Preface

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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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Cell cycle, cancer genetics, and malignancy

Chapter 1 - Cell proliferation, differentiation, and death

Introduction

This chapter describes the basic concepts of cell proliferation, cell differentiation, and cell death with reference to the development of cancerous tissue.

Cell proliferation

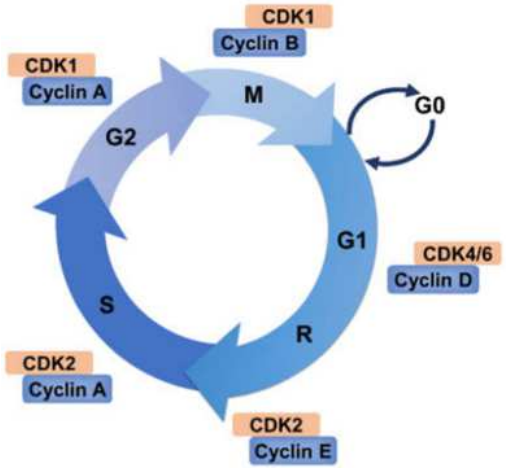
This is the process of increasing cell numbers through cell growth and division. When cells become enlarged and increase in functional capacity, this is called **hypertrophy**. The opposite of this would be **atrophy**, where cells shrink and decrease in activity. This may happen due to a loss of blood supply or stimulation. Cells can also undergo enhanced division and increase in number, which is termed **hyperplasia**. If cells decrease in number, this would be **aplasia**.

Cell differentiation

Cell differentiation is when cells change from one cell type to another, and this often happens in the development of tumours. **Metaplasia** is a reversible change where one type of mature cell is replaced by another that can better withstand the environment or stress that a tissue is under. For example, in a smoker's respiratory tract the ciliated columnar epithelium is replaced by stratified squamous epithelium as an adaptive response. In **dysplasia**, metaplastic cells proliferate and cause the growth of abnormal tissue, which marks the start of the early reversible cancer stage. Then in **neoplasia**, the proliferation becomes uncontrolled, and this stage is irreversible. A neoplasm or tumour forms and this can be malignant or benign. The loss of structural differentiation within cells is common in malignant tumours and this is called **anaplasia**.

Control of the cell cycle

Throughout the cell cycle, there are checkpoint stages to ensure that proliferation is occurring normally. At the first gap phase (G1), the DNA is checked for errors and energy and nutrient levels in the cell are checked to make sure they are sufficient for successful replication. After the DNA synthesis stage, the DNA is checked in the second gap phase (G2) to ensure that it has replicated correctly. The cell then undergoes mitosis, and in the metaphase stage of mitosis, there are checks to make sure that the chromosomes are aligned correctly and that they are attached to the metaphase plate. If there are any errors detected at these checkpoints, the cell is sent to the G0 phase until the error is corrected, or the cell is destroyed. This G0 phase is also known as the quiescent phase and is when the cell is neither dividing nor preparing to divide.



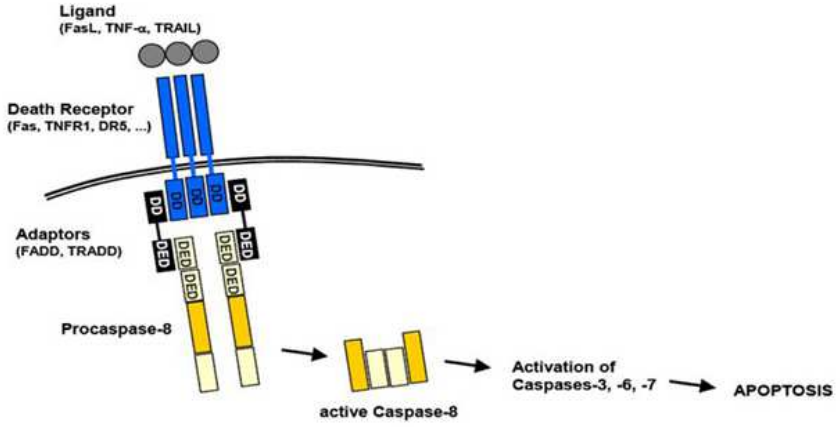
Stages of the cell cycle. *Source: facts.net*

There are proteins called cyclins that are paired with cyclin-dependent kinases (CDKs) which they activate to regulate different parts of the cell cycle. The pairs of cyclins and CDKs are found labelled in the diagram above with the corresponding stages of the cycle which they regulate. **Cyclin B** which activates **CDK1** particularly peaks during mitosis. CDK1 phosphorylates several proteins when activated to perform specific functions during mitosis. For example, **histone 1** is involved in chromosome condensation, **MAP** (microtubule-associated protein) allows stable microtubules to form in spindle formation, and **lamin** is involved in the breakdown of the nuclear envelope.

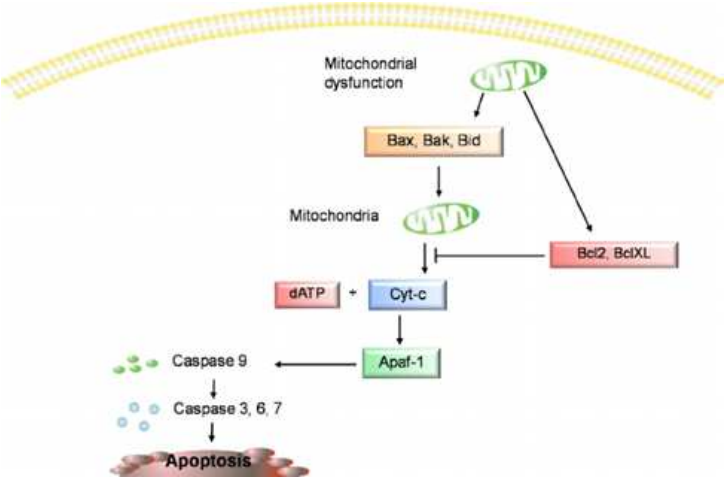
Cell death

There are several ways by which cell death can occur. One of these is **necrosis**, where there is an injury which causes accidental premature cell death. When cells undergo trauma, their cellular contents are released, and this induces an inflammatory response. This can also happen due to an infection or lack of blood flow. Necrosis is common in late-stage cancer.

Another way cells are destroyed is by **apoptosis**, also known as programmed cell death. This is the organised destruction of a cell initiated by signals from a neighbouring cell or the cell itself due to sensed internal damage. There is no inflammatory response. Apoptosis is regulated by death receptors (extracellular) and Bax proteins (intracellular). Cells such as cytotoxic T cells can send extracellular signals e.g. TNF-α to form ligands on death receptors of cells that need to be destroyed. This activates a death induced signalling complex to activate caspase enzymes which carry out apoptosis. Bax proteins regulate apoptosis via intracellular signals as they bind to and make holes in mitochondria to cause cytochrome C to be released from them. Cytochrome C activates Apaf-1 which then activates caspase enzymes to carry out apoptosis.



Extracellular regulation of apoptosis via death receptors. *Source: creative-diagnostics.com*



Intracellular regulation of apoptosis via Bax. *Source: researchgate.net*

Slim Summary!

- Cell proliferation can involve cells enlarging (hypertrophy) and also cells increasing in number (hyperplasia);
- Cell differentiation is when cells change from one cell type to another and cells may go through phases of metaplasia, dysplasia, neoplasia, and aplasia as a tumour develops;
- Within the cell cycle, there are checkpoints which are regulated by cyclins and CDKs to ensure cells replicate normally;
- Cell death may occur unintentionally by necrosis or in a programmed manner by apoptosis.

Chapter 2 - Sporadic and inherited cancers

Introduction

This chapter explains the differences between sporadic and inherited cancers and describes the distinguishable features.

Sporadic cancers are usually caused by environmental factors. They tend to have a later onset and there is no significant inherited predisposition. It usually involves **somatic** genetic alterations, which are DNA mutations that occur in somatic cells (any body cells apart from gametes). This usually causes just one tumour initially. When the genes of patients with sporadic cancers are analysed, both copies of a tumour suppressor gene are inactivated in their tumour cells, but in their other cells both copies are normal and activated. Sporadic cancers are very common and account for about 99% of cancer diagnoses.

Familial or inherited cancers have a significant inherited predisposition. This is mostly due to inherited mutated **tumour suppressor genes** and there will usually be an identifiable Mendelian pattern of inheritance. These inherited mutated genes generally cause syndromes, so there are usually several symptoms and multiple tumours of the same type, and sometimes there are other tumour types. The tumour cells of these patients have both copies of the tumour suppressor gene inactivated, but in addition their other cells also have one copy of the gene inactivated. This explains why the risk of developing tumours is higher as the cells of these individuals only have one active copy of the tumour suppressor gene rather than two. This also causes the average age of onset to be much earlier in inherited cancers. These types of cancers are much rarer and account for about 1% of cancer diagnoses.

Slim Summary!

- Sporadic cancers are very common as they are usually caused by environmental factors and involve random mutations in somatic cells;
- Inherited cancers are usually caused by mutated tumour suppressor genes being passed down to offspring, making affected individuals at a much higher risk of developing cancer.

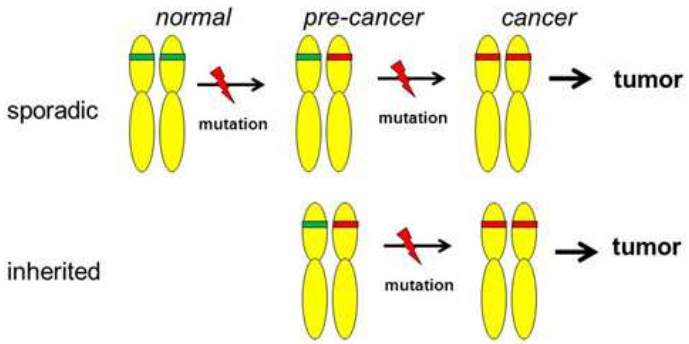
Chapter 3 - Inherited predisposition to cancers

Introduction

This chapter describes the concept of predisposition to cancers, and describes examples of inherited predispositions, such as BRCA1 and BRCA2 genes. As explained in the previous chapter, mutated tumour suppressor genes can be inherited and this greatly increases the risk of developing cancer.

Knudson's two-hit hypothesis

Knudson's two-hit hypothesis explains how two genetic "hits" are required for the development of cancer, as both copies of the tumour suppressor gene must be inactivated for cancer to develop. In sporadic cancers, both of these mutations occur randomly in somatic cells. In inherited cancers, the first hit is already inherited in all cells, so only one more mutation in somatic cells is required to develop cancer.



Knudson's two-hit hypothesis. *Source: blogspot.com*

There are several tumour suppressor genes which can become mutated. Mutated MMR (mismatch repair) genes lead to Lynch syndrome, where there is increased risk of colorectal and other cancers, and mutated TP53 genes lead to Li-Fraumeni syndrome, where several types of cancer are developed at a young age.

BRCA genes

BRCA genes are tumour suppressor genes which can become mutated and significantly increase the risk of specific cancers such as breast and ovarian cancer. They have a major role in repairing double-strand DNA breaks through **homologous recombination**, so if they are mutated then it leads to defective DNA repair. BRCA mutations are inherited in an **autosomal dominant** pattern, and their prevalence is about 1 in 200-400 people. This prevalence is higher in Ashkenazi Jews at about 1 in 40.

There are two main BRCA genes, which are BRCA1 (on chromosome 17) and BRCA2 (on chromosome 13). They are both very large genes. BRCA1 is involved in linking the detection of DNA damage with repair mechanisms, whilst BRCA2 acts as a mediator of homologous recombination. BRCA1 mutations carry a 40-72% lifetime risk of breast cancer, and BRCA2 mutations carry a slightly lower risk but are still significant. BRCA1-related breast cancer tends to be triple negative breast cancer and usually has a slightly younger onset, with cancer types being more limited to breast and ovarian. In contrast, BRCA2-related breast cancer is more similar to

non-BRCA-related breast cancer, and there is more variation in types including breast, ovarian, prostate, pancreatic, and gastrointestinal cancers.

Those with a confirmed BRCA mutation or those at risk of inheriting mutated BRCA genes receive annual MRI screening, and some may choose to have a prophylactic mastectomy. If a patient with breast cancer has a known BRCA mutation, then PARPi treatment can be used, which inhibits the action of poly(ADP) ribose polymerase. This enzyme repairs single-strand breaks in DNA, so when this is inhibited in cancer cells which already have mutated BRCA genes, it greatly increases the risk of cell death. This allows cancer cells to be destroyed.

Slim Summary!

- Knudson's two-hit hypothesis explains how two genetic "hits" are required for the development of cancer, as both copies of the tumour suppressor gene must be inactivated for cancer to develop;
- BRCA genes are tumour suppressor genes that play an important role in homologous recombination, so if they become mutated, affected individuals are at a much higher risk of developing breast and ovarian cancers.

Chapter 4 - Oncogenes

Introduction

This chapter explains the role of oncogenes in cancer development and gives examples of oncogenes.

Proto-oncogenes are genes which control normal cell growth. When these genes become mutated with a gain in protein function, then they become oncogenes, which cause uncontrolled cell growth. They may become mutated due to inherited factors or environmental factors such as exposure to carcinogens. Proto-oncogenes code for proteins which have normal growth functions in cells. These include growth factors, cell surface receptors, signal transduction system components, transcription factors, nuclear proteins, and cyclins and CDKs.

An example of one is the MYC protein, which is a transcription factor that when increased in function causes cells to enlarge (hypertrophy). The MYC gene can become overexpressed and become an oncogene if it is translocated to a more active region of the DNA, for example from a non-coding part to a coding part. Other examples of proto-oncogenes include k-Ras, PRL-3, ER, and HER2.

Slim Summary!

- Proto-oncogenes usually regulate normal cell growth, but when mutated they become oncogenes and cause uncontrolled cell growth;
- Examples include MYC, k-Ras, PRL-3, ER, and HER2.

Chapter 5 - Tumour suppressor genes

Introduction

This chapter discusses the role of tumor suppressor genes that act as the cell's protective mechanism against mutations. Information on different types of tumour suppressor genes and their mechanism of mutation will be introduced here.

Tumor suppressor genes are essential limiters of cell growth and division. They help prevent uncontrolled proliferation and repair DNA damage, acting as a safeguard mechanism against cancer. When they function normally, these genes stop abnormal cells from multiplying and make sure that cells with genetic errors are either repaired or eliminated. Mutations in TSG lead to a loss of their function, allowing cells to divide uncontrollably. In order for TSG's to become inactive, both copies of the gene must be inactivated.

Gatekeeper Genes

Gatekeeper genes, a type of TSG that has a primary role in regulating the cell cycle. These genes monitor checkpoints and can trigger programmed cell death (apoptosis), if DNA damage is detected. For example, RB1 (Retinoblastoma protein) encodes the RB protein, a gatekeeper that regulates the G1 to S phase transition in the cell cycle. In early G1, RB binds to E2F transcription factors and prevents it from activating genes needed for DNA replication. So, the cell is kept in G1 phase, unable to enter the S phase in which DNA replication is facilitated. Progression into S phase occurs when Cyclin D/CDK4/6 and Cyclin E/CDK2 phosphorylate RB. This changes RB's shape, releasing E2F, and allowing it to activate DNA replication genes. In cancer, RB is hyperphosphorylated, and therefore inactivated, so it cannot bind to E2F to keep it inactive. This results in uncontrolled progression into S phase and excessive cell division, contributing to tumour development. Similarly, TP53 (p53 protein) detects DNA damage and either halts cell cycle progression or initiates apoptosis to eliminate defective cells. By controlling these checkpoints, tumor suppressor genes prevent the accumulation of genetic errors that could lead to cancer.

Caretaker Genes

Caretaker genes maintain genomic stability by repairing DNA damage. BRCA 1 and BRCA 2 use homologous recombination (HR) to fix dangerous double-strand breaks by using the sister chromatid as an identical template, allowing the cell to repair the break accurately without introducing mutations. Mismatch repair (MMR) corrects small errors that occur during DNA replication, such as incorrectly paired bases or small insertion–deletion loops. Proteins like *MLH1* and *MSH2* recognize these mismatches, remove the faulty DNA segment, and replace it with the correct sequence.

Landscaper Genes

In addition to regulating the cell itself, some tumor suppressor genes, known as landscaper genes, influence the surrounding tissue environment to prevent conditions favorable for tumor growth. For instance, PTEN regulates cellular signaling pathways, such as PI3K/AKT, to inhibit uncontrolled growth and survival, while SMAD4 modulates the tumor-suppressive effects of

TGF-β signaling. By maintaining a balanced microenvironment, these genes reduce the likelihood of abnormal cells gaining a growth advantage.

Mechanisms of Tumor Suppressor Gene Inactivation

Cancer can develop when TSG's are inactivated through various mutations. Mutations can be sporadic, acquired during a person's lifetime (e.g., UV-induced), or inherited, present in every cell from birth, which predispose individuals to cancer. The two-hit hypothesis, first proposed by Knudson, explains that both alleles of a tumor suppressor gene must be inactivated for tumor formation. The first hit may be an inherited or spontaneous mutation, while the second hit can occur through deletion, point mutation, or epigenetic silencing such as promoter hypermethylation. Point mutations are a small change in the DNA that produces a non-functional protein. Loss of heterozygosity (LOH) occurs if one allele is already mutated, the remaining normal allele can be deleted or mutated, completely removing tumor suppressor activity.Epigenetic silencing – DNA modifications (like methylation) or histone changes (hypoacetylation) turn off the gene without changing the sequence.

Consequences of Tumor Suppressor Gene Inactivation

When tumor suppressor genes fail, cells lose the ability to control the cell cycle, allowing uncontrolled proliferation. DNA damage accumulates because caretaker genes are unable to repair errors, increasing the mutation rate. Damaged cells evade apoptosis, surviving and dividing despite harmful genetic changes. Inactivation of landscaper genes can also alter the microenvironment, promoting tumor growth and invasion. Examples of these effects include the loss of RB1 in retinoblastoma, TP53 mutations in over 50% of cancers, and BRCA1/2 mutations that predispose to breast and ovarian cancers.

Slim Summary!

- Tumor suppressor genes (TSGs) prevent cancer by controlling the cell cycle, repairing DNA, and maintaining a healthy tissue environment. Gatekeeper genes like RB1 and TP53 regulate checkpoints and apoptosis, while caretaker genes such as BRCA1/2 and MLH1/MSH2 repair DNA damage. Landscaper genes help maintain a balanced microenvironment that discourages tumor growth.
- Cancer develops when both copies of a TSG are inactivated through mutations or epigenetic changes. According to the two-hit hypothesis, loss of function can occur through point mutations, loss of heterozygosity, deletions, or gene silencing (e.g., promoter methylation).

Chapter 6 - Replication error repair genes

Introduction

This chapter introduces the importance of replication error repair genes in serving as an essential defence against cancer by preserving the accuracy of DNA replication. Their loss leads to genomic instability and increases the risk of tumour formation.

Replication error repair genes, also known as mismatch repair (MMR) genes maintain DNA accuracy during cell division. When DNA is replicated, sometimes the wrong nucleotide is inserted by DNA polymerase, creating insertion-deletion loops. During S phase and G2 phase of the cell cycle, MMR genes act as a proofreading mechanism that detects and corrects these mistakes before they become permanent mutations. Key genes in this pathway include MLH1, MSH2, MSH6, and PMS2, which work together to recognise mismatched bases, remove the incorrect DNA segment, and replace it with the correct sequence using DNA polymerase. MMR genes prevent the gradual accumulation of mutations, particularly in regions called microsatellites which are short, repetitive sequences of DNA which are highly prone to mutation.

When replication error repair genes are defective, microsatellite instability (MSI) develops, meaning that short repetitive DNA sequences become highly variable due to incorrect replication. MSI is a hallmark of a hereditary disorder called Lynch syndrome which associated with colorectal and endometrial cancers. Without functional MMR proteins, cells accumulate mutations in both tumour suppressor genes and oncogenes, accelerating cancer development.

MMR dysfunction resulting in cancer formation follows Knudson's two-hit hypothesis. Lynch syndrome is an autosomal dominant condition whereby an individual inherits one mutated MMR gene. However, cancer typically develops when the second, normal copy of the gene is damaged later in life, resulting in complete loss of mismatch repair function, accumulation of replication errors, and ultimately tumor formation.

Slim Summary!

- Function of MMR genes like MLH1, MSH2, MSH6, and PMS2 correct DNA replication errors, especially in microsatellites, preventing mutation accumulation.
- Loss of MMR function causes microsatellite instability (MSI), leading to mutations in tumor suppressor genes and oncogenes, which accelerates cancer development.
- Lynch syndrome is autosomal dominant; individuals inherit one mutated MMR gene, and cancer arises when the second copy is inactivated later in life, resulting in complete loss of repair function.

Chapter 7 - DNA repair genes

Introduction

This chapter discusses DNA repair genes which are essential for maintaining genomic stability. They are classified based on the type of DNA damage they correct and the repair mechanisms they mediate.

Mismatch repair (MMR) genes, such as *MLH1*, *MSH2*, *MSH6*, and *PMS2*, correct errors introduced during DNA replication, including mismatched bases and small insertion-deletion loops. The repair process involves recognition of the mismatched bases, excision of the incorrect DNA segment, and synthesis of the correct sequence. Defects in MMR genes result in microsatellite instability (MSI) and are commonly associated with Lynch syndrome and colorectal cancer.

Base excision repair (BER) addresses small lesions caused by oxidation, alkylation, or deamination. Key genes involved include *OGG1*, *APEX1*, and *XRCC1*. In BER, a damaged base is first removed and DNA polymerase fills in the gap before DNA ligase seals the strand. Impairment of BER can lead to accumulation of mutations and is linked to cancers such as lung and colorectal cancer.

Homologous recombination (HR) repair is responsible for fixing double-strand breaks (DSBs) in an error-free manner using a sister chromatid as a template. Critical genes include *BRCA1*, *BRCA2*, and *RAD51*. The process begins with recognition of the DSB, removal of DNA ends to produce single-stranded DNA, and inclusion of the sister chromatid to lead accurate repair. Defects in *BRCA1* or *BRCA2* impair HR, significantly increasing the risk of breast, ovarian, and prostate cancers.

Overall, defects in DNA repair genes lead to genomic instability, accumulation of mutations, chromosomal rearrangements, and aneuploidy. Faulty repair mechanisms can activate proto-oncogenes such as *RAS* and *MYC*, or inactivate tumor suppressor genes like *TP53*, accelerating cancer progression. Inherited defects in DNA repair genes are associated with cancer predisposition syndromes, including Lynch syndrome (*MLH1*, *MSH2* mutations), and hereditary breast and ovarian cancer syndrome (*BRCA1*, *BRCA2* mutations.

Slim Summary!

- Mismatch repair (MMR) genes (*MLH1, MSH2, MSH6, PMS2*) fix replication errors, base excision repair (BER) genes (*OGG1, APEX1, XRCC1*) fix small base lesions, homologous recombination (HR) genes (*BRCA1, BRCA2, RAD51*) repair double-strand breaks using a sister chromatid template.
- Consequences of defective repair: Loss of DNA repair function leads to genomic instability, accumulation of mutations, chromosomal rearrangements, and activation of oncogenes or inactivation of tumor suppressor genes, driving cancer progression.

Chapter 8 - Chromosomal abnormalities and cancer

Introduction

Chromosomal abnormalities are structural or numerical changes in chromosomes that disrupt normal gene function, leading to the activation of oncogenes, inactivation of tumor suppressor genes, and genomic instability. Chromosomal abnormalities can be broadly categorized into numerical abnormalities (changes in chromosome number) and structural abnormalities (rearrangements of chromosome segments).

Numerical Abnormalities

Numerical abnormalities, or aneuploidy, involve the gain or loss of whole chromosomes. For example, trisomy (extra chromosome) can increase the prevalence of oncogenes, while monosomy (loss of a chromosome) can reduce the effectiveness of tumor suppressor genes.

Structural abnormalities include deletions, duplications/amplifications, translocations, inversions, and insertions. Deletions often remove tumor suppressor genes. Duplicated or amplified regions can overexpress oncogenes, such as *HER2* amplification in breast cancer. Translocations can generate fusion genes with oncogenic potential, exemplified by the Philadelphia chromosome (BCR-ABL) in chronic myeloid leukemia or MYC translocations in Burkitt lymphoma. Inversions and insertions can disrupt gene integrity or regulatory regions and lead to malignant transformation.

Cancer development is closely linked to genomic instability, which exists in two main forms: chromosomal instability (CIN) and microsatellite instability (MIN). CIN refers to structural and numerical chromosomal abnormalities that allow oncogene activation, tumor suppressor gene loss, and an increased mutation rate. MIN arises from defective mismatch repair (MMR) genes such as *MLH1* and *MSH2*, leading to errors in the microsatellite region of DNA sequences. These genomic instabilities facilitate the accumulation of mutations required for cancer progression.

The process of tumorigenesis involves the sequential addition of mutations in both oncogenes and tumor suppressor genes, typically requiring 4–7 critical alterations. These genetic changes allow cells to acquire the six capabilities of cancer. Successful angiogenesis → which is the proliferation of blood vessels to support tumour growth. A disregard for growth signals which sustains proliferative signaling. Evading growth suppressors and becoming insensitive to tumor suppressor signals. Resisting cell death by avoiding apoptosis despite DNA damage. Enabling continuous replication by maintaining proliferation potential. Invading surrounding tissues through activation of invasion and metastasis.

Defects in DNA repair genes, such as MMR genes (*MLH1, MSH2*), BER genes (*OGG1, XRCC1*), or HR genes (*BRCA1, BRCA2*), allow mutations to accumulate unchecked. Combined with chromosomal abnormalities, these defects disrupt normal cellular regulation and drive cancer progression. Inherited mutations in DNA repair or tumor suppressor genes further predispose individuals to cancer, as seen in Lynch syndrome (MMR defects) and hereditary breast and ovarian cancer (*BRCA1/2* mutations).

Slim Summary!

- Numerical (aneuploidy) and structural (deletions, amplifications, translocations) changes disrupt tumor suppressor genes and activate oncogenes.
- CIN (chromosomal instability) and MIN (microsatellite instability) from defective DNA repair genes (*MLH1, MSH2, BRCA1/2*) accelerate mutation accumulation.
- 4–7 key mutations enable cells to sustain growth, evade suppression and apoptosis, induce angiogenesis, and invade tissues, driving multistage tumor development.

Chapter 9 - Anatomy of the breast

This will be covered in a separate anatomy booklet.

Chapter 10 - Lymphatics and breast cancer

Introduction

This chapter describes the lymphatic drainage of the breast and upper limb, and explains how it affects breast cancer diagnosis, staging, and treatment.

About 75% of the lymph from the breast drains into the axillary lymph nodes, but some lymph does drain into the parasternal and abdominal lymph nodes. The two lateral quadrants of the breast are mainly drained by the axillary lymph nodes, the superior medial quadrant is drained by the parasternal nodes, and the inferior medial quadrant is drained by the abdominal nodes. The upper limb has deep and superficial lymphatic vessels which accompany the deep and superficial veins. These also drain into the axillary lymph nodes. The arrangement of the axillary lymph nodes will be covered in more detail in the anatomy booklet.

The lymphatic drainage of the breast is clinically significant as cancer cells often spread via the lymphatic system. The involvement of lymph nodes is assessed in breast cancer staging using the TNM system. The status of lymph nodes is staged from N0 to N3 when assessed by a doctor. N0 means that no lymph nodes can be felt, N1 means there are palpable swollen nodes, N2 means the lymph nodes are swollen and lumpy, then N3 means that swollen nodes are palpable near the collarbone. Breast cancer which spreads to the lymph nodes would be **invasive**, as the cancer cells would have started to invade surrounding tissues. Common types of breast cancer include invasive ductal carcinoma and invasive lobular carcinoma. Ductal carcinoma may also be "**in-situ**" in its early form before it becomes invasive.

If there is lymph node involvement then more extreme treatment may be needed, such as chemotherapy and lymph node dissection surgery to remove swollen lymph nodes. This is to remove any remaining cancer cells and prevent more tumours from forming.

Slim Summary!

- The breast is mainly drained by the axillary lymph nodes and cancer cells may spread to lymph nodes via the lymphatic drainage system;
- Lymph node involvement may require more extreme treatment such as lymph node dissection surgery combined with chemotherapy.

Chapter 11 - Aetiology and epidemiology of breast cancer in the UK

Introduction

This chapter outlines the aetiology and epidemiology of breast cancer in the UK.

Breast cancer is much more common in women and is the most common cancer diagnosed in women, but it is still possible for men to get breast cancer. The risk of breast cancer increases with age, and it is more common in white women. Family history and genetic predispositions, which were mentioned in previous chapters, are also high-risk factors. Early menarche also increases the risk of breast cancer as there is increased exposure to oestrogen, and in contrast child-bearing decreases risk. Other lifestyle factors such as high alcohol consumption, heavy smoking, and obesity also increase risk. Approximately 56,900 new cases of breast cancer are diagnosed every year in the UK and there has been a slight increase in incidence rates in the last decade.

Slim Summary!

- Risk factors of breast cancer include female gender, early menarche, poor diet, old age, and heavy smoking or drinking.

Chapter 12 - Formation and spread of cancers

Introduction

This chapter describes the basic mechanisms by which cancerous tumours form and spread. A neoplasm or tumour is an abnormal mass of tissue which has exceeded and uncoordinated growth compared to normal tissues and persists in the same manner even after cessation of the stimuli which evoked the change. Benign tumours grow by expansion and displace adjacent tissue, whilst malignant tumours grow by infiltrating local tissues and spread to other parts of the body.

Formation of a tumour

As mentioned in chapter 1, the differentiation and proliferation of abnormal cells can eventually lead to the formation of a tumour. A stimulus such as a carcinogen may cause metaplasia. For example, in a smoker's respiratory tract the ciliated columnar epithelium is replaced by stratified squamous epithelium as an adaptive response. The metaplastic cells then undergo dysplasia, where they proliferate and abnormal tissue builds up. This marks the start of the early reversible cancer stage. The proliferation eventually becomes uncontrolled and irreversible in neoplasia, where a neoplasm is formed. Cancer is any malignant tumour and can affect various types of tissue. A **carcinoma** is a malignant tumour of epithelial tissue, and a **sarcoma** is a malignant tumour of stromal tissue.

Spread of malignant tumours

The original malignant tumour is referred to as the **primary tumour**, and any tumours which form from this are known as **secondary tumours**. The spread of a malignant tumour may be local, or it may be classed as metastasis, where there is distant spread and formation of a secondary tumour. There are several routes of metastasis. Epithelial malignancies typically invade the **lymphatic system** and grow in lymph nodes. Tumours can also invade the bloodstream (**hematogenous** spread), with emboli being filtered out in capillary beds, and this typically happens in stromal malignancy and later stages of epithelial malignancy. **Transcoelomic** spread is when cancer cells cross body cavities such as the peritoneal or pleural spaces and this is common in colorectal and ovarian cancers. Tumours may also spread within epithelium, for example in Paget's disease of the nipple, vulva and anus, or in epithelial lined spaces such as the alveoli. Sites of metastases include the lymph nodes, liver, lungs, bones, brain, endocrine glands, and the skin.

Slim Summary!

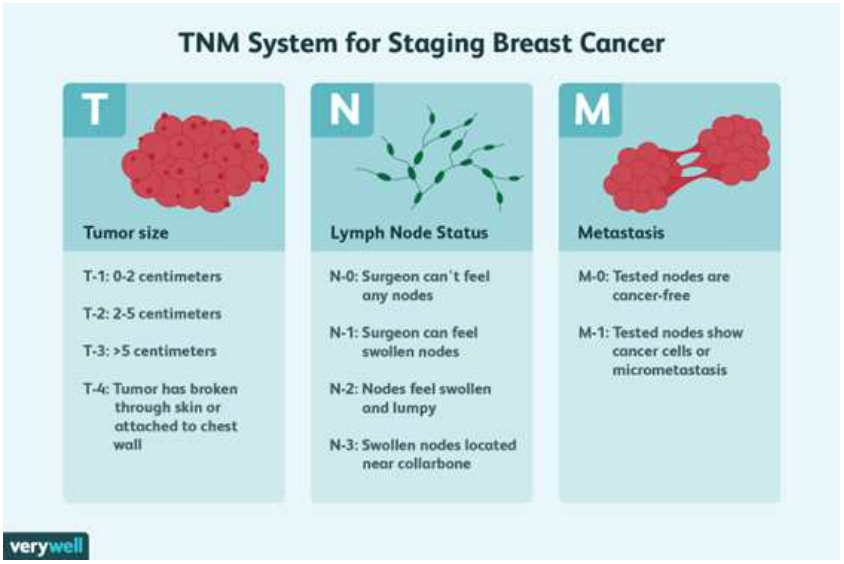
- Tumours form by the uncontrolled abnormal proliferation and differentiation of cells;
- Primary malignant tumours may spread and form secondary tumours in neighbouring tissues (metastasis) via routes such as lymphatic drainage, the bloodstream, and crossing body cavities.

Chapter 13 - Staging and grading cancers

Introduction

This chapter explains the basic principles of how cancers are staged and graded.

Tumour **staging** is based on three main features using the **TNM system**. T refers to the **size** of the tumour and is staged from T1 to T4. N refers to the extent of **lymph node** involvement, staged from N0 to N3. Finally, M refers to whether there is **distant metastasis** and is marked as either M0 or M1. Below is the specific criteria for breast cancer staging.



Breast cancer staging. *Source: www.verywellhealth.com*

Grading tumours involves estimating how aggressive they are by the degree of differentiation of the cancerous cells. Grade I is least aggressive with well-differentiated cells, grade II is moderate, and grade III is the most aggressive with little differentiation. The grading system is much more subjective than the staging system and isn't usually as accurate for predicting outcomes.

Slim Summary!

- Tumours are staged using the TNM system, with size, lymph node involvement, and metastasis being assessed;
- Tumours are graded by how differentiated the cells are and generally if there is less differentiation, the cancer is more aggressive.

Chapter 14 - Types of breast cancer

Introduction

This chapter discusses the types of breast cancer in women, their prevalence, severity, and treatments.

Types of Breast Cancer

Breast cancer is the most common cancer in women who do not smoke. The majority of breast cancers arise from the milk ducts (ductal epithelium) or lobules (milk-producing glands). The most common type is infiltrating ductal carcinoma (IDC), which begins in the ducts and invades surrounding fibrous or fatty tissue. Other types include infiltrating lobular carcinoma (ILC), which often appears larger than expected on mammograms and is typically strongly estrogen receptor (ER) positive, making it sensitive to hormonal therapy. Less common forms include mucinous carcinoma, where cancer cells produce mucous that forms a tumor, medullary carcinoma, a rare type (3–5%) that feels spongy rather than forming a firm lump, papillary carcinoma, more common in women over 60, and tubular carcinoma, a rare type representing around 2% of cases, which under the microscope looks like hundreds of small tubes.

Other rare breast cancers include adenoid cystic carcinoma, a slow-growing, often triple-negative tumor with a good prognosis but potential for recurrence, secretory carcinoma, mostly affecting younger women and presenting as a painless lump with a generally good prognosis. Apocrine carcinoma resembles sweat glands and is less responsive to hormonal therapy. Paget's disease of the nipple, affects the nipple and areola and is often associated with underlying ductal carcinoma in situ (DCIS), causing redness and scaling. Phyllodes tumor is a fibroepithelial tumor that can be benign or malignant, with the malignant form capable of rapid growth and metastasis.

Non-Invasive Breast Cancer

Non-invasive, or in situ, breast cancer refers to malignant changes in the ductal or lobular epithelial cells that have not yet breached the basement membrane. Ductal carcinoma in situ (DCIS) occurs when cells lining the milk ducts become cancerous but remain confined to the duct, preventing spread to lymph nodes or the bloodstream. This stage is usually detected via mammography and is highly curable, often treated with breast-conserving surgery. Lobular carcinoma in situ (LCIS) involves abnormal growth of cells in the lobules and increases the risk of developing invasive cancer in either breast in the future.

Invasive Breast Cancer

Invasive breast cancers have breached the duct or lobular walls and spread into surrounding tissue. Infiltrating ductal carcinoma is the most common, representing approximately 80% of cases. Infiltrating lobular carcinoma is often estrogen receptor positive and may appear larger on imaging than expected. Mucinous carcinoma forms tumors with mucus, often carrying a better prognosis than IDC. Medullary carcinoma is rare, felt as a spongy mass, and usually appears on mammograms.

Breast Cancer by Hormone Receptor Status

Hormone receptor-positive cancers express ER and/or progesterone receptor (PR) and can be treated with hormone therapy. Drugs such as tamoxifen block ER and prevent estrogen from stimulating tumor growth, commonly used in premenopausal women, while aromatase inhibitors (e.g., anastrozole, letrozole) reduce estrogen production in postmenopausal women.

Hormone receptor-negative cancers do not express ER or PR and generally grow faster, especially in younger women. These cancers do not respond to hormone therapy, so treatment relies on chemotherapy or immunotherapy.

Triple-negative breast cancer (TNBC) lacks ER, PR, and HER2 expression. TNBC is aggressive, spreads quickly, and is associated with mutations in TP53 and BRCA1/2, which impair cell cycle regulation and DNA repair. Treatment options include chemotherapy, immunotherapy (e.g., atezolizumab), and PARP inhibitors for patients with BRCA mutations.

Triple-positive breast cancer, expressing ER, PR, and HER2, can be treated with a combination of hormone therapy and HER2-targeted drugs, offering multiple therapeutic avenues.

Slim Summary!

- Non-invasive forms like DCIS and LCIS remain confined, whereas invasive cancers such as IDC and ILC breach surrounding tissue and carry a higher risk of spread.
- Tumor biology, especially ER, PR, and HER2 status strongly determines treatment, with hormone receptor–positive cancers responding to endocrine therapy, HER2-positive cancers to targeted drugs, and triple-negative cancers requiring chemotherapy, immunotherapy, or PARP inhibitors due to their aggressive nature.

Chapter 15 - Immunocytochemistry

Introduction

This chapter discusses the technique of immunocytochemistry, the role of biomarkers in detecting breast cancer subtypes, and the subtypes of breast cancer as categorized by their receptor, as well as luminal subtypes.

Immunocytochemistry (ICC): Overview

Immunocytochemistry (ICC) is a laboratory technique used to detect specific proteins (antigens) within individual cells using antibodies. By labeling antibodies with detectable markers, ICC allows researchers and clinicians to visualize where particular proteins are located inside the cell. To perform ICC, cells are placed on a slide, exposed to antibodies that bind specific antigens, and then visualized under a microscope after a signal-producing reaction occurs. This process helps identify protein expression patterns important for diagnosis and research.

Principles of ICC

Antibody–Protein Interaction

ICC relies on the specific interaction between antibodies and their target proteins. Two types of antibodies are commonly used. Primary antibodies bind directly to the antigen. Secondary antibodies recognize the primary antibody are typically attached to markers such as fluorescent dyes or enzymes which help the antigen–antibody complexes to be visualized under a microscope.

Detection and Visualization

The markers attached to secondary antibodies produce an observable signal. Enzymatic markers generate a color change when exposed to a substrate, whereas fluorescent markers emit light under specific wavelengths. After staining, the cells are examined under a light or fluorescence microscope, allowing the viewer to assess not only whether the protein is present but also where it is located within the cell.

Steps in ICC for Breast Cancer Biomarkers

The first step is **sample preparation**. It involves fixing the cells on a slide using chemical fixatives. Fixation preserves the cell's architecture and prevents degradation of proteins so that their true location and amount can be measured accurately. The next step is **blocking** → before antibodies are added, a blocking solution is applied. This step reduces nonspecific binding, meaning it prevents antibodies from sticking to parts of the cell where they do not belong. Blocking increases staining accuracy and reduces background signal. Next up is **antibody incubation**. To detect breast cancer biomarkers, primary antibodies that specifically recognize ER, PR, HER2, or Ki67 are added to the slide. After they bind to the target proteins, secondary

antibodies carrying visible markers are applied. This amplifies the signal and improves detection. Further on, **visualization** is performed. The slide is processed so the markers on the secondary antibody produce either a colored or fluorescent signal. Under the microscope, the presence and location of the biomarker can then be observed. Finally, the staining results are analyzed through **quantification**. This may involve estimating how strongly the cells stain for the marker (intensity) and how many cells show staining (proportion). Quantifying these patterns helps determine how much of each protein is present and whether the cancer is likely to respond to certain treatments.

Role of Biomarkers in Determining Breast Cancer Subtypes

ICC is used to detect key biomarkers in breast cancer cells, helping guide diagnosis and treatment. The Estrogen Receptor (ER) and Progesterone Receptor (PR) are nuclear proteins whose presence can be visualized using ICC, indicating that the tumor is hormone-responsive and likely to respond to therapies such as tamoxifen or aromatase inhibitors. HER2, a growth factor receptor located on the cell membrane,overexpression or amplification signals aggressive tumor growth but predicts responsiveness to targeted therapies like trastuzumab. Ki67 is a nuclear protein expressed during active cell division, and ICC detection of high Ki67 levels indicates a rapidly proliferating tumor, helping clinicians assess aggressiveness and guide treatment decisions. Through ICC, the location and intensity of these biomarkers can be evaluated, providing critical information for personalized breast cancer management.

Subtypes of Breast Cancer

Hormone Receptor–Positive Breast Cancer are tumors that express ER and/or PR and are usually HER2-negative. They typically grow more slowly and respond well to hormone therapy. This is the most common subtype. HER2-Positive Breast Cancers overexpress the HER2 receptor. Although they tend to be more aggressive, the availability of HER2-targeted treatments has greatly improved outcomes. ER and PR may be either positive or negative in this subtype.
Triple-Negative Breast Cancer lacks expressions of ER, PR, and HER2. Because it does not respond to hormone or HER2-targeted therapies, chemotherapy is often required. TNBC tends to be aggressive and is more common in younger patients.

Luminal subtypes are categories of breast cancers that originate from the luminal (inner) cells of the breast ducts. These cancers are typically hormone receptor–positive, meaning they express estrogen receptors (ER) and/or progesterone receptors (PR). These tumours are further classified by Ki67 level and HER2 status. One subtype is Luminal A → ER/PR positive, HER2 negative, and low Ki67. These tumors grow slowly and have the best prognosis. Another subtype is Luminal →ER/PR positive but with high Ki67 or HER2 positivity. These tumors grow faster and may need more aggressive treatment than Luminal A.

Slim Summary!

- ICC Technique: Uses antibodies to detect proteins in cells, visualized via color or fluorescence; steps include fixation, blocking, antibody incubation, and quantification.
- Biomarkers: ER/PR indicate hormone responsiveness, HER2 signals aggressive growth but predicts targeted therapy response, Ki67 shows proliferation.
- Breast Cancer Subtypes: Hormone receptor–positive (ER/PR+), HER2-positive, Triple-Negative (ER−/PR−/HER2−), Luminal A (ER/PR+, HER2−, low Ki67), Luminal B (ER/PR+, HER2+ or high Ki67).

Chapter 16 - Oestrogen receptors

Introduction

Estrogen receptors (ERs) are nuclear hormone receptors in breast epithelial cells that regulate gene expression in response to estrogen, controlling cell proliferation, differentiation, and survival. In ER-positive breast cancer, this signaling drives uncontrolled tumor growth, making ER a critical target for hormonal therapies.

Role of Oestrogen Receptors in Breast Cancer

Oestrogen receptors (ERs) are nuclear hormone receptors found primarily in breast epithelial cells. They respond to the hormone, estrogen and then control gene expression through activating transcription factors. When estrogen binds to the receptor, ER undergoes a structural change that allows it to dimerize (pair with another ER molecule). The dimer then enters the nucleus (or is already in the nucleus, depending on the receptor's location), where it binds to specific DNA sequences known as estrogen response elements (EREs). This interaction activates or represses genes involved in cell proliferation, differentiation, and survival. Two major ER genes are ER-α and ER-β, but ER-α is the primary form associated with breast development and breast cancer. In healthy tissue, ER plays a normal role in development and reproductive physiology. In breast cancer, however, this same signaling pathway drives uncontrolled cell growth.

Normal Physiological Role of Oestrogen in the Breast

During puberty (menarche) and reproductive years, estrogen is produced by the ovaries which stimulates the growth and maturation of the breast ducts. When oestrogen binds to ER in breast epithelial cells, it triggers the transcription of genes that cause these cells to proliferate. This proliferative action is essential for normal breast development and maintenance of reproductive function. However, long-term exposure to oestrogen, such as in individuals with early menarche or late menopause, increases the number of repeated cycles of cell division. Over a lifetime, this prolonged oestrogen stimulation increases the chance of DNA replication errors, and therefore the likelihood of developing breast cancer. Thus, while estrogen-ER signaling is physiologically necessary, chronic exposure has important epidemiological implications for cancer risk.

How ER Signaling Contributes to Breast Cancer Development

Approximately 70–80% of breast cancers are estrogen receptor–positive (ER+), meaning the tumor cells express ER and rely on estrogen-mediated signaling for growth. In ER-positive cancers, estrogen binding to its receptor activates genes that promote cell cycle progression and cell survival. For example, Cyclin D1, accelerates movement through the G1 phase of the cell cycle, increasing proliferation and BCL-2 is an anti-apoptotic protein that prevents programmed cell death and allows abnormal cancer cells to survive longer.

Some cancers also exhibit overexpression of ER (often due to increased activity of the ESR1 gene). This makes tumor cells even more sensitive to small amounts of estrogen, contributing to aggressive growth despite seemingly normal hormone levels. The cumulative effect is continuous

stimulation of cancer cell division and survival, making estrogen a critical driver of tumor progression in ER-positive disease.

Hormonal Therapy in ER-Positive Breast Cancer

Because ER-positive breast cancers depend on oestrogen for growth, hormonal (endocrine) therapy is designed to block estrogen action or reduce oestrogen production. This "starves" the cancer of its required growth signal. Endocrine therapy is highly effective and significantly reduces recurrence and mortality in ER-positive breast cancer. Treatment approaches fall into four main categories: Selective Oestrogen Receptor Modulators (SERMs), Aromatase Inhibitors (AIs), Selective Estrogen Receptor Degraders (SERDs), and ovarian suppression.

Selective Estrogen Receptor Modulators (SERMs)

SERMs, such as tamoxifen, bind to the estrogen receptor but do not activate it in breast tissue. This means they act as competitive antagonists, blocking estrogen from binding and preventing ER-driven transcription. Because tamoxifen blocks ER without lowering estrogen levels, it is effective in both premenopausal and postmenopausal women. Interestingly, SERMs can behave as oestrogen agonists in some tissues (e.g., bone, uterus), but their breast-specific antagonistic effect is what makes them effective cancer treatments. By preventing estrogen-ER binding, tamoxifen slows tumor growth and reduces recurrence risk after surgery.

Aromatase Inhibitors (AIs)

Aromatase inhibitors such as anastrozole, letrozole, and exemestane work by blocking the enzyme aromatase, which converts androgens into oestrogen in peripheral tissues. After menopause, this aromatase-mediated conversion becomes the primary source of estrogen since the ovaries no longer produce significant amounts. By inhibiting aromatase, these drugs reduce circulating oestrogen, depriving ER-positive cancer cells of their growth signal. Because they target peripheral estrogen production, AIs are most effective in postmenopausal women. They are a standard part of long-term treatment to prevent cancer recurrence.

Selective Estrogen Receptor Degraders (SERDs)

SERDs, such as fulvestrant, provide a different method of blocking estrogen signaling. These drugs bind to the oestrogen receptor and cause it to become unstable and misfolded. The cell recognizes the abnormal receptor and destroys it through proteasomal degradation. As a result, there are fewer oestrogen receptors available, reducing the cell's sensitivity to oestrogen. Unlike SERMs, SERDs have no agonist activity, meaning they are pure antagonists and fully block ER function. SERDs are often used in advanced, metastatic, or tamoxifen-resistant ER-positive cancers.

Ovarian Suppression (in Premenopausal Patients)

In premenopausal women, the ovaries are the main source of oestrogen. Ovarian suppression can be achieved through medication, such as GnRH agonists (e.g., goserelin), which shut down ovarian estrogen production, or surgical removal of the ovaries (oophorectomy). This is often combined with tamoxifen or, in some cases, aromatase inhibitors (once ovarian function is fully

suppressed). By eliminating ovarian oestrogen production, ovarian suppression reduces estrogen availability and improves outcomes in younger patients with ER-positive breast cancer.

Slim Summary!

- Estrogen binding to ER promotes cell cycle progression (via Cyclin D1) and survival (via BCL-2), with overexpression of ER enhancing tumor proliferation.
- Treatments block estrogen action or production using SERMs (e.g., tamoxifen), aromatase inhibitors (e.g., anastrozole), SERDs (e.g., fulvestrant), or ovarian suppression in premenopausal women.
- SERMs competitively block ER, AIs reduce estrogen synthesis, SERDs degrade ER, and ovarian suppression stops estrogen production, collectively starving ER-positive tumors of growth signals.

Chapter 17 - HER2 receptors

Introduction

This chapter HER2 (Human Epidermal Growth Factor Receptor 2) which is a transmembrane tyrosine kinase receptor that regulates cell growth, survival, and proliferation through downstream signaling pathways. In breast cancer, overexpression or amplification of HER2 drives aggressive tumor behavior but also creates opportunities for targeted therapies.

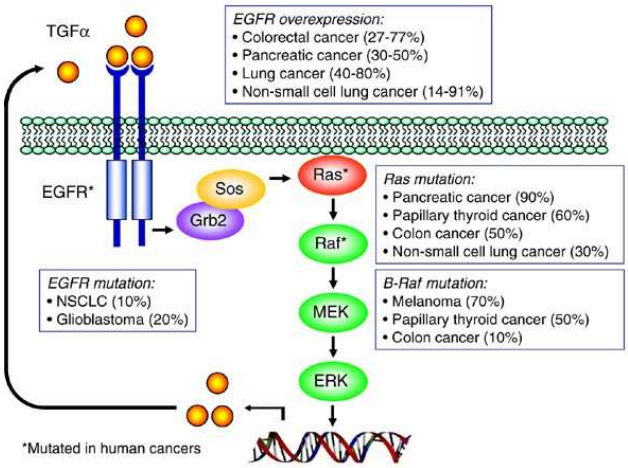
Role of HER2

HER2 (Human Epidermal Growth Factor Receptor 2) is a transmembrane tyrosine kinase receptor encoded by the ERBB2 gene on chromosome 17. HER2 has an extracellular domain, which typically binds growth factors, a transmembrane portion, and an intracellular tyrosine kinase domain, which activates signaling pathways inside the cell.

Normal HER2 Signaling and Downstream Pathways

When HER2 usually dimerizes other HER receptors, the intracellular kinase domain undergoes autophosphorylation, activating major signaling pathways that control cell survival, proliferation, and metabolism. Two major pathways are involved.

RAS–RAF–MEK–ERK (MAPK) Pathway



RAS Pathway. *Source: nature.com*

Her 2 is activated through the dimerization of Her 1 and Her 2 which activates GRB2 and SOS, leading to activation of RAS. RAS then stimulates the RAF–MEK–ERK cascade. Once activated, ERK enters the nucleus and phosphorylates transcription factors such as ETS, which promotes the transcription of genes involved in cell-cycle progression, especially Cyclin D1. Increased Cyclin D1 allows cells to progress from G1 to S phase, increasing cell division.

PI3K–AKT Pathway

HER2 dimerization with HER 3 can trigger PI3K, which activates AKT, promoting cell survival, growth, and anti-apoptotic effects.

HER2 Overexpression in Breast Cancer

In approximately 15–20% of breast cancers, the ERBB2 gene becomes amplified, so that many extra copies of the gene are produced. This leads to the overexpression of the HER2 protein on the cell surface. Excessive Cyclin D1 production which binds to CDK4/6, promoting the transition from G1→ S phase. Increased proliferation of ductal epithelial cells, greater survival and resistance to apoptosis, enhanced invasiveness, and metastatic potential.

Distinguishing HER2-Positive and HER2-Negative Breast Cancers

HER2 status is determined using Immunohistochemistry (IHC) and sometimes FISH testing. HER2-positive tumors: IHC 3+ or FISH-positive → show high HER2 protein expression or gene amplification. HER2-negative tumors: IHC 0–1+ or FISH-negative; do not respond to HER2-targeted therapy. HER2-positive breast cancers are typically more aggressive but have excellent targeted treatment options. HER2-negative cancers are instead classified according to hormone receptor status (ER and PR).

Targeted Therapy for HER2-Positive Breast Cancer

HER2-positive tumors respond well to therapies that specifically block HER2 signaling. These treatments dramatically improve survival by inhibiting the receptor's function or delivering chemotherapy directly to HER2-expressing cells.

Trastuzumab (Herceptin) is a monoclonal antibody that binds to the extracellular portion of HER2. It blocks the ability of HER2 to receive and transmit growth signals and also recruits the immune system to attack tumor cells. This therapy has transformed HER2-positive cancer from a highly aggressive disease into one that is much more manageable. Pertuzumab blocks HER2 from dimerizing with other HER family receptors. Since HER2–HER3 dimerization is one of the most potent activators of the PI3K pathway, pertuzumab significantly reduces pro-survival signaling. It is often used together with trastuzumab. Trastuzumab Emtansine (T-DM1) and Enhertu are antibody–drug conjugates, meaning they combine a HER2-targeting antibody with a small dose of attached chemotherapy. T-DM1 carries a microtubule-blocking drug, while Enhertu carries a drug that blocks topoisomerase I (an enzyme needed for DNA to unwind during replication). Because the antibody directs the chemotherapy specifically to HER2-positive cancer cells, these treatments deliver the drug exactly where it's needed while causing less damage to normal cells.Neratinib is an oral tyrosine kinase inhibitor that blocks HER2's intracellular kinase activity. By preventing HER2 from transmitting growth signals, it helps control residual disease and reduces recurrence risk.

Slim Summary!

- HER2 activates key pathways such as RAS–RAF–MEK–ERK to promote cell cycle progression and Cyclin D1 production, and PI3K–AKT to enhance cell survival and prevent apoptosis.
- Amplification of the ERBB2 gene in 15–20% of breast cancers leads to uncontrolled proliferation, increased invasiveness, and metastatic potential.
- Treatments include monoclonal antibodies (trastuzumab, pertuzumab), antibody–drug conjugates (T-DM1, Enhertu), and tyrosine kinase inhibitors (neratinib), which specifically block HER2 signaling or deliver chemotherapy to HER2-positive cells, improving patient outcomes.
-

Chapter 18 - Cancer treatments

Introduction

This chapter describes chemotherapy, radiotherapy, and targeted cancer treatments, and explains the benefits and disadvantages of each approach.

Chemotherapy involves the use of drugs to destroy rapidly growing cancer cells, with the drugs being administered by injection, intravenous infusion, or orally. It is usually effective at killing rapidly dividing cells, but it is non-selective and therefore causes unpleasant side effects like hair loss and immunosuppression.

Radiotherapy involves using ionising radiation to destroy cancerous cells. The radiation is usually as targeted as possible to the affected tissue, but some nearby tissues can still be damaged in the process. It can also cause side effects such as hair loss, skin issues, gastrointestinal disturbances, and fatigue. It also may not always be effective if there is low blood supply to the tumour, since oxygen is required for the radiation to destroy the cancer cells, and patients cannot receive radiotherapy too often due to the risk of damage to healthy tissues.

Targeted therapy uses specific drugs to target specific molecules associated with certain cancers, such as receptors on breast cancer tumours. These have been mentioned in other chapters of this booklet, and they are usually effective and very targeted, reducing the risk of unwanted side effects. However, their use is limited to the patients who have the corresponding targets because they are so specific.

Slim Summary!

- Chemotherapy and radiotherapy usually cause side effects in healthy tissues as they are less targeted, for example hair loss, skin issues, and immunosuppression;
- Targeted therapy usually is more effective and causes less unwanted side effects, but its use is limited to patients who have the corresponding targets.

Chapter 19 - Help-seeking behaviour

Introduction

This chapter explains how health beliefs and social context influence help-seeking behaviour, using the biopsychosocial and health belief model.

Help-seeking behaviour is the process of deciding to seek professional help for a health-related issue. The **health belief model** describes how demographic variables influence the likelihood of seeking help. This includes susceptibility, for example if a family member had cancer and the individual may also be at risk, and severity, which would be how serious the health condition could be. Biological factors like age, gender, and genetics also influence people's perception of health issues and how seriously they impact an individual's life. The costs and benefits of seeking help would be weighed by the individual and a cue to action such as seeing an advert on TV may prompt help-seeking behaviour and increase health motivation. Individuals also have perceived control over the health issue, such as being confident that they can attend a GP consultation.

There is a **clinical iceberg theory**, which suggests that only a very small proportion of health conditions are known to health professionals due to people not seeking help. Individuals often delay help-seeking and the time between detecting a sign or symptom and the first contact with a health professional is referred to as the **patient interval**. Delaying help-seeking then has an impact on the health issue itself, as it may get progressively worse and have worse outcomes if treatment is given later.

There is a proposed set of stages which brings in features of the self-regulatory and health belief model for the process of choosing to seek help. Patients first experience something and recognise it as a symptom, and the recognition of symptoms can be dependent on perception and social context. Patients then determine if the symptom is normal or not and consider if it is severe enough to need help. They then decide if contacting a health professional would be helpful and make contact with health professionals if they decide to.

Slim Summary!

- Several factors encompassing the health belief, biopsychosocial, and self-regulatory models influence help-seeking behaviour;
- Individuals often delay help-seeking, which only makes the health issue worse as treatment is provided later.

Chapter 20 - Psychosocial factors and decision making

Introduction

This chapter explains how psycho-social factors influence decisions about treatment and care for breast cancer by patients and healthcare professionals.

Decision making about treatment is the process by which a healthcare choice is made by a patient or significant other with one or more healthcare professionals. There is shared doctor and patient responsibility to make the decision in the patient's best interest but with the influence of their preferences as well. Key parts include defining and explaining the health problem, presenting the treatment options with pros and cons, and clarifying the patient's values and preferences. Personal preferences of the patient may affect the treatments prescribed, as some patients may tolerate certain side effects better than others. Especially with cancer treatment it's important that patients are provided with sufficient information about the diagnosis and treatment to make an informed decision. Psychosocial factors which are considered may include mental and emotional health, religious beliefs, social support, and economic situations.

Slim Summary!

- Psycho-social factors including mental and emotional health, religious beliefs, social support, and economic situations are important to consider when making decisions about treatment for cancer patients;
- Doctors should ensure that the treatment provided is in the patient's best interest and consider their preferences.

Chapter 21 - Impact of life-threatening illness

Introduction

This chapter describes the impact of serious and life-threatening illness, such as cancer, on self, identity and biography.

The concept of **biographical disruption** involves the fundamental rethinking of biography and self-concept with the impact of severe illness. Patients often grieve their previous life and experience anxiety and depression.

There are also **cognitive adaptation theories** that explore the processes patients go through as they adjust to the impact on their lives. They may search for meaning and causality behind their illness, such as analysing potential causes of the illness (stress, diet, carcinogens), and try to improve their self-knowledge and reprioritise aspects of their lives. They may also seek to achieve mastery by controlling their illness and negative thoughts with psychological techniques, such as a positive attitude or meditation. Patients may compare themselves to others to improve their own self-esteem, making statements like “At least the cancer didn’t spread”, and through this they undergo a process of self-enhancement.

Slim Summary!

- Serious and life-threatening illness can cause biographical disruption, where there is the fundamental rethinking of biography and self-concept;
- Patients may go through processes called cognitive adaptation theories to try and reflect and adjust how they live their lives having gone through this experience.

Chapter 22 - Adjusting to serious illness

Introduction

This chapter discusses the management of serious or long-term illness which requires strategies that support emotional, cognitive, and practical adaptation to maintain quality of life.

Managing and adjusting to serious illness or long-term conditions involves strategies that address emotional, cognitive, and practical challenges. Cognitive Adaptation Theory (CAT) highlights three key elements: maintaining positive beliefs, regaining a sense of control, and finding meaning in the experience, all of which foster resilience and well-being.

Patients use strategies like emotional coping (therapy, support groups), self-management (education, realistic goal-setting), social support, and practical adaptations (adjusting routines or using assistive devices). Healthcare professionals support these efforts through patient-centered care, shared decision-making, psychological support, practical assistance, and holistic approaches that consider social and cultural factors.

Together, patients and professionals collaborate on goal-setting, resilience-building, and educational initiatives, helping patients to regain control and improve their quality of life.

Slim Summary!

- Patients build resilience and well-being through coping strategies, self-management, social support, and practical adaptations, while healthcare professionals facilitate this process via patient-centered care, shared decision-making, and holistic support.

Chapter 23 - Shared decision-making

Introduction

This chapter discusses the requirements that must be met for consent to be valid.

Valid consent requires that a decision is made voluntarily, by a person who is appropriately informed and has the capacity to consent, whether this is the patient, someone with parental responsibility for a patient under 18, or an individual with lasting power of attorney.
The GMC outlines seven key principles for decision making and consent. First, all patients have the right to be involved in decisions about their treatment and care. Second, decision making should be an ongoing, collaborative process that relies on meaningful dialogue and the exchange of relevant information. Third, patients must be listened to and provided with the information they need in a way they can understand. Fourth, doctors must identify what matters most to the patient so they can explain the benefits, risks, and reasonable alternatives in a way that aligns with the patient's values. Fifth, capacity must always be presumed in adults unless there is clear evidence that the patient lacks capacity for that specific decision at that specific time. Sixth, when a patient does lack capacity, any decision made on their behalf must be in their overall best interests. Finally, patients whose right to give consent is limited by law, such as those under certain mental health legislation, should still be supported to participate in decision-making as fully as possible.

Slim Summary!

- Valid consent requires that a decision is made voluntarily by someone who is informed and has the capacity to decide.
- The GMC outlines several key criteria which can be read above.

Chapter 24 - Informed consent

Introduction

This chapter discusses the importance of informed consent and situations in which it would be limited.

Informed consent is an important part of the doctor–patient relationship because it respects a patient's autonomy which is their right to make decisions about their own body and health. For consent to be meaningful, patients must receive clear, honest information about their diagnosis, the purpose and risks of proposed treatments, the alternatives available, and the likely outcomes of doing nothing. This allows them to make choices based on their own values, priorities, and understanding of what matters most in their lives.

However, there are limits to informed consent. One limit is lack of capacity, a patient may be temporarily or permanently unable to understand or weigh information well enough to make a decision (for example, due to unconsciousness, severe confusion, or a learning disability). In these cases, doctors must make decisions based on the patient's best interests while still involving them as much as possible. Another limit is emergency situations, where immediate action is required to save a life or prevent serious harm, and there is no time to obtain full consent. Here treatment can proceed without detailed discussion. A further limit involves legal restrictions, such as when public health laws require certain actions (like notifying authorities of specific infectious diseases), even though consent would normally be sought. These limits do not override the importance of informed consent, they simply recognize that in some circumstances, the patient's safety or legal obligations must guide decision-making.

Slim Summary!

- While informed consent is a part of ethical practice, it may be limited by factors such as lack of capacity, emergencies, or legal requirements, which prioritize patient safety and legal obligations.

Chapter 25 - Consent and genetic information

Introduction

This chapter discusses how genetic information challenges the idea of consent as an individual decision by introducing shared risks, uncertain future implications, and complex privacy questions that must be addressed openly and sensitively in the consent process.

A patient's test result may indicate that siblings, parents, or future children are also at risk of a serious inherited condition. This means a patient's decision not to be tested or not to share results, can affect others' ability to make informed health decisions. Doctors must consider the patient's confidentiality with the potential duty to warn relatives who might be harmed by lack of information. Genetic tests can reveal unexpected information, such as risks for unrelated conditions (incidental findings), variations of unknown significance, or implications for future health. Truly informed consent requires explaining these possibilities, which can be difficult because the meaning of some results may change as science advances. Genetic information may be stored in databases and used for future research. Patients must understand how their data may be used, who can access it, and the limits of anonymity.

Slim Summary!

- Genetic testing requires careful consent because results can affect relatives, reveal unexpected or uncertain information, and involve data storage and future use, creating ethical and practical challenges for patient autonomy and confidentiality.

Afterword

Phew, you did it! You've finished reading your summary. 🎉
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📞 010 214 32 45

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