is referred to as 2N. This means that a gamete or germ cell would be referred to as N as it is haploid. When there are multiples of N greater than 2N, this is referred to as **polyploidy** and any cells which have exact multiples of N are referred to as euploid. For example, triploidy is when there are three copies of each chromosome instead of two and this would be referred to as 3N. It is the most common form of polyploidy and can occur if an ovum is fertilised by two spermatozoa (dispermy) or if a diploid gamete has been fertilised (failure of maturation of ovum or sperm). Triploidy usually results in a miscarriage. Tetraploidy (4N) can also occur if the first zygotic mitotic division fails to complete and this is not compatible with life.

An individual can also have extra copies or fewer copies of one particular chromosome, resulting in a total number of chromosomes which is not a multiple of N. This is referred to as **aneuploidy**. An extra copy of one particular chromosome is referred to as trisomy and the loss of a copy of a chromosome is referred to as monosomy. Trisomy of certain chromosomes can result in conditions such as Down's syndrome, Edward's syndrome and Patau syndrome which are correspondingly named trisomy 21, trisomy 18 and trisomy 13 based on which chromosome there is an extra copy of. All complete monosomies of autosomes are not compatible with life, but complete monosomy of the X chromosome results in Turner syndrome and is compatible with life. There can also be partial monosomies and partial trisomies in unbalanced translocations which will be discussed in the structural abnormalities section.

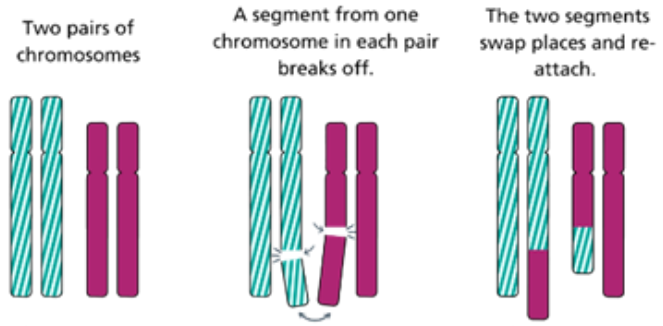
Aneuploidy can occur by **non-disjunction**, which is when chromosomes or sister chromatids fail to separate at anaphase during meiosis. It can also occur by **anaphase lag**, which is when there is delayed movement of chromosomes after separation at anaphase during meiosis. Both of these result in gametes either having an extra copy or one less copy of a chromosome and consequently the fertilised gamete also has this abnormality.

Structural chromosomal abnormalities
Structural abnormalities are characterised by the breakage of chromosomes and changing of the genetic material or DNA. They can be spontaneous, but the rate is usually increased by exposure to mutagens such as ionising radiation and by genetic conditions which affect DNA replication such as Bloom's syndrome.

We will first look at abnormalities which affect a single chromosome. A **deletion** involves the loss of part of a chromosome as part of the DNA sequence is lost. An **inversion** involves a segment of a chromosome's DNA sequence being inverted. Inversions can be pericentric (involving the centromere) or paracentric (not involving the centromere). **Duplications** of chromosomal segments can also occur and these can be in tandem or in inverse with the original segment. An **isochromosome** forms when one arm of a chromosome is duplicated and another arm is lost so that the chromosome has two identical arms.

Abnormalities can also affect two or more chromosomes. **Insertions** involve the breakage of genetic material from one chromosome and the insertion of it into another. **Translocations** are the exchange of material between two chromosomes. These can be **reciprocal** or **Robertsonian**.

Reciprocal translocations involve segments of two non-homologous chromosomes being exchanged. This results in a **balanced translocation** and has no phenotypic effect on the carrier. This is because the amount of genetic material has not changed but it is now in a different location. However, this can cause problems during meiosis and fertilisation.



Reciprocal translocation. *Source: genomicseducation.hee.nhs.uk*

For example, if genetic material from chromosomes 1 and 10 was exchanged, a carrier would have a 1:10 reciprocal translocation and their genetic configuration could be represented as:

1, 1:10, 10, 10:1

This is because the exchange only occurs between one chromosome in each pair, so there is still one normal chromosome in each pair.

The partner of the carrier would have a normal configuration of:

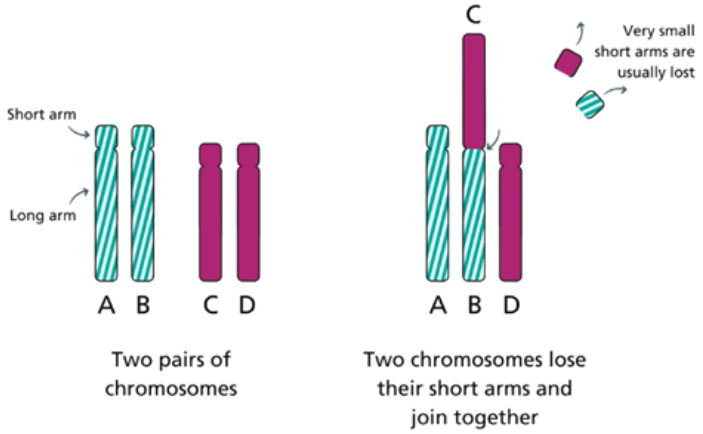
1, 1, 10, 10

Their gametes and possible combinations in the offspring post-fertilisation would be as follows:

Carrier gametes	Partner gametes	Combination in offspring	Outcome
1, 1:10	1, 10	1, 1:10, 1, 10	PT1, PM10
1, 10	1, 10	1, 10, 1, 10	Normal
1, 10:1	1, 10	1, 10:1, 1, 10	PT1, PM10
1:10, 10	1, 10	1:10, 10, 1, 10	PT10, PM1
1:10, 10:1	1, 10	1:10, 10:1, 1, 10	BT
10, 10:1	1, 10	10, 10:1, 1, 10	PT10, PM1

Outcomes of reciprocal translocation carrier's offspring. *Source: SlimAcademy.* PT=Partial trisomy, PM=Partial monosomy, BT=Balanced translocation.

Therefore, the possible outcomes for the offspring are a normal genotype, a partial trisomy of one chromosome and partial trisomy of the other, or a balanced translocation.
Robertsonian translocations involve the fusing of the long arms of two non-homologous chromosomes. This can only occur in **acrocentric** chromosomes which have short arms. These are chromosomes **13, 14, 15, 21 and 22**. The short arms are usually lost and because their genetic sequence is repeated on other chromosomes this does not have an important effect. This again results in a balanced translocation for the carrier but can cause problems during meiosis and fertilisation.



Robertsonian translocation. *Source: genomicseducation.hee.nhs.uk*

For example, if a Robertsonian translocation occurred between chromosomes 13 and 21, a carrier would have a 13:21 Robertsonian translocation and their genetic configuration could be represented as:

13, 21, 13:21

Again, the exchange only occurs between one chromosome in each pair so there is still one normal copy of each chromosome.

The partner of the carrier would have the normal configuration:

13, 13, 21, 21

Their gametes and possible combinations in the offspring post-fertilisation would be as follows:

Carrier gametes	Partner gametes	Combination in offspring	Outcome
13	13, 21	13, 13, 21	M21
21	13, 21	21, 13, 21	M13
13:21	13, 21	13:21, 13, 21	BT
13, 21	13, 21	13, 21, 13, 21	Normal
13, 13:21	13, 21	13, 13:21, 13, 21	T13
21, 13:21	13, 21	21, 13:21, 13, 21	T21

Outcomes of Robertsonian translocation carrier's offspring. *Source: SlimAcademy.* M=Monosomy, T=Trisomy, BT=Balanced translocation.

Therefore, the possible outcomes for the offspring are a normal genotype, a balanced translocation, complete trisomy of one chromosome, and complete monosomy of one chromosome. Complete monosomy of one of the involved chromosomes would be lethal. Trisomy of a chromosome could result in a condition such as Down syndrome which is trisomy of chromosome 21.

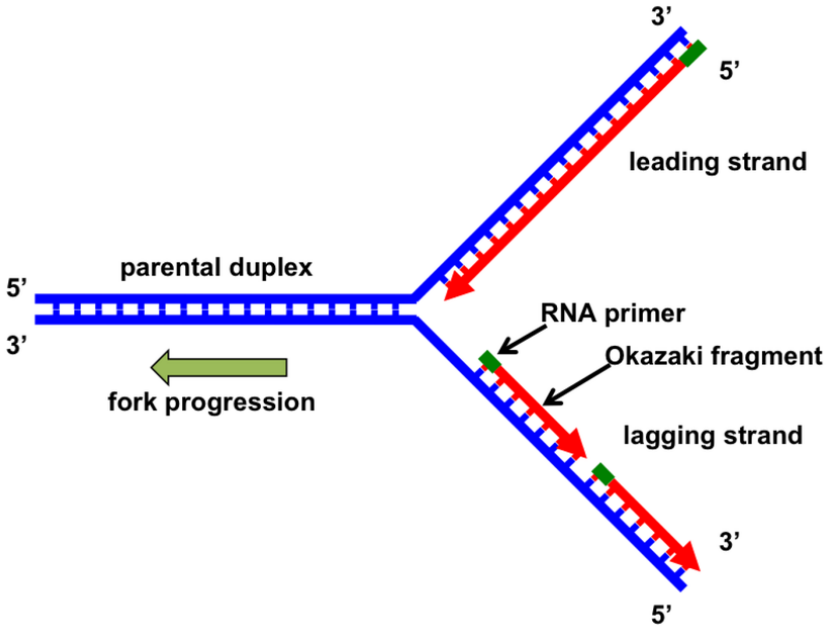
The phenotypic consequences of these abnormalities can vary greatly depending on the amount of genetic material affected and some of them have been mentioned above. They can result in the loss of a protein product or several and cause mild or severe conditions and syndromes.

Slim Summary!

- Numerical abnormalities are when the number of chromosomes differs from the normal 46. They include aneuploidy and polyploidy;
- Structural abnormalities are when breakage occurs in chromosomes which causes the genetic material to change. They can affect single chromosomes (e.g. deletion, inversion, duplication and isochromosome formation) or two chromosomes (e.g. insertions and translocations);
- Translocations can be reciprocal, where segments of two non-homologous chromosomes are exchanged, or Robertsonian, where the long arms of two acrocentric chromosomes fuse;
- These translocations present as balanced translocations in the carrier but can cause complications in their offspring including monosomies and trisomies. An example of this is Down syndrome (trisomy 21) being caused by a parent being a carrier of a Robertsonian translocation.

Chapter 3 - Mitosis and Meiosis

Introduction
Cell division, through mitosis and meiosis, is fundamental for growth, tissue repair, and reproduction. Accurate DNA replication, chromosome segregation, and regulatory mechanisms ensure genetic stability, while errors or age-related changes can impact cellular function and fertility.



DNA Replication. *Source: https://www.researchgate.net/*

The Cell Cycle
The cell cycle is a series of steps where a cell grows, copies its DNA, and finally divides to make new cells. It is mainly divided into two parts→ interphase and the mitotic phase. Interphase is split into G1, S, and G2 phases.

Directionality of DNA
DNA strands have a directional quality which is crucial for replication. The structure of DNA, with a phosphate group attached to the 5′ carbon of the sugar and a hydroxyl (→OH) group attached to the 3′ carbon, means that DNA polymerase can only add new nucleotides to the 3′ end of the RNA primer. This is important as DNA strands are antiparallel, meaning one strand runs in the 5′→3′ direction, while the other runs in the 3′→5′ direction. As a result, DNA polymerase 3 can only synthesize new DNA in the 5′→3′ direction of the base strand, which affects how the leading and lagging strands are replicated.

DNA Replication
DNA replication is essential in keeping genetic information intact as we grow and repair tissue. It begins at multiple origins of replication all at once, making sure the entire genome is copied quickly and accurately

Origin of Replication
Helicase enzymes bind at specific spots along the DNA strand called origins, it unwinds and separates the strands of the double helix by breaking the hydrogen bonds between the base pairs. This action creates replication forks at multiple points on the DNA strand. Following this, RNA primase helps hold the separated DNA strands apart to prevent them from realigning.

Primer Formation
RNA primase lays down short RNA primers in a 5'→3' along the DNA template that runs from the 3' to 5' direction. DNA polymerase 3 builds off the 3' end of the RNA primer and extends DNA continuously so that its directionality is in the 5'→ 3' following the replication fork**.**

Elongation
On the leading strand, DNA polymerase 3 facilitates synthesis smoothly and continuously, as the orientation of the strand allows the enzyme to add nucleotides in the same direction as the movement of the replication fork. Helicase unzips the strand, and DNA polymerase 3 follows this route creating a continuous strand that extends towards the replication fork.
On the lagging strand, the orientation is the opposite, so the DNA template runs 5'→ 3' in direction towards the replication fork. RNA primase lays down short RNA primers in the 5' → 3' direction and DNA polymerase attaches in the 3' end of each RNA primer synthesized DNA in short segments built away from the replication fork to form okazaki fragments. In conclusion, as helicase unwinds a short fragment and RNA polymerase builds a primer fragment, DNA polymerase 3 works to build fragments away from the replication fork on the lagging strand. This repeats continuously until the lagging strand is fully replicated.

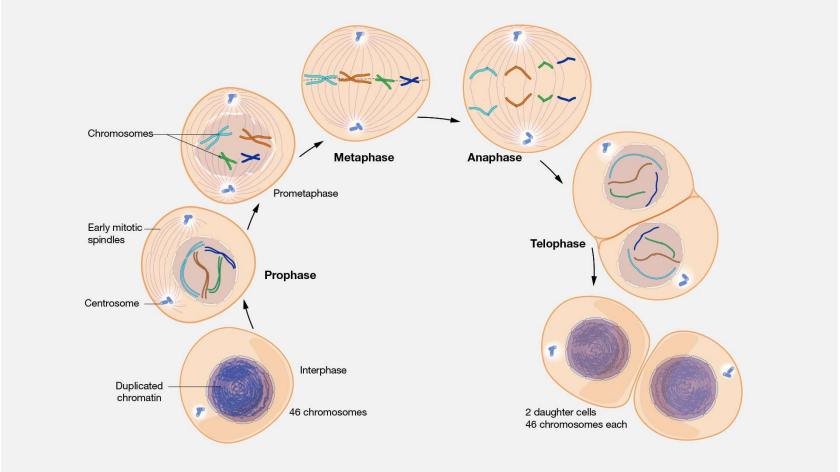
Therefore, the lagging strand is copied in little pieces because of the directional limitation of DNA polymerase 3, while the leading strand is copied continuously.

Primer Removal and Replacement
After elongation, DNA polymerase I removes the RNA primers on the lagging strand between the okazaki fragments and fills the gaps with DNA using the existing DNA as a template to keep the genetic code intact.

Ligation
Finally DNA ligase completes DNA replication on the lagging strand. After DNA polymerase 1 removes the RNA primers and fills the gaps in with DNA, the newly synthesized Okazaki fragments are still discontinuous → it seals the breaks within the sugar→phosphate backbone between these fragments by forming a phosphodiester bond → which joins adjacent nucleotides together.

Although DNA replication is highly accurate due to the proofreading activity of DNA polymerase, errors can occur and result in mutations, disrupting gene function and contributing to genetic disorders.

Mitosis



Mitosis *Source: https://www.genome.gov/*

Interphase (Pre-Mitosis)
Interphase is the phase when a cell performs its normal activities→growing, functioning, and preparing to divide. The nucleus remains whole, and all the cell's DNA is found inside. At a certain stage, the cell replicates its DNA. Each chromosome copies itself, resulting in pairs known as sister chromatids, joined at the centromere. In humans, all 46 chromosomes duplicate, leading to 92 chromatids in total. However, these pairs are not visible during interphase→DNA stays in a loose, tangled form called chromatin. This relaxed state keeps DNA accessible, allowing the cell to make proteins and replicate DNA efficiently. So, interphase is a busy, productive period that prepares the cell for division.

Prophase: The Start of Mitosis
Prophase marks the onset of mitosis. At this stage, things intensify. The nuclear membrane dissolves, releasing the genetic material. Chromosomes, which previously looked like a disorganized mass, begin to coil tightly, making it possible to distinguish the individual sister chromatid pairs. Meanwhile, the spindle apparatus starts to develop. Centrioles move to opposite ends of the cell, and spindle fibers extend between them. By the conclusion of prophase, the spindle stretches across the cell, ready for the next steps→organizing and separating the chromosomes.

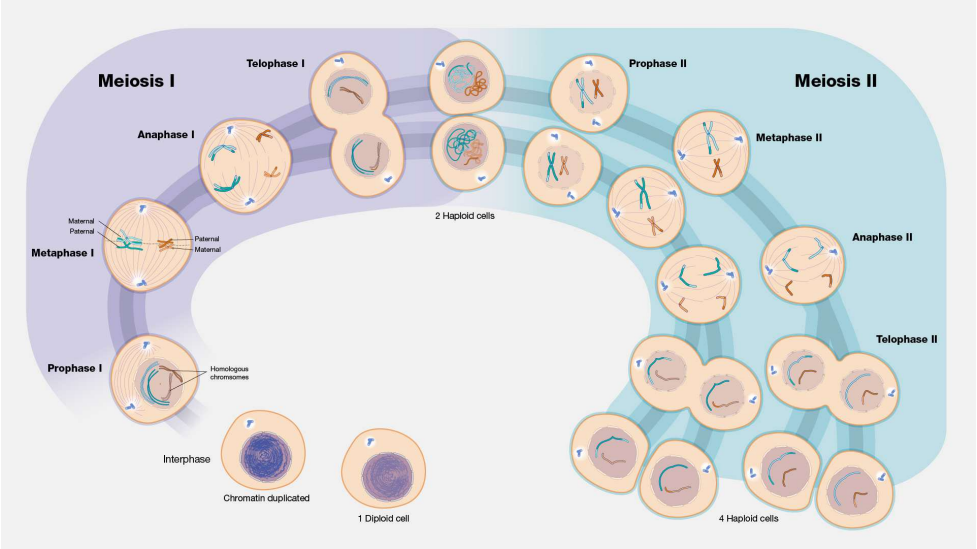
Metaphase
During metaphase, everything aligns. The spindle apparatus is fully assembled, with a centriole at each cell pole. The sister chromatid pairs connect to spindle fibers at the center of the cell, creating the equatorial plate. Each chromatid pair is attached to its own spindle fiber, so in human cells, there are at least 46 spindle fibers→one for each pair. The nuclear membrane is no longer present, letting the chromosomes move freely for the next phase.

Anaphase
Anaphase is where the real movement occurs. Each sister chromatid pair separates at the centromere, and the identical chromosomes travel toward opposite poles of the cell→one set to each side. This ensures both ends of the cell receive a complete set of 46 chromosomes. As the chromosomes progress, the spindle fibers break down behind them. By the end of anaphase, there are 46 chromosomes at each cell pole, matching the original set.

Telophase
Now, the cell begins to conclude division. In telophase, a new nuclear membrane forms around each group of 46 chromosomes at opposite sides of the cell. The cell membrane starts to pinch inward between them→a process called cytokinesis. Eventually, the cell divides into two new daughter cells. Each has a complete set of chromosomes, just like the original cell.

Post-Mitosis: Return to Interphase and the Cell Cycle Continues
After mitosis and cytokinesis are complete, the two new cells re→enter interphase. Their chromosomes unwind into chromatin again, so the cells can resume their work→producing proteins, growing, and carrying out their roles. When the time is right, each new cell will prepare for division once more. This cycle repeats consistently, supporting growth, repair, and upkeep throughout the body.

Meiosis



Meiosis *Source: https://www.genome.gov/*

Interphase (Pre-Meiosis)
Interphase in meiosis is much like interphase in mitosis for the key steps i, ii, and iii. It is a growth and activity phase of the cell cycle, making up most of a cell's life as it moves, feeds, grows, and carries out its normal biological tasks. During this stage, the nuclear membrane remains intact, the nucleus is present, and it contains the DNA. At a certain point, the cell replicates its DNA or chromosomes, turning each chromosome into a sister chromatid pair (SCP). These SCPs are not noticeable during interphase because the chromosomes are unraveled and tangled in the form of chromatin. One major difference between mitosis and meiosis is that most cells do not start meiosis; they continue with mitosis as part of the ongoing cell cycle. Only two types of cells in humans can undergo meiosis→oogonia in females and spermatogonia in males. No other cells can begin meiosis. These two types are special because they can choose between two processes: mitosis to create more oogonia or spermatogonia, or meiosis to create gametes. So, oogonia can go through mitosis to produce more oogonia or undergo meiosis to produce eggs (gametes). Likewise, spermatogonia can use mitosis to create more spermatogonia or meiosis to form sperm (gametes).

Prophase I (of Meiosis I)
Remember that every phase in meiosis occurs twice, since meiosis involves two rounds of cell division. Prophase I shares similarities with prophase in mitosis. It marks the true start of meiosis, during which the nuclear membrane breaks down (though the DNA remains intact). The chromosomes untangle from the chromatin and wind into separate, tightly packed, and clearly recognizable sister chromatid pairs. At this stage, they become visible and countable→there are 46 SCPs (92 chromosomes) in a human cell. Meanwhile, the spindle apparatus begins to form from the centrioles and parts of the cytoskeleton. The two centrioles move to opposite ends of the cell, creating spindle fibers that extend between them. By the end of prophase, the spindle stretches across the entire cell. There are two key differences between meiosis and mitosis in this phase. The first is the formation of tetrads, where homologous SCPs join together. For instance, the two chromosome 1 SCPs from the mother and father (1M and 1D) pair up to create one tetrad made up of two SCPs and four chromosomes. The second difference is crossing over, where chromosomes in each tetrad exchange parts of DNA. This creates four unique, homologous chromosomes, still linked as two SCPs, but no longer strictly maternal or paternal. They are now labeled as 1a, 1b, 1c, and 1d→four unique combinations of the same chromosome pair.

Metaphase I
Metaphase I also shares several aspects with mitosis. The spindle fully forms, consisting of two centrioles at opposite ends of the cell linked by multiple spindle fibers spanning its width. The nuclear membrane is completely dissolved by the start of metaphase. The main difference lies in how the chromosomes are arranged. In meiosis, each tetrad connects to its own spindle fiber, instead of each SCP connecting individually as in mitosis. The tetrads align along the center of the cell, known as the equatorial plate, resulting in at least 23 spindle fibers, each with a tetrad attached at its center. Each chromosome within the tetrad is now unique, following the 1a, 1b, 1c, 1d notation.

Anaphase I
Anaphase I closely resembles anaphase in mitosis, but it differs in that tetrads, not SCPs, separate. Each tetrad splits into its two SCPs, which stay connected. One SCP moves along its spindle fiber toward one pole of the cell, while the other moves toward the opposite pole. Each SCP follows its spindle fiber, and by the end of anaphase I, each side of the cell holds one SCP from each tetrad. There are still 46 SCPs total, with 23 SCPs located at each pole. The chromosomes continue to use the spindle fibers for movement, and as they move, the spindle fibers gradually break down, disappearing completely by the end of anaphase. Thus, anaphase I starts with 46 SCPs arranged as tetrads and ends with 46 SCPs divided into two groups of 23. Each chromosome remains unique, following the 1a, 1b, 1c, 1d notation.

Telophase I
After anaphase I, there is one set of 23 SCPs (46 chromosomes) at each pole of the cell, and each chromosome is unique. A new nuclear membrane forms around each set of SCPs, resulting in two new nuclei within the cell. Then, cytokinesis takes place as the cell membrane begins to pinch inward between the two sets of chromosomes. This process divides the cell into two genetically unique cells, each with 46 chromosomes organized into 23 SCPs. Cytokinesis is the actual physical split of the cell, producing two cells, each with its own nucleus and unique genetic makeup.

Post-Meiosis I
After Meiosis I, there is no return to interphase, and the cell cycle does not repeat. The result of Meiosis I is two genetically unique cells, each with 23 SCPs, where every chromosome is unique. These cells immediately enter Meiosis II.

Prophase II (Initiation of Meiosis II)
At the onset of Meiosis II, both haploid cells derived from Meiosis I immediately proceed into Prophase II, a stage that closely parallels early mitotic prophase. The nuclear envelope disintegrates, and chromosomes undergo further condensation, becoming distinctly visible as pairs of sister chromatids. Spindle apparatus assembly commences from the centrioles and associated cytoskeletal structures. Centrioles migrate to opposing poles within each cell, and spindle fibers extend between them, occupying much of the intracellular space by the conclusion of this phase. Importantly, each cell contains 23 pairs of sister chromatids→half the number present during mitosis→with each chromosome representing a unique genetic composition. This process occurs concurrently in both cells.

Metaphase II
During Metaphase II, the events closely resemble those observed in mitotic metaphase. The spindle fibers complete their assembly, with centrioles positioned at opposite cellular poles. Each pair of sister chromatids attaches to spindle fibers and aligns precisely at the cell's equatorial plane. The distinguishing feature of this stage is the presence of only 23 pairs of chromatids per cell, as opposed to the 46 pairs typical of mitotic cells, and the fact that each chromosome is genetically distinct. Both cells experience this phase in parallel.

Anaphase II
Anaphase II proceeds in a manner analogous to anaphase of mitosis. Cohesin proteins are cleaved, allowing the sister chromatids of each chromosome to segregate and migrate as independent chromosomes toward opposite poles of the cell. As the chromosomes move, spindle fibers disassemble. Consequently, each pole receives 23 single chromosomes, and the chromatid pairs are no longer present. Thus, starting from 23 pairs of chromatids in each of the two cells, the result is 23 single, distinct chromosomes at each cellular pole.

Telophase II
Following the completion of anaphase II, each pole of the cell possesses 23 unique chromosomes, with all chromatid pairs separated. Nuclear envelopes reform around these chromosomes, resulting in the formation of two nuclei per cell. In aggregate, four nuclei arise across the two cells. Subsequent cytokinesis divides each cell into two, yielding a total of four distinct haploid cells, each containing a single nucleus and 23 chromosomes.

Post-Meiosis II
At the conclusion of Meiosis II, four genetically unique haploid cells→referred to as gametes→are produced, each possessing 23 chromosomes. These cells are specialized for participation in sexual reproduction. Their chromosomes decondense into chromatin, but they do not re-enter interphase or undergo further mitotic divisions. Unless fertilization occurs, leading to the formation of a zygote and initiation of a new organismal cell cycle, these gametes will ultimately degenerate and be reabsorbed.

Effect of Aging on Cellular Division

With advancing age, somatic cells exhibit a marked decline in proliferative capacity. In these cells, senescence→a state of irreversible cell cycle arrest→occurs as a consequence of cumulative cellular aging. This phenomenon is primarily driven by telomere attrition; telomeres, which are repetitive nucleotide sequences at chromosomal termini, progressively shorten with each round of DNA replication due to the end-replication problem. Compounding this effect, lifelong exposure to oxidative stress and the accrual of somatic mutations further compromise genomic integrity, thereby reducing tissue regenerative potential, impairing wound healing, and manifesting as canonical phenotypes of organismal aging. Ultimately, certain mutations may disrupt cell cycle regulation, predisposing to oncogenesis as genetically compromised cells acquire the ability to proliferate uncontrollably.

This process is not limited to somatic cells; gametogenic cells are similarly subject to age-associated decline. In females, both the quantity and quality of oocytes diminish over time, with the incidence of meiotic errors such as nondisjunction increasing significantly. Such chromosomal segregation anomalies underlie conditions like trisomy 21 (Down syndrome). Males also experience declines in reproductive parameters, characterized by reductions in sperm count, motility, and increased sperm DNA fragmentation. These changes collectively contribute to decreased fertility and elevate the risk of transmitting genetic abnormalities to offspring.

Telomeres thus occupy a central role in cellular aging. Each mitotic event results in incremental telomere shortening, as DNA polymerase cannot fully replicate chromosomal ends. When telomeres reach a critically short length, cells undergo replicative senescence. While the enzyme telomerase is capable of elongating telomeres, its expression is repressed in most differentiated somatic cells. Conversely, malignant cells frequently reactivate telomerase, circumventing replicative limits and facilitating unchecked cellular proliferation, a hallmark of tumorigenesis.

Slim Summary!

- Mitosis produces two genetically identical diploid cells for growth and repair, whereas meiosis generates four genetically unique haploid gametes for sexual reproduction;
- Aging and telomere shortening reduce cell division efficiency, increase mutation risk, and affect reproductive cell quality, contributing to decreased fertility and potential disease development.

Chapter 4 - Principles of genetic screening

Introduction
Genetic screening during pregnancy is an important part of prenatal care, aimed at identifying pregnancies at higher risk for chromosomal abnormalities, especially Down Syndrome (Trisomy 21). These screenings use a combination of maternal blood tests and ultrasound measurements, and sometimes fetal cell analysis, to assess risk. They do not provide a definitive diagnosis but estimate the likelihood of a condition. Screening is usually performed in both the first and second trimesters, allowing early detection and helping clinicians and parents make informed decisions.

First Trimester Screening (Combined Test)
During the first trimester, clinicians generally employ a combined screening approach consisting of maternal serum analysis and ultrasonographic assessment of nuchal translucency (NT), which quantifies the subcutaneous fluid accumulation at the posterior aspect of the fetal neck. The serum biomarkers evaluated include Pregnancy-Associated Plasma Protein-A (PAPP-A) and free beta subunit of human Chorionic Gonadotropin (free β-hCG). PAPP-A is integral to placental and fetal development via upregulation of Insulin-like Growth Factor 3 (IGF-3). Reduced PAPP-A levels are indicative of impaired placental function, which correlates with intrauterine growth restriction and is frequently observed in cases of Down Syndrome. Elevated free β-hCG concentrations are also characteristic of Down Syndrome, reflecting altered trophoblastic function and persistence of the corpus luteum, which is essential for sustained progesterone production and pregnancy maintenance.

The ultrasonographic measurement of NT is utilized to detect increased fluid accumulation, which is associated with anomalies in lymphatic drainage, congenital cardiac defects, or aberrations in connective tissue→all of which are prevalent in fetuses with Down Syndrome. A normal NT measurement is less than 3.5 mm; values exceeding this threshold are suggestive of chromosomal aneuploidy. The synthesis of these findings→decreased PAPP-A, increased free β-hCG, and elevated NT constitutes the basis of the first trimester combined screening protocol for Down Syndrome. It is crucial to underscore that these results yield a probabilistic risk assessment rather than a definitive diagnosis.

Second Trimester Screening (Quadruple Test)
In the second trimester, typically between gestational weeks 15 and 20, the quadruple test is performed. This assay quantifies four distinct analytes in maternal serum: Alpha-Fetoprotein (AFP), total hCG, Unconjugated Estriol (uE3), and Inhibin A. Decreased AFP levels are associated with Down Syndrome, whereas elevated AFP may indicate open neural tube defects such as anencephaly. Increased hCG and Inhibin A levels, in conjunction with reduced uE3, are also indicative of Down Syndrome; the latter reflects compromised fetoplacental steroidogenesis, as estriol synthesis requires contributions from both the fetus and the placenta. The quadruple test refines the risk stratification established by first trimester screening and provides a more comprehensive assessment of chromosomal anomaly risk.

Non-Invasive Prenatal Testing (NIPT)
Non-Invasive Prenatal Testing (NIPT) is available from ten weeks of gestation onward. This methodology involves the analysis of cell-free fetal DNA (cffDNA) circulating in maternal plasma to detect common aneuploidies, including Trisomy 21, Trisomy 18, and Trisomy 13. NIPT demonstrates high sensitivity and specificity and is noninvasive, requiring only a maternal blood sample. As such, it serves as an effective tool for risk assessment and can inform the need for further confirmatory diagnostic procedures.

Integrated Screening
Integrated screening combines data from the first trimester combined test and the second trimester quadruple test. This integrative approach enhances the accuracy of risk estimation and reduces the likelihood of false-positive results.

Diagnostic Tests
Should screening results indicate an elevated risk for Down Syndrome, confirmatory diagnostic testing is warranted. Chorionic Villus Sampling (CVS) is conducted between gestational weeks 10 and 13 and entails the collection of placental villous tissue via transcervical or transabdominal approaches for cytogenetic analysis. Amniocentesis is typically performed between weeks 13 and 20, wherein a sample of amniotic fluid containing fetal cells is aspirated for chromosomal evaluation. Both CVS and amniocentesis provide definitive diagnoses of chromosomal abnormalities, including Trisomy 21.

Slim Summary!

- First and second trimester screening, including the combined and quadruple tests, evaluates maternal serum markers and fetal ultrasonographic parameters to estimate the risk of Down Syndrome and other chromosomal anomalies;
- Non-invasive prenatal testing (NIPT) and confirmatory diagnostic procedures, such as chorionic villus sampling and amniocentesis, provide higher accuracy or definitive diagnoses when screening indicates elevated risk.

Chapter 5 - Physiological changes during pregnancy and monitoring

Introduction
This chapter describes the physiological changes during pregnancy and how they are monitored.

Physiological Changes and monitoring
Several physiological changes to different organ systems and tissues occur during pregnancy due to the higher rate of metabolism. These can be monitored during the routine visits to clinics which are detailed in the section on healthcare for pregnancy in the UK.
In the cardiovascular system, plasma volume, cardiac output, stroke volume and heart rate all increase whilst serum albumin concentration and serum colloid osmotic pressure decrease. There is also an increase in coagulation factors and fibrinogen in the blood. Tidal volume and minute ventilation increase in the lungs.

During a visit, measurements such as pulse and respiratory rate along with **blood pressure** would be taken to monitor them and check for abnormalities. The normal range for blood pressure would be below 120/80 mmHg and a blood pressure above 140/90 would be classed as high and may indicate **pre-eclampsia**.

The pregnant person experiences nausea and vomiting as well as gastrointestinal reflux due to prolonged small bowel transit time and delayed gastric emptying. The gut microbiome changes and influences the developing microbiome of the fetus. Pregnancy symptoms like this would be discussed during visits and medications could potentially be prescribed if symptoms are severe.
A placenta specific hormone called placental lactogen is released which causes insulin resistance and reduces maternal glucose uptake so that more glucose can be absorbed by the fetus for growth. This may lead to a condition called **gestational diabetes** where there is excessive mobilisation of glucose and natural insulin resistance. **Blood glucose levels** would be regularly tested during visits to check for signs of gestational diabetes such as high glucose levels.

Immunological transfer – Trophoblast-derived signals create a pro-inflammatory environment in early pregnancy. These signals cause maternal immune cell recruitment and most antibodies cannot cross the placenta. However, IgG antibodies are able to cross via the IgG receptors on syncytiotrophoblast cells. These maternal IgG antibodies can last up to 12 weeks of age. The fetus is protected from immune attack from the mother by the display of HLA-G proteins on trophoblast cells.

Whilst some immune responses in the mother are enhanced, there is suppression of other parts of the immune system to protect the fetus from immune attack, so this causes the pregnant person to be more susceptible to infection by pathogens. **Urine tests** are done to check for abnormalities such as protein in the blood which may indicate an infection or pre-eclampsia.
As the fetus grows, **fundal height** (level of the fundus of the uterus) notably changes.

Gestational Age (Weeks)	Fundal height landmark
12	Pubic symphysis
20-22	Umbilicus
36	Xiphisternum
37-40	2-3cm below xiphisternum (regresses as fetal head descends)

Changes in fundal height. *Source: SlimAcademy*

This is regularly measured at each visit using a measuring tape and a fundal height measurement chart. This allows the overall growth of the fetus to be monitored throughout the pregnancy as well as its development via **ultrasound scans**.

Slim Summary!

- Physiological changes in the cardiovascular system cause an increase in pulse and respiratory rate which can be measured during visits to monitor them. Blood pressure is also important to be monitored to check for signs of pre-eclampsia;
- Pregnancy symptoms such as vomiting and gastrointestinal complications can be discussed and medications prescribed if they are severe;
- Blood tests and urine tests are also important to test blood glucose levels and check for protein in the urine;
- Fundal height is also measured regularly to monitor the growth of the fetus.

Chapter 6 - Risks during pregnancy

Introduction
Pregnancy induces significant physiological changes in the maternal body, most of which facilitate fetal development. However, maladaptations can occur, resulting in clinically significant complications for both the mother and fetus. Major maternal risks include gestational diabetes mellitus, pre-eclampsia, postpartum hemorrhage, placental abruption, anemia, and uterine atony.

Gestational Diabetes Mellitus (GDM)
Gestational diabetes mellitus arises when pregnancy-associated hormones disrupt normal glucose metabolism. Human placental lactogen (hPL) induces insulin resistance, leading to hyperglycemia. Although the maternal pancreas increases insulin secretion to compensate, this response is sometimes inadequate. Cortisol further stimulates hepatic gluconeogenesis, while progesterone exacerbates cellular insulin resistance. The cumulative effect is elevated maternal blood glucose concentrations, culminating in GDM if regulatory mechanisms are insufficient. GDM increases the risk of fetal macrosomia, complicating labor and delivery.

Pre-Eclampsia
Pre-eclampsia typically manifests after 20 weeks' gestation, characterized by sustained hypertension (blood pressure >140/90 mmHg) and proteinuria, indicating renal involvement. Under normal conditions, vasodilatory hormones such as nitric oxide and relaxin promote vascular relaxation and remodeling. Cytotrophoblast invasion and the subsequent remodeling of maternal spiral arteries are essential for adequate uteroplacental perfusion.

In pre-eclampsia, this vascular remodeling is defective; spiral arteries remain narrow and unresponsive to vasodilatory stimuli, resulting in reduced placental perfusion and hypoxia. The hypoxic placenta releases anti-angiogenic factors that inhibit vascular endothelial growth factor (VEGF) and placental growth factor (PIGF), impairing endothelial function and reducing nitric oxide bioavailability. This pathophysiology exacerbates systemic hypertension and induces widespread endothelial injury. Disease progression may lead to eclampsia, characterized by maternal seizures, which poses significant morbidity and mortality risk. Magnesium sulfate is the standard prophylactic and therapeutic agent for seizure control in this context.

Postpartum Hemorrhage (PPH)
Postpartum hemorrhage is defined as excessive maternal bleeding following delivery. The predominant etiology is uterine atony, wherein the uterus fails to contract effectively after placental expulsion. Normally, myometrial contractions constrict the spiral arteries at the placental implantation site, achieving hemostasis. In uterine atony, persistent vasodilation results in continued bleeding from these vessels, which can rapidly progress to hypovolemic shock and is a leading cause of maternal morbidity and mortality postpartum.

Placental Abruption
Placental abruption refers to the premature separation of the placenta from the uterine wall prior to delivery. This event can precipitate significant maternal hemorrhage and acute disruption of fetal oxygen and nutrient supply, posing immediate risk to both mother and fetus. Predisposing factors include maternal hypertension, abdominal trauma, and abnormal placental implantation. Placental abruption constitutes an obstetric emergency due to its potential for rapid decompensation.

Anemia in Pregnancy
Anemia is highly prevalent in pregnancy, attributed to increased maternal demand for hematopoietic nutrients required to support expanded blood volume and fetal development. Insufficient intake or absorption of iron or folate leads to decreased hemoglobin synthesis, resulting in reduced oxygen-carrying capacity and increased susceptibility to infection. Severe anemia is associated with increased risk of preterm labor and low birth weight.

Other Maternal Complications
Additional maternal complications may arise from maladaptive vascular responses intended to maintain placental perfusion. For example, chronic vasoconstriction in pre-eclampsia can result in long-term endothelial dysfunction and vascular injury.

Risks to the Fetus
Maternal complications directly impact fetal outcomes. Adverse sequelae include preterm birth, congenital anomalies, stillbirth, macrosomia, and neonatal abstinence syndrome secondary to maternal substance use. Impaired placental function, as seen in pre-eclampsia or abruption, can result in chronic fetal hypoxia, intrauterine growth restriction, or perinatal mortality.

Slim Summary!

- Maternal complications such as gestational diabetes, pre-eclampsia, uterine atony, placental abruption, and anemia increase risks for both mother and fetus, including hypertension, hemorrhage, hypoxia, fetal growth restriction, preterm birth, and perinatal mortality;
- Understanding the pathophysiology, risk factors, and clinical management of these conditions is essential to optimize maternal and fetal health and to provide effective monitoring and interventions throughout pregnancy.

Chapter 7 - The first trimester

Introduction

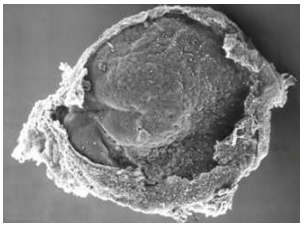
This chapter describes the events in the first trimester of a pregnancy, in chronological order. Major morphogenic events are summarized. This was covered in Theme 1b but has been repeated here for consolidation.

Moment	Event
Day 3/4	Morula formed
Day 5/6	Blastocyst formed
Day 8/9	Implantation, Bilaminar Disc forms
Day 14/15	Gastrulation
Day 15	Embryo elongates
Day 17	Nervous system starts to develop, cephalic and caudal regions form
Day 19	Neural tissue forms, somites start to appear
Day 22	Heartbeat starts
Day 27-28	Circulation starts
Week 4	Otic and optic placodes visible, forelimb then hindlimb buds visible
Week 5	Embryo is approximately 2mm long
Week 7	Hand and foot visible
Week 8	Digits appear
Week 9	All essential structures initiated, growth period begins
Week 12	First trimester ends

General timeline. *Source: Slimacademy*

Human gastrula

The embryo changes shape between days 15 and 19 to form a **cephalic** (head) and **caudal** (tail) end in an **elongated** structure compared to the previous disc-like structure.

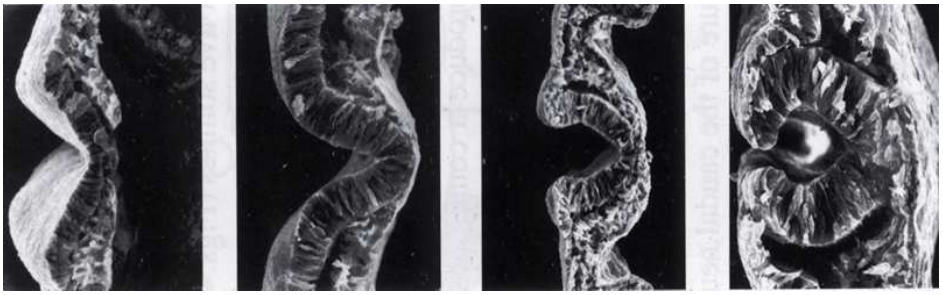


Embryo at Days 15-17. *Source: https://php.med.unsw.edu.au/embryology/index*

Embryo at Days 17-19. *Source: https://php.med.unsw.edu.au/embryology/index*

Nervous System
After gastrulation around 19-21 days post-fertilisation the nervous system starts to develop. Neural tissue forms from the **ectoderm** with the neural plate forming in the **cephalic region** and the **neural tube** forming along the dorsal region which will go on to form the spinal cord.

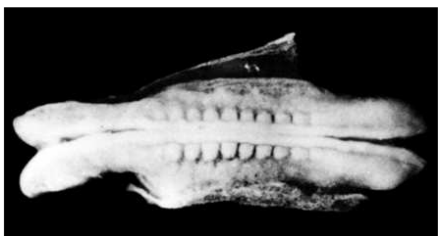
The neural plate rolls to form a tube and **neural crest cells** form at the boundary with the ectoderm at 23-26 days post-fertilisation. There are two openings in the tube called **neuropores** at the cephalic and caudal ends. These can fail to close and cause defects such as **anencephaly** and **spina bifida** respectively.



Formation of the neural tube. *Source: https://php.med.unsw.edu.au/embryology/index*

Neural crest cells migrate out of the dorsal neural tube and are incorporated in many tissues to form **neurones** and supporting cells in the **peripheral nervous system**.

Somite Development
Somites start to form around Day 19 alongside the neural tube and they develop successively from anterior to posterior. There are 44 pairs of somites in total and they go on to form muscle, vertebral and rib bones.



Somite development. Source: https://php.med.unsw.edu.au/embryology/index

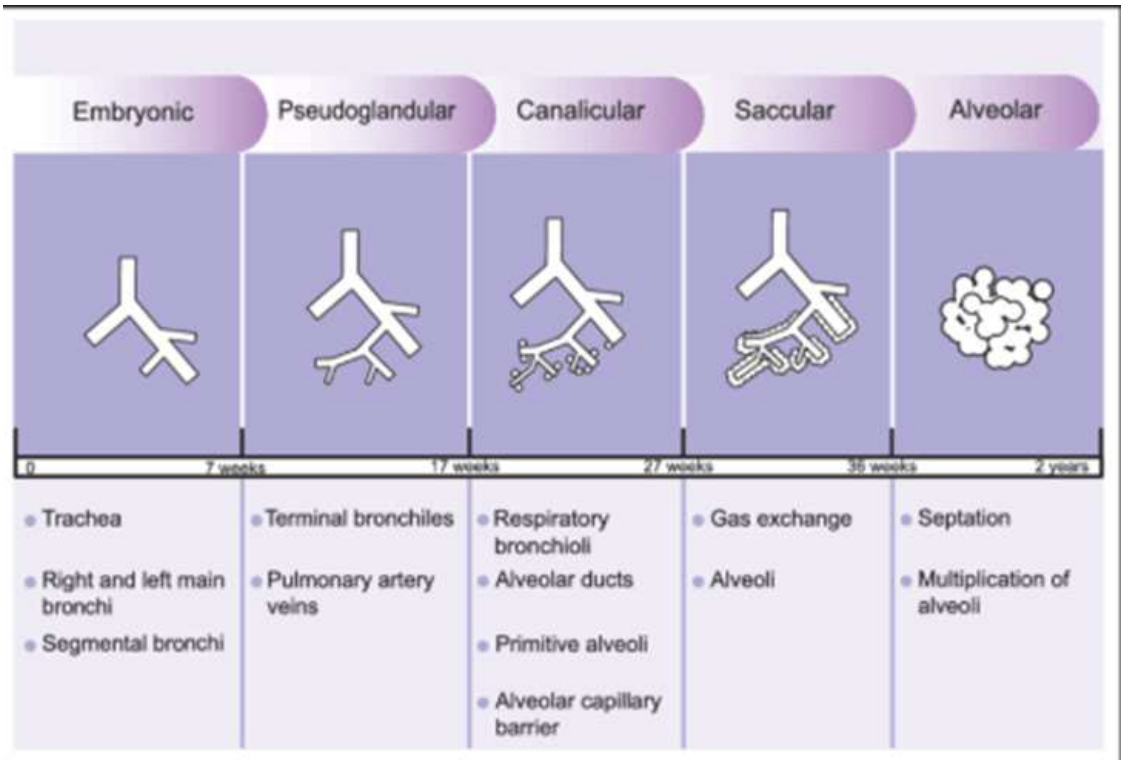
Ear and eye development
The ears and eyes develop from ectodermal thickenings on the surface of the embryo called placodes. The **otic placode** is visible from the 4th week and it disappears in the 5th week as the inner ear components form. The **optic placode** is visible from the end of the 4th week.

Limb development
Limb buds start to become visible from early in the 4th week with the **forelimb bud** being present before the **hindlimb bud**. The patterning of these buds is important for specifying the proximal, distal, dorsal and ventral axes in the development of the **digits**.

During weeks 7 and 8 the outgrowth of the buds progresses to form distinguishable hands and feet. There are condensations of cartilage which show precursors of digits and apoptosis occurs between the digits to separate them.

Heart development
The ventral surface of the heart is clearly visible from around day 22 and the development of the heart continues through to week 8. The heart is the first organ to function as the heartbeat begins at day 22 and circulation begins at day 27. The function of the heart is essential for the continued growth of the fetus for the required nutrients to reach developing cells.

Lung development
The lungs develop via a process called branching morphogenesis in five phases: embryonic, pseudoglandular, canalicular, saccular and alveolar. Different germ layers contribute to different parts. The endoderm and mesoderm supply most of the alveoli, the ectoderm contributes to the neural innervation and the mesoderm contributes to the musculoskeletal support.

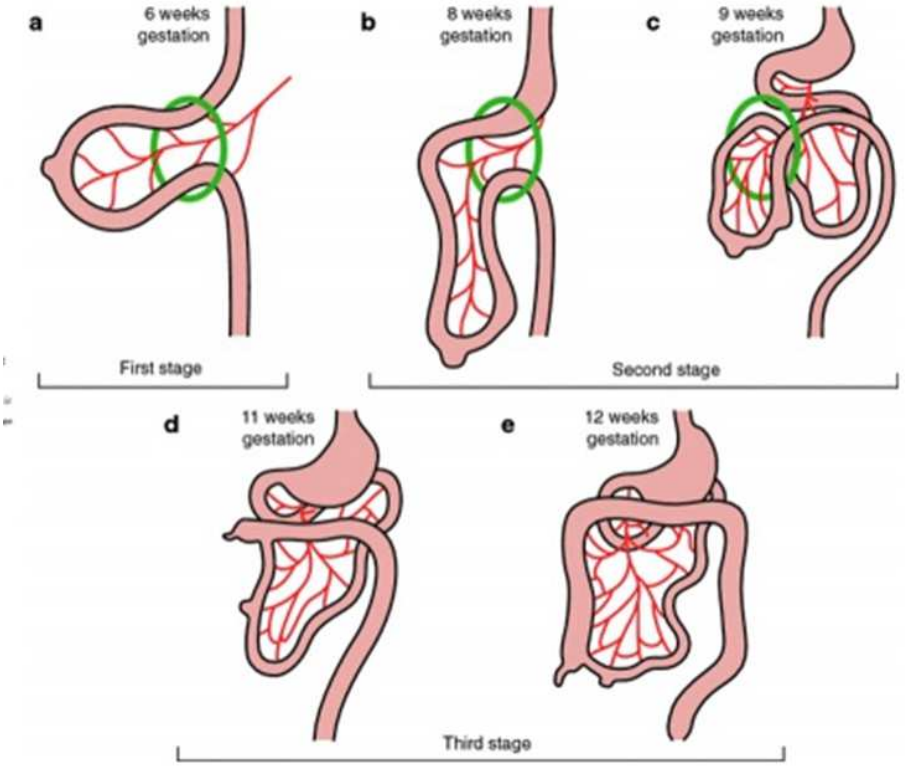


Stages of lung development. *Source: www.researchgate.net*

Kidney development
The kidneys also develop via branching morphogenesis in close association with the genitals from the **urogenital ridge**. There are three stages to the development: **pronephros** (day 18), **mesonephros** (day 24) and **metanephros** (day 35).

Gastrointestinal system development
The GI system originally arises from the **endoderm** in week 2 or 3. From week 4 onwards, different germ layers contribute to different parts: the **mesoderm** contributes to the mesentery, smooth muscle and blood vessels and the **ectoderm** contributes to the enteric nervous system.

There are three divisions which go on to form different structures. The **foregut** forms the oesophagus, oral cavity, trachea, stomach and pancreas. The **midgut** forms the small intestine and the ascending colon which is herniated during development. **Herniation** means the intestines develop outside the abdominal wall initially and then rotate to acquire the adult morphology. The **hindgut** then forms the remainder of the colon and rectum.



Development of the midgut. *Source:* www.researchgate.net

Slim Summary!

- During the first trimester (weeks 1–12), embryonic development advances rapidly. The process commences with the morula and blastocyst, progresses through gastrulation, and continues into organogenesis. By approximately week 9, the embryo has transitioned into a fetus, marking an important developmental milestone;
- Neural development begins as early as day 19, when the neural plate forms and subsequently folds into the neural tube. Timely closure of the neuropores is critical, as failure can result in congenital defects such as anencephaly or spina bifida. Alongside the neural tube, somites appear and will eventually differentiate into muscles, vertebrae, and ribs, establishing much of the musculoskeletal framework;
- Sensory organ development initiates early. The otic and optic placodes, which give rise to the ears and eyes, are evident by week 4. Limb buds also emerge during this period, and through processes such as apoptosis, digits are separated by week 8;
- The heart stands out as the first functional organ, beginning to beat around day 22. By day 27, it establishes circulation, ensuring the efficient delivery of nutrients necessary for ongoing embryonic growth.

Chapter 8 - Pregnancy Healthcare

Introduction
This chapter describes how healthcare for normal pregnancy and birth is structured in the UK and then compares it to when the pregnancy is not following a normal course.

Structure of care
UK pregnancy healthcare is directed by three groups of professionals: midwives (community/hospital), GPs (community) and obstetricians (hospital). Many people will book midwives who carry out most of the care duties during pregnancy. All pregnant people have at least two scan visits. If abnormalities are detected during tests and scans, further investigations may be performed.
There are four normal phases of care:

- First trimester (0-12 weeks) – This is when booking happens which involves creating a risk assessment, dating of different milestones in the pregnancy and initial screening to check development. Investigations include testing for urine infections, HIV, hepatitis B, syphilis and red cell antibodies. An ultrasound is performed around the 10-12th week which is both transabdominal and transvaginal to check location, visibility and the number of fetuses.
- Second trimester (12-25 weeks) – A **fetal anomaly assessment** and ultrasound scan is performed at 20 weeks as the fetus should be fully formed with no further organogenesis. The scan can screen for syndromes such as Down's syndrome and other structural abnormalities.
- Third trimester (25-40 weeks) – This mainly involves monitoring with a **fetal growth assessment** and considering obstetric complications. Blood pressure and urine are measured to check for pre-eclampsia.
- Puerperium (delivery – 6 weeks after) – Breast feeding, recovery and neonatal care are monitored. The hand over to a health advisor begins after 4 weeks.

In someone's first pregnancy, there are ten visits and an anomaly scan at 20 weeks. From the second pregnancy onwards, there are seven visits and still an anomaly scan at 20 weeks.

Timing of visits/scans

Week	Specifics
10	Booking and ultrasound
16	
20	Ultrasound
25*	
28	
31*	
34	
36	
38	
40*	
41	

Timing of visits/scans. *Source: SlimAcademy* *Only for first pregnancy

During antenatal screening, if abnormalities are detected then treatment can be given, or further investigations can be performed depending on the situation.

If an **infectious disease** is detected such as HIV, hepatitis B or syphilis, then early treatment can be given to prevent **vertical transmission** to the fetus.

The pregnant person may also be aware of genetic risks such as inherited disorders in their family so these would be specifically screened for.

Blood tests can detect levels of **biochemical markers** such as beta-HCG, PAPP-A, inhibin A and alpha fetoprotein which can indicate certain conditions. For example, higher concentrations of beta-HCG and inhibin A and lower concentrations of PAPPA-A and alpha fetoprotein can indicate Down's syndrome. High alpha fetoprotein levels can indicate spina bifida.

Further tests would then be performed if abnormal biochemical markers were detected. **Chorionic villus sampling** involves taking a sample of the placenta and is performed between the 10^{th} and 13^{th} week. **Amniocentesis** involves taking a sample of amniotic fluid and analysing fetal cells' chromosomes. It is performed later between the 15^{th} and 20^{th} week. Both of these investigations are invasive and carry a 1% risk of miscarriage. **Non-invasive pre-natal testing** can also be done which involves taking a blood sample and finding fragments of fetal DNA to analyse. This can be done from the 9^{th} week.

If an abnormality was confirmed to be found and would significantly harm the life of the fetus or pregnant person, then they would be given the option to terminate the pregnancy.

Slim Summary!

- Fetal anomaly and growth assessments are performed during every pregnancy to check for abnormalities;
- If abnormalities are detected then further investigations such as biochemical marker tests, chorionic villus sampling and amniocentesis can be performed to confirm diagnosis of specific conditions;
- Severe abnormalities may allow the pregnancy to be terminated.

Chapter 9 - Cultural assumptions and screening

Introduction
Cultural, religious, and sociocultural factors shape whether families pursue screening, accept invasive testing, or consider pregnancy termination.

Perceptions of disability significantly influence approaches to prenatal screening and diagnostic testing. In certain societies, disability is associated with considerable stigma, social exclusion, and negative stereotypes. Families embedded within such cultural frameworks are more likely to pursue prenatal screening and, upon receiving diagnoses such as Down syndrome, may opt for pregnancy termination. However, this is not universally applicable. In other cultural or religious contexts, there is an inherent belief in the intrinsic value of all human life, regardless of disability status. Within these groups, disability may be conceptualized as a normative variation of human existence or as an integral component of a broader existential framework. Consequently, families with these perspectives frequently decline prenatal screening or invasive testing, and the option of pregnancy termination is generally precluded irrespective of diagnostic outcomes.

Additionally, broader sociocultural factors, such as prevailing attitudes toward decision-making authority, levels of trust in medical professionals, and the relative importance of collective versus individual autonomy, further inform interpretations of risk and influence reproductive decision-making processes. For this reason, healthcare providers must exercise particular sensitivity when discussing prenatal screening with patients. The objective should not be to direct patients toward any specific course of action, but rather to facilitate informed decision-making by respecting familial values, providing comprehensive information, and offering appropriate support tailored to each family's unique context.

Slim Summary!

- Sociocultural factors, including trust in medical professionals and decision-making norms, require healthcare providers to practice sensitive, non-directive counseling that supports informed, family-centered choices.

Chapter 10 - Influences of decisions about screening

Introduction
Antenatal screening decisions are influenced by personal, cultural, ethical, social, and medical factors. Effective communication and ethical guidance from healthcare professionals are essential for informed choices.

The decision-making process regarding antenatal screening is multifaceted, encompassing not only medical considerations but also personal, cultural, ethical, and social dimensions. Individual beliefs about disability, pregnancy termination, and the meaning of parenthood can significantly influence attitudes toward screening. Cultural and religious values also play a substantial role; for example, some individuals may perceive destiny as predetermined, while others may express concerns regarding the moral implications of genetic testing. Each person brings a unique background and perspective to these decisions.

Socioeconomic factors, such as financial resources and access to healthcare, are also critical determinants. Limited affordability or insufficient information may lead individuals to forgo screening entirely. Psychological factors, including anxiety related to potential results or apprehension about invasive procedures, further complicate the decision-making process. From a clinical standpoint, variables such as maternal age, family medical history, and assessed risk levels are significant considerations.

Furthermore, the manner in which healthcare professionals communicate information about antenatal screening→including the clarity, openness, and accuracy regarding its capabilities and limitations→profoundly affects patient understanding and decision-making. Ultimately, it is incumbent upon healthcare providers to adhere to core ethical principles: respecting patient autonomy, promoting beneficence, minimizing harm, and ensuring justice. These ethical obligations are essential to facilitating genuinely informed choices about antenatal screening and to ensuring that patients do not experience coercion.

Slim Summary!

- Individuals' decisions are influenced by a range of factors, including personal beliefs, cultural and religious background, psychological state, financial considerations, and medical factors such as age, family history, and perceived risk;
- Engaging in transparent communication and adhering to fundamental ethical principles, such as respect for autonomy, beneficence, non-maleficence, and justice, facilitates decision-making processes that align with individuals' values and preferences.

Chapter 11 - Risk and probability

Introduction
This chapter explains the different ways of calculating and presenting risk and probability.

Presenting probability
There are several ways to represent the chances of something happening in terms of probability. Different terminology is used in research studies to compare outcomes of trials and evaluate how different factors affect the risk of something happening, such as contracting a certain disease.

Risk is the probability of something happening and it doesn't always have negative connotations. It is often represented as a percentage or decimal. **Odds** is the ratio of something happening to it not happening. For example, if the odds of an event occurring are 3 to 1 then there is a 0.75 probability or risk of it happening.

Prevalence is the probability of having a condition at a particular point in time. **Incidence** is the probability of a new case of the condition in a particular population over a particular time period. **Relative risk** is the relative likelihood of an outcome in people exposed or not exposed to a risk factor. **Absolute risk** is the risk of developing a condition over a certain time period.
When comparing risk, **risk ratios** or **odds ratios** can be used to represent relative risk and it is important to state which is being used and differentiate them.

!! **Risk/Odds ratio** = Risk/odds in one group divided by Risk/odds in other group
Risk/odds absolute difference = Risk/odds in one group – Risk/odds in other group

Risk and odds ratios will be similar if the chance of the event is very small.
For example: A 35-year-old woman has a 1 in 800 chance of having a baby with Down's syndrome. A 50-year-old woman has a 1 in 250 chance.

The risk ratio would be:
(1/250) / (1/800) = 3.20

The odds ratio would be:
(1/249) / (1/799) = 3.21

Therefore, from this data, a 50-year-old would be 3.20 or 3.21 times more likely to have a baby with Down's syndrome depending on if risk or odds was used.

Slim Summary!

- Risk is the probability of something happening, whereas odds is the ratio of an event occurring to it not occurring;
- Relative risk is calculated using risks or odds to find the relative likelihood of an outcome in people exposed or not exposed to a risk factor.
- Prevalence is the probability of having a condition at a particular point in time, whereas incidence is the probability of a new case of the condition in a particular population over a particular time period.

Chapter 12 - Perception of risk

Introduction
Perceptions of risk are influenced by both personal and contextual factors.

Personal factors include age, past experiences, health literacy, psychological state, and cultural or religious beliefs. For example, a parent who has previously had a child with a genetic condition may perceive recurrence risk as higher than statistical estimates. Emotional responses such as anxiety or optimism bias also shape risk interpretation. Contextual factors include family and community attitudes, societal norms about disability, access to healthcare and reliable information, quality of counselling, media influence, and socioeconomic or policy-related conditions. Overall, perceptions of risk reflect not only objective probabilities but also individual experiences, beliefs, and social context, all of which are important in clinical decision-making and antenatal counselling.

Slim Summary!

- Personal factors include age, past experiences, health literacy, psychological state, and cultural or religious beliefs;
- Contextual factors include family and community attitudes, societal norms about disability, access to healthcare and reliable information, quality of counselling, media influence, and socioeconomic or policy-related conditions.

Chapter 13 - Abortion

Introduction
This chapter summarises the legal criteria specified in the Abortion Act in the UK and describes the ethical implications for patients and professionals.

The Abortion Act
The original **Abortion Act 1967** has undergone several recent changes but still remains the main legislation for abortion in the UK. It allows an abortion if the pregnancy is less than **24 weeks** (originally 28 weeks) and **two** registered practitioners agree that continuing the pregnancy will risk damage to the physical or mental health of the pregnant person or children. However, an abortion can be performed even after 24 weeks if there is **severe risk** to the pregnant person's life or if the child will be born with a **severe abnormality**.

In June 2025, abortion was **decriminalised** as the House of Lords voted to amend the Crime and Policing Bill. It used to have to be performed directly following the guidelines in the Act in a clinic or hospital, otherwise the individuals involved would risk criminal prosecution. Despite decriminalisation, the medical framework in the Act remains in place and should be followed by medical professionals. The full impact and implementation of the amendment is also yet to be released.

A doctor or medical professional is allowed to **opt out** of performing an abortion if they conscientiously object and believe it is not in the patient's best interest. However, they can give support and information to consult another practitioner.

Medical professionals should consider the four pillars of medical ethics when making decisions about abortion. These are: **autonomy, beneficence, non-maleficence** and **justice**. Both the life of the pregnant person and fetus should be considered and patients should be fully informed of the consequences of their decision.

Slim Summary!

- Abortion is allowed in the UK if the person is less than 24 weeks pregnant and two registered practitioners agree that continuing the pregnancy will risk damage to the physical or mental health of the pregnant person or children;
- If there is a severe abnormality then abortion may be allowed even after 24 weeks;
- Medical professionals should consider the ethical implications and physical and mental consequences for both the pregnant person and fetus when making decisions about abortion. They are allowed to opt out of performing an abortion but should still provide support and information to consult another practitioner.

Afterword

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