

Module Four – Cancer Treatment Principles

Overview

The aim of this module is to develop the ability of the beginning specialist cancer nurse to provide care to people undergoing treatment for cancer.

Key concepts

The key concepts associated with cancer treatment principles are listed below:

- Common classification systems for cancer.
- Tumour, treatment and person related factors influencing treatment planning.
- Evidence based treatment guidelines.
- Principles for facilitating decision making by people affected by cancer.
- Principles of clinical trials in cancer control.
- Principle mechanisms of action of surgery, radiotherapy, antineoplastic agents, biological and targeted therapies and haematopoietic stem cell transplantation in cancer control.
- Nursing role in cancer clinical trials.
- Commonly used complementary and alternative health practices and their implications.
- Sources of information and support for people using complementary and alternative health practices.

Learning activities

At times, you will have learning activities to complete. The questions will relate to the content you've just read or the video you've just watched.

Videos

You will be prompted to access EdCaN videos throughout this module.

Resource links

Resource links may be included throughout the module. These links lead to interesting resources, articles or websites, and are designed to encourage you to explore other available information.

Estimated time to complete

40 hours

Learning objectives

On completion of this module, you should be able to:

1. Outline the implications of staging and grading on a person's cancer journey.
2. Explain the principles of cancer treatment planning.
3. Identify the role of evidence based treatment guidelines in the context of a multidisciplinary approach to planning treatment.
4. Identify the nurse's role in supporting the person affected by cancer to participate in decisions about their treatment and care.
5. Describe the principle mechanisms of action for the major treatment modalities used in the management of cancer.
6. Identify early and late effects commonly associated with cancer treatments.
7. Outline the role of clinical trials in cancer treatment.
8. Identify nursing implications associated with caring for the person considering, or undergoing, a cancer clinical trial.
9. Identify sources of evidence based information and support for people who use complementary and alternative health practices.

Cancer grading and staging

Following a cancer diagnosis, the person undergoes a series of investigations to determine the characteristics of the tumour tissue and the extent of spread of disease in the body. This process— known as disease staging— is generally commenced before treatment begins.

The information gathered from staging investigations is used to classify a tumour. Accumulated evidence about the clinical behaviour of other tumours with similar characteristics is used to guide treatment planning and estimations of disease prognosis.^{1, 2}

Histopathological review

Histopathological review (the microscopic examination of tumour tissue) identifies a number of properties that enable assessment of a tumour's aggressiveness. The amount of necrosis, inflammation, haemorrhage, cellular genetic changes and the degree of mitotic activity within a tumour tissue specimen are some of the properties examined in the laboratory. These histopathological characteristics are used to categorise a tumour into a grade, ranging from well-differentiated (grade 1), through moderately (grade 2) and poorly differentiated (grade 3) to undifferentiated (grade 4). In general, higher grade tumours are more aggressive and carry a worse prognosis than lower grade malignancies.¹⁻³

Anatomical extent

In addition to classifying a cancer on the basis of histopathological characteristics, a malignancy is usually classified according to the anatomical extent of disease. Extensive observation of the clinical behaviour of cancers allows prediction of the natural history of growth and progression of a cancer. In general, the greater the anatomical extent of the cancer, the more limited the successful treatment options and the poorer the prognosis becomes.^{2, 4}

The tumour-node-metastasis (TNM) staging system

One of the most commonly used staging systems for solid tumours is the tumour-node-metastasis or TNM system. Used internationally, the TNM system is regularly reviewed to incorporate changing knowledge about the behaviour of tumours. The system assesses and classifies three properties:

- the extent of the primary tumour (T)
- the presence and extent of lymph node involvement (N)
- the presence of metastases (M).

Numerical values are assigned to various levels within each of the three categories, reflecting increasing extent of disease. The summing of the numerical values for each of the three categories allows the tumour to be classified into one of four stages, numbering stage I through to stage IV. High stage disease (stage III or IV) reflects greater anatomical extent and is correlated with poorer prognosis.

There are a number of other staging systems devised by the interest groups of oncology clinicians. Each system defines the clinical aspects of particular cancers that correlate with favourable and unfavourable outcomes and is used to guide treatment decisions.^{1, 2, 4}

Learning activities	
Completed	Activities
<input type="checkbox"/>	1. Access a current text and/or the Tumor Grade: Questions and Answers fact sheet ⁵ on the National Cancer Institute website and prepare a brief explanation of the term 'high grade tumour' for a person affected by cancer.
<input type="checkbox"/>	2. Access a current text or website (such as www.cancer.gov ⁶) and compare the methods of staging lung and breast cancers.
<input type="checkbox"/>	3. Review the records of two individuals in your unit (or access the EdCaN case studies). For each person, list the following: <ul style="list-style-type: none">• Staging and/or grading of their cancer• Implications of the staging for prognosis.

Principles of treatment planning

The aim of treatment for cancer may be: cure, control and prolongation of life, or palliation of symptoms. These goals are re-evaluated when an individual's disease status changes.⁷ A number of factors are taken into account when determining a treatment plan.

Tumour factors

- Accurate diagnosis and staging is imperative to inform treatment options and decisions.⁸
- Tumour size, anatomic location, histology, sensitivity to antineoplastic agents or radiation, natural history and related survival statistics are also considered.⁹
- Prognostic and risk factors identified in staging can determine the need for standard approaches or recommendation for participation in clinical trials.⁷

Treatment factors

- Treatment decisions may vary in complexity depending on disease types. While some diseases have established therapeutic regimens, for others research data has not led to prescriptive guidelines.⁸
- Evidence of treatment effectiveness can also be considered in conjunction with questions about affordability.⁸

Individual factors

Choice of therapy can be influenced by a person's:^{8,9}

- general health
- age
- performance status
- preferences, values, and beliefs.

Recognition of these individual factors is important in ensuring a health care approach which is sensitive to the needs and expectations of the person affected by cancer.

Standardised methods of assessing responses to treatment and individual factors (such as quality of life and performance status) form an essential element of treatment planning and informed decision making throughout the care continuum.

Quality of life evaluations, developed to complement tumour response and length of survival outcomes, have a range of applications. The following list summarises uses of quality of life information in cancer control:¹⁰

- determine whether a new therapy is preferable to standard therapy
- compare two standard therapies with similar survival outcomes
- identify the long-term negative effects of therapy when survival time is long

- discover whether a therapeutic regimen is better than supportive care only when survival time is short
- determine the negative effects of therapy given to prevent recurrence
- identify the need for supportive care
- target problems and facilitate communication in clinical practice.

Assessment tools

The Psycho-oncology Outcomes Database (PoD)

PoD¹¹ is a searchable online database of validated psychosocial and quality of life measures. It contains information about more than 300 patient-reported questionnaires measuring outcomes such as quality of life, supportive care needs, psychological states and social support. Access to PoD is free via the [Psycho-oncology Co-operative Research Group members' website](#)¹² (This is a free resource but you must register as a member and then click 'Remember me' to bypass the login page in future.)

Performance scales

Performance scales that measure an individual's functional status may be used in eligibility criteria for clinical trials, and also to determine an individual's prognosis and survival time. A person with a lower functional score may have reduced likelihood to respond to treatment favourably.¹¹

The most commonly used performance scales are the:

- [Karnofsky scale](#)¹³
- [Karnofsky \(Australian\) performance scale](#)¹⁴
- [ECOG scale](#)¹⁵

Learning activity

Completed

Activity

1. Review the records of two individuals in your health care facility (or access the EdCaN case studies) who have recently been diagnosed with cancer, and where possible interview them. For each case:
 - Identify their cancer diagnosis
 - Describe the disease, treatment, and individual factors that were considered in the treatment planning process.

Communication principles to support treatment decision making

When faced with treatment options, the person affected by cancer can be required to make difficult decisions. A systematic review concluded that preferences vary considerably, and while most individuals prefer a collaborative role, a significant minority prefers to take a passive or inactive role. Evidence about specific individual factors such as age and gender and their impact on preferences and improved satisfaction related to collaborative decision making is inconclusive, prompting the recommendation for further research in this field.¹⁶

Health professionals are encouraged to assess individual preferences for involvement, acknowledging that preferences are likely to change over time and as a result of many influences. Consequently, assessment of preference is a process that should be conducted throughout the duration of the person's cancer journey.¹⁶ Nurses play an important role in educating and supporting people affected by cancer as they evaluate the benefits and risks associated with treatments.

Key communication principles in treatment decision making

Communication has been identified as an important element of treatment decision making. A tool kit has been developed to support health professionals and people affected by cancer communicate effectively to support decision making. Key principles in the toolkit include:¹⁷

Principle 1: Good communication between healthcare consumers and healthcare professionals has many benefits.

Principle 2: Healthcare consumers vary in how much participation in decision making they desire.

Principle 3: Good communication depends on recognising and meeting the needs of healthcare consumers.

Principle 4: Perception of risks and benefits are complex and priorities may differ between healthcare consumers and healthcare professionals.

Principle 5: Information on risks and benefits needs to be comprehensive and accessible.

Learning activities

Completed	Activities
<input type="checkbox"/>	1. Access the publication <i>Making decisions about tests and treatments</i> ¹⁷ and complete the following: <ul style="list-style-type: none">• Discuss the meaning of informed consent in the context of treatment decision making• Outline how you can promote autonomy in patient decision making.
<input type="checkbox"/>	2. Interview an individual to assess their experience of treatment decision making. <ul style="list-style-type: none">• Outline the information they were provided• Appraise the effectiveness of strategies used to deliver this information• Identify barriers and enablers to their decision making process

Multidisciplinary teams and treatment planning

A multidisciplinary approach is recommended during treatment planning and throughout the cancer journey.

Multidisciplinary care has been described as 'an integrated team approach to health care in which medical and allied health care professionals consider all relevant treatment options and develop collaboratively an individual treatment plan for the person affected by cancer'.¹⁸

The principle objectives of a multidisciplinary meeting in the context of treatment planning are:¹⁹

- to provide an opportunity for multidisciplinary discussion of all newly diagnosed people, and to review cases of cancer within an appropriate timeframe to facilitate effective treatment planning
- to determine, in light of all available information and with reference to the evidence base, the most appropriate treatment plan for each individual
- to provide educational opportunities for team members and trainees.

People affected by cancer (including health care teams and services) can benefit from a multidisciplinary approach in the following ways:²⁰

- Treatment planning is improved through consideration of full therapeutic range, and as a result survival benefit has been reported.
- Emotional needs of individuals are recognised.
- Less service duplication, improved coordination of services and development of clear lines of responsibility between members of the MDT.
- Shared decision making in the MDT is more likely to result in recommendations that align with best practice and evidence based care.
- Reduction in minor psychological morbidity of team members.
- Learning and educational opportunities for team members.
- Improved MDT communication.
- Understanding and adherence to agreed treatment and care plan with knowledge of the investigations and results.

Learning activities

Completed

Activities

- 1. Describe ways in which you are able to contribute to multidisciplinary treatment planning.
- 2. Outline how you would respond to a person who asks why they need to see so many health professionals and attend so many clinic appointments.
- 3. Observe a multidisciplinary team meeting (or watch EdCaN's lymphoma case-based learning resource²¹ – [Arthur's story 6](#)) and reflect on:
 - the outcomes of the meeting for the person affected by cancer and for members of the team
 - the role of different members of the team in the meeting
 - what opportunities existed for professional development during the team meeting.

Older people with cancer: treatment planning

Physiological changes that occur with ageing, as well as multiple co-morbidities, can complicate management of cancers in older persons. For example, older people treated for cancer have increased susceptibility to therapeutic complications such as severe and prolonged myelosuppression and mucositis, and increased risk of cardiomyopathy and central and peripheral neuropathy.²²

Individual treatment planning for older people affected by cancer is imperative, particularly considering that the elderly are less likely to receive antineoplastic agents, and when they do it is often dose-reduced leading to poorer outcomes.²³ This population is also under-represented in clinical trials for new cancer therapies.²⁴

Domains that need to be considered in determining a treatment plan for the older person include:^{22, 25}

- mental and emotional status
- activities of daily living
- home environment
- social support
- comorbidities
- nutrition
- polypharmacy.

Two commonly used assessment tools – the Karnofsky Performance Score and Eastern Cooperative Oncology Group performance status – have been criticised due to their inability to capture functional decline, and because they do not take mental status or co-morbid conditions into account.

The Comprehensive Geriatric Assessment is used in some centres as one approach to assess these domains, but can be time-consuming and is not yet routinely used in practice.^{22, 25}

Learning activities	
Completed	Activities
<input type="checkbox"/>	1. Access Chemotherapy in the Elderly ²⁶ , and: <ul style="list-style-type: none">• summarise the impact of ageing on pharmacokinetics and pharmacodynamics• discuss the implications of these issues on treatment planning.
<input type="checkbox"/>	2. Compare the treatment plan of an individual in their 40s to someone over 70 with the same/similar cancer diagnosis. Discuss reasons for similarities or differences in the plan.

Children and young people with cancer: treatment planning

Treatment and supportive care approaches used for children and young people depend on the underlying diagnosis and, to some extent, the child's age. Survival outcomes and impact of toxicities also differ according to the age of the child.^{27, 28} For example, radiotherapy is avoided in children aged under three due to increased associated long term effects.²⁷

The principal differences in cancer treatment for children compared with adults are:

- increased intensity
- toxicities may have more significant and lasting effects.

Treatment and supportive care strategies must consider the child's developmental stage. For example, during treatment with radiotherapy, the child may be required to remain still for up to 25 minutes. Treatment planning may involve discussions around use of anaesthetics and play therapy.²⁷

The impact of diagnosis and treatment of childhood cancer impacts on the individual and extends into the family. Treatment planning for children and young people with cancer occurs in the context of this extended group.²⁸

Learning activity

Completed

Activity

1. Access [*Improving outcomes in children and young people with cancer*](#)²⁷, and summarise challenges associated with planning antineoplastic therapy in children compared with adult populations.

Evidence based approaches to cancer treatment

Evidence based clinical practice guidelines are systematically developed statements that assist the practitioner and person affected by cancer to make decisions about appropriate health care for specific clinical circumstances. In the area of cancer control, evidence based clinical guidelines have been developed by the National Health and Medical Research Council (NHMRC) and the Australian Cancer Network (ACN).

A commentary on the development of guidelines in Australia is given in the article, Development of evidence-based clinical practice guidelines for best practice: Towards better outcomes.²⁹ A full list of current guidelines and resources can be found on the [Cancer Learning website](#).³⁰

From the perspective of a nurse working in cancer care settings, best practice requires an understanding of the evidence base underpinning various cancer treatments and nursing interventions. In addition to the clinical guidelines for treatment of specific cancers, a number of useful sources provide evidence based guidelines to inform core domains of practice for nurses working in cancer settings. Examples include:

- [Oncology Nursing Society\(ONS\) resources](#)³¹
- [National Comprehensive Cancer Centre \(NCCN\) guidelines](#)³²
- [NHMRC guidelines on supportive care](#)³³
- [The Joanna Briggs Institute](#)³⁴

Learning activities

Completed	Activities
<input type="checkbox"/>	1. Access the article, Nursing-Sensitive Patient Outcomes: The Development of the Putting Evidence into Practice Resources for Nursing Practice . ³⁵ Identify three examples of nurse-sensitive patient outcomes in your work environment.
<input type="checkbox"/>	2. Access the article, Oncology Nurses' Use of National Comprehensive Cancer Network Clinical Practice Guidelines for Chemotherapy-Induced and Febrile Neutropenia . ³⁶ Summarise the barriers and enablers which have been described regarding the use of these clinical practice guidelines in clinical care.
<input type="checkbox"/>	3. Identify a nursing intervention or practice and: <ul style="list-style-type: none">• summarise recommendations from the evidence based guidelines• reflect on the extent to which the recommendations are implemented in your practice setting and the reasons for this.

Clinical trials in cancer treatment

The findings of clinical trials are integral to the practice of evidence based cancer care.³⁷⁻³⁹

The purpose of clinical trials is to evaluate the safety, effectiveness and toxicities of new agents and combinations of agents or interventions in humans. Clinical trials involve the following four phases of research or evaluation of an investigational drug or intervention:³⁹

- **Phase I trials** involve determination of safe drug levels and/or schedules of a new drug using human subjects.
- **Phase II trials** involve determination of therapeutic efficacy when applied to clients with various diagnoses.
- **Phase III trials** are used once efficacy is established to compare the drug to an existing effective standard therapy for the same diagnosis.
- **Phase IV trials** involve utilisation as standard therapy to determine optimal use of the drug with large client populations.

A review of cooperative clinical trials in cancer in Australia found that fewer than 3% of new adult cases each year enter a clinical trial. It has been suggested that at least twice as many adults with cancer would benefit from trial entry.³⁸

Barriers to access and enrolment to trials are:⁴⁰

- system barriers (particularly limited funding for clinical trials)
- healthcare provider barriers (protocol complexity, general lack of knowledge)
- participant barriers (discomfort about the research process, fear of potential side effects).

Learning activities

Completed	Activities
<input type="checkbox"/>	1. Access the Priority driven research web page ⁴¹ on the Cancer Australia website and summarise the organisation's current research priorities.
<input type="checkbox"/>	2. After accessing the following clinical trials information and resources: Access CR ³⁹ National Health and Medical Research Council: Clinical trials ⁴² <ul style="list-style-type: none">• describe the four different phases of a clinical trial• outline the essential elements of a clinical trial protocol.
<input type="checkbox"/>	3. Access the Australian and New Zealand Clinical Trials Registry ⁴³ and: <ul style="list-style-type: none">• identify the purpose of the registry• select one type of cancer common to your area of practice and search for current clinical trials relevant to this cancer.

The nurse's role in research and clinical trials

Cancer nurses can contribute to many aspects of the clinical trial process including:

- conceptualising and designing studies as part of a multidisciplinary team
- providing information to people affected by cancer
- assessing and monitoring people involved in clinical trials
- implementing treatments as part of a clinical trial protocol
- ensuring adherence to ethical principles associated with clinical trials.

The nurse also has a key role in providing continuity of care, advocating for the person affected by cancer, interacting with the research team, and documenting care provided.⁴⁴

Learning activities

Completed

Activities

1. Access a current text and the following websites to answer the learning activities below.

[National Cancer Institute: educational materials about clinical trials](#)⁴⁵

[Access CR](#)³⁹

[National Health and Medical Research Council: Clinical trials](#)⁴²

- Describe the roles of the clinical trials nurse/research nurse.
- Outline the complementary roles and role overlap that may occur between your role as a nurse working with cancer patients and the clinical trials nurse.

2. A person newly diagnosed with cancer asks you if they should enrol in a clinical trial. Discuss how you would respond.

3. Identify a clinical trial currently underway within your health care facility. Where possible, discuss this trial with the research nurse or data manager.

- Outline the purpose and process of this trial.
- Identify any implications for nursing care of participants within the trial.

Overview of treatment modalities

Surgery in cancer control

There are a number of roles and indications for surgery in cancer control including:⁴⁶

- **Prophylactic surgery**
Some underlying conditions or congenital or genetic traits are associated with a significantly higher incidence of cancer. When these cancers are likely to occur in non-essential organs, the potentially involved organ may be removed or the anatomical, developmental or genetic defect corrected to prevent or reduce risk of subsequent malignancy.^{46, 47}
- **Diagnostic surgery**
The major role of surgery in diagnosing cancer involves the acquisition of tissue for exact histologic diagnosis. Endoscopic approaches are replacing many open surgical procedures for diagnostic purposes.⁴⁶ Laparoscopic staging procedures may identify metastatic or unresectable disease so the person affected by cancer may avoid a major operation.⁴⁷
- **Definitive (or curative) surgery**
Surgery can be a simple, safe method to cure individuals with solid tumours when the tumour is confined to the anatomic site of origin. Resection of the primary cancer involves definitive surgical treatment encompassing a sufficient margin of normal tissue to achieve a cure with surgery alone.^{46, 47}
- **Rehabilitative (or reconstructive) surgery**
Surgical techniques are being refined to enhance reconstruction and rehabilitation after definitive therapy. The ability to reconstruct anatomic defects can substantially improve function and cosmetic appearance.⁴⁶ Reconstruction may be immediate or delayed, depending on circumstances.
- **Palliative surgery**
Surgery to relieve distressing symptoms in an individual with no hope of cure or intent to lengthen their lifespan is considered palliative.⁴⁶ Five main purposes have been identified for palliative surgical procedures:⁴⁸
 - evaluation of the extent of the disease
 - control of locoregional spread
 - control of a fungating tumour, discharge or haemorrhage
 - control of pain
 - surgical reconstruction or rehabilitation to improve quality of life.

For further information on this treatment approach, complete Module Six Part One – Providing care for the person having cancer surgery.

Learning activities

Completed	Activities
<input type="checkbox"/>	<p>1. Review two individuals in your health care facility and identify which of the following surgical approaches they have had at some point throughout their cancer journey:</p> <ul style="list-style-type: none">• prophylactic surgery• diagnostic surgery• definitive surgery• rehabilitative surgery• palliative surgery.
<input type="checkbox"/>	<p>2. Access a current text and outline the differences between definitive or curative surgery and cytoreductive surgery.</p>

Radiotherapy in cancer control

Radiotherapy can be used alone, or as an effective neoadjuvant and adjuvant treatment in combination with other treatment modalities such as surgery, antineoplastic agents and hormonal therapy.⁴⁹⁻⁵⁶

The aim of radiotherapy may be cure, control, or palliation to offer benefits in terms of:^{57, 58}

- organ preservation
- quality of life
- survival outcomes
- effective alleviation of symptoms.

There are a variety of external or internal treatment delivery methods including:

- External beam radiotherapy (EBRT)
- Brachytherapy
- Combined modality treatment.

This enables a range of radiotherapy schedules that best suit the tumour type and stage of a cancer to be considered.^{54, 59}

Understanding radiobiologic principles and their application to nursing care is integral to achieving optimal outcomes.⁶⁰ Radiotherapy aims to treat cancer through delivering sufficient doses of ionising radiation to a specific area of the body to damage target DNA that eventually results in cell death.⁶¹ Ionising radiation causes cell death (either directly or indirectly).

Direct damage to the atoms that make up the DNA results in either single or double-strand breaks, faulty cross-linking of chains after breakage, damage or loss of a nitrogenous base, or breakage of the hydrogen bond between the two chains of the DNA molecule causing impaired cellular functioning or cell death.⁴⁹

Indirect damage is caused by the interaction of ionising radiation with the molecules of the cellular fluid, resulting in toxic changes due to the creation of unstable free radical ions that impair cellular functioning. While a direct hit causes the most lethal damage, the most common injury occurs as a result of the interaction of radiation and the water molecule.⁶²

Radioactive substances emit both gamma rays and radiation particles until all their atoms are stable in a process called radioactive decay. The activity and rate of decay varies from one radioactive source to another. The most important feature of any type of ionising radiation in determining its application in radiotherapy is its penetrating power. The deeper the tumour within a patient, the higher the penetrating power of the radiation required.⁶³

The basic principles of radiobiology (four Rs) are:^{49, 62, 64, 65}

- **reoxygenation:** occurs when radiation is delivered in multiple fractions to cells that may be relatively resistant due to hypoxia; cells may become reoxygenated and therefore more radiosensitive.
- **redistribution:** is defined by cells that survive a dose of radiation due to synchronisation in resistant phases of the division cycle and redistributing into more sensitive phases of the cell cycle during subsequent doses of radiation.
- **repopulation:** describes cells responding to lethal injury by repopulating or regenerating themselves.
- **repair:** occurs following sub lethal cellular injury which represents damage to the strands of the DNA and which can be repaired by enzymatic processes.

The four Rs of radiation biology, the tumouricidal dose, and the tolerance of surrounding critical tissues determine the prescription for a site specific tumour with a particular histology and pathology.⁶⁴ To quantify the amount or dose of absorbed radiation within a recipient, the unit of Gray (Gy) is used.

$$1 \text{ Gray (Gy)} = 1 \text{ Joule of energy absorbed per kg of mass} = 1 \text{ J/kg.}$$

This absorbed dose is an indicator of the level of biological effects that may occur in the different tissues of the body due to ionising radiation.⁶³

Based on the principles of radiobiology, the total dose of radiation prescribed to treat a particular tumour is divided into a number of daily doses or fractions. This aims to protect normal surrounding tissue while maximising the radiation effect on the tumour.⁴⁹ Different tissues have varying tolerance levels to radiation exposure which, if exceeded, results in high morbidity of the treatment.⁴⁹

For further information on this treatment approach, complete Module Six Part Two – Providing care for the person having radiotherapy for cancer.

Learning activities	
Completed	Activities
<input type="checkbox"/>	1. Explain why some tissues are more prone to radiation effects than others, using the principles of radiobiology described above.
<input type="checkbox"/>	2. List common acute and chronic effects associated with radiotherapy.

Antineoplastic therapy in cancer control

The role of antineoplastic agents in cancer control includes:^{66, 67}

- **Induction:** initial therapy administered with the aim of achieving significant cytoreduction, and ideally, complete remission of disease.
- **Consolidation / intensification:** administered following induction to prolong freedom from disease and overall survival. While consolidation therapy uses the same agents as induction therapy, intensification therapy uses agents which are non-cross resistant to induction therapy.
- **Adjuvant treatment:** antineoplastic agents used in conjunction with another treatment modality i.e. biotherapy, radiotherapy or surgery, and aimed at treating micro-metastases and preventing local recurrence.
- **Neo-adjuvant treatment:** use of antineoplastic agents to reduce the size of a tumour before definitive treatment.
- **Maintenance therapy:** prolonged, low-dose therapy administered to extend the duration of remission and achieve cure.
- **Primary therapy:** antineoplastic agents administered as the definitive therapy.
- **Combination therapy:** use two or more agents to treat the disease.
- **Myeloablative therapy:** prepares individuals for haematopoietic stem cell transplantation.
- **Salvage therapy:** agents given after failure of other treatments to control disease or provide palliation.

Antineoplastic agents frequently disrupt replication at the cellular level by obstructing the synthesis of new genetic material or by causing irreversible damage to the DNA itself. While this affects both normal and malignant cells, normal cells have a greater ability to repair minor damage and continue living. The increased weakness of malignant cells is exploited to achieve the therapeutic effects seen with the administration of antineoplastic agents.⁶⁸

The mechanisms of action of antineoplastic agents are based on the concepts of cellular kinetics – cell cycle time, growth fraction, and tumour burden listed below:⁶⁹

- **Cell cycle time** is the amount of time needed for the cell to complete an entire cycle from mitosis to mitosis. Cycle times for cancer cells vary from 24 to 120 hours, with most ranging from 48 to 72 hours. Those cells with shorter cycle times are more easily damaged by cell-cycle phase specific cytotoxic agents. Continuous infusions of these agents results in higher cell kill percentages as a greater number of cells are exposed to the agent.
- **Growth fraction** is the percentage of cells in the tumour that are reproducing (cycling). For cancer cells there is really no difference to that of normal cells – the main difference is that cancer cells proliferate continuously.⁷⁰ Higher growth fractions result in higher cell kills with cell-cycle phase specific agents. In tumours that have most of the cells in G 0 or the resting phase, using cell-cycle phase non-specific cytotoxic agents results in a higher cell kill.

- **Tumour burden** is the number of cells in the tumour. Tumours with a small burden are more sensitive to antineoplastic agents. As the tumour burden increases, the growth fraction and sensitivity to systemic treatment reduces.

It is theorised that cancer cells exposed to a certain dose of antineoplastic agents will destroy a constant percentage of cells in the tumour. This concept is known as first-order kinetics.^{68, 71} In line with this theory, repeated doses of therapy are needed to reduce the total number of cells. The number of cells left after therapy depends on the results of previous therapy, the time between repeated doses, and the doubling time of the tumour. Repeated treatments are delivered to reduce the tumour to a small enough number of cells so that the immune system can kill any remaining cells.⁷¹

Most antineoplastic agents are classified according to their structure or cell cycle activity – either cell cycle phase specific or cell cycle phase non-specific:⁷²

- **Cell cycle phase specific agents** act on the cells in a specific phase. They are most effective against tumours that have a large proportion of cells actively moving through the cell cycle and cycling at a fast rate. Rapid cycling ensures that the cell passes through the phase in which it is vulnerable to the drugs' effects.
- **Cell cycle phase non-specific agents** are not dependent on the cell being in a particular phase of the cell cycle for them to work – they affect cells in all phases of the cell cycle. Resting cells (phase G0) are as vulnerable as dividing cells to the cytotoxic effects of these agents. As a result, phase non-specific agents have been found to be some of the most effective drugs against slow-growing tumours.

Antineoplastic agents are also traditionally divided by their origin or mechanism of action. The main groups include:^{68, 71, 73}

- *Alkylating and alkylating-like agents*
- *Antimetabolites*
- *Antitumour antibiotics*
- *Plant alkaloids*
- *Topoisomerase inhibitors*
- *Miscellaneous agents*
- *Hormonal agents.*

For further information on this treatment approach, complete Module Six Part Three – Providing care for the person having antineoplastic agents for cancer.

Learning activities

Completed



Activities

1. Discuss why most treatment protocols deliver multiagent regimens rather than single agents.



2. Identify the cell cycle time for the cells in the following tissues and describe the impact of this on the effects of antineoplastic agents:

- bone marrow
- mucous membranes
- cardiac muscle
- hair follicles.

Biological and molecular targeted therapies in cancer control

Biological and molecular targeted therapies have therapeutic and supportive roles in cancer control.⁷⁴

Therapeutic roles in cancer control include:

- curative when used in the primary or adjuvant setting
- improving treatment response by improving disease free survival when used in conjunction with conventional therapies
- controlling or stabilising disease in advanced cancers in the palliative care setting
- maintaining or enhancing quality of life.

Supportive roles in cancer control include:

- minimising the severity of toxicities associated with other therapeutic treatments.

The mechanisms underlying biological and molecular targeted therapies include:⁷⁵

- enhancement of the individual's immune system
- alteration of the environment in which cancer cells grow
- increasing the vulnerability of cancer cells to the body's immune system
- alteration of the pathway by which normal cells transform to malignant cells
- prevention of metastasis of cancer cells
- enhancing the repair of normal cells damaged by treatment
- changing cancer cells so they behave like healthy cells.

Biotherapeutic agents currently approved for use in cancer control in Australia fall into the following broad categories:^{74,76}

- cytokines
 - interferons
 - interleukins
 - haematopoietic growth factors
- monoclonal antibodies
 - unconjugated
 - armed or conjugated antibodies
- cellular therapies
 - dendritic cells
 - tumour-infiltrating lymphocytes
 - antibody-activated T cells
- vaccines
- gene therapy
- angiogenesis inhibitors.

For further information on this treatment approach, complete Module Six Part Four – Providing care for the person receiving cancer biological and molecular targeted therapies.

Learning activity

Completed



Activities [copy activities to your notebook]

1. Access [*Overview: Progress in targeted therapies for cancer*⁷⁷](#), and summarise current challenges that have been identified in the use of targeted therapies.

Haematopoietic Stem Cell Transplantation in cancer control

Haematopoietic stem cell transplantation (HSCT) has evolved over the past 20 years from experimental to first line therapy for many malignant and non-malignant diseases.⁷⁸

In non-malignant diseases, the role of transplantation is to replace defective marrow. In malignant diseases, stem cell infusions rescue the marrow following disease-eradicating myelosuppressive therapy.

Autologous transplants use an individual's previously collected and cryopreserved haematopoietic stem cells (HSC) to reconstitute the immune system following antineoplastic agents (with or without radiotherapy).

In Australia in 2014, indications for autologous transplants in recipients aged over 16 years included:⁷⁹

- multiple myeloma - 56%
- non-Hodgkin's lymphoma - 31%
- Hodgkin lymphoma - 5.5%.

Other indications included:

- acute myeloid leukaemia
- primary amyloidosis
- chronic lymphocytic leukaemia.

The most common indications for autologous transplantation in recipients aged 0-15 in 2014 were:⁷⁹

- neuroblastoma
- medulloblastoma
- other central nervous system tumours and
- Ewing sarcoma.

Allogeneic transplants use a related or unrelated donor's HSC to reconstitute the immune system of an individual who has received myeloablative or non-myeloablative chemotherapy (with or without radiotherapy). Improved understanding of the bone marrow microenvironment and chimerism has enabled the use of newer processes such as non-myeloablative haematopoietic stem cell transplantation (NMHSCT).⁸¹

In Australia in 2014, indications for allogeneic related donor transplants in recipients aged over 16 years included:⁷⁹

- acute myeloid leukaemia - 41%
- acute lymphoblastic leukaemia - 13%
- non-Hodgkin's lymphoma - 8%
- myelodysplasia - 14%.

Other indications included:

- multiple myeloma

- chronic lymphocytic leukaemia
- severe aplastic anaemia
- chronic myeloid leukaemia.

The effects of haematopoietic stem cell transplantation are numerous and range in severity. Conditioning regimens prior to HSCT alter an individual's immunity for months to several years post transplantation.⁸¹

For further information on this treatment approach, complete Module Six Part Five – Providing care for the person undergoing haematopoietic stem cell transplantation.

Learning activity	
Completed <input type="checkbox"/>	Activity 1. Access the National Cancer Institute webpage Bone Marrow Transplantation and Peripheral Blood Stem Cell Transplantation ⁸² and identify acute and chronic effects associated with HSCT.

Complementary and alternative medicines (CAMs)

Complementary therapies are supportive methods used to complement, or add to, mainstream treatment. Complementary methods are not given to cure disease, rather they may help control symptoms, improve wellbeing and manage psychological distress. Examples include guided imagery, relaxation training, massage therapy, support groups, music therapy and mindfulness meditation.⁸³ Alternative therapies are promoted as treatments to be used instead of conventional medicine. Some CAMs have effects as powerful as traditional medical treatments, which may impede, alter or enhance the treatment prescribed by western medical practitioners. This may lead to potentially negative treatment results.⁸⁴ There is no valid scientific evidence to support claims of cure or in slowing the progress of cancer with their use.⁸³

The use of CAMs is often associated with a person's need to take control, be involved in their treatment, and maximise their chance of cure, survival time or quality of life. Many people are reluctant or unwilling to speak about their use of health and wellbeing therapies with health professionals.⁸⁵ It is recommended that health professionals become more diligent in assessing the use of CAMs by people affected by cancer.

Effective communication skills including assessing the person's use of CAMs, understanding the objectives of use and exploring the evidence regarding their use remain the basic principles for initiating and exploring the use of CAMs.

Resource link

Cancer Council Victoria, (2009). [*Complementary and alternative medicine \(CAM\): communicating with patients*](#)⁸⁶

Learning activities

Completed

Activities

1. Identify the various sources of information available for the public in relation use of CAMs in cancer, and the strengths and limitation of these sources.
2. Outline reasons that a person with cancer may choose to use CAMs.
3. Access [*Mrs Li's case study*](#)⁸⁷ and watch the video '[*alternative medicines*](#)'.



Complete the following learning activities:

- Discuss how you would respond to Mrs Li's use of traditional Chinese medicines. Provide evidence based rationales for your response.
- Describe how you would assess the benefits and risks associated with the CAMs Mrs Li may be using.
- Consider some of the barriers that impact on discussing complementary therapies. How would you facilitate communication between Mrs Li and her family and health professionals about her use of CAMs?

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