Fundamentals of antineoplastic agent therapy for cancer

Key concepts

- Classification of antineoplastic agents.
- Factors influencing the selection of antineoplastic agents for cancer.
- Role of antineoplastic agents in the treatment and palliation of cancer.
- Methods for administering antineoplastic agents.
- Principles of safe handling of antineoplastic agents.
- Future directions of antineoplastic therapies in the management of cancer.
- Experience and impact of antineoplastic therapies on various health domains.
- Prevention, detection, and management of common health alterations experienced by people receiving antineoplastic therapies for cancer.

Assumed knowledge and related information

- EdCaN module: The Biology of Cancer.
- EdCaN module: Fundamentals of targeted therapies for cancer.

Objectives

On completion of this supporting resource, you should be able to:

1. Explain the role of antineoplastic therapies in the treatment and palliation of cancer.
2. Outline the classifications of antineoplastic agents.
3. Discuss principles for administering antineoplastic therapy.
4. Apply principles of safe handling when providing care for a person receiving antineoplastic therapy.
5. Discuss the experience and impact of antineoplastic therapies on the various domains of health.
6. Implement interventions to prevent, detect and manage common health alterations experienced by people receiving antineoplastic therapies for cancer.

Learning activities

At times, you will have learning activities to complete. Click on the learning activities button and a list of questions will pop up. The questions will relate to the content you've just read or the video you've just watched.

Resource links

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

PDF of EdCaN module: Fundamentals of antineoplastic agent therapy for cancer
You can download a PDF version of the module.

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The role of antineoplastic therapy in cancer control

Antineoplastic drugs, alone or in combination, may be used in the management of cancer to achieve:[1-3]

- chemoprevention (the use of natural or synthetic products or antineoplastic agents to prevent or suppress carcinogenesis in people highly susceptible to certain cancers)
- cure (all cancer cells destroyed, life expectancy unchanged)
- control (preventing or slowing the growth of a tumour to prolong survival)
- palliation (management of symptoms).

A number of terms describe the role of antineoplastic agents in cancer control:[2, 4]

- **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, radiation therapy 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.

Learning activities	
Completed	Activities
☐	1 Access a current text or evidence based clinical guidelines and describe clinical examples of the use of antineoplastic agents with the goals of: • Chemoprevention. • Cure. • Control. • Palliation.

Key concepts of antineoplastic agent therapy

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.[1]

Cellular kinetics

The mechanisms of action of antineoplastic agents are based on the concepts of cellular kinetics - cell cycle time, growth fraction, and tumour burden:[5]

- 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 that have shorter cycle times are more easily damaged by cell-cycle phase specific cytotoxic agents. Continuous infusions of these agents result in higher cell kill percentages as a greater number of cells are exposed to the agent.

- The 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.[6] 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.

- The 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.[1, 7]

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.[7]

Learning activities	
Completed	Activities
☐	1 Access a current text and review the biology of the cell, including cell structures and functions.
☐	2 Summarise the process of normal cell repair and contrast this with the process of malignant cell repair.
☐	3 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 membrane. • Cardiac muscle.
☐	4 Provide three examples of how cellular kinetics can be manipulated in the treatment of cancer.

Pharmacodynamics

Pharmacodynamic properties of antineoplastic agents, including their actions and behaviour in a body, define the therapeutic effects of the agent.[1] The effective dose must be neither too high (side effects will be too severe) nor too little (the tumour will continue to grow, and may develop resistance.). Key pharmacological factors impacting on antineoplastic actions include:[1]

- **Route of administration**
  Dictated by the characteristics of individual drugs and chosen to optimise drug availability. Anti-cancer effects may be improved with higher concentrations at the tumour site.

- **Drug distribution**
  The distribution and transport of drugs within the body can affect the proportion of free or pharmacologically active drug in the bloodstream.

- **Biotransformation**
  The metabolic biotransformation of antineoplastic agents includes oxidation, reduction, hydrolysis, or configuration which is done mainly in the liver.

- **Excretion**
  Agents are commonly excreted via the kidneys or liver.

- **Drug interactions**
  Agents may either inhibit or potentiate the action of another, thus modifying the therapeutic or toxic effects, or its enzyme inhibition or induction.

- **Drug resistance**[8, 9]
  Primary resistance refers to the lack of tumour response when agents are administered. Secondary resistance occurs after initial tumour regression. Factors contributing to secondary resistance include:
  - variations in drub bioavailability
  - drug metabolism or elimination
  - tumours possibly located in 'sanctuary sites'
  - changes in cell kinetics
  - drug-related toxicity in the recipient
  - reduced blood supply to the tumour.

  Multidrug resistance (MDR) refers to the phenomenon whereby exposure to a single drug is followed by cross-resistance to other apparently unrelated drugs.

Learning activities	
Completed	Activities
☐	1 Choose two antineoplastic agents. For each drug summarise the pharmacodynamic properties and outline any considerations for nursing management: • route of administration • drug distribution • biotransformation • excretion • drug interaction
☐	2 Detail the proposed mechanisms of multidrug resistance.
☐	3 Outline current evidence based strategies to overcome multidrug resistance.

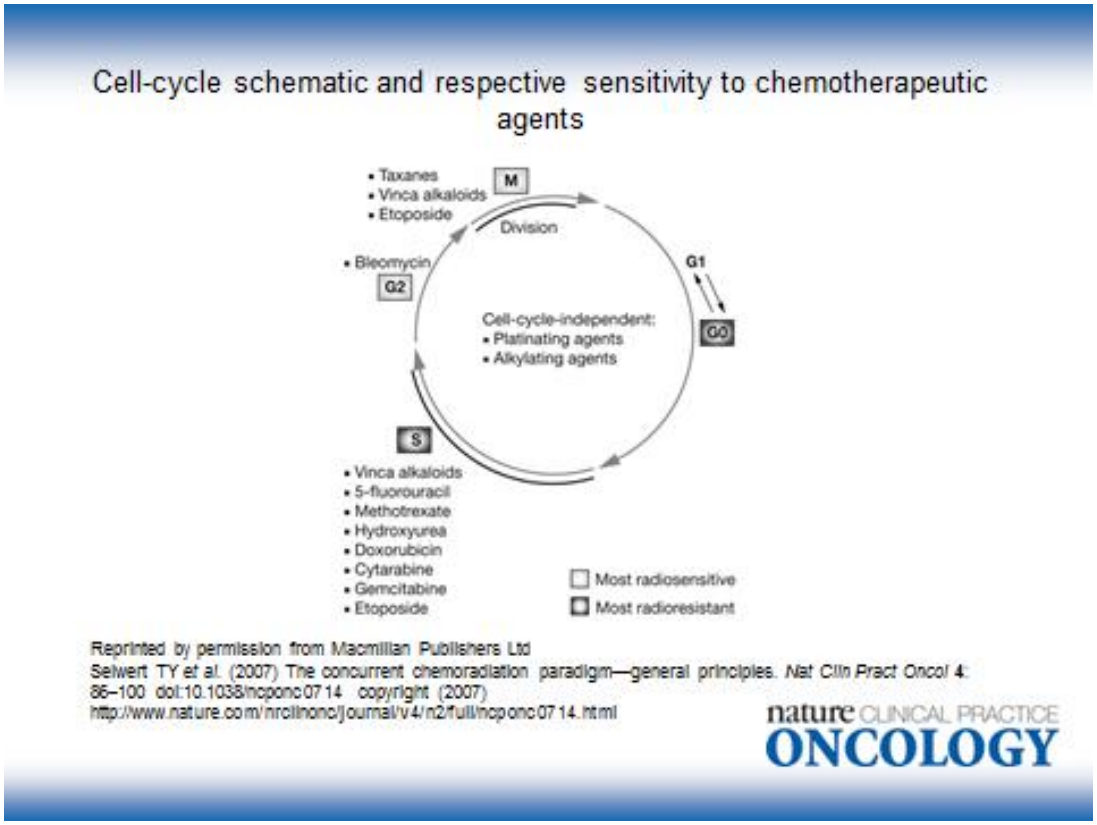
Classification of antineoplastic agents

Most antineoplastic agents are classified according to their structure or cell cycle activity - either cell cycle phase specific or cell cycle phase non-specific:[9]

- 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 dependant 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.

The following figure highlights the action of common agents at each point of the cell cycle.[10]



Antineoplastic agents are also traditionally divided by their origin or mechanism of action. The main groups include:[1, 7, 11]

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

Alkylating and alkylating-like agents

Classic alkylating agents interfere with DNA replication by crosslinking DNA strands, DNA strand breaking, and abnormal pairing of base pairs. They exert their lethal effects on cells throughout the cell cycle but tend to be more effective against rapidly dividing cells.[1, 7, 11]

Because alkylating agents are active against cells in G0, they can be used to debulk tumours, causing resting cells to be recruited into active division. At this point, those cells are vulnerable to the cell cycle-specific agents. These agents are active against lymphomas, Hodgkin's disease, breast cancer, and multiple myeloma.[1, 7, 11]

Major toxicities occur in the haematopoietic, gastrointestinal and reproductive systems. Individuals treated with these agents are also placed at a higher risk of developing secondary malignancies. Examples include Cyclophosphamide, Ifosfamide, Chlorambucil, Busulfan and Melphalan.[1, 7, 11]

The nitrosureas are a subgroup of the alkylating agents. They also interfere with DNA replication and repair. They are highly lipid soluble and readily cross the blood-brain barrier. An example is Carmustine.[1, 7, 11]

Another subgroup of alkylators called Platinum-containing compounds include agents such as Cisplatin, Carboplatin and Oxaliplatin.[12] Their cytotoxic properties also extend to alteration of the cell membrane transport systems and suppression of mitochondrial function.

Learning activity	
Completed ☐	Activity 1 Choose an alkalyting agent and discuss its: • Indications in cancer control. • Mechanism of action. • Adverse effects. • Administration considerations.

Antimetabolites

Antimetabolites interfere with DNA and RNA synthesis by acting as false metabolites, which are incorporated into the DNA strand or block essential enzymes, so that DNA synthesis is prevented.[13] Most agents are cell cycle phase specific for S phase. These agents are most effective when used against rapidly cycling cell populations and are consequently more effective against fast-growing tumours than slow-growing tumours. Major toxicities occur in the haematopoietic and gastrointestinal systems. Examples include Methotrexate, 5-Fluorourocil and Cytosine Arabinoside.[1, 7, 11]

Hypomethylating agents represent a class of drugs that may restore normal gene function to genes responsible for cell division and differentiation.[14] Hypomethylating agents may function as biological response modifiers by affecting cytokine cell signaling.[12] These agents may be identified as antimetabolites and they include 5-azacytidine and Decitabine.

Learning activity	
Completed ☐	Activity 1 Choose an antimetabolite and a hypomethylating agent and discuss its: • Indications in cancer control. • Mechanism of action. • Adverse effects. • Administration considerations.

Antitumour antibiotics

Antitumour antibiotics (also called Anthracyclines) interfere with RNA and DNA synthesis. Most drugs are cell cycle non-specific. Major toxicities occur in the haematopoietic, gastrointestinal, cardiac and reproductive systems. Cardiac toxicity may be manifested as acute changes in the electrocardiograph (ECG) and arrhythmias. Individuals with preexisting heart disease are most at risk.[12] Examples include Bleomycin, Daunorubicin, and Doxorubicin.[1, 7, 11]

Learning activity	
Completed ☐	Activity 1 Choose one anthracycline and discuss its: • Indications in cancer control. • Mechanism of action. • Adverse effects. • Administration considerations.

Plant alkaloids

Plant alkaloids bind to microtubule proteins during metaphase, causing mitotic arrest. The cell cannot divide and dies. This group is mainly cell cycle phase specific for M phase. Major toxicities occur in the haematopoietic, integumentary, neurologic and reproductive systems. Hypersensitivity reactions also may occur during administration of these agents.[1, 7, 11] This group contains three subgroups:[1, 7, 11]

- the vinca alkaloids e.g. vincristine and vinblastine
- the epipodophyllotoxins e.g. etoposide and teniposide
- the taxanes e.g. paclitaxel and docetaxel.

Learning activity	
Completed ☐	Activity 1 Choose an antineoplastic agent from each subgroup of the plant alkaloids and discuss their: • Indications in cancer control • Mechanism of action • Adverse effects • Administration considerations.

Miscellaneous agents

Miscellaneous agents differ from any of the major classes of cytotoxic agents.
Common miscellaneous agents are asparaginase and hydroxyurea.[1, 7, 11]

Topoisomerase inhibitors prevent realigning of DNA strands and maintain single-strand breaks. Major toxicities occur in the haematopoietic and gastrointestinal systems. Examples include irinotecan and topotecan.[1, 7, 11]

Learning activity	
Completed ☐	Activity 1 Choose a miscellaneous agent and discuss the: • Indications in cancer control. • Mechanism of action. • Adverse effects. • Administration considerations.

Hormonal agents

Hormonal agents alter the internal / extracellular environment. Most agents are cell cycle phase non-specific. Breast, thyroid, prostate and uterine cancers are examples of tumours that are sensitive to hormonal manipulation. With these diseases, the action of hormones or hormone antagonists depends on the presence of hormone receptors in the tumours themselves (i.e. oestrogen receptors in breast cancers). [1, 7, 11] There are individual classifications of hormonal agents:[13]

- adrenocorticoids, eg. prednisone
- androgens, eg. testosterone propionate
- oestrogens, eg. diethylstilbestrol
- selective oestrogen receptor modulators, eg. tamoxifen citrate
- selective aromatase inhibitors, eg. anastrozole
- progesterones, eg. megestrol acetate
- antitestosterone , eg. flutamide.

Major toxicities occur in the gastrointestinal, sexual / reproductive systems and mood and sleep pattern changes.[1, 7, 11]

Learning activity	
Completed ☐	Activity 1 Choose one hormonal agent and discuss its: • Indications in cancer control. • Mechanism of action. • Adverse effects. • Administration considerations.

Factors influencing agent selection and administration

There are a number of key issues to consider when planning delivery of antineoplastic agents:

Tumour characteristics:[5]

- Tumour burden: the larger the tumour, the greater the likelihood of the development of metastases.
- Tumour growth rate: the more rapidly growing the cancer, the more responsive its cells are to cytotoxic therapy.
- Tumour cell heterogeneity: increases the risk for the development of resistance.
- Tumour location.
- Hormone receptor status.
- Blood supply to the tumour.

The blood-brain barrier is a cellular structure inhibiting various substances from entering the brain, protecting both the brain and the cerebrospinal fluid from harmful agents.[15]

Individual characteristics:[8]

- Performance status: those with a better status may have a smaller tumour burden, and better ability to tolerate and respond to cytotoxic therapy. Cancer treatment centres use performance status as a prognostic indicator. Additional factors include stable weight, absence of concomitant illnesses, and optimal symptom management.
- Reduced immunity and weight loss decreases the individual's tolerance to treatment effects. If dose reductions and treatment delays are a result, tumour cells have a chance to develop resistance.
- Circadian rhythm refers to routine fluctuations in the biological functions of living creatures. These variables may affect drug absorption, metabolism, distribution, and elimination, and may be controlled to allow for intensification of drug dosages, and the reduction of side effects of being treated with cytotoxic drugs.[2] For example, administering Fluorouracil in the evening may assist in reducing toxicities as the cells of the gastrointestinal system and the bone marrow are most actively dividing during the first half of the day.[8]

Single-agent therapy

Single-agent therapy was often used in the early history of cancer chemotherapy. The major disadvantages of single-agent therapy led to clinical trials, starting in the 1960s, with combinations of drugs. Some of these disadvantages were:[7]

- poor success at achieving long-term remissions
- development of resistance to further drug therapy - the most common reason for treatment failure
- severe or lethal toxicities when given in doses adequate to eradicate the tumour.

Combination therapy

With a few exceptions, combination therapy has replaced single-agent therapy in the medical management of cancer. Combinations of agents have been associated with less likelihood of resistance, increased fractional cell kill, and improved response rates. Principles underpinning the selection of agents within combination therapy include:[1]

- all drugs used should be of proven value in the disease they are intended to treat
- agents should have different modes of cytotoxic action
- if possible, the dose-limiting toxicities of the chosen agents should be different.

Learning activities		
Completed		Activities
☐	1	Describe the physiology of the blood-brain barrier.
☐	2	Outline the implications of the blood-brain barrier for cancer control efforts.
☐	3	Outline common methods of assessing an individual's performance status pre-treatment.
☐	4	Define the term 'dose intensity'.
☐	5	Discuss the implications of dose reduction and treatment delays on dose intensity.
☐	6	Provide evidence based examples of the impact dose intensity has on a person's outcomes.
☐	7	Discuss the rationale for continuous infusional and intermittent antineoplastic therapy.
☐	8	Provide three examples of how an individual's hormone receptor status impacts on treatment determination.

Principles of administration of antineoplastic agents in professional nursing practice

There are a number of key professional issues which must be considered in the administration of antineoplastic agents:

- nurse competency
- health professional roles and responsibilities
- policy and procedure.

To prepare nurses to administer antineoplastic agents, educational programs should include both theoretical and supervised clinical experience.[16] Regular assessment of nurses' competence should occur to ensure theory and practice remains evidence based, and to help prevent errors in administration.[17]

EdCaN has developed a competency assessment tool[18] for evaluating a specialist cancer nurses' competence in administering antineoplastic agents.

The Cancer Institute NSW has developed the Antineoplastic Drug Administration Course (ADAC) which supports health professionals develop the necessary knowledge and clinical skills to administer antineoplastic drugs via different routes and handle related waste safely. It is becoming nationally recognised as a minimum requirement nurse competence in administration of antineoplastic agents.

Risk assessment and quality assurance are key elements of safe practice associated with antineoplastic agents. Systems, policies and procedures are required to support the reporting of adverse events, incidents and near misses. Identification of 'error prone' practices may indicate the need for practice modification.[16]

The Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] is a national document developed to provide guidance on the safe prescribing, dispensing and administration of antineoplastic agents used in the treatment of cancer. This document should be used as a guidance tool to inform local practice and be adapted according to local service needs.

Learning activities	
Completed	Activities
☐	1 Outline the roles and responsibilities of the nurse in antineoplastic agent administration.
☐	2 Access the EdCaN Competency assessment tool for antineoplastic agent administration[18], The Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] or the editorial Medication errors in hospitals: what can be done?[19] as well as current state or territory guidelines. • Discuss processes that are in place in your health facility to ensure safe standards of antineoplastic administration. • Discuss the strengths of your facility's current antineoplastic agent administration practices in light of the recommendations within these documents. • Identify any areas for improving your facility's current antineoplastic agent administration practices in light of the recommendations within these documents. • Describe how you would manage an administration error involving an antineoplastic agent.

Safe handling

Exposure to antineoplastic agents poses a potential health risk to staff who:[16]

- prepare, handle, or administer the drugs
- care for individuals following administration
- dispose of these drugs or related waste.

Many antineoplastic agents, proven to be carcinogenic, mutagenic and teratogenic, are classified as hazardous substances. Direct exposure to antineoplastic agents can occur during administration or handling, and involves inhalation, ingestion or absorption.[20-22]

Safe levels of occupational exposure to hazardous agents and a reliable method of monitoring exposure have proven difficult to determine.[3] The health risk of any procedure involving antineoplastic agents stems from the inherent toxicity of the drug and the extent to which individuals are exposed.

Health professionals working with antineoplastic agents are guided by guidelines, policies, and procedures to ensure maintenance of standards of care and to reduce occupational exposure.[16]

Learning activities	
Completed	Activities
☐	Access your state or territory policy document guiding practice with antineoplastic agents (examples below), and your own institution's policy and procedure for handling cytotoxic substances. • Safe Handling of Cytotoxic Drugs and Related Wastes: Guidelines for South Australian Health Services 2012 • Guide for handling cytotoxic drugs and related waste. Workplace Health and Safety Queensland, 2014 • The Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] • Cancer Nurses Society of Australia Position Statement on the Minimum Education Requirements for Nurses in the Administration of Anti-Cancer Drugs within the Oncology and Non-Oncology Setting[23]
	1 Appraise the current policy and procedures in your facility in light of the key guidelines. 2 Outline the key elements of an in-service program for nurses new to cancer control on safe handling of antineoplastic agents and their waste products. 3 Outline the principles of safe practice you would apply when advising a person regarding cytotoxic precautions in their home and community. 4 Discuss strategies used to ensure cytotoxic safety for the following groups and individuals: • Support staff (i.e. cleaners, orderlies). • Nurses in specialties other than cancer. • Radiology staff. • Pathology staff. • Accident and emergency staff.

Providing information and supportive care

A key role of the SCN is to meet the informational needs of people affected by cancer receiving antineoplastic agents. Education of people receiving antineoplastic agents can: [1]

- provide support and knowledge to empower them to manage self-care effectively
- reduce fear
- increase self-confidence
- improve compliance.

Before administering antineoplastic agents, valid informed consent is required.[1]

Education for the person receiving antineoplastic agents should involve:[16]

- a coordinated multidisciplinary approach
- timely documentation
- verbal and written information providing the aims, effects and likely outcomes of treatment
- a list of appropriate websites
- information reinforced on subsequent visits
- medication guides and diaries.

For further information access the supporting modules:

- EdCaN module: Cancer Treatment Planning.
- EdCaN module: Cancer Supportive Care Principles.

Learning activities		
Completed		Activities
☐	1	Access pp. 12-14 of the Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16], and document a detailed education plan for a person receiving antineoplastic agents.
☐	2	Access Evaluation of the addition of video-based education for patients receiving standard pre-chemotherapy education[24] (free article, but you must register and login to access it) and critically discuss the role of various forms of media (print, internet, video) in providing education for people receiving antineoplastic agents.
☐	3	Identify key websites you would recommend to support the information needs of people receiving antineoplastic agents, providing a justification for your recommendation.
☐	4	Outline the process of obtaining and documenting informed consent prior to administration of antineoplastic agents.
☐	5	Discuss the ethical and professional responsibility of the SCN in the process of informed consent.

Pre-treatment considerations

Assessment of the individual before starting treatment is necessary to identify and prevent treatment effects, provide a baseline measure to compare response, and ensure correct dosage and administration processes.[1] Individual assessment involves:[16, 25]

- relevant diagnosis, medical and medication history
- drug allergies
- body parameters and laboratory values
- questions regarding compliance, treatment tolerance, and adverse events
- risk assessment of anaphylaxis or extravasation
- venous access.

Treatment protocol considerations:

- medication such as antiemetics should be given as per protocol to ensure effective therapeutic levels[16]
- cytoprotectants are used to prevent or reduce specific system toxicities while safeguarding the antineoplastic effects[2]
- drug sequencing
- test dosing.

Dose calculation considerations[16]

- the dose of a drug is generally based on the individual's body surface area (BSA) or weight
- a standardised method of calculation of the BSA[26] should be used by all clinicians within a healthcare facility
- the use of printed tables and slide-rules for the calculation of the BSA is not recommended
- dose adjustments may be made in consideration of toxicities and factors affecting drug elimination.

Learning activities	
Completed	Activities
☐	1 Access the Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] , and summarise an individual's pre-treatment assessment using the framework provided in table 14.
☐	2 Discuss specific pre-treatment considerations associated with administration of the following agents: • Bleomycin. • L-asparaginase. • Paclitaxel. • Doxorubicin.
	3 Identify two agents used as cytoprotectants and discuss the indications for their use.
	4 Access the Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] , and: • Appraise antineoplastic agents protocols in your facility in light of recommendations in the guidelines. • Conduct an in-service for new nurses on how to utilise an antineoplastic agents protocol.
	5 Access the medical record for a person who has received antineoplastic agents, and: • Calculate the individual's BSA. • Calculate dose requirements as per the protocol.

Routes of administration

Antineoplastic agents can be administered via various routes including:[1]

Intravenous

- peripheral venous access
- central venous access
    - percutaneous lines
    - peripherally inserted central catheters (PICC)
    - implantable devices (Port-a-caths)
    - tunnelled venous access devices (Hickman catheter).

Oral

- Enables shorter treatment time, greater independence of the individual, and improved tolerability.
- Disadvantages may be that the individual is not monitored as intensively, there is a risk of noncompliance, possibility of under- or over-dosing, and inconsistency of absorption from the gastrointestinal tract.

Intrathecal/intraventricular

- Agents are administered directly into the cerebrospinal fluid, usually as prophylaxis in leukaemia or lymphoma.

Intraperitoneal

- Direct administration of agents into the peritoneal cavity.
- It allows ovarian or colorectal cancers to be 'bathed' in high concentrations of antineoplastic agents.

Intrapleural

- Direct administration of agents into the pleural cavity.
- It allows treatment of malignant effusions, which may be associated with lung, breast, prostate, gastrointestinal and ovarian cancers.

Intravesical

- Administration of agents directly into the bladder to treat superficial cancer of the bladder.

Topical

- Commonly prepared as ointments, and usually used to treat sun cancers.

Subcutaneous and intramuscular

- Uncommonly, agents may be administered by these routes.

Learning activities	
Completed	Activities
☐	1 Access a current text and: • Outline the risks and benefits for different methods of intravenous access. • Discuss considerations in choosing the most appropriate intravenous access device for a person receiving antineoplastic agents. • Summarise the principles of venipuncture for antineoplastic agent administration.

		• Appraise current policy and procedures for intravenous antineoplastic agent administration in light of state and national guidelines. • Define vesicant and irritant agents and outline implications for their administration.

☐	2	Access the following documents and complete the activities below.
		• Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16]
		• Role of the nurse in patient education and follow-up of people receiving oral chemotherapy treatment: an International survey[27]
		• Multinational Association for Supportive Care in Cancer MASCC Oral Agent Teaching Tool (MOATT)[28]
		  • Outline the common concerns associated with oral administration of antineoplastic agents.
		  • Develop an in-service (including PowerPoint or written resources) for nursing staff in non-specialist settings for the administration of oral antineoplastic agents.
		  • Discuss the information which would be provided to a person going home with oral antineoplastic agents.

☐	3	Access a current text and local policy and procedures relevant to intrathecal (IT) administration of antineoplastic agents, and Guidelines for the Safe Prescribing, Supply and Administration of Cancer Chemotherapy[16] and: • Outline the key steps in preparing of a person for IT administration of an antineoplastic agent • Outline the role of each member of the MDT in IT administration of an antineoplastic agent • Discuss common adverse effects which may occur during IT drug administration and strategies to prevent and manage these issues • Summarise the evidence based post-procedural care of the person following IT administration of an antineoplastic agent.
☐	4	Access a current text and local policy and procedures relevant to intraventricular administration of antineoplastic agents, and: • Outline the key steps in preparing a person for intraventricular administration of an antineoplastic agent. • Outline the role of each member of the MDT in intraventricular administration of an antineoplastic agent. • Discuss common adverse effects which may occur during intraventricular drug administration and strategies to prevent and manage these issues. • Summarise the evidence based post procedural care of the person following intraventricular administration of an antineoplastic agent.
☐	5	Outline the indications, adverse effects and nursing considerations associated with the following routes of administration for antineoplastic agents: • Intraperitoneal. • Intrapleural. • Intravesical. • Topical. • Subcutaneous. • Intramuscular.

Models of care

Day therapy and home-based therapy offers advantages of maintaining lifestyle and minimising disruption of day-to-day activities.[1] The establishment of shared care oncology outreach services and nurse-led services are examples of new approaches to improving access to cancer treatment services.[29]

Reported benefits of shared care models include:[30]

- reduced fragmentation of care; that is, a better integrated, more continuous system of care
- more efficient use of scarce resources and related cost efficiencies
- strengthened links between primary, secondary and tertiary sectors
- improved working relationships between providers
- improved satisfaction among people affected by cancer and providers
- increased access to care for people affected by cancer.

These models of care also raise a number of logistical and safety issues that need to be addressed. Challenges include:[30]

- power and status differences between health providers (eg. between nurses and GPs or GPs and medical specialists)
- professional territorialism and perceived threat to professional autonomy and/or scope of practice
- current funding arrangements that require the GP to see each patient in order to receive service payment/reimbursement
- dedicated time and personnel to implement and manage shared care
- limited methods to measure the outcomes of shared care models.

Learning activities	
Completed	Activities
☐	1 Describe the community and hospital supports available for people receiving antineoplastic agent treatment in their home.
☐	2 Access Shared Care Models: A high-level literature review[29] and WA Cancer & Palliative Care Network's Integrated Primary Care & Cancer Services Model of Care[31], and: • Outline the shared care model of care for the person affected by cancer receiving antineoplastic agents. • Discuss the role of the SCN in the shared care model outlined above.

Responses to antineoplastic therapy

While the target of antineoplastic agents is the cancer cell, these agents are unable to distinguish between normal and cancer cells. Some temporary damage will occur to normal cells, especially those cells that are rapidly dividing, such as bone marrow, gonads, gastrointestinal mucosa and hair follicles.

Some drugs have an affinity to certain organs in the body (e.g. bleomycin and lung tissue), and toxicity may occur in these organs over time.

Responses to antineoplastic therapy can be classified as:

- Anticipatory.
- Immediate.
- Short-term.
- Long-term.

Anticipatory responses

Anticipatory nausea and vomiting is a learned response after prior episodes of antineoplastic agent-induced nausea and vomiting.

The symptoms occur when individuals are reminded of a prior emetic experience.[1]

Learning activity	
Completed ☐	Activity 1 Access a current text, and: • Discuss the pathophysiology of anticipatory nausea and vomiting. • Outline strategies to minimise anticipatory nausea and vomiting.

Immediate responses

A number of immediate effects may occur within 30 minutes of the start of treatment. These include:[1]

- pain at insertion site
- venous pain
- cold sensation along vein
- red flush along the vein
- facial and bodily flushing
- hypotension
- abnormal tastes or smells
- hypersensitivity reaction
- extravasation.

Hypersensitivities

Some antineoplastic agents are associated with hypersensitivity reactions mediated by an immune mechanism (IgE), and involve the release of vasoactive agents. It occurs when an individual is exposed to a drug a second time, after prior exposure and when the immune cells are sensitised. Systemic responses include urticarial, rash, hypotension and more severe bronchospasm or anaphylaxis with profound vasomotor collapse.[13]

It is also important to consider that individuals may be allergic to other substances in the medical environment such as latex, other supportive drugs, blood transfusions, or food.

Extravasation

Extravasation occurs when a drug inadvertently leaks into the surrounding subcutaneous or subdermal tissues rather than into the intravenous compartment during administration. The degree of tissue destruction is directly related to the properties of the drug extravasated, duration of tissue exposure, and amount of infiltrate.[1]

Extravasation of vesicant drugs can have devastating consequences for individuals. Effects include pain, tissue necrosis and possible limb dysfunction. Some agents have antidotes that will minimize or prevent local tissue damage.[13]

Related resource

Resource Document – Extravasation Management [32] (free resource, but you must register and click 'Remember me' to bypass the login page in future).

Learning activities	
Completed	Activities
☐	1 Identify agents associated with hypersensitivity reactions and outline strategies to minimise their occurrence and manage any adverse events.
☐	2 Access Resource Document – Extravasation Management [32] (free resource, but you must register and click 'Remember me' to bypass the login page in future) website, and: • Identify common vesicant, irritant and non-irritant agents. • Appraise the current policy and procedure in your health care facility for managing extravasation of antineoplastic agents in light of the published guidelines • Discuss immediate actions to manage a vesicant extravasation.
☐	3 Identify agents associated with pain at administration and discuss strategies to prevent and manage discomfort during and after their administration.

Short-term responses

Short-term effects occur between 3 and 7 days after therapy begins.[1] These may include:

- nausea and vomiting
- anorexia
- mucositis
- myelosuppression
- possible recall of radiation skin reactions
- pain at tumour site or jaw area
- flu-like syndrome, including fever
- chemical cystitis
- haematuria
- malaise
- diarrhoea
- constipation
- cold-induced paraesthesia (oxaliplatin).

Nausea and vomiting

- Acute nausea and vomiting develops within the first 24 hours after administration of antineoplastic agents.
- Delayed nausea and vomiting occurs more than 24 hours after administration of antineoplastic agents and may persist for a week.
- The emetogenic potential of an antineoplastic agent and the individuals response determines the approach to management of nausea and vomiting.[33]

Related resources

- National Cancer Institute Nausea and Vomiting (PDQ®)[34]: PDQ cancer information summary provides comprehensive, peer-reviewed information for health professionals about the pathophysiology and treatment of nausea and vomiting.
- National Comprehensive Cancer Network NCCN Clinical Practice Guidelines in Oncology Antiemesis Free resource, but you need to register and log in to access it. Consensus guidelines on the management of chemotherapy induced nausea and vomiting.
- Multinational Association for Supportive Care in Cancer Antiemetic Guidelines[35]: Presentations and publications providing detailed summary of the deliberations from this consensus guideline meeting conducted in Perugia, Italy, in late March 2004.
- Multinational Association for Supportive Care in Cancer MASCC Antiemesis Tool (MAT)[36]: The MASCC Antiemesis Tool (MAT) was developed by members of MASCC. The concept of the MAT is to provide an easy-to-use and easy-to-evaluate tool to assist in providing the best individual care to people affected by cancer and facilitate the assessment of the effectiveness of antiemetic strategies.
- Chemotherapy-Induced Nausea and Vomiting (CINV) Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.

Mucositis

- Mucositis is an inflammation of the lining of any part of the gastrointestinal tract, including the oral mucosa. This lining is highly vulnerable to treatment-related toxicity because of its rapid cell turnover. Individuals affected often present with pain, difficulty eating, and ulceration or erythema in the mouth.
- Agents known to induce mucositis include bleomycin, doxorubicin, daunorubicin, docetaxel, 5-FU, and methotrexte, in addition to high dose therapy with busulphan, etoposide, melphalan, and thiotepa.[1]

- Combining antineoplastic agents and radiation modalities usually increases the normal tissue reactions.

Related resources

- National Cancer Institute Oral Complications of Chemotherapy and Head/Neck Radiation (PDQ®)[37] This summary describes oral complications caused by chemotherapy and radiation therapy, and various methods of prevention and treatment.
- Mucositis Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.

Myelosuppression

- Myelosuppression is the most frequent dose-limiting toxicity of antineoplastic agents, and is potentially life-threatening.[1]
- Infections, anaemia and thrombocytopenia are related to bone marrow suppression.

Related resources

- National Comprehensive Cancer Centre NCCN Clinical Practice Guidelines in Oncology Cancer- and Chemotherapy- induced anaemia Free resource, but you need to register and log in to access it. Consensus guidelines on the prevention and management of cancer and chemotherapy-induced anaemia.
- National Comprehensive Cancer Centre NCCN Clinical Practice Guidelines in Oncology Myeloid Growth Factors Free resource, but you need to register and log in to access it. Consensus guidelines on the use of myeloid growth factors in cancer control.
- National Comprehensive Cancer Centre NCCN Clinical Practice Guidelines in Oncology Prevention and treatment of cancer-related infections Free resource, but you need to register and log in to access it. Consensus guidelines on the prevention and management of cancer-related infections.
- Prevention of Infection Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.

Constipation

Constipation can result from disease, nutritional deficits, and medications including antineoplastic agents, analgesics, and antiemetics[1].

Related resources

- Constipation Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.

Learning activity	
Completed ☐	Activity 1 Choose three acute effects of antineoplastic agents, and summarise current evidence based strategies to prevent and manage these effects.

Long-term responses

Long-term effects may create significant problems, as they can cause lasting damage to the body and affect the person's quality of life. These effects, which are often cumulative, include physical effects, second primary malignancies, and sexuality and psychological issues. Specific effects include:[1]

- alopecia
- skin reactions
- nail ridging
- thrombophlebitis
- organ damage, e.g. renal, hepatic, pulmonary and cardiac
- neurological problems and CNS toxicity
- sexual dysfunction
- psychological issues.

Fatigue

- Fatigue may be related to the disease and/or treatment effects such as pain, nutritional problems, and myelosuppression.
- Associated with feelings of tiredness, lack of energy and inability to continue, fatigue has been suggested to affect 60-90% of individuals receiving antineoplastic agents.[1]

Related resource

- Fatigue. Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Cancer-Related Fatigue

Nutritional deficits

- These include taste changes, pain from mucositis, nausea and vomiting, and reduced hunger sensations.[1]

Related resources

- Self-Care Strategies to Cope With Taste Changes After Chemotherapy[39]
- National Cancer Institute: Nutrition in Cancer Care[40]: This PDQ cancer information summary provides comprehensive, peer-reviewed information for health professionals about nutrition before, during, and after cancer treatment.

Nerve damage

- Peripheral neuropathy induced by antineoplastic agents impacts on physical functioning and quality of life.
- Antineoplastic agents associated with peripheral neuropathy include platinum compounds, taxanes, vinca alkaloids, thalidomide, and bortezomib.[41]

Related resource

- Peripheral Neuropathy. Putting Evidence into Practice (PEP) resource, Oncology Nursing Society.

Alopecia

- Hair loss may be apparent 1-2 weeks after administration of antineoplastic agents and reaches a peak in 1-2 months.
- Agents associated with hair loss include: amsacrine, bleomycin, busulfan, cyclophosphamide, cytarabine, dactinomycin, daunorubicin, dacarbazine, doxorubicin, etoposide, 5-FU, hydroxyurea, ifosfamide, interleukin-2, methotrexate, nitrosureas procarbazine, vinblastine, and vincristine.
- Distress and anxiety related to altered body image and self-concept may occur.[1]

Sexual and reproductive issues

- Women may experience amenorrhoea with hot flushes, insomnia, and vaginal dryness as well as decreased fertility or permanent infertility.
- Actual and potential gonadotoxic agents include nitrogen mustard, cyclophoshamide, L-phenalalanine mustard, busulfan, and chlorambucil.[1]
- Men may experience decreased or absent production of sperm, which may recover over a period of years.
- Sperm production is affected by alkylating agents, cisplatin, vinblastine, and bleomycin[1].

Related resources

- National Cancer Institute Sexuality and Reproductive Issues (PDQ®) This PDQ cancer information summary provides comprehensive, peer-reviewed information for health professionals about sexuality and reproductive issues that cancer patients may experience during or after treatment.
- The psychosexual care of women affected by gynaecological cancers[42]: These learning modules will help all health professionals develop the knowledge and skills to support women and their partners experiencing psychosexual concerns following gynaecological cancer. This resource can be used for self-directed learning or by educators in both clinical and academic settings as part of a facilitated learning program.

Cardiac effects

- Cardiotoxicities may develop as intermediate to late effects after treatment with antineoplastic agents.
- Agents associated with cardiotoxic effects include doxorubicin, epirubicin, mitoxantrone, idarubicin, trastuzumab, bleomycin, high dose cyclophosphamide, 5-FU, ifosfamide, mitomycin-C, and paclitaxel.[1]

Pulmonary effects

- Pulmonary toxicities occur due to damage to the endothelial cells of the lungs, and result in pneumonitis or fibrosis.
- Agents associated with pulmonary effects include bleomycin, BCNU and CCNU, busulfan, carmustine, chlorambucil, cyclophosphamide, cytarabine, docetaxel, fludarabine, lomustine, melphalan, methotrexate, mitomycin C, and paclitaxel.[1]

Second primary malignancies

- Secondary malignancies can be categorised as treatment-related, syndromic, or due to shared etiologic influences (lifestyle, environment, individual factors or genetic or other influences).[43]
- Secondary malignancies are most commonly related to the use of alkylating agents, the duration of therapy and the use of antineoplastic agents in people aged over 40.[43]
- The most common antineoplastic agent induced second malignancy is acute leukaemia. Second cancers have distinctive chromosome abnormalities, and survival after antineoplastic agent-related leukaemia is generally quite poor. Non-Hodgkin's lymphomas or solid tumours also can occur as second malignancies.[43]

Learning activity	
Completed ☐	Activity 1 Choose three long-term effects of antineoplastic agents, and summarise current evidence based strategies to prevent and manage these effects.

Toxicity grading scales

Toxicity grading scales provide consistency in reporting, and provide a framework for assessment and documentation of adverse effects. Objective assessment of the impact of treatment may inform the need for adjustments to the treatment plan.

CTCAE (Common Terminology Criteria for Adverse Events) is a list of adverse event (AE) terms commonly encountered in oncology. Each AE term is defined and accompanied by a grading scale that indicates the severity of the AE. With the availability of new agents and the multimodality interventions, it is critical to systematically monitor the AEs that are linked to oncology research. CTCAE is intended to be an agreed on terminology for the designation, reporting and grading of AEs that occur in oncology research.[44]

CTCAE serves several purposes, such as:[44]

- to standardise AE reporting within the NCI oncology research community, across groups and modalities
- to facilitate the evaluation of new cancer therapies, treatment modalities, and supportive measures
- to aid in AE recognition and severity grading
- to monitor safety data and for regulatory reporting
- to define oncology research protocol parameters (eg. eligibility criteria; dose limiting toxicity; maximum tolerated dose; dose modification).

Related resource

— Common Terminology Criteria for Adverse Events (CTCAE)

Learning activity	
Completed ☐	Activity 1 Access the National Cancer Institute toxicity criteria[45], and provide a clinical example of how the use of objective criteria facilitates safe and effective care.

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