

CLINICAL CLERKSHIP ONCOLOGY SELECTIVE HANDBOOK

Revision 9
2017 – 2018



Department of Oncology

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WELCOME

Welcome to the oncology block of your clinical clerkship. We hope to provide you with a very enjoyable educational experience to stimulate further interest in this rapidly developing field.

Oncology as a medical field is constantly changing, but deals at the same time with the "timeless" existential issues that are at the core of a physician-patient interaction.

This handbook is meant to serve as a guide for you, more than as a comprehensive reference. It is not expected that you can become an oncologist in two weeks, but it is hoped you can learn a good amount about the management of common malignancies in this time. A session to go over the clerkship learning outcomes is scheduled as part of the rotation.

We welcome you to your selective in Oncology and look forward to your learning experience with us.

Sincerely,

Michael Sanatani, MD, FRCP(C)
Belal Ahmad, MD, FRCP(C)

Handbook Edited
By
Drs. Belal Ahmad, Michael Sanatani & Kimberly Trudgeon
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ROTATION STRUCTURE

Students will rotate through the outpatient clinics for two weeks. They will be assigned to a selection of oncologists as preceptors; the exact schedule is available at the start of the rotation. A student may not see, in the course of two weeks, patients of *all* the common types of cancer, but will see a reasonable selection of tumour sites.

Clerks will have no official duties on the ward and will not do in-house call. Pagers will be provided, and the students will be contacted to see oncological emergencies.

Students will see at least one radiation treatment simulation, one patient on radiotherapy and spend time in the chemotherapy unit seeing how chemotherapy is administered. Students will attend multidisciplinary rounds where patients are discussed and treatment decisions are made. Formal teaching will be given on several topics such as the basic science of oncology, pain and symptom management, and communication skills, accessing oncology literature and oncology emergencies. Informal teaching will occur in the clinic.

DUTIES OF CLERK:

Orientation on the first day of the rotation begins at 09:00am sharp with Kimberly Trudgeon, in Room A4-901C of the London Regional Cancer Centre (4th Floor) (Victoria Hospital Campus). If there is a statutory holiday, orientation falls to the next day of the week at the same time and location.

REFERENCE MATERIAL:

- Integrated oncology modules for medical students are located at “Learnoncology.ca”
- Teaching material provided by consultants and rotation supervisors in Windsor and London
- Oncology at a Glance by Graham G. Dark will also be available
- A copy of the “*Clinical Clerkship Oncology Selective Handbook*” will only be available on line.
- More information about the rotation is also available online at:
http://www.schulich.uwo.ca/oncology/education/undergraduate/year_3.html

SCHEDULE:

You will also receive a printed copy of your Selective rotation schedule to follow during the 2 weeks on your Oncology rotation.

Clerks will be assigned to a specific rotation schedule usually with several clinics to choose from for each day; this flexibility is to ensure coverage in case of clinic cancellations or restrictions. Clerks are however encouraged to attend similar clinics during both weeks, so as to allow some “longitudinal” individual time with the consultants. Use the “Scheduling” function of PowerChart at the beginning of each week to check that there are an appropriate number of patients booked for each clinic you plan to attend on your schedule. Physicians will be made aware ahead of time by our office to expect a medical student in their clinic that week.

SPECIAL / TEACHING SESSIONS:

- Prostate examination teaching
- Chemo suite tour
- Ward teaching – Dr. Fred Sexton / Dr. Assuras / Dr I Kerr:
- Case Based teaching by Residents
- Review of clerkship learning outcomes
- Tumour board meetings are generally held on the following days, times and locations
Note: clerks can attend these providing it fits into their clerkship schedule (not mandatory to attend)

2016–2017 LRCP Multidisciplinary Cancer Conferences

Disease Site	Frequency	Date	Times	Location
**Sarcoma (with Kingston)	2 nd & 4 th Monday	Mondays	4:00 – 5:00 p.m.	LRCP A1-155 & UH (A3-100)
Sarcoma (videoconferenced with Hamilton)	Weekly	Thursdays	1:00 – 2:00 p.m.	LRCP Admin. Conf. Room A3-945 & UH (A3-252)
(*TCL – Thyroid Cancer London)	Bi-weekly	Tuesdays (2 nd & 4 th)	7:00 – 8:00 a.m.	VH B3-439 & UH (A3- 100)
Gynecology	Weekly	Tuesdays	7:30 – 9:00 a.m.	LRCP A3-924 A/B & UH (A3-252)
London Liver Cancer Network (LLCN)	Weekly	Tuesdays	4:30 – 6:00 p.m.	A3-924 'B' & UH radiology conf. room C2-210
Neuroendocrine (NET)	2 nd & 4 th Wednesdays	Wednesdays	8:00 – 9:00 a.m.	LRCP A1-155 and UH (A3-252)
Skin (<i>Cutaneous Group</i>)	2 nd Friday of each month	Fridays (2 nd of each month)	7:00 a.m. to 8:00 a.m.	LRCP A1-155 <i>or</i> UH A3-252 & St. Joe's E1-134
**Thoracic (camera #17)	Weekly	Wednesdays	1:00 – 2:00 p.m.	LRCP A3-924 'A/B' & UH A3-252 & C2-210
**Gastrointestinal (GI)	Weekly	Thursdays	7:00 – 8:30 a.m.	LRCP A1-155 and UH (A3-100)
Hematology	Weekly	Thursdays	8:15 – 9:15 a.m.	LRCP Conf. Room A3- 924 'B'
Genitourinary (GU)	Weekly	Thursdays	8:00 – 9:00 a.m.	LRCP Conf. Room A3- 924 'A' & UH (A3-252)
**GU Telemedicine	2 nd & 4 th Thursdays	Thursdays (2 nd & 4 th)	7:00 – 8:00 a.m.	LRCP Conf. Room A3- 924 'A' & UH (A3-252)
GU (Renal)	(1 st of each month)	Thursdays	7:30 – 8:00 a.m.	LRCP Conf. Room A3- 924 'A' & UH (A3-252) & St. Joe's D0-138
**Head & Neck	Weekly	Fridays	12:30 – 1:30 p.m.	LRCP Conf. Room A3- 924 'A/B' & UH (A3-100)
**Breast	Weekly	Fridays	7:30 a.m. to 9:00 a.m.	LRCP Conf. Room A3- 924 A/B & D0-138 (St. Joe's) & UH A3-100
Central Nervous System (CNS)	Weekly	Fridays	8:00 – 9:00 a.m.	LRCP A1-155 & UH A3- 252
*Melanoma (<i>Cutaneous Group</i>)	4 th Friday (monthly)	Fridays (4th of each month)	7:00 – 8:00 a.m.	LRCP A1-155, St. Joe's E1-134 & UH (A3-252)

Revised: March 2017

EVALUATION:

- Based on preceptor feedback; CanMeds format (scholar, professional attributes, etc.)
- Examination (Combined multiple choice and short answer – based on the objectives listed below)

ACADEMIC AWARDS:

Elena B. Wolf Award (2)

Awarded annually for essays in the field of cancer research or treatment submitted by students in the clinical clerkship.

Class of Meds '49 Award for Excellence in Teaching by Residents (2)

Recognize and reward excellence in teaching by residents. You will have an opportunity to spend time with a Resident in Medical Oncology or Radiation Oncology for you case teaching session.

Dr. Ed Brecevic Award

The award is for any clinical clerk or resident who demonstrates an exceptional bedside manner and compassionate care and is nominated by any staff member, colleague or fellow student.

PROGRAM CONTACTS:

Medical Oncology Undergraduate Education Director:

Dr. Michael Sanatani
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Learning Outcomes
ONCOLOGY CLERKSHIP ROTATION

Clinical Clerkship Selective – Department of Oncology – Objectives

Preamble: The overall goal of the rotation is to introduce the student to clinical oncology, focusing on the four major cancer sites (Lung, breast, colorectal, prostate).

Knowledge is to be gained of the presentation of these cancers, the treatment modalities used and their side effects, and of the general biological behavior of these cancers.

Skills to be demonstrated include the adaptation of the patient assessment (history and physical) to the clinical situation (prioritization and focus of assessment), as well as exploration of the cancer patients' ideas, expectations, feelings/symptoms, and function.

Empathic, respectful and compassionate attitudes are expected, as is an awareness of factors in oncology which could lead to compassion fatigue and physician and trainee burnout, and of personal strategies which can help build resiliency.

References:

Oncology at a Glance, 2013, Wiley & Sons, sections 2,4,5,6,7,9,10,12,13, 14,17,20,21,23,29,30,34,41 and cases 3,4,6,7,8,9,15,16

Learnoncology.ca website, whiteboard presentations and oncology modules

Objectives

1. Obtain and history and perform a physical examination adapted to the patient's clinical situation

- Demonstrate appropriate content and focus of the history and physical (Medical expert)
- Demonstrate appropriate structure and control of the encounter (Medical expert)
- Show evidence of clinical reasoning and underlying scientific foundations (Medical expert/Scholar)
- Display sensitivity towards the patient's circumstances (Professional)
- Show rapport and empathy in exploring the patient's overall prognosis, fears and hopes, and will assess their activities of daily living and support systems, recognizing the need for social work, psychiatry, OT, RD, palliative care, or spiritual care referral when appropriate (Communicator)

If presented with a cancer patient seen in consultation or follow-up, assessment should include:

- I. Presentation of cancer (new consult) or cancer symptoms (from primary/systemic/due to metastases) (new consult and follow-up)
- II. Review of specific side-effects possible with treatment received (follow-up)
- III. Review of systems and the Edmonton Symptom Assessment System scores
- IV. Physical exam tailored to areas highlighted by history, the cancer illness, and assessment of treatment side effects and risks

Specific components for the four main tumour sites:

- a. If presented with a patient with non-small cell or small cell lung cancer, patient assessment should include (*Reference: page 68/69, Oncology at a Glance*):
 - i. History: smoking, environmental, COPD history, dyspnea/cough/hemoptysis history, anorexia, fatigue, pain, cardiac and renal comorbidities.
 - ii. Physical exam: Inspect for signs of hypoxia, pleural or pericardial effusions, liver metastasis, pulmonary osteopathy, hypercalcemia, Cushing's syndrome, brain metastasis, vertebral metastasis, lymphadenopathy, Horner's syndrome and brachial plexus involvement
- b. If presented with a patient with colorectal cancer (*Reference: page 76/77, Oncology at a Glance*):
 - i. History: Bowel habits, abdominal pain, anorexia, nausea, dyspnea, pain
 - ii. Physical exam: Evaluation for liver metastasis, bowel obstruction, ascites, pleural effusions and lung masses, and lymphadenopathy. Rectal exam where specifically indicated – note contraindicated if immunosuppressed!
- c. If presented with a patient with adenocarcinoma of the breast (*Reference: page 66/67, Oncology at a Glance*):
 - i. History: breast changes, bone pain, abdominal pain, confusion/headaches
 - ii. Physical exam: signs of pleural or pericardial effusions, local breast involvement, liver metastasis, bone metastasis, brain metastasis, axillary lymphadenopathy, and brachial plexus involvement
- d. If presented with a patient with adenocarcinoma of the prostate (*Reference: page 90/91, Oncology at a Glance*):
 - iii. History: urinary tract symptoms/hesitancy, pain, bone pain, edema, bowel function, weakness
 - iv. Physical exam: digital rectal examination if indicated, a screening neurological examination, and assessment for bone metastasis and complications of androgen deprivation therapy (cachexia, osteoporosis complications, loss of libido, depression, gynecomastia)

2. **Formulate and justify a prioritized differential diagnosis** of the symptoms and findings assessed, including whether the condition is cancer or treatment-related or

non-malignant **and formulate an initial plan of investigation based on the diagnostic hypotheses** demonstrating appropriate test selection

3. Formulate management plans

- I. Outline of general management principles and intents for early vs intermediate vs late stage non-small cell and small cell lung cancer, and including general estimation of the approximate median overall survival (by stage). Contrast chemotherapy and targeted therapy for NSCLC
- II. Outline general management principles for early and late stage colorectal cancer, including general estimation of the approximate median overall survival (stage IV) or recurrence rates (resected) with optimal therapy
- III. Outline general management principles for early and late stage breast cancer, including hormones, targeted agents, and chemotherapy as well as radiation and surgery approaches.
- IV. Be able to describe treatment options (Surgery, external beam radiation, brachytherapy) for men with localized prostate cancer and the common side effects of each. Contrast the general management principles for hormone-sensitive vs hormone-refractory prostate cancer and list the classes of systemic agents used to treat prostate cancer along the disease trajectory. Differentiate central LHRH agonist vs peripheral androgen blockade, adrenal androgen suppression, chemotherapy, bone health Rx – bisphosphonates, denosumab

Cancer treatment and supportive care – Selections from the “Canadian Oncology Goals and Objectives for Medical Students”, version April 2015. The knowledge-related objectives below will be addressed during the “Objectives Review Session” with one of the clerkship selective directors

1. Demonstrate an understanding of the concepts of curative, neoadjuvant, adjuvant and palliative treatments and demonstrate an understanding of the concepts of localized versus systemic treatments
2. Demonstrate an understanding of the definition of prognosis and describe general factors that affect prognosis in cancer patients.
3. Describe the components of commonly used performance status assessment tools such as the ECOG and Karnofsky performance status scales.
4. Identify factors that would affect the formulation of a treatment plan for a cancer patient (i.e. tumour, treatment and patient-related factors).
5. Demonstrate an understanding of the general principles of how radiation is used to treat cancer and different types of radiation (e.g. external beam, brachytherapy, stereotactic radiation).

6. List the common acute, subacute, and late adverse effects of radiation.
7. List factors that would make a cancer patient a poor candidate for chemotherapy.
8. Know the general differences between traditional chemotherapy and targeted therapy
9. Understand that Canadian treatment guidelines for common cancers are available through provincial organizations (e.g. Cancer Care Ontario, British Columbia Cancer Agency, Alberta Health Services, etc).
10. List common side effects of chemotherapy and radiation, and common symptoms of cancer. Outline diagnostic and supportive care algorithms for each, appropriate for the severity based on clinical assessment:
 - Diarrhea
 - Mucositis
 - Myelosuppression
 - Renal failure, dehydration
 - Cardiac effects
 - Neuropathy
 - Dyspnea including treatment and cancer-related causes
 - Anorexia, nausea/vomiting including treatment and cancer-related causes
 - Pain (see Medicine seminar)
 - Fatigue including treatment and cancer-related causes

5. Recognize a patient requiring urgent or emergent care, provide initial management and seek help

- If presented with a febrile cancer patient, the student will choose the appropriate investigations and initial empiric treatment options
- If presented with a patient with leg weakness the student will order the appropriate tests to rule out cord compression
- If presented with a patient with malignant hypercalcemia, the student will demonstrate correction calculations for serum albumin and order the appropriate initial therapeutics
- If presented with a patient with symptoms and findings attributable to elevated intracranial pressure, the student will recognize the need to investigate for malignancy spread to the CNS

6. Educate patients on basics of cancer management, health promotion during and after treatment – only with consultant or resident direct supervision.

Demonstrate awareness of role limitations and scope of practice of medical students (vis-à-vis controlled acts e.g. communicating prognosis, diagnosis, obtaining consent, giving advice) including deference of patient questions to appropriate members of the healthcare team where necessary.

6. Present oral and written reports that document a clinical encounter

- Appropriate structure and content of the presentation (Communicator) – organized, focused, prioritized, incl. treatment intent, primary site, cancer treatment history, stage, grade, histology
- Appropriate delivery of the presentation (Communicator)
- Demonstration of sensitivity and understanding towards the patient (Professional, Collaborator)

7. Have an approach to communication in difficult situations

- Demonstrate an understanding of the psychosocial or existential issues around life-threatening illnesses, such as cancer, relevant to different cultures, faiths and traditions, by addressing them with the patient and/or during case presentation.
- Recognize the inherent tension between society's need for the just allocation of finite resources and an individual physician's responsibility to advocate for a patient's access to effective therapies.
- Describe the components of informed decision making, including discussion of complications of cancer therapy in the curative and palliative setting, recognizing that potentially life-prolonging cancer therapies can induce potentially life-threatening adverse reactions.
- Have an approach to discussing withholding or ending cancer treatment considered inappropriate by the physician/oncology team, but requested by the patient.
- Realize that caring for cancer patients can lead to compassion fatigue and physician burnout which can negatively impact patient care, and outline a personal strategy by the end of the selective if possible.
- Demonstrate the ability to communicate information in a sensitive manner, addressing concerns, fear and expectations.
- Describe the SPIKES strategy for breaking bad news. **Note: use/do this only with direct supervision of physician in the room**

References: <https://www.ariadnelabs.org/wp-content/uploads/sites/2/2015/08/Serious-Illness-Conversation-Guide-5.22.15.pdf>, and for the SPIKES approach: *The Oncologist* 2000; 5:302-311

Reminder – This rotation may provide opportunity for many of these clinical experiences, please seek them out!

ESSENTIAL ONCOLOGY EXPERIENCES FOR MEDICAL STUDENTS

By graduation, medical students should have had the following clinical experiences with cancer patients ⁽¹⁾

- Observe a physician disclose to a patient they have cancer.
- Observe a physician discussing resuscitation status with a cancer patient.
- Observe a physician discussing the prognosis of a terminal cancer with a patient.

- Discuss the risks and benefits of screening for breast, colon and cervical cancer with patients.
- Perform a breast examination and if possible examine a patient with a breast mass due to breast cancer (under supervision).
- Perform a prostate examination and if possible examine a patient with a prostate nodule who has prostate cancer (under supervision).
- Speak with a patient who has had a potentially curative surgery for cancer regarding their treatment experience.
- Speak with a cancer patient who has had radiation treatment for cancer regarding their treatment experience.
- Speak with cancer patients who have had adjuvant chemotherapy for breast, colorectal and/or lung cancer regarding their experience.
- Speak with cancer patients who have had palliative chemotherapy for breast, colorectal and/or lung cancer regarding their experience.
- Review cancer-related diagnostic imaging with a radiologist (e.g. mammograms, chest X-rays with a solitary pulmonary nodule, CT scans showing primary and metastatic cancers)

⁽¹⁾ *Canadian Oncology Goals and Objectives for Medical Students – Canadian Oncology Education Working Group, version April 2015*

REFERENCE MATERIAL: RECOMMENDED READING MATERIAL

A copy of the “*Clinical Clerkship Oncology Selective Handbook*” will only be available on line.

Teaching material provided by rotation supervisors (Teaching sessions/Objectives Review Slidesets)

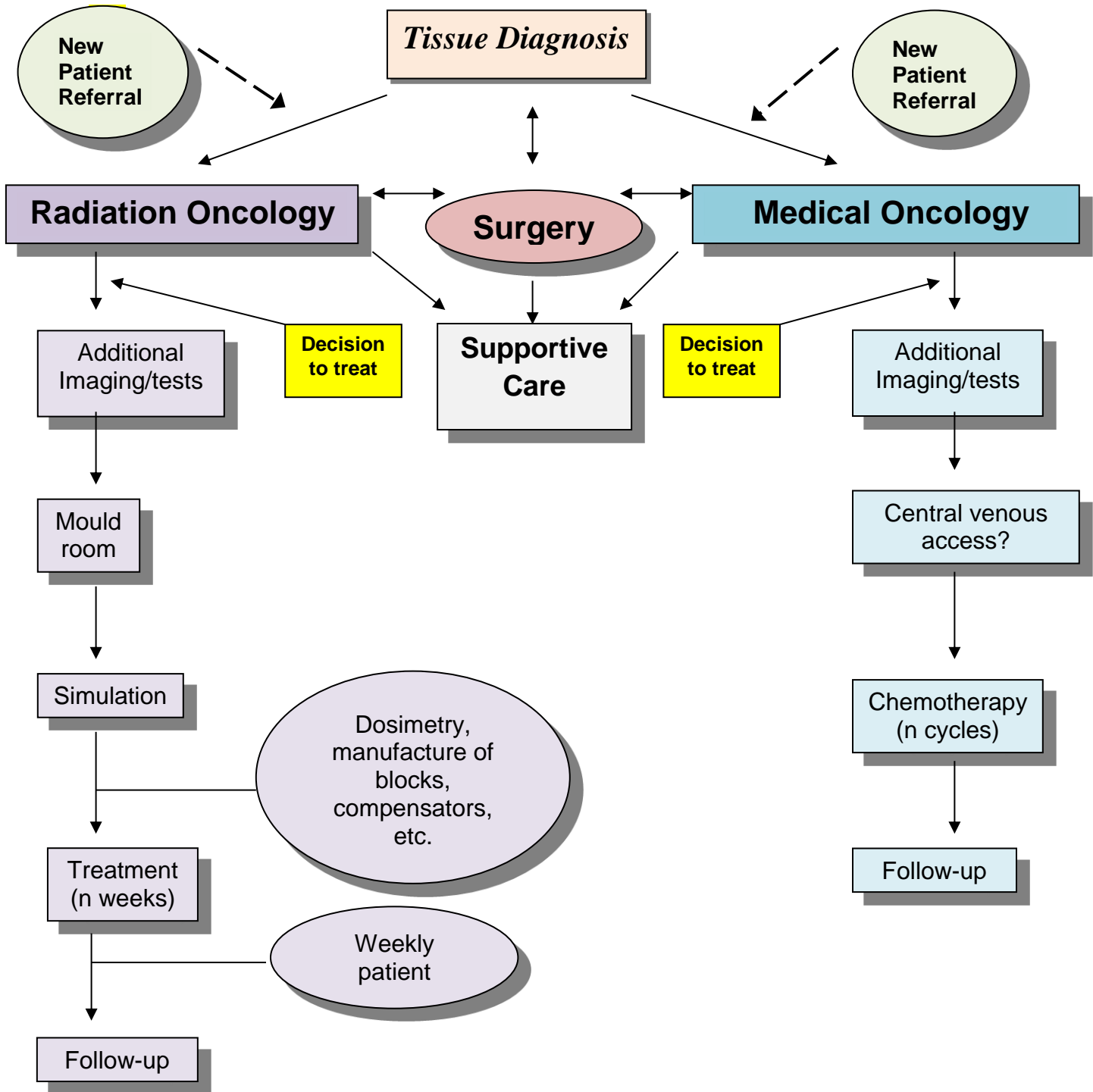
Integrated oncology modules for medical students are located at “Learnoncology.ca” and at the NCI (www.cancer.gov)

Supplemental References:

Further disease-site specific references:

- European Society for Medical Oncology (ESMO) minimal clinical recommendations (updated regularly)
<http://www.esmo.org/education-research/esmo-clinical-practice-guidelines.html>
- www.bccancer.bc.ca - BC Cancer Agency Cancer Management guidelines / drug manual
- More information about the rotation is also available online at:
http://www.schulich.uwo.ca/oncology/education/undergraduate/year_3.html
- http://www.nccn.org/professionals/physician_gls/default.asp - National Comprehensive Cancer Network (U.S.A.)
- <http://www.cancercare.on.ca/> - Cancer Care Ontario
- Canadian Cancer Statistics: http://www.cancer.ca/canada-wide/about%20cancer/cancer%20statistics/canadian%20cancer%20statistics.aspx?sc_lang=en
- www.adjuvantonline.com - Estimates of treatment effect (lung, colon, breast cancers)
- www.clinicaltrials.gov
- Quality of Life Assessment -
http://www.uwo.ca/oncology/undergraduate/pdf_documents/Quality%20of%20life%20assessment.pdf
- CNS Brochure
http://www.uwo.ca/oncology/undergraduate/pdf_documents/CNS_brochure.pdf
- Radiation Oncology Overview www.radiationoncology.ca
- Call of Death Article (Journal of Clinical Oncology – Volume 28, Number 16, June 1, 2010)
- “*Certain Death in Uncertain Time: Informing Hope by Quantifying a Best Case Scenario*”
Belinda E. Kiely, Martin H.N. Tattersall, and Martin R. Stockler

THE REFERRAL AND TREATMENT PROCESS



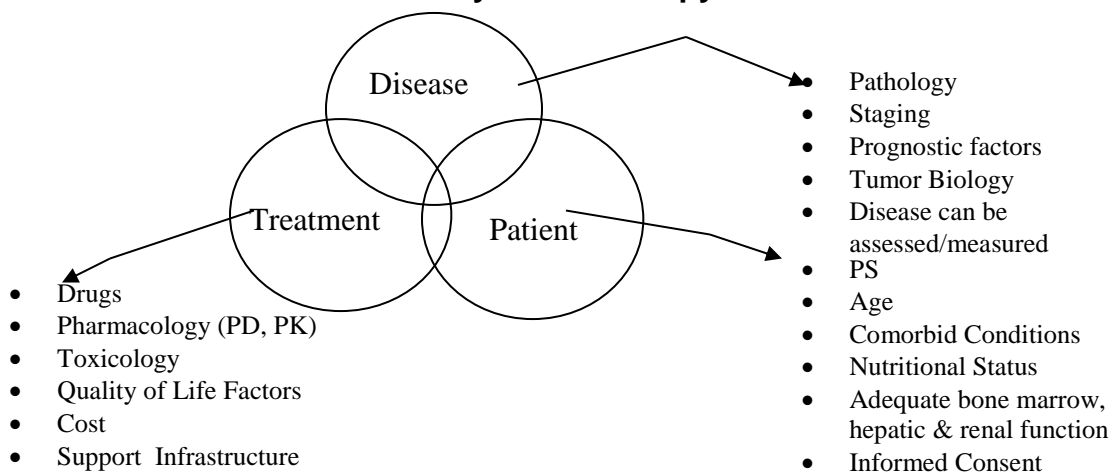
SYSTEMIC THERAPY OF CANCER: AN OVERVIEW

Ian Kerr, MSc, MD, FRCPC

The treatment of cancer is carried out with the appropriate use of local/regional therapy (eg. surgery, radiotherapy) as well as with the use of systemic therapy (eg. chemotherapy, biologics, hormones). Systemic therapy is the predominant therapeutic tool of the medical oncologist. Today, many cancer treatment approaches are multidisciplinary, utilizing local/regional as well as systemic therapies in various combinations (e.g. chemotherapy and XRT before surgery for locally advanced rectal cancer; chemotherapy and XRT after definitive surgery for breast cancer).

Before a treatment plan is generated it is important to know the specific diagnosis of cancer (eg. pathology), the stage of disease (eg. results seen at surgery, imaging tests, clinical assessment), the various prognostic features, as well as the status of the patient/host (eg. performance status, comorbidities, hepatic/renal function).

Factors to be considered for systemic therapy:



The treatment/therapy can then be determined (standard? investigational?) taking into consideration its expected benefit (efficacy), ease of delivery, and expected/potential side-effects (toxicity). In addition the goals of treatment (cure? palliation?) need to be taken into account. Some cancers that cannot be cured can be usefully palliated by chemotherapy (e.g. metastatic breast, small cell lung or colon) while others may have more limited benefit from chemotherapy (eg. pancreatic cancer) and may be considered for priority in clinical trials investigating new drugs (IND).

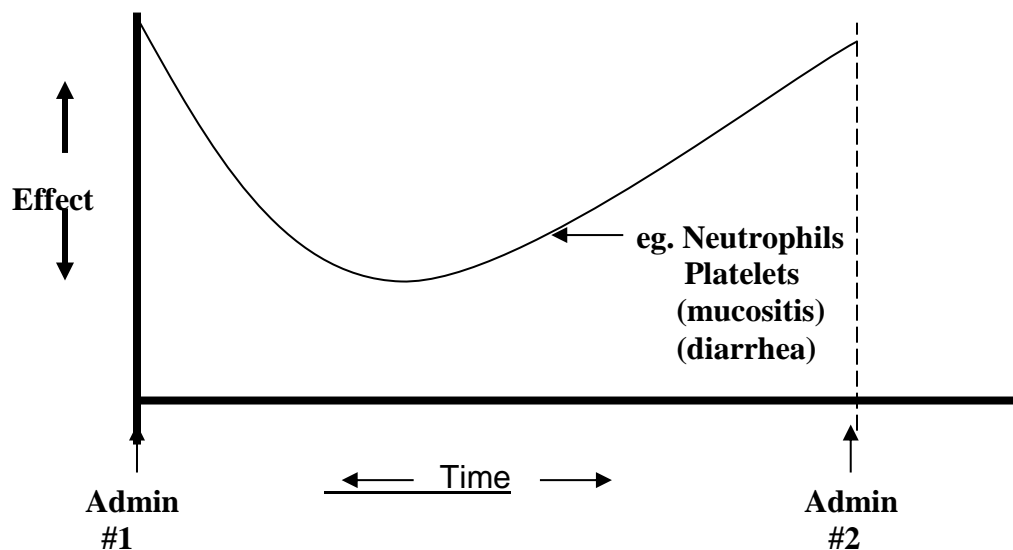
Specific treatment related factors to be considered for systemic therapy include:

- Drug(s) (e.g. which drugs or combinations are most appropriate)
- Dose and Dosing Interval (eg. cycle interval; standard dose vs. dose reduction)
- Schedule (eg. bolus, infusion)
- Route (eg. po, IV, regional administration such as hepatic arterial infusion or intraperitoneal chemotherapy)
- Combinations of drugs or single agents?

Today most systemic therapy (eg. chemotherapy) is carried out using combinations of drugs (eg. doublets or several drugs together). The principles behind the concept of combination chemotherapy include the following:

- each agent should be individually active

- each agent should have a different mechanism of action
- each agent should have (ideally) a different spectrum of toxicity (and resistance?)
- each agent should be used in an appropriate dose
- combinations (same as agents given alone) should be administered in the shortest interval between therapy cycles to allow for recovery of normal tissues (within practical limits) (see figure below).



As seen above, the administration of chemotherapeutic drugs (and many biologics) on an intermittent basis is dictated by schedules that allow enough drug (eg. dose) to be given but at intervals that allow normal tissues to recover from the toxic effects of treatments on the normal host (patient). These intervals may vary depending on therapy related factors (e.g. specific drug or dose) as well as host/patient factors (e.g. prior XRT, extensive prior chemotherapy which may limit the reserves of the bone marrow).

The effect of the drugs (e.g. pharmacodynamics), measured as efficacy (e.g. response rates, survival) or toxicity (e.g. side effects) are not only dependent on the dose of the drug and intervals between treatments, but also on the pharmacokinetics of the drug in a particular patient (e.g. bioavailability, clearance, concentration-time profiles).

Systemic therapy can be used in several circumstances:

- aim of potential cure (e.g. choriocarcinoma, germ cell cancers, lymphomas)
- in a neoadjuvant setting (e.g. given before surgery such as in locally advanced rectal cancer or breast cancer)
- in an adjuvant setting (e.g. given after surgery with the aim of decreasing relapse and increasing the chance of cure, such as following resection of colon or breast cancer)
- for palliation (e.g. metastatic cancer that is not curable, but therapy may decrease symptoms or improve length of survival).

Details regarding specific drugs can be found in the chapter dealing with the pharmacology of chemotherapeutic agents. It should be noted again that systemic therapy includes not only the conventional chemotherapeutic agents (e.g. cyclophosphamide, cis-platin, doxorubicin, taxol), but also hormones (e.g. progesterone) and modifiers of hormone metabolism/effect (e.g. tamoxifen, letrozole), as well as the increasing numbers of “molecularly targeted agents” (e.g. gefitinib or Iressa, erlotinib or Tarceva, trastuzumab or Herceptin).

PHARMACOLOGY OF ONCOLOGY: AN OVERVIEW

Brian Dingle, M.Sc. (Pharmacology), M.D., F.R.C.P.(C)

The following provides a very short outline to familiarize the student with our tools. Whenever a specific drug is encountered, we strongly suggest you review the excellent (and also relatively brief) monographs found through the BC Cancer Agency at: <http://www.bccancer.bc.ca/HPI/DrugDatabase/DrugIndexPro/default.htm>

1. Conventional Chemotherapy

ANTI-METABOLITES

History:

Anti-folates were first used in the form of Aminopterin by Farber in 1948. First analogues produced and tested for biologic activity were the 5-halogenated pyrimidines, 5-chloro-, 5-bromo-, and 5-iodouracil: tested for anti-malarials; thought to function as nucleic acid analogue. Gemcitabine was developed as an anti-viral in 1986.

Methotrexate

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Antifolate. Inhibit dihydrofolate reductase, which decreases available tetrahydrofolate, a methyl donator for thymidine synthesis	ALL, Breast, Head and Neck Intra-theal injection for CNS meningeal disease	myelosuppression, mucositis, renal toxicity in high dose (prevent by alkalinization of urine and hydration)	ASA, particularly with high dose, NSAIDs, Trimethoprim (which reduces folate stores)

Pearls:

- don't use with third space fluids: leaches out slowly causing toxicity
- must alkalinize urine when high dose used to avoid crystallization

5-Fluorouracil

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Antifolate. Thymidylate Synthetase (uracil to thymine in DNA) inhibitor, especially when modulated by leukovorin or CIV, nucleoside analogue in mRNA ? when bolus	Colo-rectal, Breast	myelosuppression, mucositis, hand foot syndrome	methotrexate through regulation of folates

Capecitabine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Antifolate. Orally administered pro-drug of 5-FU.	Colo-rectal, Breast	myelosuppression, mucositis, hand foot syndrome	methotrexate through regulation of folates

Pearls:

- 1650 mg/M2/Dayx14 gives same drug levels as CIV 5FU 300mg/M2/d

Cytosine Arabinoside

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
inhibition of nuclear DNA synthesis	AML, intra-theclal injections	myelosuppression, GI epithelial injury, hepatic cholestasis and CNS toxicity in high dose	

Pearls:

- One of only a very few drugs that can be used intra-theclally (but not with the common diluent which is supplied with powder form)
- An example of a drug which has greater myelotoxicity when given by continuous infusion than when given equidose bolus

Gemcitabine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
inhibition of DNA synthesis	Pancreas, NSCLC	myelosuppression, N&V, flu-like symptoms	

Pearls

- FDA approval granted for first time on basis of clinical benefit, not response rate!

6-Mercaptopurine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
inhibits purine biosynthesis	ALL	myelosuppression, rapidly reversible	Avoid allopurinol

Pearls

- One of the earliest examples of pharmacogenomic effects... ~10% heterozygous for single nucleotide polymorphism in thiopurine methyl transferase leading to toxicity

Fludarabine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Inhibits DNA synthesis	CLL, lymphoma	myelosuppression, delayed neurotoxicity	

Pearls

- may cause auto-immune hemolytic anemia,
- immune suppression persists beyond myelosuppression due to T-cell depletion, patients AIDS like for four months post treatment

Cladribine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Inhibits DNA synthesis and repair	Hairy Cell leukemia	Myelosuppression, ALS like syndrome	

Pearls

- 'miraculous' efficacy in Hairy Cell leukemia, one seven day treatment induces remissions for several years, possibly even cures, a disease which had little else to help until this class of drugs

ALKYLATING AGENTS

History:

Alkylating agents were the first non-hormonal agents used in the treatment of Cancer. Physicians caring for soldiers gassed in WWI with sulphur mustards, and WWII with nitrogen mustards noted myelosuppression, and lymphoid aplasia. Treatment of leukemia and lymphoma was attempted, and subsequent trials against solid tumours in USA were kept secret for a period after the war because of military use. Some of the first work with these agents in lung cancer patients was conducted by Dr. O.H. Warwick (former Dean of Medicine and Vice President of University of Western Ontario) while he was studying and working in England after the war.

All alkylating agents, including platinum, form strong chemical bonds with thiol sulphurs and amino nitrogens, often forming cross-links.

Cyclophosphamide

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA	Breast, Lymphoma	N&V, myelosuppression, alopecia, rarely pulmonary, hemorrhagic cystitis	

Pearls

- Formerly the mainstay of many treatments, including lung
- Meta-analysis of advanced lung cancer showed patients did worse on alkylating agents

Melphalan

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA	Myeloma	N&V, myelosuppression,	

Pearls

- Oral drug
- One of the first to be used as adjuvant treatment in Breast cancer
- Crosses the blood brain barrier

Chlorambucil

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA	CLL, lymphoma	skin rash, myelosuppression,	

Platinums - History: The first platinum compounds were discovered in 1965 (Rosenberg and colleagues) when studying the effects of electrical current on bacterial growth.

Cisplatin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA, intrastrand probably more than interstrand	Most solid tumours	Renal, neuro myelosuppression, N&V, symptomatic hypo-magnesemia	Avoid aminoglycosides soon after cisplatin

Pearls

- The most commonly used anti-tumour agent
- Trans platinum agents have no anti-tumour effect

Oxaloplatin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA, intrastrand probably more than interstrand	Colon cancer adjuvant and metastatic	myelosuppression, N&V, pharyngolaryngeal dysesthesia	Synergistic with 5FU

Pearls

- Pharyngolaryngeal dysesthesia is a neurologic phenomenon characterized by the sensation of being unable to breath, particularly on exposure to cold.

Carboplatin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Cross linking of DNA, intrastrand probably more than interstrand	Most solid tumours, often a substitute for cisplatin when renal impairment	myelosuppression, N&V less than cisP,	

Pearls

- Most oncologists find carboplatin slightly less active than cisplatin
- Calculated AUC (area under the curve) gives more consistent drug levels in correlation with renal function than does the BSA, and so is routinely used with this drug

INTERCALATING TOPOISOMERASE-TARGETTING DRUGS

Anthracyclines: History Fermentation product of *Streptomyces*, these were originally described as anti-tumour antibiotics. Anti-tumour activity was first discovered in the 1960s. First used in the Toronto General Hospital in 1973.

Adriamycin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Poisoning Topoisomerase II, intercalate dsDNA	Breast, most solid tumours (particularly in the past), lymphoma, leukemia	myelosuppression, N&V, alopecia cardiotoxicity, vessicant	Trastuzumab causing cardiotoxicity

Pearls

- Excreted in bile, less than 10% in urine
- Radiation recall can lead to unexpected complications

Epirubicin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Poisoning Topoisomerase II, intercalate dsDNA	Breast, most solid tumours (particularly in the past), lymphoma, leukemia	myelosuppression, N&V, alopecia less cardiotoxicity than Adria, vessicant	

NON-INTERCALATING TOPOISOMERASE-TARGETTING DRUGS

Epipodophylotoxins - History: Developed to improve on podophylotoxin, and extract from the Mandrake plant and anti-microtubule agent, epipodophylotoxins lost their anti-tubulin activity, but gained the ability to poison Topoisomerase II.

Example: Etoposide

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Poisoning Topoisomerase II,	Lung, testicular	myelosuppression, N&V,	

Pearls

- May be used orally

Camptothecins – History: From the wood bark of the Chinese tree *Camptotheca*, identified for its anti-tumour activities in the 1960s. The salts of this drug were at first deemed too toxic.

Example: Irinotecan

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Poisoning Topoisomerase I,	Gastrointestinal	myelosuppression, N&V, diarrhea (acute/delayed)	Avoid within 6 weeks of radiation, reduce dose with prior RTX

Pearls

- Because of metabolism by glucuronidation, more toxic in Gilbert's Syndrome (~9% homozygous, 30% heterozygous in NA)

MICROTUBULE TARGETTING DRUGS

Vinca Alkaloids –History:

The extract of periwinkle, a common groundcover, was thought to cause hypoglycaemia according to folk lore. Extracts from this plant were prepared and investigated by Dr. Robert Noble, an Endocrinologist and Director of Medical Research at the Collip Laboratories of the University of Western Ontario, along with his colleagues Drs. C.T. Beer and J.H. Cutts. Their original animal experiments failed to show any effect on carbohydrate metabolism, but they noted septicaemia due to granulocytopenia, and later, activity against breast cancer in mice and sarcoma in rats. Subsequent clinical trials in humans were conducted by Dr. O.H. Warwick (mentioned above) and his colleagues at the Princess Margaret Hospital shortly before Dr. Warwick came to UWO as Dean of Medicine.

In recognition of this local discovery, the periwinkle plant forms the logo for the London Regional Cancer Centre.

Example: Vincristine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Many effects, but disruption of microtubules best described	Lymphoma, ALL	myelosuppression, neuropathy (constipation), vesicant, tumour lysis	

Pearls

- Always lethal if given intra-theccally (which has occurred all too frequently)

Example: Vinblastine

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Many effects, but disruption of microtubules best described	Lung, Breast, Hodgkins	myelosuppression, neuropathy (constipation), vesicant, tumour lysis	

Pearls

- Also lethal intra-theccally, though a less common error

Taxanes – History:

Isolated in 1971 from the Western Yew tree, taxanes were initially in short supply for lack of trees. Eventually more efficient methods of production were developed, and Docetaxel is extracted from the leaves of the European Yew, sparing the tree.

Paclitaxel, Taxol

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Stabilizes microtubules	Lung, Breast,	myelosuppression, type 1 hypersensitivity, myalgia	

Pearls

- Must separate use of doxorubicin from paclitaxel to avoid serious cardiac
- Pre-treatment with Decadron and histamine blockers important

Docetaxel, Taxotere

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Stabilizes microtubules	Lung, Breast,	myelosuppression, alopecia, nausea, stomatitis, rashes (some acute), edema	

Pearls

- Cardiotoxicity with anthracyclines has not been demonstrated with Docetaxel
- Pre-treatment with Decadron and histamine blockers important
- Patients allergic to Paclitaxel may be fine with Docetaxel, as the former contains Cremophor; however, patients allergic to Docetaxel should be assumed to be allergic to Paclitaxel

2. Targetted therapies

Monoclonal antibodies – History:

Kohler and Milstein reported on the “Continuous cultures of fused cells secreting antibody of predefined specificity” in Nature in 1975. Since then several anti-bodies, usually over 95% human fused to murine segments at the variable light chain end, have been developed for use in malignancy.

Herceptin has found activity in Breast cancer patients with Her2neu (EGFR2) over-expression, both in the palliative and adjuvant setting. Rituxan improves response rates in lymphomas with chemotherapy, or as a single agent in indolent disease. Cetuximab and Bevacizumab are finding increased use in solid tumours.

Rituxan

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Anti-CD20 antibody: may react with receptor or induce cell mediated cytotoxicity	Lymphoma, auto-immune disease	hypersensitivity	Synergy with CHOP in large cell lymphoma

Herceptin

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Anti EGF receptor	Her 2 neu expressing Breast Cancer	hypersensitivity	Cardiotoxicity with adriamycin; synergistic with taxanes, vnoelbine

Cetuximab

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Anti EGF receptor	Colon cancer	hypersensitivity	

Bevacizumab

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Anti VEGF receptor	Colon cancer	Hypersensitivity, hypertension, thrombosis and hemorrhage	

Tyrosine kinase inhibitors – History:

The genetic mutation typical of CML leads to an aberrant trans-membrane protein, a tyrosine kinase which requires no ligand to stimulate signal transduction. STI571 was designed to inhibit this protein, and paved the way for a new paradigm in cancer treatment. In lung cancer, Tarceva shows improvement in survival in third line treatments. Iressa shows activity primarily in patients with mutations of the EGF-receptor.

Imatinib (“Gleevec”, STI 571)

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Tyrosine kinase inhibitor	Ph + CML, GIST	Fluid retention	

Gefitinib (“Iressa”) and Erlotinib (“Tarceva”)

Mechanism of Action	Common Use	Common Toxicity	Drug Interactions
Tyrosine kinase inhibitor	NSCLC (both), Pancreas (Tarceva)	Skin rash, possible interstitial lung disease (Iressa)	

3. Immunotherapy

See link at the beginning of this chapter

- Interferon
- BCG (Bacille Calmette-Guerin)

4. Hormonal therapy

See link at the beginning of this chapter

- Tamoxifen
- Letrozole, exemestane
- Goserilin
- Bicalutamide

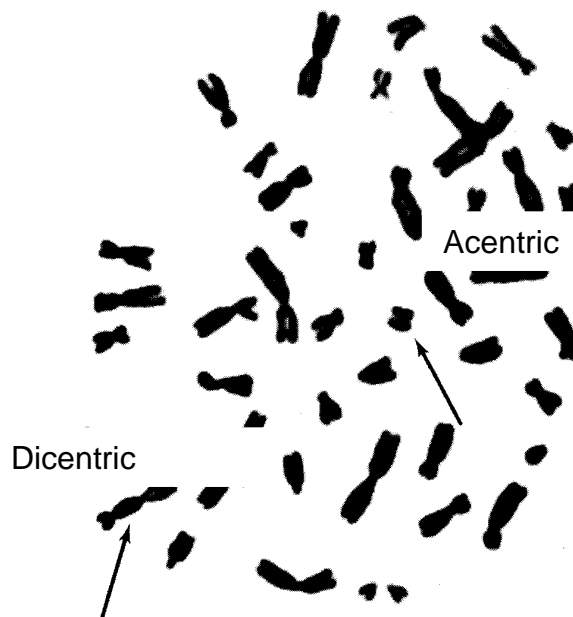
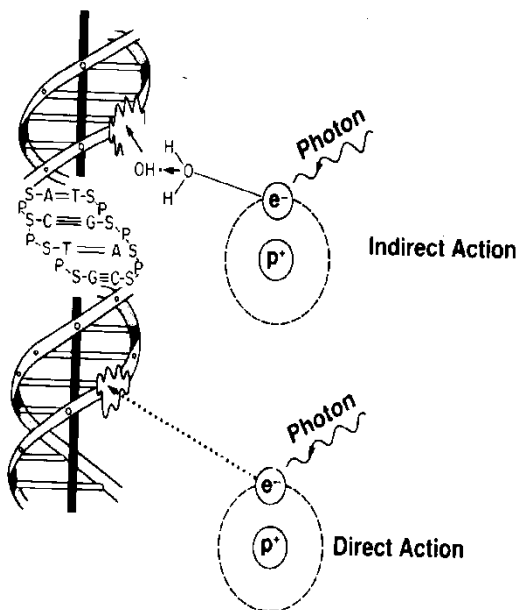
RADIOBIOLOGY: A PRIMER

J. Battista, Ph.D.

(condensed from *Radiobiology for the Radiologist* by E. J. Hall)

How does radiation kill cells ?

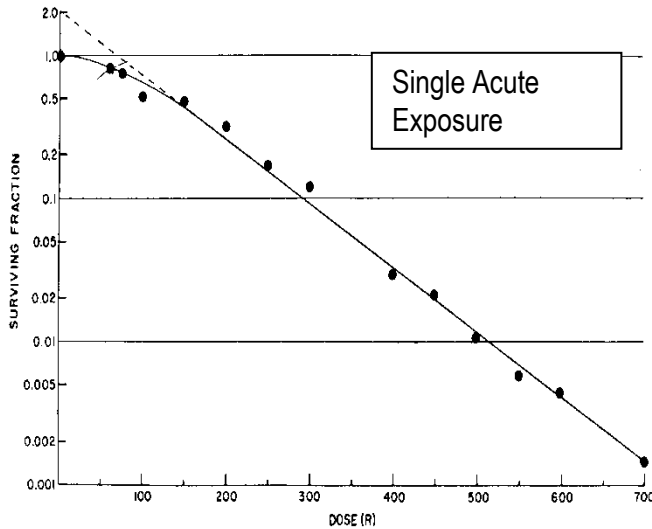
Radiobiology is the study of the effects of radiation on living organisms. Mammalian cells are damaged by radiation through a complex sequence of physical, radiochemical, and biological events. While the number of damaged cells increases with the radiation energy deposited or “dose”, there are other non-physical factors that ultimately determine the fate of an irradiated cell. The damage has been classified as being “direct” when biomolecules are directly ionized by the radiation particles, and “indirect” when the damage is caused by free radicals released in water by the radiation. More specifically, the production of double strand breaks (DSBs) in the DNA molecule gives rise to chromosomal breaks on a larger scale. Some of the chromosome breaks can be spliced back together symmetrically but incorrectly giving rise to mutations and carcinogenesis. On the other hand, asymmetric recombinations, such as dicentric chromosomes, inhibit cell replication and colony formation (i.e. cell death). There is also recent evidence that such DNA damage can also trigger a signal for programmed cell death or apoptosis.



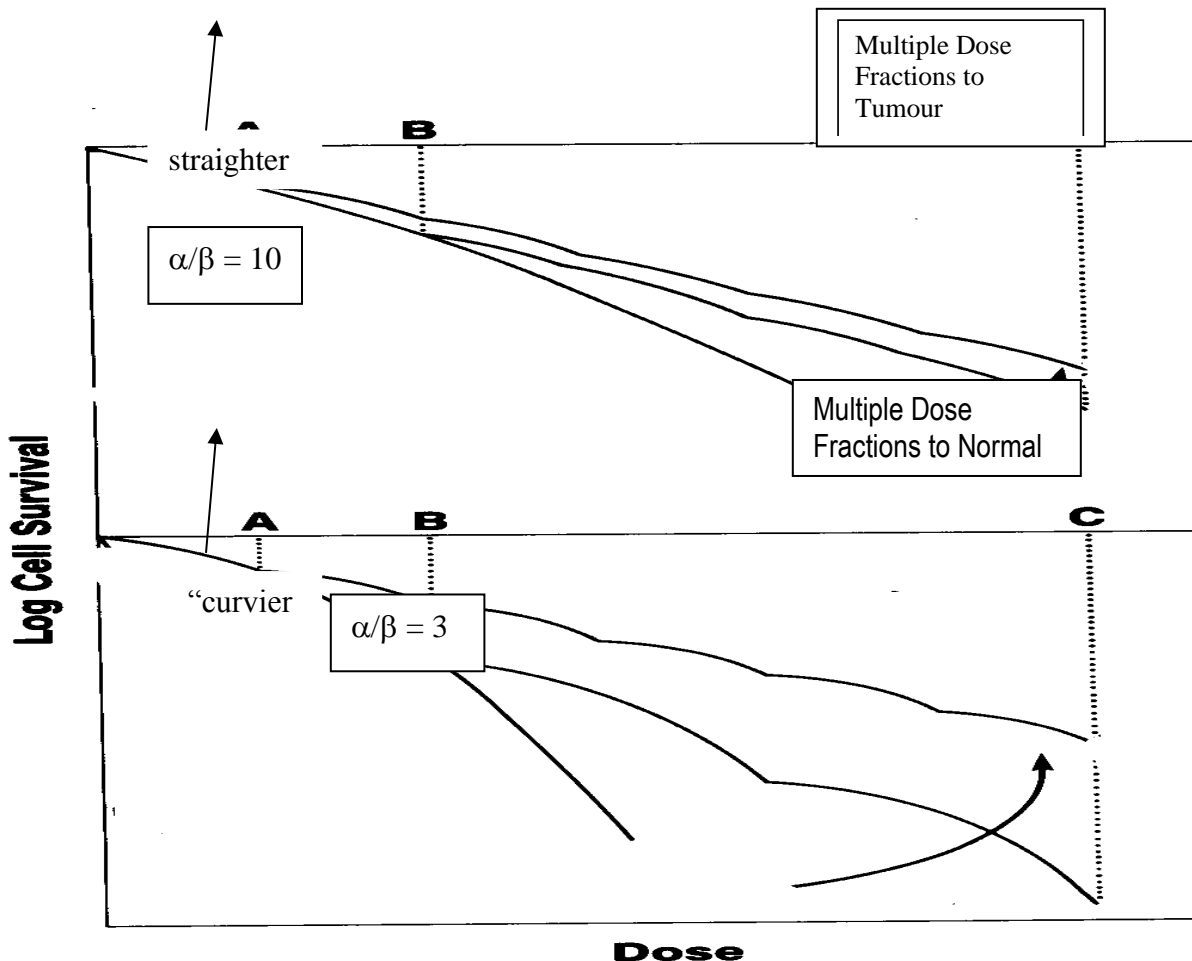
A cell survival curve is a semi-logarithmic plot of the fraction of cells surviving a given radiation dose level. Survival curves can be fitted to a linear-quadratic (LQ) equation of the form:

$$S(D) = e^{-(\alpha D + \beta D^2)}$$

where D is the physical dose (in units of cGy) and the α and β coefficients (i.e. α/β ratio) characterize the “curviness” of the survival curve. Fortunately, tumour cells ($\alpha/\beta = 10$) and normal tissue cells ($\alpha/\beta = 3$) have different “curviness” and differential cell killing is achievable not only by lowering the dose to normal tissues using advanced technology (see next section of this booklet), but also by splitting the dose into incremental daily dose fractions. This allows the treatment of many radiotherapy patients with a beneficial therapeutic ratio of tumour control with



a low risk of complications in adjacent normal tissues.



The radiation gives rise to double-strand DNA breaks, which are then manifested as chromosome damage. Many of the DNA breaks, including doublets, which can be repaired by cellular enzymes over a time period of several hours. However, if there are too many residual double-strand breaks per cell or they are misrepaired in an asymmetrical way, then cell death ensues. The evidence for repair can be inferred from the low dose region of the survival curve, which has a “shoulder” portion.

Repair takes place between radiation exposures to external beams or it can take place concurrently during continuous irradiation at low dose rates with brachytherapy. Thus during a course of radiotherapy, there is ample time available for repair of normal tissues. The therapeutic advantage of dose fractionation is illustrated in the previous Figure, where the tumour cells are killed more efficiently than normal tissue cells because their survival curve is “straighter” at dose levels corresponding to a standard daily fraction (200 cGy or 2 Gy).

Re-assortment within the Cell Cycle

The cell cycle describes the timing of events which take place during the lifecycle of a mammalian cell and typically requires approximately 24 hours to complete. After mitosis (M phase), a new cell first undergoes a first growth phase (G1 phase), then synthesizes and replicates its DNA (S phase) and finally enters a second growth phase (G2 phase) before entering mitosis. By synchronizing mammalian cells *in vitro*, it is possible to demonstrate that cells are more sensitive to radiation during the G2 and M phases of the cell cycle. This is a “point of no return” during which there is an ample amount of DNA present and its movement and splitting must be well orchestrated. In the other phases of the cell cycle there is less DNA present and it is molecularly more open for access by repair enzymes. During the synthetic period (S) there is also evidence for ‘up-regulated’ levels of radioprotective agents that scavenge free radicals that would otherwise reach and damage the DNA. With regard to the fractionation of dose, splitting the total dose into daily fractions gives an opportunity for asynchronized cells to move into and perhaps accumulate in the sensitive G2 and M phases of the cell cycle. Similarly continuous brachytherapy over prolonged periods ensures exposure of all cells as they traverse the sensitive phases. There have been attempts to sensitize radiation cells to radiation damage by forcing cells to stall in the G2 and M phases of the cell cycle prior to irradiation.

Repopulation of Tumor Cells

Radiation therapy aims to slow or halt the progression of the tumor by killing more tumour cells than are generated through rapid replication. However, this gain must also be achieved by allowing the normal tissues to regenerate. Thus, repopulation of tumor cells is to be avoided and the re-population of normal tissues is to be encouraged.

Tumor cell kinetics are characterized by three time parameters defined below:

- Cell cycle time refers to the average time between mitosis for individual cells actively grown *in vitro* in culture.
- Potential doubling time (T_{pot}) is the time required for the number of cells to double, taking into account that only a subpopulation of cells are actively growing and these are referred to as the “growth fraction”. The potential doubling time can be measured in individual human tumors using flow cytometry. T_{pot} is considerably longer than the cell cycle time because some of the cells are dormant.
- Tumour doubling time is the time required for a tumor to double its volume *in vivo* within an animal or a patient. This is the most clinically relevant time since rapidly-proliferating tumors must be treated more aggressively in a timely fashion. This

volume can be measured by three-dimensional (3D) imaging techniques such as CT or ultrasound scanning or by direct palpation if the tumor is accessible. The tumor doubling time is longer than the potential doubling time because of cell losses which occur *in vivo* through immunologic or apoptotic elimination. Typical volume doubling times for human tumors are shown below.

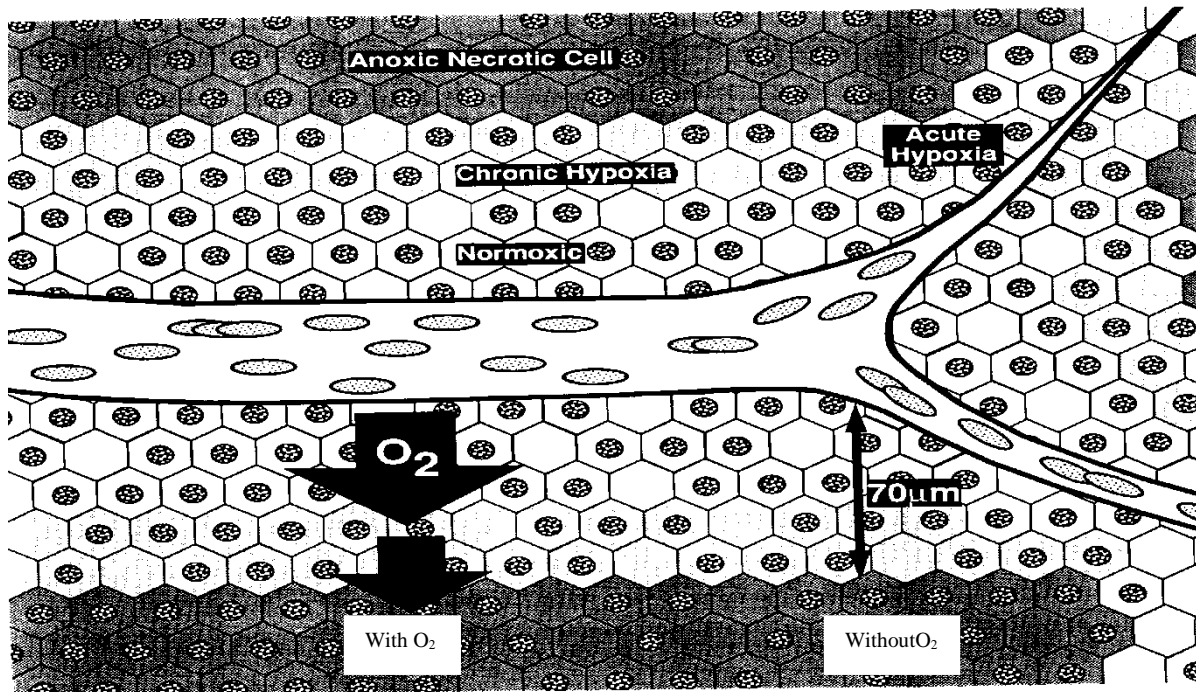
AUTHOR(S)	SITE	VOLUME-DOUBLING TIME (DAYS)	RANGE (DAYS)
Breuer	Lung metastases	40	4-745
Collins et al.	Lung metastases	40	11-164
Collins	Lung metastases from colon or rectum	96	34-210
Garland	Primary bronchial carcinoma	105	27-480
Schwartz	Primary bronchial carcinomas	62	17-200
Spratt	Primary skeletal sarcomas	75	21-366

(Based on data from Steel GG: Cell Tissue Kinet 1:193-207, 1968)

With regard to dose fractionation, it is important to minimize the overall time course of radiation treatment so as not to allow excessive tumor proliferation during treatment. This is especially true since there is evidence for accelerated repopulation (i.e. induces a shorter doubling time) in tumors after a radiation stimulus. On the other hand, repopulation of normal tissue cells is a desirable effect in-between dose fractions.

Re-Oxygenation of Tumor Cells

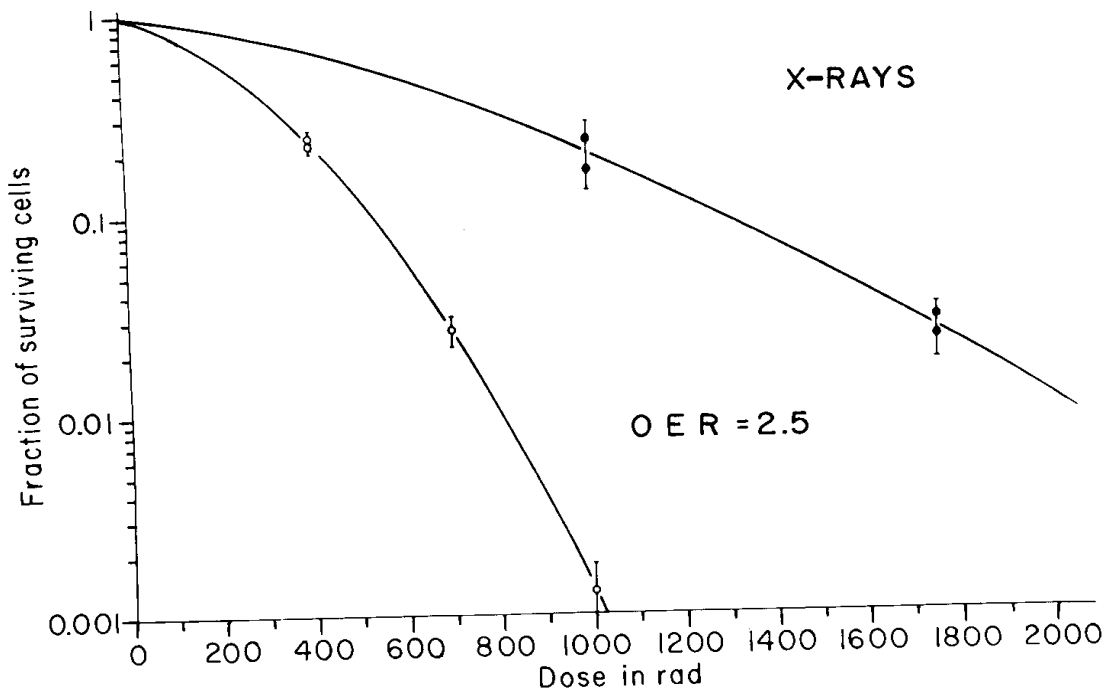
Well-oxygenated cells are up to three times more sensitive to x-rays than poorly-oxygenated cells. This “oxygen effect” has been one of the most studied phenomena in radiation biology



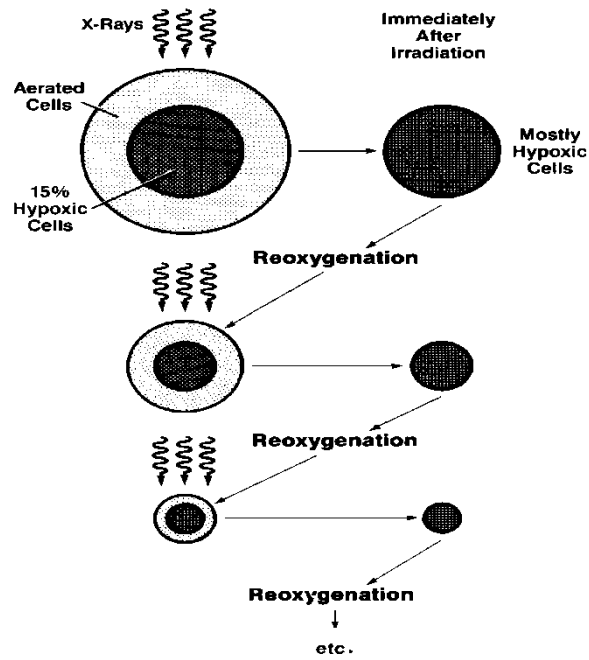
because its understanding and control could lead to more effective radiotherapy. In a solid tumor, there are regions of full oxygenation near blood vessels, and region of moderate oxygenation (hypoxia) or minimal oxygenation (anoxia) at more remote locations from blood vessels. Since tumours often trigger new blood vessel formation (angiogenesis), the tumor cell killing by radiation can be very heterogeneous and transient, depending on the local levels of oxygenation.

The oxygen enhancement ratio (OER) is the ratio of doses required under hypoxic conditions to the doses required under the oxygenated conditions to achieve the same cell killing level. For the x-rays most used in radiotherapy, the OER has a value of 2.5 indicating that the hypoxic regions of a tumor would need a dosage level almost three times higher than the well-oxygenated cells.

The oxygen effect is caused by the radiation chemistry of water that may yield oxidized DNA-radicals that inhibit the extent of its enzymatic repair. To be effective, the oxygen must be present during the irradiation since the radiation chemistry occurs rapidly (typically microseconds) following the start of radiation exposure. It should be also noted that full oxygenation is not required to achieve maximum sensitization. An oxygen pressure of 30 mm of mercury (1/5 of the oxygen content in atmospheric air) is sufficient to achieve near-maximum effects. Hypoxic cells in a *milieu* of less than 3 mm of mercury of oxygen, on the other hand, are well protected against radiation damage.



It is believed that in solid tumors, the hypoxic fraction of cells is significant (typically 15 %) and thus the lack of oxygenation limits the effectiveness of radiation therapy. During a course of fractionated radiotherapy, oxygenated tumor cells are initially killed more easily and when these cells are lost, there is renewed access to oxygen by the hypoxic cells. Thus through repeated fractionations, oxygen is made more and more available to the hypoxic cells which can then be more effectively damaged by subsequent exposure to radiation. The time required for re-oxygenation is approximately six hours which sets the minimum time required between dose fractions for curative fractionated therapy of solid tumours with proven hypoxia.



Summary

Fractionated or continuous radiation therapy with external beams or brachytherapy has been adopted during 50 years of clinical experience to exploit the above “4 R’s” of radiobiology in the eradication of tumors and the preservation of normal tissue function. The following Table summarizes the desired effects on tumour and normal cells when doses are fractionated

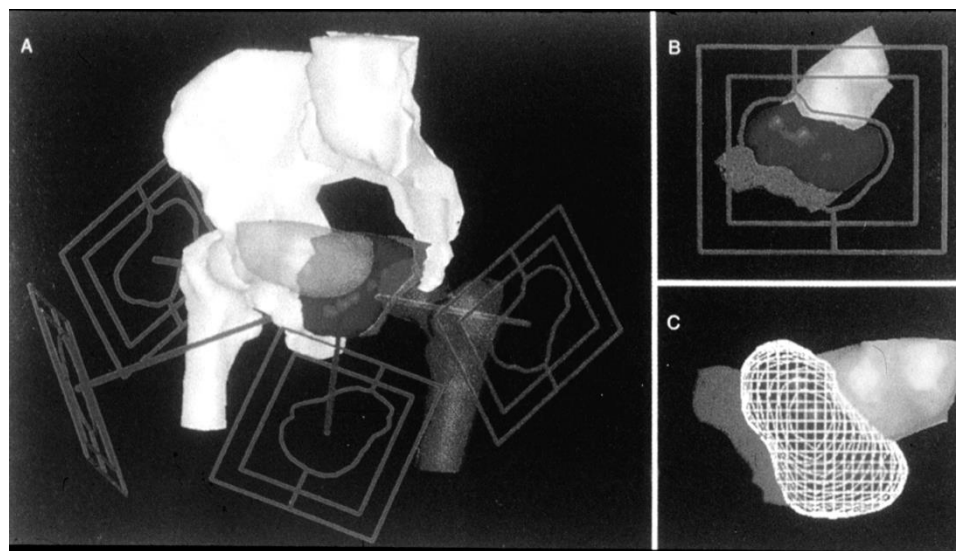
Effect on	<i>Repair</i>	<i>Re-Assortment</i>	<i>Repopulation</i>	<i>Re-Oxygenation</i>
Tumour	Straighter shoulder	Opportunity to kill G2-M cells	Increased rate of proliferation	Sensitize hypoxic fraction
Normal Tissues	“Curvier” Shoulder	Opportunity to spare G1-S cells	Preserve organ function	Already oxygenated

In addition to achieving higher doses in the target tumor and lower doses in normal tissues through better treatment planning and 3D dose distributions, the “4R’s” must be respected in the ultimate optimization of radiation therapy. Full understanding and control of both the physical and biological factors will lead to better tumor control rates and fewer normal tissue complications.

Simulation and Dosimetry

CT Planning

Before starting treatment, the patient is imaged in the treatment position. In the past, radiotherapy fields were designed with reference to bony landmarks using fluoroscopy and plain simulator radiographs (“conventional simulation”). Following simulation, manual acquisition of patient contours and delineation of the target volumes for computerised dosimetry was necessary. This manual registration of tumour volumes derived from diagnostic imaging onto the simulator radiographs/contours was both tedious and of limited accuracy. For modern conventional radiation treatment planning, the acquisition of a set of axial “planning CT” images through the volume of interest is required. The planning CT scan differs from diagnostic CT



**Fig. 1-CT
Simulation:**

Illustrates target volume, critical structures, and radiation portals. “Beam’s eye view (b) is also shown.

scans in that the planning CT images are acquired under the same conditions (on a flat couch with a custom immobilisation device) that the patient will be treated on the linac. CT contains the electron density information needed for radiation dose calculations but may not be the ideal imaging for some tumours. Fusion of MRI (pre and/or post-operative) and planning CT images may facilitate tumour volume definition. Dedicated “CT simulators” are becoming available in many radiation oncology departments. These CT simulators incorporate powerful imaging workstations for efficient target contouring and image manipulation such as image fusion between CT and other modalities such as MRI as well as “virtual” simulation of beam arrangements.

“Inverse Planning” Dosimetry

Dosimetry refers to the process of determining the distribution of radiation dose in tissues. Once the target volume and critical structures have been identified by the radiation oncologist on the planning CT images, the radiation dosimetrist will design a plan to deliver a uniform radiation dose to the target while minimising dose to critical structures. In the past, due to limitations of imaging and computerised dosimetry this task was usually accomplished using a limited number of simply shaped radiation beams of uniform density. The resulting dose distribution usually erred on the side of caution, irradiating large volumes of normal tissue to minimise the chance of a “geographical miss” of the tumour. Modern conformal radiotherapy seeks to minimise the high dose deposited outside the target by the use of multiple, non-overlapping radiation beams shaped to the configuration of the tumour in the beam’s eye view. Currently, most treatment planning is performed manually, through the iterative “forward” optimisation of 2-6 radiation beams with conventional beam angles, beam’s eye view blocking and beam modifiers (compensators, wedges). Dose volume histograms provide a graphical summary of the dose received by the target as well as surrounding critical structures and may be used to compare rival treatment plans for relative “goodness”.

A recent innovation is the availability of “inverse treatment planning” software whereby the radiation oncologist specifies the desired dose distribution (conforming to the target) as well as organs at risk to be avoided. Back calculations (analogous to the image reconstruction algorithms used by CT scanners) then yield the appropriate beam delivery parameters (angle, shape, intensity profile) to produce the distribution desired in the patient. The delivery of such “inversely planned” treatments may require the use of intensity modulation to dynamically alter the beam intensity across the beam profile (see below). Such treatments may produce a very conformal dose deposition with reasonable dose homogeneity throughout the target and a very rapid dose falloff outside the target.

Treatment Delivery and Verification

Multileaf Collimator

Collimators define the radiation beam edge as the beam leaves the radiation machine. Standard collimators consist of two sets of jaws, which define a rectangular beam. These jaws can change the field size in two dimensions (x and y).

Multileaf collimators (MLC) also change the field size in two dimensions, but because the “jaws” in the x-axis are composed of several “leaves”, the beam can be shaped into non-rectangular conformations. Although beams can be shaped similarly with custom-made cerrobend blocks, this process is labour intensive and doesn’t allow the degree of flexibility afforded by MLCs.

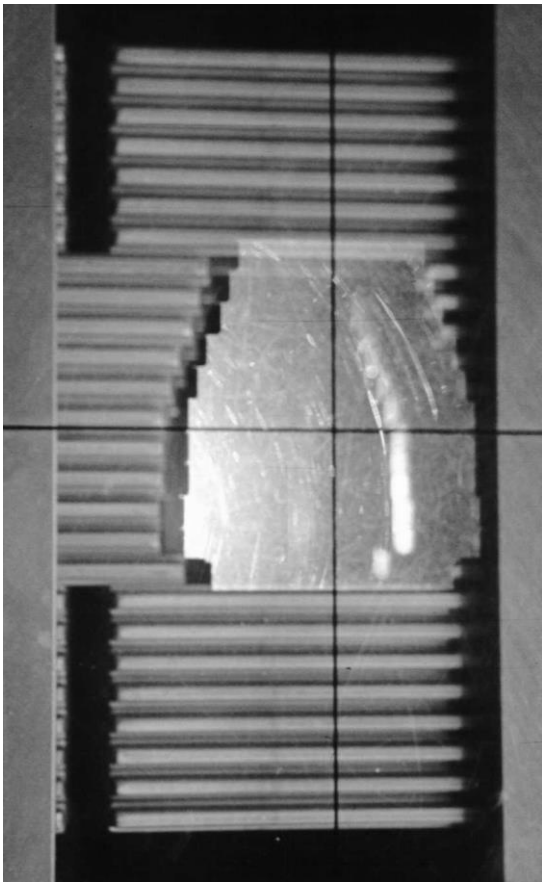


Fig 2 – Multileaf Collimator(MLC):

Multiple leaves shape the portal to the desired target volume.

Intensity Modulated Radiotherapy (IMRT)

This process utilises a standard linac equipped with MLCs. The beam's intensity is “modulated” by the MLC's “leaves” which move in and out as the beam is turned on to produce a very complex dose distribution. IMRT allows conformation of high dose to more complex shapes while sparing surrounding normal tissues.

Tomotherapy

Essentially a CT scanner equipped with a therapeutic X-ray tube. This device is still in development. The patient would be treated with a narrow fan beam, shaped by a special MLC, which would rotate around the patient similar to the way CT images are acquired. Tomotherapy offers the theoretical advantages of delivering very conformal treatment (a form of IMRT), and allowing three-dimensional portal imaging with each fraction delivered.

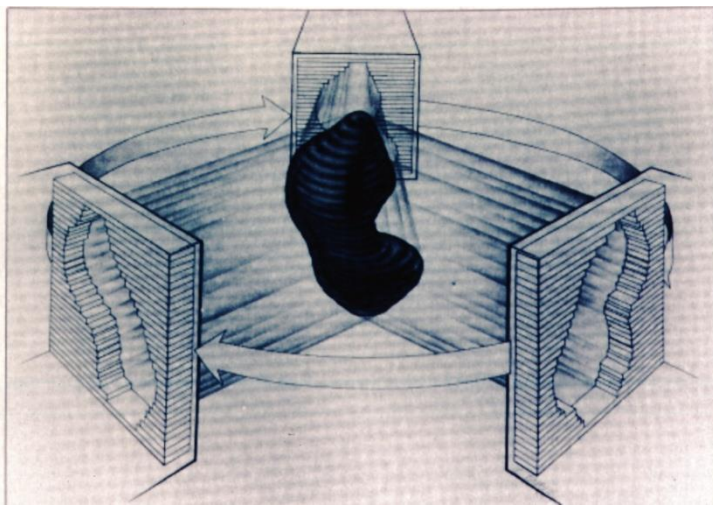


Fig. 3 – Intensity Modulated Radiotherapy (IMRT):

MLCs “shift on the fly” as the gantry rotates to allow dose conformity to complex shapes, resulting in better sparing of normal tissues.

Stereotactic Radiosurgery

This technology is used almost exclusively for the treatment of CNS neoplasms. It allows highly focused radiotherapy to small volumes, sparing normal structures in very close proximity to the target. Radiosurgery can be delivered by a linac (available in London), or by a “gamma knife” (not available in London).

Stereotactic radiosurgery requires precise immobilization and localization. This is accomplished by attaching a stereotactic frame to the patient’s skull. The frame serves as an immobilizing device and as a reference coordinate system. Determination of the treatment volume is assisted by a planning CT taken with the stereotactic frame in place. The treatment is delivered by multiple overlapping highly collimated radiation beams.

Others

Prostate Brachytherapy

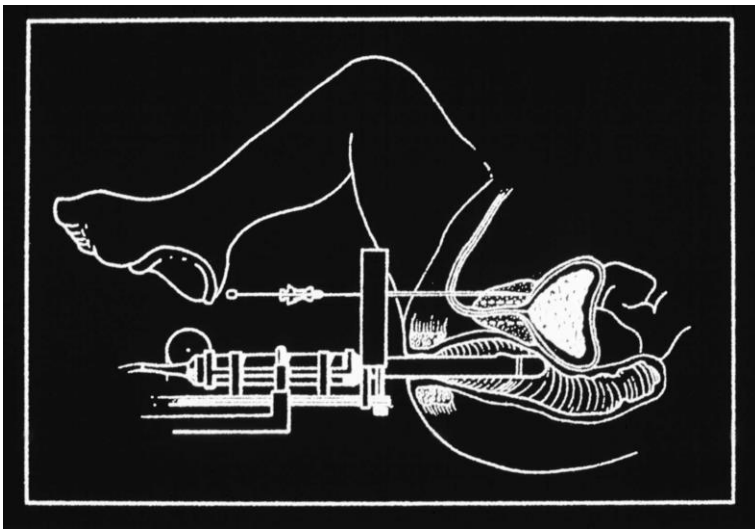
Prostate brachytherapy is coming back into favour as a viable treatment option. In the 1970s and 1980s, prostate implants were done retroperitoneally through a laparotomy incision. Radioactive seeds were placed blindly in the target volume using a freehand technique. Outcomes with this procedure were poor and it lost popularity.

More recently, interest has renewed in prostate brachytherapy using a transrectal ultrasound-guided (TRUS-guided) transperineal technique. 5-10 year biochemical control is comparable in historical series to surgery or external beam radiotherapy for early stage prostate cancer.

The technique involves implanting Iodine 125 or Palladium 103 seeds (about 60-100) using template guided transperineal needles based on a TRUS preplan. The patient is admitted to hospital the day of the procedure, which takes approximately one hour to do under general anaesthesia, and is usually discharged the next day. Acute side effects consist of perineal pain, hematuria, diarrhea/constipation, ejaculatory pain and urinary outlet obstruction. The patient is sent home with adequate oral analgesia and a Foley catheter in place. The catheter can usually be discontinued within one to two weeks post-implant. Long term side effects consist of impotence (25%), urinary retention (3%), and TURP).

Fig. 4 – Prostate Brachytherapy:

Template guided needles are used to deposit radioactive seeds in the prostate using real-time transrectal ultrasound imaging



Eligible patients for prostate brachytherapy at the LRCC are restricted to those with early stage disease (clinical stage <T2b, Gleason score <7, pre-treatment PSA <10) and smaller glands (<60 cc). Other centres also use this technique as a boost for later stage disease after external beam radiotherapy.

Photodynamic Therapy

Photodynamic therapy (PDT) is a rapidly expanding field with many potential applications in both benign and malignant conditions. The three components necessary for PDT are a photosensitising agent, light, and oxygen.

The main advantages of PDT in oncology relate to its high selectivity for malignant or premalignant tissues, and relative sparing of surrounding normal tissues. There appears to be no additive toxicity with either chemotherapy or radiation, and PDT can be repeated many times if necessary. Its main limitations relate to the limited depth of penetration of the photoactivating light in tissue (usually 1-3 mm), and the technique is best suited for superficial lesions such as skin cancers or carcinoma in situ.

ONCOLOGIC EMERGENCIES

T. Vandenberg, MD, FRCPC

1. *Febrile Neutropenia*
2. *Spinal Cord Compression*
3. *Hypercalcaemia*
4. *Hyponatremia*
5. *Tumour Lysis Syndrome*
6. *Leukostasis Syndromes*
7. *Respiratory Emergencies*
8. *Superior Vena Cava Obstruction*

FEBRILE NEUTROPENIA

Assessment of febrile neutropenic patient

- Factors predisposing cancer patients to infection
 - Reduced humoral immunity
 - Reduced cell mediated immunity
 - Obstruction
 - Granulocytopenia
 - Mucosal disruption
 - Prosthetic devices
 - Hypo or asplenism CLL, myeloma
 - Lymphomas, steroids
 - Lung, colon cancer
 - Leukaemia, chemotherapy
 - Mucositis from chemo
 - Central line
 - Hodgkin's disease
- Many patients will have a normal physical exam, but it is important to assess clues for the likely organism.
 - Oral cavity (mucositis, thrush, gingivitis, caries, abscess)
 - Skin (venipuncture sites, zoster)
 - Central line site
 - Optic fundi
 - Perianal area (fissure, abscess). NEVER DO RECTAL.
 - Lungs
 - G.I.
 - G.U.
 - C.N.S.
- Laboratory tests
 - Blood (including all lumens of central line), urine and sputum cultures.
 - Stool cultures if diarrhoea. Often physical findings (rales) may precede evidence of pneumonia on CXR. Only after neutrophils recover will an infiltrate become

radiologically apparent. 50% of clinically infected patients will not have positive cultures. Only 15% will have positive blood cultures.

Management

- Broad spectrum monotherapy with imipenem, meropenem, or piperacillin/tazobactam, or combination therapy as per current ID guidelines.
- Q24 hour dosing for aminoglycosides.
- Antibiotic choice tailored to clinical situation (previous infections, spectrum of resistant bacteria).
- Reassess after 48 hours. If still febrile, reculture. Consider coverage for pseudomonas.
- Bronchoalveolar lavage for lung infiltrates.
- Ultrasound to assess for occult sites (subphrenic, pelvic abscesses).
- Central lines may need to be removed if clinically infected and infection not responding to appropriate antibiotics.
- Role of vancomycin as part of initial therapy in patients with central lines should be questioned (toxicity, cost, no change in outcomes).
- Rule out C. Difficile if diarrhoea.
- Consider amphotericin B if continued fever and neutropenia. Newer antifungals may offer advantages.
- Could fever be viral (HSV, CMV)?
- Could it be related to cancer, especially if lymphoma or liver metastases? Naprosyn test?
- Could it be a drug fever?

Controversies

- Role of open lung biopsy vs. empirical treatment
- Combination therapy vs. monotherapy
- Antibiotic prophylaxis

SPINAL CORD COMPRESSION

Clinical picture

- Symptoms present median two months before diagnosis
- Usually previously diagnosed cancer, occasionally initial presentation
- Early diagnosis essential
- First Symptoms:
 - pain 95%
 - weakness 5%
 - sensory loss 1%
- Symptoms at Diagnosis:
 - pain 96%
 - weakness 76%
 - sensory loss 51%
 - bladder/bowel dysfn 57%
 - Fewer sensorimotor or autonomic symptoms at diagnosis since widespread use of myelography and MRI scans
- Pain sites:
 - cervical 15%
 - thoracic 70% (breast, lung)
 - lumbosacral 15% (G.I., pelvic)
 - Nature of pain: Local or radicular, progressive, may mimic visceral disease, worse when lying down or with valsalva (eg: bowel movement)

- Other symptoms: Ataxia 7%, Brown-Sequard syndrome 2%, others (acute urinary retention, Lhermitte's sign, fasciculations, facial paresis) uncommon
- Signs:
 - weakness 85%
 - ambulatory 50%
 - paraparetic 35%
 - paraplegic 15%
 - abnormal DTRs (usually hyperactive) 65%
 - sensory loss 65%
 - also check, abdominal, cremasteric reflexes, anal tone

Pathophysiology

1. Compression of cord parenchyma-demyelination, axonal destruction?
2. Vascular compression-ischemia, edema, infarction
3. Vasogenic edema-Compression of venous outflow

Causes

1. Breast 22%
2. Lung 13%
3. Prostate 10%
4. Lymphoma 10%
5. Sarcoma 8%
6. Colorectum 7%
7. Kidney 6%
8. Melanoma 4%
9. Myeloma 3%
10. Neuroblastoma 1%
11. Unknown 11%

85% arise from the vertebral body or pedicle, 10% through the intervertebral foramina, and 5% are intramedullary metastases

Investigations

1. History and physical examination.
2. Spine X-ray: 80% are positive, bone scan increases rate to 85%.
3. CT scan more sensitive than x-rays or scans.
4. MRI gold standard: Assesses soft tissue as well as bone, does not miss levels if multiple areas of compression, clearly shows non-malignant causes (herniated disk), can assess for meningeal metastases, does not require invasive procedure (myelogram). Difficult for people with claustrophobia so give sedative before.

Differential diagnosis

- Extradural lesion
- Herniated disk
- Haematoma
- Abscess
- Fat (steroids)
- Extramedullary haemopoiesis
- Rheumatoid nodule
- Intradural lesion
- Primary tumour
- Metastasis

- Meningeal metastasis
- Myelopathy (radiation or chemo)

Treatment

- Immediate referral to radiation oncologist, neurosurgeon or spinal orthopaedic surgeon.
- Dexamethasone (10mg, 100mg)? IV then 4mg Q6H P.O.
- Role of diuretics, mannitol?
- Chemo role undefined. Useful for selected patients with meningeal metastases.
- Surgery indicated if diagnosis required, localised and completely resectable tumour, previous radiation or radioresistant tumour, instability (esp. C-spine). Role of anterolateral vs. posterior resections?

Special Considerations High C-spine compression:

- Rule out atlanto-axial subluxation with open-mouth odontoid x-rays. 2/3 from breast cancer.
- If early/no subluxation, use steroids, Philadelphia collar, radiation therapy.
- If subluxation, need cervical traction, posterior cervical fusion followed by radiation.

Spinal subdural hematoma:

- Usually bleeding after lumbar puncture especially if low platelets (<20,000).
- Need emergency myelogram and surgical evacuation of clot.

Prognosis

Preop Status	% Ambulatory Postop
Ambulatory	60%
Paraparetic	35%
Paraplegic	7%

Poorer prognosis:

- Rapid progression of signs/symptoms
- Loss of sphincter control
- High T-spine; 24% recover T1-4, 43% recover T5-12

Pathology	Response
Lymphoma/myeloma	50%
Breast/prostate	33%
Lung/kidney	10%

CANCER ASSOCIATED HYPERCALCEMIA

Know
this!

INCIDENCE - varies with cancer site, overall 10 - 20%

Calculation of corrected calcium: add 0.2 to reported calcium level, for each 10 g/L drop in albumin below 40. Normal range of calcium = 2.2 – 2.65 approx.

Example: Albumin= 20, calcium reported as 2.59. Corrected calcium = $2.59 + (0.2 \times 2) = 2.99 = \text{hypercalcemia}$.

Common Sites:

- Breast 30 - 40%
- Myeloma 20 - 40%
- Lung Cancer 12.5 - 35%
- Head Neck 2.9 - 25%
- Renal Cell 3 - 17%
- Lymphoma 0.5 - 4%

PATHOPHYSIOLOGY

- multiple etiologies
- humeral hypercalcemia of malignancy probably several mediators PTHrP, TGF, IL1, TNF causing increased breakdown and decreased formation

Symptoms - have a high index of suspicion

Clinical Presentations of Cancer-Related Hypercalcemia

General: Dehydration, weight loss, anorexia, pruritus, polydipsia

Neuromuscular: Fatigue, lethargy, muscle weakness, hyporeflexia, confusion, psychosis, seizure, obtundation, coma

Gastrointestinal: Nausea, vomiting, constipation, obstipation, ileus

Genitorenal: Polyuria, renal insufficiency

Cardiac: Bradycardia, prolonged P-R interval, shortened Q-T interval, wide T-wave, atrial or ventricular arrhythmias

Differential Diagnosis

In hospitalised patients:

- 77% due to malignancy
- 4% due to hyperparathyroidism
- 2% Vitamin D intoxication
- 2% due to tamoxifen
- 16% idiopathic

Treatment

Should you treat?

Best treatment - treat underlying malignancy

Other therapeutic options:

1. Hydration and diuresis
 - NS hydration at least 3 litres/day
 - Consider lasix after rehydrated but usually not necessary with bisphosphonates.
 - 30-40% will normalise
2. Bisphosphonates inhibit Ca reabsorption by binding to bone. Pamidronate is the treatment of choice. Effective in up to 90% cases within 48 hrs. Dose 30 - 90 mg over 4 hrs IV. Zoledronate 4 mg IV if ineffective.
3. Calcitonin but tachyphylaxis in 24-72 hours
4. Glucocorticoids - Prednisone 40-100mg/d (not very effective)

TUMOUR LYSIS SYNDROME

- Rapid destruction of malignant cells usually associated with high tumour burden and rapid response to treatment. Most commonly associated with high grade lymphomas, acute leukaemia, but may occur with other tumours.
- Hypocalcemia, hypoglycemia, hyperphosphatemia, hyperuricemia, hyperkalemia.
- Acute renal failure, arrhythmias are life-threatening complications.
- Patients with high tumour burden, increase in LDH, rapidly growing cancer should receive prophylactic hydration to maintain good urine output, allopurinol to increase in uric acid solubility and alkalinise urine to pH>7.0 with bicarb ± acetazolamide.
- Continue above if syndrome develops, add K+ binding resins, cautiously add calcium carbonate. Antiarrhythmics and hemodialysis may be necessary for some people.

LEUKOSTASIS SYNDROMES

- Depends on which blood cells are elevated
- CLL>200,000
- ALL>100,000
- AML/CML>100,000
- Increase in viscosity causes specific syndromes in various organs (pulmonary congestion-->ARDS, tumour lysis syndrome, retinal hemorrhages, CNS symptoms)
- Treatment includes leucopheresis, treatment of underlying leukaemia (including steps to prevent tumour lysis syndrome)
- Radiation to CNS, if symptomatic

RESPIRATORY EMERGENCIES

Respiratory failure

- Localised infiltrates
- Diffuse infiltrates
- Clear CXR

Specific causes

- Infection: bacterial, fungal, viral
- Tumour: Obstruction, effusion, lymphangitic carcinomatosis
- Leukostasis syndrome
- Pulmonary emboli
- Drug induced injury (bleomycin, nitrosoureas, mitomycin-C)
- Radiation

Massive hemoptysis

- Bronchogenic carcinoma
- Bronchiectasis
- Tuberculosis
- Lung abscess
- Aspergilloma

Upper airway obstruction is usually due to recurrent tumour. Often heavily pretreated. Consider treatment with heliox, narcotics. Occasionally, patients are candidates for YAG laser endobronchial ablation:

Relative contraindications

- Asymptomatic
- Obstruction at lobar/segmental level only
- Total lumen obstruction
- Extraluminal compression
- Upper lobe lesion
- Tracheoesophageal fistula

Complications

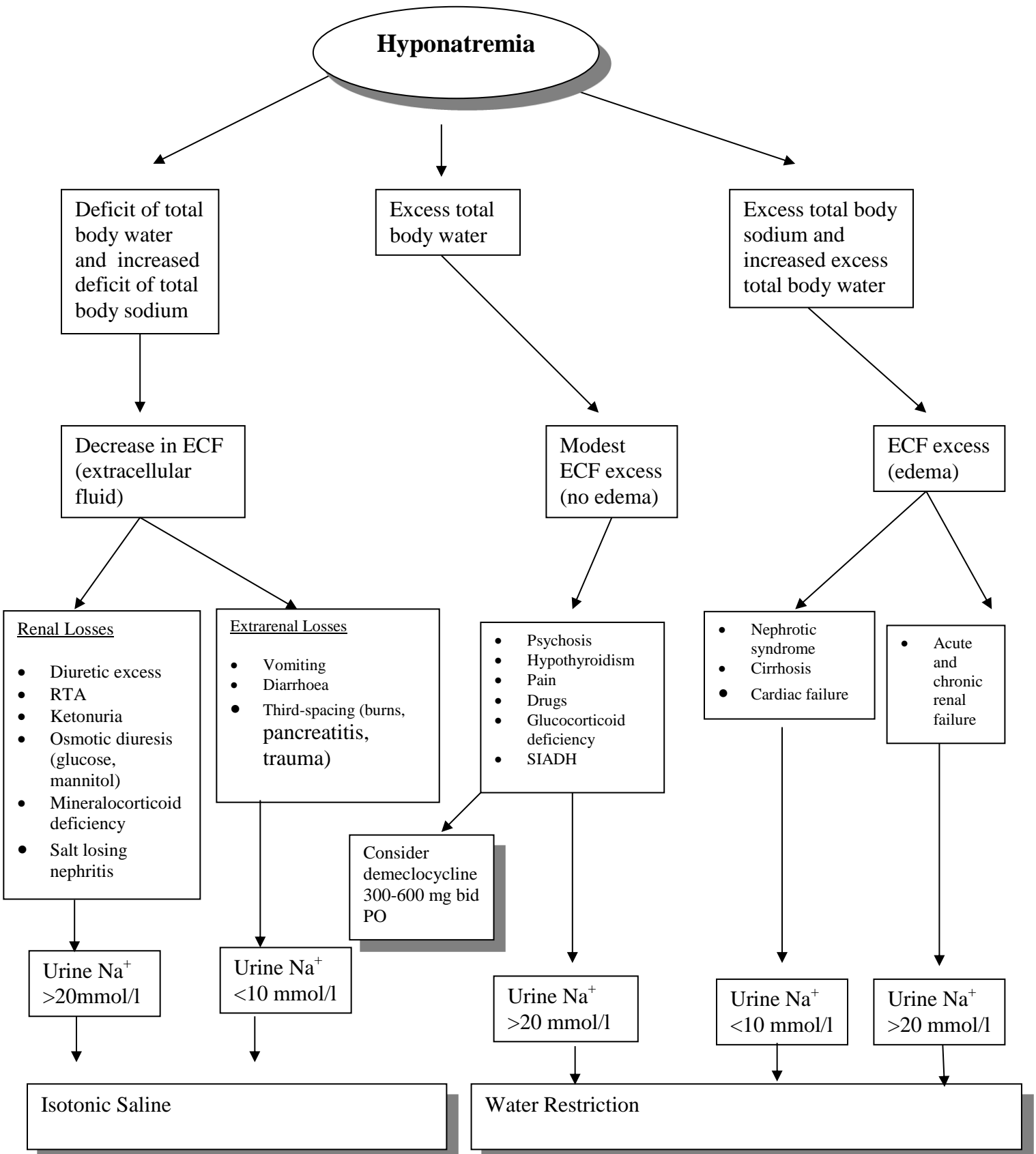
- Haemorrhage
- Perforation
- Cardiac arrhythmia
- Endobronchial combustion

SUPERIOR VENA CAVA OBSTRUCTION

- Can be an emergency if patient symptomatic
- Most cases (80%) are secondary to bronchogenic carcinoma. Other causes include lymphoma (10-18%), and benign causes such as goitre (2-3%)
- Symptoms/signs include facial plethora, dilated superficial veins on upper extremities and thorax, shortness of breath and confusion

Management

- History and Physical
- CBC, electrolytes, BUN, creatinine, calcium, albumen, other bloodwork and ABGs as indicated
- CXR and CT chest/upper abdomen
- Tissue diagnosis if possible
- Elevate head of bed with supplemental O₂
- Dexamethasone (*Decadron*) 10mg IV followed by 4mg PO q4h. Consider concurrent ranitidine (*Zantac*) 150 mg PO bid
- Referral to Radiation Oncology
- Alternatively, can consider initial treatment with chemotherapy if diagnosis of small cell carcinoma or malignant lymphoma confirmed



MANAGEMENT OF CANCER PAIN

An Abstract from the “SWOMEN Palliative Medicine Clerkship Syllabus”

C. Leighton, MD; C Johnston, MD; C Jones, MD; D Moulin, MD; Donna Danelson; Carol Jones; Joyce McManus

Overview

“**Palliative Care**” is whole-person care that “affirms life and regards dying as a normal process. It neither hastens nor prolongs death and provides relief from pain and other distressing symptoms (WHO definition). Psychological, social, and spiritual problems should be addressed simultaneously with symptom management. Palliative care should facilitate a support system to help persons live as actively as possible until death.

“**Palliative Medicine**” is “the study and management of patients with active, progressive, far advanced disease for whom the prognosis is limited and the focus of care is quality of life” (American Academy of Hospice and Palliative Medicine definition).

Therefore the focus of the Palliative Care Team is “symptom oriented” rather than disease oriented. The aim is to maintain or preferably, to improve the quality of life experienced by the patient throughout the process of disease progression and dying. A holistic approach to patient care is necessary. Psychosocial issues such as depression, loss of career, financial strains from lost income, loss of intimacy, spirituality, and adjustment by family members are all important considerations. The best approach involves multiple disciplines: oncologist, palliative medicine physician, family physician, nursing support, health care aids, social work, clergy and others.

Pain is experienced by many cancer patients during the course of their illness. The overall prevalence of pain among all cancer patients is approximately 50%, and is about 80% among advanced cancer patients. The importance of controlling all symptoms, especially pain, cannot be over emphasized. Persistent symptoms not only immediately worsen quality of life, but serve as a constant reminder to the patient that he or she has a terminal illness. Sleep, appetite, and activity level are all tightly woven into the level of pain control. Depression and hopelessness are common repercussions from uncontrolled pain. These feelings exacerbate the perception of pain and thus, create a vicious circle.

The management of cancer pain is more than prescribing a long acting opioid. A holistic approach is necessary – one that considers all the disease, treatment and psychosocial factors impacting the patient’s quality of life. Treatment must be tailored to the individual. Potential drug interactions must be anticipated before initiating an analgesic regime. One must first identify the source of the pain syndrome and treat underlying disease whenever possible (for example, with a palliative cancer treatment such as radiotherapy for bone metastasis). Neuropathic pain syndromes must be diagnosed given the pharmacologic treatment will differ to that of pure nociceptive pain syndromes. This guide, in companion with the Clinical Oncology Clerkship syllabus will help you to develop a holistic approach to the care of the cancer patient.

References:

http://www.ccac-ont.ca/Upload/esc/General/Palliative_Care_Managment_Tool_v3_0.pdf

www.painCare.ca

www.aahpm.org

www.thehealthline.ca

www.palliativecareswo.ca

1.0 Clinical Approach to the Cancer Patient in Pain

As with any patient, the etiology for the onset of pain must be clearly understood by the clinician before prescribing a treatment regime. The cancer patient in pain provides a challenging therapeutic dilemma.

A careful history and physical examination must be completed. The differential diagnosis can be extensive. Table 5.1 outlines common pain syndromes. The clinician must consider premorbid medical conditions and rule out cancer progression, or treatment toxicity. One must consider the temporal onset of the pain in the context of recent interventions. It is helpful to consider: "Why is this patient having pain now?"

A thorough history, physical examination, and psychosocial assessment are required. It is well understood that the perception of pain often changes (in intensity) as psychosocial stressors come and go in the patient's experience.

History:

- **Temporal onset** or variation of pain: Neuropathic pain often peaks late in the afternoon
- **Exacerbating or Relieving factors:** effects of ambulation or rest, medication, movement
- **Sensory descriptors** of pain, preferably documented in patients' own words: "shooting", "dull". "constant", "burning" etc "Tell me about your pain? What does it feel like?"
- **Radiation of pain**, into extremities for example
- Paroxysmal; constant or intermittent; worsening or improving;
- **Pain Intensity:** Visual analogue score of pain severity, 0-10 (0 no pain, 10 worst ever experienced) – record current pain, average for past 2 weeks, and best score
- **Associated symptoms:** nausea, vomiting, constipation, incontinence, sensory changes, headache (patients sometime consider 'headache' separate from 'pain')
- **Functional Impact:** How has pain interfered with ADLs, sleep, work, elimination, nutrition etc, Degree of disability. State of home (apartment v. house, bathroom accessibly—same floor as bedroom in end of life situations)
- **Corroboration of history** from immediate family and care givers – provides additional insight into the degree of disability caused by the patients symptoms
- **Treatment History of Pain:** Which medications/maneuvers have worked or failed.
- **Psychosocial History** – "Do you have any worries other than your pain presently?"
- **ESAS scores** (patient self-rated Quality of Life Assessment Tool, page x)
- **Concurrent medication history and use of alcohol or illicit drugs**

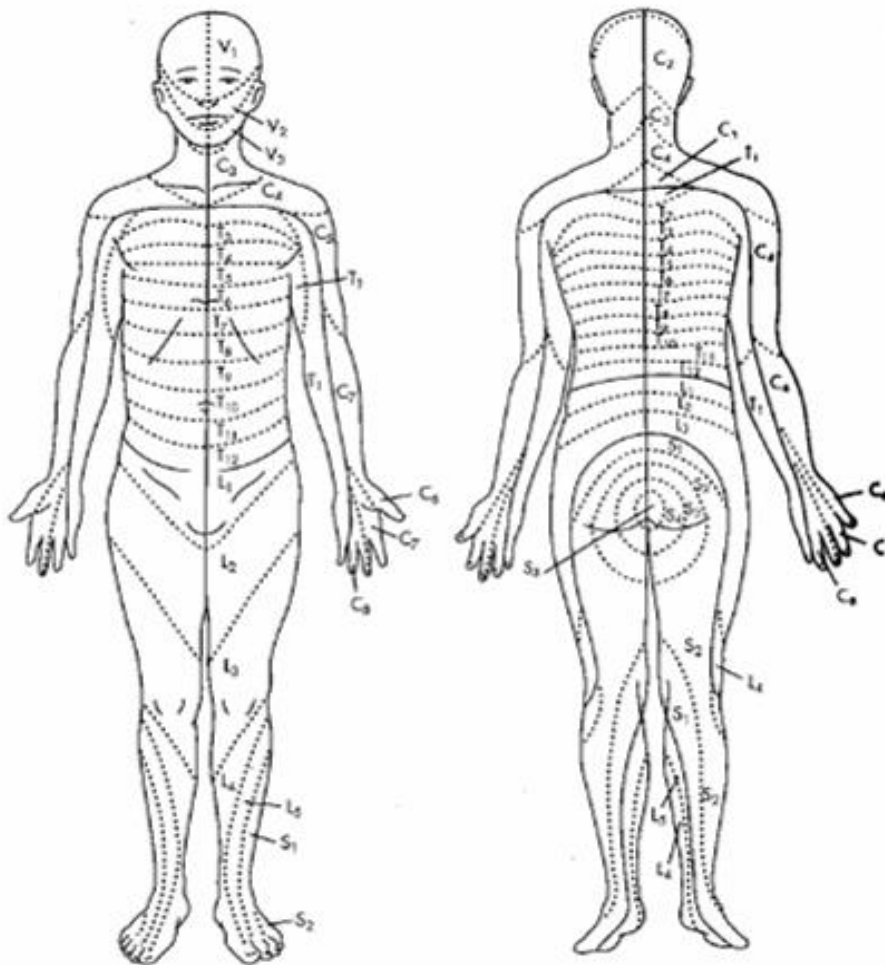
Physical Examination:

- Screening assessment should include: level of nutrition, state of hydration, color, vital signs if not stable, cognitive status if altered, level of consciousness (alert, drowsy, moribund), presence of aphasia, conversation if not appropriate, affect
- Identify common pain behaviors: grimacing, moaning, lying supine etc.
- Ambulatory or mobility aid required?
- Cardiopulmonary and abdominal assessments are routine.

- Musculoskeletal exam important to identify sites of bone tenderness, which may represent bone metastasis
- **A thorough neurological examination is a must on an initial assessment!**
 - Mental Status (usually assessed by history, MMS if concerns)
 - Speech – fluent or non-fluent; appropriate or inappropriate
 - Cranial Nerves
 - Motor – Bulk, Tone, Strength (pronator drift; heel and toe walking are good general screening assessments); distinguish between guarding from pain and true motor weakness; fasciculations or atrophy should be noted.
 - Co-ordination – heel-toe, finger-nose, Romberg
 - Deep Tendon Reflexes (record diminished or absent reflexes; clonus; hyperreflexia – Babinski sign, Hoffman’s reflex)
 - **Sensory Exam (at least Pin Prick and Light touch, temperature helpful)**
 - Report sensory disturbances:
 - **Allodynia*** – pain caused by a normally non-painful stimulus
 - eg. Patient had dynamic touch allodynia caused by a cotton ball moving across the skin
 - eg. Patient had thermal allodynia from a ice cube stimulus (burning sensation from cold)
 - **Hyperalgesia/Hyperpathia*** – exaggerated pain response following a noxious stimulus. Patient had hyperalgesia to pin prick at the right T6 dermatome posteriorly
 - **Hypoalgesia*** – decreased response or sensitivity to a normally painful stimulus
 - proprioception; vibration sensation
 - Note levels of sensory disturbances (see Figures 5.1 & Table 5.2)
 - Summarize the neurologic exam and identify where the lesion(s) is and provide the probable etiology of the lesion
- *NB: *Indicators of Neuropathic pain*
- **Investigations:** CT/MRI to rule out spinal cord compression, nerve root entrapment when suspected
- EMG/Nerve conduction studies may confirm nerve injury/dysfunction however, normal studies do not rule out neuropathic pain syndromes

Table 1.1 Considerations for Evaluation of Pain Syndromes in Cancer Patients

Pain Syndrome	Appropriate Questions	Ominous Signs
Headache	<p>Early morning? Associated with Vomiting? Intermittent or every day? Progressive? Responds to simple analgesics?</p>	<p>Severe, progressive headaches (often early am initially) associated with vomiting = r/o metastasis DDx – atypical meningitis, intracerebral hemorrhage</p>
Back Pain	<p>Temporal Onset? Prevent Sleep? Respond to analgesics? Associated Problems? - Sphincter disturbance - Constipation - Numbness/Tingling below painful level - Severe radicular pain - limb weakness</p>	<p>Nocturnal back pain, associated with sleep disturbance, severe, and progressive in nature must be consider metastatic disease until ruled out. Back pain with focal neurologic deficits, a sensory level, or sphincter impairment is an emergency – MRI is required the same day to rule out extradural spinal cord compression.</p>
Abdominal Pain	<p>Intermittent v. Frequent? Progressive v. stable? Constipation? Associated with Vomiting? Polydipsia? Associated Fever?</p>	<p>Vomiting or constipation >3 days suggest bowel obstruction or fecal impaction. Consider carcinomatosis if known history of metastatic colorectal ca or ovarian ca. Hypercalcemia: abdominal pain, thirst, constipation, neuro-excitation, vomiting Fever +/- abdominal tenderness or guarding – think of peritonitis NB. Large malignant abdominal masses may cause low grade fever also....always r/o infection</p>
Bone Pain	<p>Chronic or new? Pain on weight bearing? Pain worse in evening or overnight? Near joints? Associated stiffness. P/E – pain elicited by boney pressure far removed from painful site?</p>	<p>Bone metastasis typically causes progressive pain, worse in the evening initially. It rarely causes joint pain or stiffness. Pain produced by pressure on the same bone many cm away suggests periosteal elevation – suggestive of bone met. Sensory innervation of bones is periosteal only. Sudden onset of pain and immobility suggests pathologic # - urgent evaluation by a Radiation Oncologist or Orthopaedic Surgeon is indicated if confirmed</p>



Key Areas:

- C3 Supraclavicular Fossa
- C4 AC joint
- C6 Thumb
- C7 Middle finger
- C8 Little finger
- T1 medial antecubital fos
- T3 third intercostals spc
- T4 nipple line
- T6 Xiphisternum
- T10 umbilicus
- T12 Inguinal ligament
- L1 Upper anterior thigh
- L3 medial femoral condyl
- L5 dorsum of foot at 3rd MTP
- S1 lateral heel
- S2 popliteal fossa
- S3 ischial tuberosity
- S4/5 Perianal area

Figure 1-1 Dermatomes, anterior and posterior representations

Table 1.2 Key muscles and their corresponding primary motor level

C1-4	Diaphragm
C5	Biceps, elbow flexion
C6	Wrist extensors
C7	Triceps, elbow extension
C8	Finger flexors
T1	Intrinsic hand (interossei), finger adduction
L2	Hip flexors (iliopsoas)
L3	Knee extension (quadriceps)
L4	Ankle dorsiflexion (tibialis anterior)
L5	Great toe extension
S1	Ankle planter flexors (gastroc.)
S2-5	Anal sphincter

Synopsis:

Take a moment away from the patient and family to review the history, ESAS (Objective Symptom Assessment Scale, see page 18), physical examination findings, and prior treatments

(successes and failures). *Prioritize the patients' problems and your recommendations. It is helpful to first reflect on the following questions:*

- 1) **Does this patient possibly have a potential cancer emergency?** Spinal cord compression, superior vena cava obstruction, brain metastasis, bowel obstruction, hypercalcemia
- 2) **Does this patient have a new cancer problem, which requires re-assessment and possible treatment by an oncologist?** New adenopathy; recurrence of cancer related symptoms; imaging evidence of progressive or new sites of disease.

The next step is to identify the probable source of the current pain syndrome and classify it: **Nociceptive, Neuropathic, or a Mixed Nociceptive-Neuropathic Pain Syndrome.**

1.1 Classification of Pain Syndromes:

Pain transmission occurs via activation of somatosensory primary afferent fibers. A β fibers are large diameter, myelinated fibres and transmit low threshold, non-noxious stimuli such as touch, from the dermis. A δ fibres are less myelinated, smaller diameter fibres and transmit both noxious and non-noxious stimuli. Unmyelinated C fibers transmit high-threshold noxious inputs and have the slowest conduction velocity.

Transmission of pain is complex and involves activation of sensory receptors (nociceptors) and then, sodium channel propagation along the nerve fiber to the terminus. Calcium channel activation thereafter stimulates neurotransmitter (glutamate, SP, CGRP, etc.) release which activate spinal neurons. NMDA receptor activation occurs after repetitive stimuli (chronic pain stimulus) and may produce a "wind-up" phenomenon whereby dorsal horn neurons become more sensitive to sensory stimuli. This is thought to be the basis for **central hyperexcitability** which occurs after nerve or spinal cord injury – leading to chronic neuropathic pain syndromes.

A more detailed description of pain transmission is available: Chapter 1, Nociception: Basic **Principles, in Cancer Pain. Assessment and Management.** Bruera E, and Portenoy R. Cambridge University Press, 2003.

Nociceptive Pain: Pain which involves a stimulus of sensory receptors via a noxious stimulus (pressure, temperature, chemical (acute inflammation); and can be classified as somatic or visceral:

- i) **Somatic Pain:** Well localized, typically in the superficial cutaneous or musculoskeletal system. (e.g. surgical wound, bone metastasis, muscle strain).
- ii) **Visceral Pain:** Poorly localized often. Origin in deeper structures (viscera – e.g. constipation, appendicitis, renal calculi). Inflammation may sensitize local areas and promote increased sensitivity (hyperalgesia) through activation of mediators which lower nerve conduction thresholds.

Neuropathic Pain: Occurs as a result of neural dysfunction or injury in the central or peripheral nervous system. It may be a result of compression/crush, chemical, ischemic, metabolic, neoplastic or paraneoplastic insults. Neuropathic pain is characterized by **dysthetic** or **lancinating** components, sometimes with **hyperalgesia** or **allodynia**. Patients often use pain descriptors such as "burning", "shooting", "stabbing", or "knifelike". Pain is often severe (greater than 6 on the ESAS pain domain). Diurnal variation sometimes occurs where the pain worsens in the late afternoon and early evening. Often this discomfort is associated with sensory disturbances such as a non-noxious stimulus causing pain (light touch -- allodynia) or an exaggerated sensory response from a non-noxious stimulus (hyperalgesia).

The following reference is required reading:

2.0 Objective Assessment of Pain and Symptoms

Quality of life and symptom assessment scales are increasingly used by palliative care physicians to provide objective assessments of pain severity, response to treatment, and the impact of symptoms on the patient state of health. Scales must be reliable and validated prior to widespread clinical use. The Edmonton Symptom Assessment Scale is one such instrument, widely implemented in Ontario. It has been validated in advanced/metastatic cancer populations and renal dialysis patients. It allows patients to self-rate their symptoms on a number of domains via a categorical visual analog scale, 0-10, Figure 6.1. Summary graphs are used to plot changes in domain scores overtime and to identify trends or abrupt changes in patient quality of life. In patients with multiple or complex problems, this tool allows the clinician to concentrate on those problems most severe at the time of clinical assessment. Finally, objective scales allow health care providers from different disciplines to uniformly understand and communicate the severity of individual patient symptoms.

A second assessment tool widely employed in Ontario is the Palliative Performance Scale (Figure 2.2). This is a global quality of life score which provides a clear communication tool in which to follow the status of patients near end of life. It employs 5 domains: level of ambulation, activity level and evidence of disease in daily activity, level of self-care, oral intake, and level of consciousness. This is a categorical scale, rating PPS levels from 0% (death) to 100% (no impact of disease on daily living). One example of the practical application of the PPS is noted: The Palliative Medicine Program at the Windsor Regional Hospital, and the Windsor and Essex County Hospice recommend that the treating physician order a Symptom Response Kit (SRK) into the patient's home, to assist in end of life care, when the PPS score reaches 30%. This kit has medications commonly used to palliate patients with metastatic disease who are unable to take medications orally and have (previously) made arrangements to die at home.

Additional assessment scales are used by some cancer centers. For example, a diagnostic tool is available to help the clinician discern between pain which may be neuropathic pain or not (DN4). (3) Also, a more comprehensive pain inventory is sometimes employed (Brief Pain Inventory), especially in the setting of clinical trials.

It is likely these scales will be employed more frequently by the health care team as the electronic health record becomes more common.

Figure 2.1 The Edmonton Symptom Assessment Scale (1)

Edmonton Symptom Assessment System (ESAS)

Date of Completion: _____ Time: _____

Please circle the number that best describes:

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst possible pain
Not tired	0	1	2	3	4	5	6	7	8	9	10	Worst possible tiredness
Not nauseated	0	1	2	3	4	5	6	7	8	9	10	Worst possible nausea
Not depressed	0	1	2	3	4	5	6	7	8	9	10	Worst possible depression
Not anxious	0	1	2	3	4	5	6	7	8	9	10	Worst possible anxiety
Not drowsy	0	1	2	3	4	5	6	7	8	9	10	Worst possible drowsiness
Best appetite	0	1	2	3	4	5	6	7	8	9	10	Worst possible appetite
Best feeling of well being	0	1	2	3	4	5	6	7	8	9	10	Worst possible feeling of well being
No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Worst possible shortness of breath
Other problem	0	1	2	3	4	5	6	7	8	9	10	

Not completed
 Printed
 Computer-assisted

	DATE			HOUR	HOSP. DAY											
	MO	DAY	YEAR													
	10	11	12													
PAIN	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
ACTIVITY	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
NAUSEA	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
DEPRESSION	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
ANXIETY	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
DROWSINESS	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
APPETITE	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
WELLBEING	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12
SHORTNESS OF BREATH	10	11	12	00	01	02	03	04	05	06	07	08	09	10	11	12

ASSESSED BY: _____

Code P - Patient N - Nurse NA - Nurse Assisted F - Family

Mini-Mental State Score: _____

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Figure 2.2 Palliative Performance Scale

Palliative Performance Scale (PPSv2)
version 2

PPS Level	Ambulation	Activity & Evidence of Disease	Self-Care	Intake	Conscious Level
100%	Full	Normal activity & work No evidence of disease	Full	Normal	Full
90%	Full	Normal activity & work Some evidence of disease	Full	Normal	Full
80%	Full	Normal activity <i>with Effort</i> Some evidence of disease	Full	Normal or reduced	Full
70%	Reduced	Unable Normal Job/Work Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or Confusion
50%	Mainly Sit/Lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or Confusion
40%	Mainly in Bed	Unable to do most activity Extensive disease	Mainly assistance	Normal or reduced	Full or Drowsy +/- Confusion
30%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Normal or reduced	Full or Drowsy +/- Confusion
20%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Minimal to sips	Full or Drowsy +/- Confusion
10%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Mouth care only	Drowsy or Coma +/- Confusion
0%	Death				

References

1. Breuer E, Kuehn N, Miller MJ, et al. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care* 7:6-9, 1991.
2. Anderson F, Downing GM, Hill J, et al. Palliative Performance Scale (PPS): new tool. *J Palliat Care* 1996; 12 (1):5-11.
3. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005 Mar;114(1-2):29-36. Epub 2005 Jan 26.

3.0 Pharmacological Approach to Pain Management

3.01 Complete a careful medication history: past and present.

Cancer patients near end of life often have a number of medications by the time an assessment for pain management is made. A careful history is required to review prior and current medications. Prior administration of chemotherapy drugs, such as cisplatin for example, may have caused nephrotoxicity. Many opioid metabolites are eliminated via the kidneys, and therefore dose adjustments may be required. It is good practice to review hepatic and renal function by biochemistry, prior to prescribing a new narcotic, especially for those at risk of chemotherapy related toxicity or in the elderly.

3.02 Confirm or rule out an opioid allergy when reported.

A true allergic reaction to an opioid analgesic is an immunological response with the development of hives, urticaria, and possibly bronchospasm. This can be due to release of histamine from mast cells.

True opioid allergies are unusual. A careful history will often reveal what the patient reported as an allergy, is in fact, intolerance or symptoms associated with neuro-toxicity.

3.1 WHO Laddered Approach to Treating Pain

This approach is a gross generalization but a helpful starting point. It directs physicians to prescribe different classes of pain medication based on the severity of the pain. “Mild Pain” is rated 1-3 (0-10 categorical scale, where 0=no pain and 10=maximum severity) and non-opioid analgesics are recommended for treatment – NSAIDS (non-selective COX inhibitors (ASA, acetaminophen, naproxen, ibuprofen) and selective COX-2 inhibitors (celcoxib, meloxicam) are examples).

For “Moderate Pain”, rated 4-6, opioid +/- non-opioid co-analgesics are recommended initially. When combined with Class 1 medications (acetaminophen, ASA) there is a ceiling for a 24 hour dosage. Commonly used medications in this class may be Tylenol #2 or #3 (acetaminophen + codeine) or Percocet (oxycodone + acetaminophen). Long acting preparations of codeine are now available (codeine contin).

For “Severe Pain”, rated 7-10, more potent opioid analgesics are recommended. Chronic malignant pain will generally require a long acting opioid with a short acting opioid for “breakthrough pain”, in between doses of the long acting opioid. Knowledge of equi-analgesic doses of the various opioids is required. **When converting a patient from an immediate-acting opioid to a long-acting opioid, one must:**

1) **Calculate the 24 hour equi-analgesic dose** of the new medication to be prescribed based on the present dosing of pain medication. [eg. A patient taking 2 Tylenol#3s (60 mg codeine + 600 mg acetaminophen), every 6hours i.e. 8 per day, has taken an equivalent dose of 24 mg of morphine in 24 hours, or approximately 5 mg of hydromorphone. An appropriate starting dose of a long acting opioid would therefore be 3 mg Hydromorphone Contin Q 12 H]. Opioid naïve patients should start with an immediate acting opioid preparation with frequent intervals permitted (Q2-4 hours as tolerated). After 48-72 hours a long acting preparation could be prescribed based on the 24 hour requirements. (see Table 3.1)

2) **Prescribe the Breakthrough dosage of narcotic:** The usual BT dose is 10% of the 24 hour long acting dose requirement. (eg, above example, 0.6 mg is the calculated BT dose – the prescription may read: 0.5-1 mg hydromorphone (1/2 – 1 tablet) PO Q 2H PRN, Dispense: 40 one mg tablets). Dose frequency of BT medication according symptom severity, level of activity, and side effects experienced. For Q1H for end of life care, and Q2-4H for someone ambulatory.

3.2 Opioid Analgesia for Moderate to Severe Pain

- Opioid analgesics commonly used are noted in Table 7.1.
- Please note their half-lives – it takes approximately 5 half-lives to reach a steady serum concentration of a short acting opioid, assuming normal elimination.

Therefore, this provides a rough guide to the clinician as to when to evaluate the efficacy of dose adjustments. A rough guide is short acting opioid (not methadone) may be adjusted Q24 hours and controlled release preparations Q 48-72 H.

- Equi-analgesic doses are also provided and refer to chronic dosing schedules. Note the difference between oral and intravenous dose equivalents
- Meperidine (Demerol) has neurotoxic metabolites which may accumulate over time and induce seizures with regular dosing. It should not be used to treat chronic pain.
- $T_{1/2}$ for controlled release preparations will differ
- Dose reduce by 20-50% in the elderly
- Dose reduce in the setting of renal impairment or hepatic impairment
- Up to 10% of population lack the active enzyme CYP2D6 necessary to digest codeine to morphine – a high risk of nausea and vomiting exists in this group, with minimal analgesic gain.

3.3 Action of Opioids:

- Opioids act on receptors located in the dorsal horn of the spinal cord, periaqueductal gray matter, thalamus, cortex, and in some peripheral tissues
- Activated receptors block pain transmission
- Four primary opioid receptors have been identified thus far: μ , δ , κ , and ORL-1
- NMDA receptors are important targets for neuropathic pain states
- Morphine acts on μ receptors primarily, located in the central nervous system
- Morphine metabolites include M3G (morphine-3-glucuronide) and M6G (morphine-6-glucuronide): M6G contributes to the analgesic effect and is cleared by the kidney. M3G is the predominate metabolite and has neuroexcitatory effects and may be responsible for neurotoxic effects seen in chronic high dosage use
- Oxycodone may have additional characteristics favorable for neuropathic pain given it acts on μ and κ receptors
- Fentanyl is delivered by a transdermal patch which creates a 12 hour reservoir of narcotic – this provides a 12 hour delay in onset and offset. Short or long acting narcotics should continue to be employed for 12 hours after the patch is initiated.
- Methadone requires a special license (an exemption in Ontario) to prescribe and has excellent properties for controlling refractory neuropathic pain, given activity at δ and NMDA receptors
- Converting from oral opioids to methadone generally requires a hospital admission and careful patient monitoring given the possible toxicities (including cardiac arrhythmias, respiratory suppression, and oversedation) in the acute transition period. Multiple drug interactions are possible with methadone administration and this has led to a number of deaths in North America. The physician who prescribes methadone must review and approve new drug prescriptions given to the patient.

3.4 Common Opioid Side Effects

- A laxative regime should be prescribed to all patients receiving regular dosing of opioids – constipation is common, and often severe.
- Nausea is caused by diminished peristaltic action – a prokinetic agent is often helpful.
- Neuro-excitatation may occur and is usually a manifestation of opioid toxicity
 - Early, myoclonic jerks may be observed, and are an early indication
 - Later, delirium, or seizures may occur.

3.5 Challenges to Pain Management

- Escalating pain not responsive to a current opioid regime
 - Rule out disease progression, neurologic compromise,
 - Consider an **Opioid Rotation**: By changing to a different class of opioids, improvement in pain control may be obtained. Decrease the dose of the new drug by 30% to account for incomplete cross-tolerance. Use a short acting opioid for breakthrough pain and titrate to effect
 - **Opioid Rotations** are especially helpful when renal function has worsened in the setting of early neuro-toxicity i.e. myoclonus; intractable nausea or vomiting; persistent sedation
- **Pain Crisis**
Administer Dexamethasone 10-40 mg IV then reassess for etiology of pain – spinal cord compression will usually dictate ongoing dexamethasone, 4 mg po QID until definitive surgical or radiotherapy management

3.6 Co-Analgesics:

- Neuropathic Pain – See section 8.0
- Bone Pain – NSAIDS, biphosphonates, steroids, radiation
- Visceral Pain – hepatic capsule distension – steroids

Spinal cord compression – steroids, urgent radiotherapy, opioid analgesia +/- pregabalin or gabapentin for neuropathic pain, biphosphonates for lytic bone metastasis

Table 3.1 Equi-analgesic doses and properties of commonly prescribed opioids

Narcotic	Dose /Route	T _{1/2} oral prep	Metabolite	Route of Action-Receptor	Comments
Codeine	200 mg PO 120 mg SC/IV	3 hr	Metabol. to Morphine	μ	10% population have intolerance with nausea, vomiting. 1 Tylenol #3 = 30 mg codeine, 300 mg acetaminophen, 15 mg caffeine (in Canada)
Oxycodone	10 mg PO	2-3 hr		μ, κ	κ receptor blockade may contribute to relief of neuropathic pain states
Morphine	20 mg PO 10 mg SC/IV	2-3.5 hr	M3G, M6G	μ	Metabolites cleared by kidney, dose adjust when Cr. Cl elevated
Hydromorphone	4 mg PO 2 mg SC/IV	3 hr	HM6G	μ	Better tolerated than morphine and preferred medication for sc/IV CADD pump infusion
Fentanyl	Starting dose 12-25 ug/hr Q 72 H transdermal NB: 25 ug./hr Q 72 H equivalent to 60-100 mg oral Morphine/24 hr	22 hr (transdermal)		μ, δ	BT dose for 25 ughr/Q72 H would be 10 mg morphine po or Hydromorphone 2 mg Q1H PRN. Should not be prescribed in opioid naïve patients. Apply with last dose of long acting (Q12) oral opioid Withdrawal: Initiated oral opioid dosing 12 hours after removing the patch.
Methadone	2 mg PO	15-30 hr		μ, δ, NMDA antagonist	Excellent properties for neuropathic pain treatment. Requires special license/exemption to prescribe

4.0 Management of Neuropathic Pain

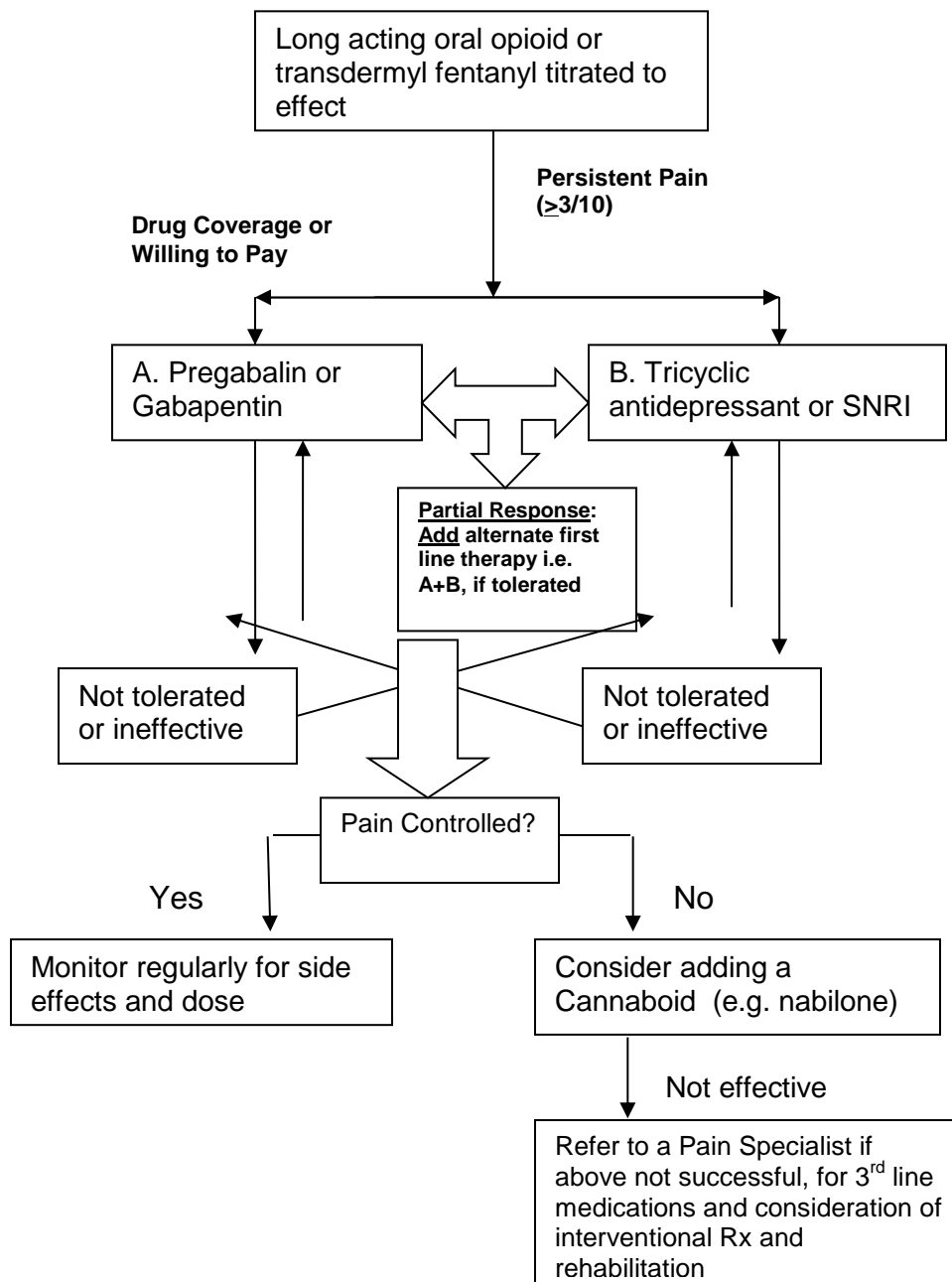
- Requires a dedicated physician and a number of patient visits
- In the setting of severe malignant pain (nociceptive or neuropathic origin), opioid analgesia should be considered first line treatment, according to the WHO ladder approach to pain management described in Sections 3.1 and 3.2.
- Opioid analgesics provide improvement in neuropathic pain intensity (20-30% reduction) in about 40% of patients (NNT 2.5) with non-cancer related neuropathic pain (e.g. diabetic pain and post-herpetic neuralgia).
- It is important to note that current guidelines for the treatment of cancer-related neuropathic pain are therefore extrapolated from non-cancerous neuropathic pain syndromes. Treatment efficacy derived from opioids may therefore differ, given the mechanism of neuropathic pain from tumor infiltration may be dissimilar from the mechanism occurring in benign neuropathic pain states.
- Frequently, opioid analgesics alone are inadequate to control neuropathic pain. Adjuvant analgesics may help to reduce pain intensity further.
- An anticonvulsant, either gabapentin or pregabalin is the adjuvant drug of first choice if available to the patient (affordable or covered by a drug plan). Gabapentin is a voltage gated calcium channel antagonist. It is associated with improved pain control, better mood and sleep. Pregabalin is an analogue with a higher calcium channel affinity and much better bioavailability. The major side effect is sedation and tends to subside after a few weeks of use. In Ontario, pregabalin (Lyrica) is approved for treatment of postherpetic neuralgia but is often used "off label" to treat neuropathic pain. NNT (number needed to treat) is approximately 3-4 (i.e. about 25% of patients with neuropathic pain will have improved pain control with this medication)
- If gabapentin or pregabalin are neither helpful nor affordable, then a tricyclic antidepressant is a reasonable alternative with a NNT of 3. A more sedating TCA, i.e. amitriptyline, may be appropriate if the patient has insomnia. Otherwise, desipramine or nortriptyline are preferred because of fewer anticholinergic side effects
- Neuropathic pain from tumor infiltration often responds to dexamethasone, at least in the short term. A reasonable dose is 10 mg PO STAT followed by 4 mg PO Q6H.
- Other medications to consider are SNRI (serotonin-norepinephrine reuptake inhibitors, e.g. venlafaxine)
- Methadone may be particularly useful for cancer related neuropathic pain when conventional controlled release opioid analgesics fail (3)
- Slow titration of medication, adjusted upward for effect is required. This is especially important in the elderly or in those with renal/hepatic impairments
- Please refer to the references below for more comprehensive prescribing information
- An algorithm follows as a guide to managing severe chronic malignant neuropathic pain syndromes. Note each treatment must be tailored to the individual patient.

Table 4.1 Pain medications commonly used to treat malignant neuropathic pain (note opioids are absent, see Table 3.1).

Drug	Adverse effects	Therapeutic Dosage	Comments
Pregabalin (Lyrica)	Sedation, edema, dry mouth, ataxia/dizziness	25 mg TID in the elderly increase dose by 50 to 150 mg/d weekly. Common starting dose otherwise: 75 mg po BID x1 week. Max dose is 600 mg PO BID. Usual therapeutic dose: 300-600 mg/day	Anticonvulsant. Dose adjust in renal impairment. More bioavailable than gabapentin.
Gabapentin	Sedation, edema, ataxia/dizziness, dry mouth	Common starting dose: 300 mg PO TID In elderly start with 100-200 mg PO TID and increase Q3-7 days as tolerated. Otherwise, increase by 300 mg/day Q weekly to effect. Max dose 3600 mg/day.	Anticonvulsant. Dose adjust in renal impairment. Usual therapeutic dose 300-2400 mg/day.
Tricyclic antidepressants (e.g. amitriptyline, desipramine, etc.)	Anticholinergic side effects (dry mouth, constipation, sedation, heart block, urinary retention) weight gain	10-25 mg PO QHS as a starting dose. Increase Q4-7 days as tolerated by 10-25 mg increments. Usual effective dose at 50-75mg. Maximum dose: 150 mg.	Contraindicated in glaucoma or in patients with moderate to severe urinary outflow obstruction (amitriptyline worse for side effects). Cannot be taken with MAOIS.
Venlafaxine (Effexor)	Sleep disturbances, dry mouth, constipation, hypertension, ataxia, sweating, anxiety, anorexia	37.5 mg PO once daily to start. May increase weekly by 37.5 mg/day to maximum of 375 mg/day. Usual therapeutic dosage: 150-225 mg/day	SNRI. Dose adjustment in renal impairment. Cannot be taken with MAOIs.
Nabilone (cesamet)	Sedation, vertigo, blurred vision, dizziness, dry mouth, mood changes, headache	Start with 0.5 – 1 mg po qhs (split ½ 0.5 mg capsule in the elderly for the first few doses, then increase). Increase by 1 mg po/day per week. Max dose 6 mg/day. Usual Therapeutic dose 1 mg PO QHS to 2 mg PO BID	Cannabinoid Synthetic analog of THC T _{1/2} 2 hours Targets endocannabinoid receptors, CB1 and CB2

References 1 and 2 provide a comprehensive review of adjuvant analgesics for neuropathic pain

Figure 4.2 Algorithm for the Treatment of Severe Chronic Malignant Neuropathic Pain (Mixed Neuropathic-Nociceptive or Neuropathic Pain Syndromes). *Adapted from*



Note: The Canadian Pain Society recommends initiation of a tricyclic antidepressant or Gabapentin/Pregabalin for neuropathic pain, not specific to patients with advanced/metastatic cancer. Please refer the reference by Moulin DE et al below (2). Gabapentin now covered by Ontario Drug Benefit.

References

1. Gilron I et al. *Neuropathic pain: a practical guide for the clinician.* CMAJ 2006;175(3):265-75.
2. Moulin DE, Clark AJ, Gilron I, et al. *Pharmacological management of chronic neuropathic pain – Consensus statement and guidelines from the Canadian Pain Society.* Pain Res Manage Vol 12 No 1 Spring 2007: 13-21.
3. Lynch ME. *A review of the use of methadone for the treatment of chronic non-cancer pain.* Pain Res Manag 2005;10:133-44.

ADDITIONS FOR THE
SWOMEN PALLIATIVE MEDICINE CLERKSHIP SYLLABUS

Oncologists commonly rely on prognostic assessments to predict which patients are likely to benefit from oncology treatment interventions. Many of these decisions are based on the patient's functional status. The following performance scales are frequently used by oncologists:

1. ECOG- Eastern Cooperative Oncology Group is a scale of 0-4; if the ECOG score is greater than two, patients are usually considered unsuitable for most chemotherapy treatments. The ECOG scale has been shown to be predictive of survival in both advanced cancer and terminal cancer.
2. Karnofsky Performance Status scores are expressed as a percentage of the normal performance status in 10% increments, with 100% representing normal.

Palliative Care physicians tend to use the Palliative Performance Scale as a framework for measuring progressive decline of the patient over the course of their illness and as a guide to projection of length of survival. The PPS has been described earlier in the syllabus. Patients with a PPS of 10-20 have a median survival of 6 days on average; PPS of 30-50 have a median survival of 41 days on average; PPS of 60-70 have a median survival of about 108 days.

A comparison chart of these three performance scales is attached for quick reference.



Edmonton Symptom Assessment System (ESAS)

Description

The **Edmonton Symptom Assessment System (ESAS)** is a valid and reliable assessment tool to assist in the assessment of nine common symptoms experienced by cancer patients. The ESAS is one of the key assessment tools used in the Palliative Care Integration Project. The original tool was developed by the Regional Palliative Care Program, Capital Health in Edmonton, Alberta and slightly modified for this project.

Purpose of the ESAS

This tool is designed to assist in the assessment of: pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, well being, and shortness of breath. One blank scale is available for patients to use to assess an “other problem” as needed. The severity **at the time of assessment** of each symptom is rated from 0 to 10 on a numerical scale; with 0 meaning that the symptom is absent and 10 that it is the worst possible severity.

The ESAS was designed so that the patient, or his/her family caregiver, could self-administer the tool. Therefore, the patient should be taught how to complete the scale. It is the **patient’s opinion** of the severity of the symptoms that is the **gold standard** for symptom assessment.

The ESAS provides a clinical profile of symptom severity over time. It provides a context within which symptoms can be understood. However, it is not a complete assessment in itself. For good symptom management to be attained, the ESAS must be used as one part of a holistic clinical assessment.

How to do the ESAS

The patient circles the most appropriate number to indicate where the symptom is between the two extremes.

No pain 0 1 **2** 3 4 5 6 7 8 9 10 Worst possible pain

The circled number is then transcribed onto the medical chart (e.g., flow sheet) or the ESAS form is addressographed and placed in the medical chart.

Edmonton Symptom Assessment System (ESAS)

Please circle the number that best describes:

No pain	0	1	2	3	4	5	6	7	8	9	10	Worst possible pain
Not tired	0	1	2	3	4	5	6	7	8	9	10	Worst possible tiredness
Not nauseated	0	1	2	3	4	5	6	7	8	9	10	Worst possible nausea
Not depressed	0	1	2	3	4	5	6	7	8	9	10	Worst possible depression
Not anxious	0	1	2	3	4	5	6	7	8	9	10	Worst possible anxiety
Not drowsy	0	1	2	3	4	5	6	7	8	9	10	Worst possible drowsiness
Best appetite	0	1	2	3	4	5	6	7	8	9	10	Worst possible appetite
Best feeling of wellbeing	0	1	2	3	4	5	6	7	8	9	10	Worst possible feeling of wellbeing
No shortness of breath	0	1	2	3	4	5	6	7	8	9	10	Worst possible shortness of breath
Other problem	0	1	2	3	4	5	6	7	8	9	10	

Patient's Name _____
Date _____ Time _____

Complete by (*check one*)
 Patient
 Caregiver
 Caregiver assisted

BODY DIAGRAM ON REVERSE SIDE

August, 2006

HOW TO USE THE LOG FOR SYMPTOM SCORES

What Is this Form Used For?

This log is a place for you to write your Edmonton Symptom Assessment System (ESAS) scores. It is used when you use the ESAS. Your nurse or doctor will look at this report to see how well your symptoms are being managed.

When Should I Use this Form?

Please use this form every day when you do your ESAS.

How Do I Use the Form?

You will see on the ESAS form that each symptom has a rating scale from “0” to “10”. A score of “0” means that you do not have the symptom. A score of “10” means that your symptom is at its very worst. Write your score for each symptom in the space provided.

Example: No pain 0 1 **2** 3 4 5 6 7 8 9 10 Worst possible pain
 You record a “2” under Pain Score under today’s date.

Date	Aug 12 2002									
Time:	10 AM									
Pain score	2									
Activity score	2									
Nausea score	3									
Drowsiness score	4									
Appetite score	4									
Anxiety score	0									
Depression score	0									
Well being score	6									
Shortness of breath score	0									
Who did the assessment? (Patient or family member)	patient									

Other words you can use for some of the symptoms:

- Instead of depression: feeling sad or blue
- Instead of anxiety: feeling nervous or restless
- Instead of activity: your energy
- Instead of drowsiness: feeling sleepy
- Instead of wellbeing: your overall comfort level. Or, think of how you would truthfully answer the question “How are you?”

There is one blank scale that you can use if you have another symptom that is not on the list. Please record who completed the ESAS, such as the patient or a family member.

Palliative Performance Scale (PPS)

Description

The Palliative Performance Scale is a reliable and valid tool used for palliative care patients. Developed by Victoria Hospice Society, British Columbia, the PPS guides the assessment of a patient's functional performance.

The PPS is divided into 11 categories that are measured in 10% decremental stages (100% to 0%). These 11 categories are organized into 3 stages:

- 1) Stable
- 2) Transitional
- 3) End-of-Life

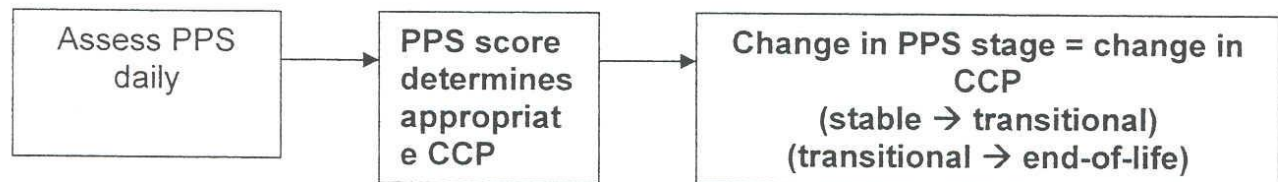
There are five observable parameters included in the functional assessment:

- 1) Degree of ambulation
- 2) Ability to do activities
- 3) Ability to do self-care
- 4) Intake
- 5) Level of consciousness

Purpose of the PPS

The PPS provides a framework for measuring progressive decline over the course of illness. It also provides a "best guess" projection of length of survival (i.e. suggests if patient is moving closer to death) and serves as a communication tool for the team. It also can act as a workload measurement tool. For example, patients who score between 0-40% usually require increased hands-on nursing care and their family members often need more support compared to those patients with higher PPS scores.

For the purpose of the Project, the PPS will also be used to guide the appropriate selection of the Palliative Collaborative Care Plan (i.e., Stable, Transitional, or End-of-Life).



How to do the PPS

The PPS score is determined by reading horizontally at each level to find the “best fit” for the patient. Leftward columns are “stronger” determinants, thereby taking precedence over others.

- 1) Begin at the left column until the appropriate ambulation level is found
- 2) Read across to the next column until the correct activity/evidence of disease is located
- 3) Read across to the self-care column, intake and conscious level columns before assigning the PPS score to the patient

Ambulation:

- “Reduced” ambulation occurs at PPS 70% and 60%. The difference between 70% and 60% is subtly related to the activity columns – that is whether the patient is unable to do work (70%) or unable to do hobbies or house work (60%). Also note that the patient at 60% requires occasional assistance with self-care.
- There are subtle differences between “mainly sit/lie” and “mainly in bed”. The difference is subtly related to items in the self-care and intake columns. Use these adjacent columns to help decide. As well, the difference between mainly sit/lie and mainly in bed is proportionate to the amount of time the patient is able to sit up versus the need to lie down.

Activity & Evidence of Disease:

- “Some”, “significant” and “extensive” disease refer to physical and investigative evidence showing degree of disease progression.
Example: Breast Cancer
 - local recurrence = “some” disease
 - 1 or 2 metastases = “significant” disease
 - multiple mets = “extensive” disease
- The extent of disease is also judged in the context of the patient’s ability to maintain work, hobbies and activities. For example, “reduced” activity may mean playing 9 holes of golf instead of 18, or continuing with morning walks but at a reduced distance.

Self Care:

- “Occasional Assistance” - Most of time the patient can transfer, walk, wash, toilet, eat own meals but sometimes needs help (e.g., once a day or few times a week)
- “Considerable Assistance” – Regularly every day the patient needs help (e.g., to get to the bathroom but can brush own teeth; needs food cut but can feed self)
- “Mainly Assistance” – This is an extension of the “considerable assistance” category. (e.g., patient needs help getting to bathroom and washing)
- “Total Care” – The patient is unable to eat, toilet or do any self care without help

Intake:

- “Normal” – refers to patient’s usual eating habits while healthy
- “Reduced” – a reduction of the patient’s normal eating habits
- “Minimal” – very small amounts, usually pureed or liquid, which are well below nutritional sustenance

Conscious Level:

- “Full consciousness” – full alertness, orientation, good cognitive abilities
- “Confusion” – presence of delirium or dementia and a reduced level of consciousness, which may be mild, moderate or severe.
- “Drowsiness” – may be due to fatigue, drug side-effects, delirium, closeness to death
- “Coma” – absence of response to verbal or physical stimuli. Depth of coma may fluctuate.

Making “Best Fit” Decisions

- Only use the PPS in 10% increments (e.g., cannot score 45%)
- Sometimes one or two columns seem easily placed at one level but one or two columns seem better at higher or lower levels. In these cases, use your clinical judgment and the leftward dominance rule to determine a more accurate score the patient.

(Example case studies are provided at end of PPS section.)

When to do the PPS

a) Patients at Home

It is good practice to complete the PPS each visit. The PPS should only be completed on a daily basis for those patients receiving more than one nursing visit per day.

b) Patients Admitted to Hospital, Palliative Care Unit, or Long-Term Care Facility

It is good practice to complete the PPS every day. It may be more helpful to complete the PPS at the end of the day shift.

Who Should Complete the PPS

The PPS can be used by any regulated health care provider. It is anticipated that in most cases, the PPS will be completed by a registered nurse or registered practical nurse.

Where to Document the PPS

The PPS score is transcribed into the medical chart, e.g., on the flow sheet or in progress notes as per organization policy.

Example Case Study #1

The patient spends the majority of the day sitting in bed or lying down due to fatigue from advanced disease. She requires considerable assistance to walk even short distances. She is fully conscious. She has good nutritional intake.

What is the patient’s PPS score? (see bottom of page for “best fit” score)

Example Case Study #2

The patient is very weak and remains in a chair a couple of hours a day. The rest of the time, he is in bed. He has advanced disease and is requiring almost complete assistance with self-care and feeding. He is experiencing decreased food intake, with a few small snacks that remain mostly unfinished. He has adequate fluid intake. The patient is drowsy but not confused.

Palliative Performance Scale Feb 05

1st printing January, 2003.

Revised February 2005

What is the patient's PPS score? (see bottom of page for "best fit" score)

Example Case Study #3

The patient is up and about on her own. She has experienced a recent recurrence of disease. She can do household chores with adequate rest periods. The patient requires occasional assistance with self-care whereby her caregiver watches her get in and out of the shower. Her intake is reduced from normal but still adequate. The patient is fully conscious with no confusion.

What is the patient's PPS score? (see bottom of page for "best fit" score)

PPS Case Study Answers:

Case study #1: PPS score 50%

Case study #2: PPS score 40%

Case study #3: PPS score 70%

[Reference: Victoria Hospice Society]

Palliative Performance Scale (PPSv2)
version 2

PPS Level	Ambulation	Activity & Evidence of Disease	Self-Care	Intake	Conscious Level
100%	Full	Normal activity & work No evidence of disease	Full	Normal	Full
90%	Full	Normal activity & work Some evidence of disease	Full	Normal	Full
80%	Full	Normal activity <i>with</i> Effort Some evidence of disease	Full	Normal or reduced	Full
70%	Reduced	Unable Normal Job/Work Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable hobby/house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or Confusion
50%	Mainly Sit/Lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or Confusion
40%	Mainly in Bed	Unable to do most activity Extensive disease	Mainly assistance	Normal or reduced	Full or Drowsy +/- Confusion
30%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Normal or reduced	Full or Drowsy +/- Confusion
20%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Minimal to sips	Full or Drowsy +/- Confusion
10%	Totally Bed Bound	Unable to do any activity Extensive disease	Total Care	Mouth care only	Drowsy or Coma +/- Confusion
0%	Death	-	-	-	-

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“Pearls” from your Palliative Medicine Team March 2006

Performance Scales: a side by side comparison for quick reference

	ECOG	PPS	Ambulation	Activity and Evidence of Disease	Self-Care	Karnofsky
Asymptomatic	0	100%	Full	Normal activity and work No evidence of disease	Full	100
Symptomatic fully ambulatory	1	90%	Full	Normal activity and work Some evidence of disease	Full	90
		80%	Full	Normal activity <i>with effort</i> Some evidence of disease	Full	80
Symptomatic In bed < 50% day	2	70%	Reduced	Unable normal job/work Significant disease	Full	70
		60%	Reduced	Unable hobby/housework Significant disease	Occasional Assistance necessary	60
		50%	Mainly sit/lie	Unable to do any work Extensive disease	Considerable Assistance Required	50
Symptomatic In bed > 50% day	3	40%	Mainly bed	Unable to do most activity Extensive disease	Mainly Assistance	40
Symptomatic Bedridden	4	30%	Totally bed bound	Unable to do any activity Extensive disease	Total care	30
		20%	Totally bed bound	Unable to do any activity Extensive disease	Total care	20
		10%	Totally bed bound	Unable to do any activity Extensive disease	Total care	10
Dead	5	0%	Death			0

ROLE OF PALLIATIVE CARE IN CANCER

Gil Schreier, MD

The WHO defines palliative care as an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.

At the LHSC and LRCP an interdisciplinary team approach has been adopted by the palliative care service. Consultation for pain and symptom management in the ambulatory and inpatient oncology settings is provided by the palliative care service for cancer patients. Admission to the palliative care unit for investigation and management of complex physical, psychosocial or family issues in advanced cancer patients is also available. Additionally, the palliative care service works closely with family physicians and other community palliative care providers to assist those patients that have chosen to die in the home setting.

There is a 10 bed palliative care unit at the Victoria Campus of the LHSC. Patients admitted in this unit are managed by physicians specializing in palliative medicine. These physicians also provide the palliative care consultation service throughout the hospital and see patients in the weekly ambulatory palliative care clinic in the LRCP. At the University campus there is a 4 bed palliative care unit where patients are managed by community family physicians. They are supported by a physician specializing in palliative medicine and by palliative nurse practitioners. The palliative care clinician and NPs at University campus also provide consult coverage to the hospital. Currently there is also a 10 bed palliative care unit at Parkwood Hospital and patients there are cared for by community family physicians. These patients have less acute symptom management needs.

Palliative care affirms life and regards dying as a normal and inevitable process. The provision of palliative care is applicable early in the course of illness, in conjunction with other cancer therapies such as chemotherapy or radiation therapy that are intended to prolong life. Palliative care does not hasten or postpone death, but provides relief from pain and other unpleasant and distressing symptoms while offering support to patients and helping their families cope during the course of the illness.

MANAGEMENT OF TREATMENT RELATED COMPLICATIONS AND MEDICAL SUPPORTIVE CARE

Michael Sanatani, MD

(with material from a chapter by Jonathan Greenland, MD and the EPEC program)

Both the patient's disease process and the treatment offered can at times lead to situations where medical intervention is needed to support the patient through the complication that has arisen. This is generally termed "supportive care", although some oncologists include wider-ranging issues (including emotional and spiritual concerns) in the definition of this field, overlapping it with palliative care. This chapter will give an overview over the most common complications and symptoms you may encounter in clinical oncology practice.

Fatigue:

The most common symptom; more prevalent than pain in patients with advanced cancer. May be due to advancing disease, endocrine abnormalities (primary or secondary to disease or treatment), or treatment.

Approach:

Rule out medical causes (anemia, glycemic control, thyroid dysfunction, uremia)

Rule out depression

Counsel:

Promote energy conservation (not consistently shown to work)

Evaluate medications

Optimize fluid, electrolyte intake

Permission to rest - but also **promote exercise periods as tolerated**

Clarify role of underlying illness

Consider dexamethasone if disabling; promotes feeling of well-being, increased energy - effect may wane after 4-6 weeks - taper off as tolerated

Methylphenidate? Ginseng? (being evaluated)

Anorexia/Cachexia:

Loss of appetite and lean muscle mass. This is not just starvation, but a state of increased metabolic rate associated with inflammation and loss of appetite. Poor prognosis. Cannot be reversed with feeding alone (difference vs. starvation!). Few interventions shown to be of benefit other than steroids, exercise, and treating the cancer itself; current approaches:

Rule out hyperthyroidism (rare)

Exercise

Dietician advice to maximise caloric intake

Anorexia-treating strategies - frequent small bland meals, avoid strong aromas

Dexamethasone (appetite stimulant) - short term

Megace (appetite stimulant) - longer term but inc. thrombosis risk; other SE

?Anabolic steroids, other agents - experimental

Nausea/Vomiting:

The most feared complication. Approach to nausea:

Assess most likely cause of nausea:

Bloodborne (CTZ, vomiting center) - metabolic (drugs/chemotherapy, hypercalcemia, uremia), sepsis, etc -

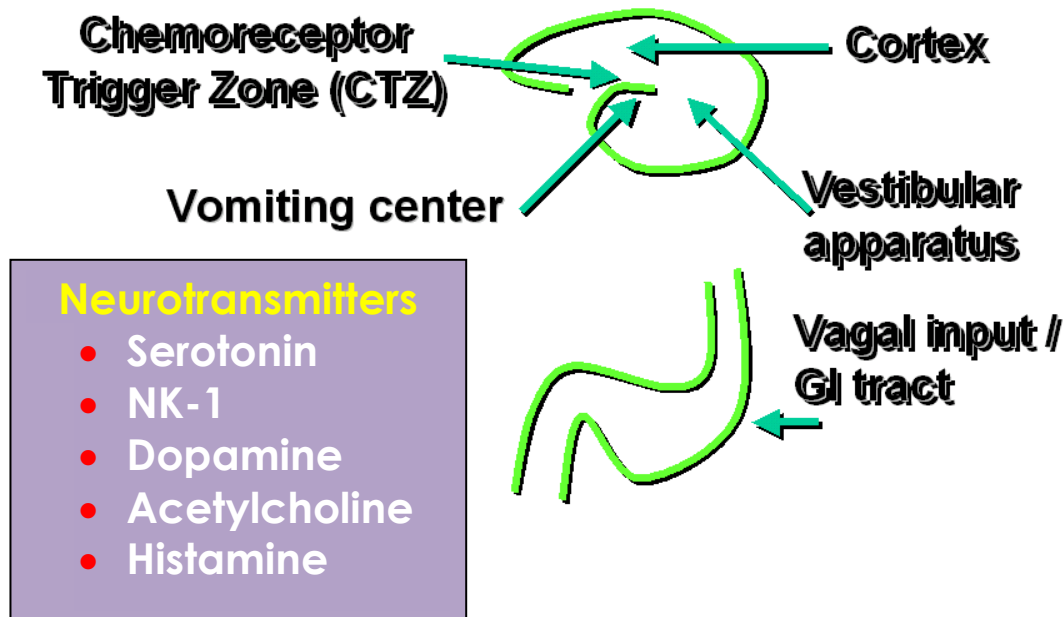
Vagal - MI, bowel distention, liver capsule, chemo (some effects via gut vagal afferents), radiation -

Vestibular - labyrinthitis, skull tumour, brain tumour, etc.

Cortical - increased ICP, sensory input, radiation

Anxiety-related - anticipatory nausea, anxiety, pain
Undiagnosed - occasionally seen with advanced cancer

Pathophysiology of nausea / vomiting



Treatment tools:

Serotonin antagonists Ondansetron, Dolasetron, Granisetron, Palonosetron
Corticosteroids Dexamethasone
NK-1 inhibitor, Aprepitant, Casopitant
Dopamine antagonists prochlorperazine (Stemetil), metoclopramide, haloperidol
Anticholinergics dimenhydrinate (Gravol)

Notes

Serotonin antagonists work for chemo/rads induced n/v but are expensive, constipating, have drug interactions, and can cause headache.

Dopamine antagonists are good general first line antiemetic agents and have a wide spectrum of action but also have side effects (MSK) and dose must be adjusted for renal function.

Chemotherapy-induced nausea (CIN) is typically classified as follows:

Anticipatory Rx with anxiolytics (e.g. lorazepam), cognitive techniques

Acute Prophylax with antiemetics depending on the emetogenicity of the regimen
(*Hesketh class*) - look up at **nccn.org** - day of chemotherapy

Serotonin antagonists - ondansetron, granisetron,
?palonosetron

Dexamethasone

Aprepitant

Breakthrough PRN: dopamine antagonist (Prochlorperazine, metoclopramide, etc)

Delayed

Hard to treat. Usually continue Dexamethasone and breakthrough PRN x 2-3 days prophylactically. Weak evidence for serotonin antagonists (palonosetron may be better but not available in Canada 2007) but commonly used.

Pain - see chapter on cancer pain

Mucositis, Xerostomia:

Mucositis is an inflammation of the mucosa, most commonly in the mouth. However, it may occur in other parts of the aerodigestive tract (esophagitis, proctitis, etc). It may be due to chemotherapy and/or radiation. The ulcers that form are usually non-infectious in etiology, but may become secondarily infected. Systemic infection can be life-threatening, especially if occurring during an episode of neutropenia. Pain from oral ulcers can require systemic opioid administration, and/or hospitalisation for enteral/parenteral fluids / nutrition. For less severe cases, topical therapy is indicated (see below; local protocols can vary). Xerostomia refers to dry mouth, usually as a consequence of radiation to the salivary glands.

Esophagitis

- Xylocaine viscous 5-10 ml ac meals
- Nystatin 100,000 units swish and swallow qid (preventative while on radiotherapy); 500,000 qid (if suspect frank candida infection) *NB* if esophageal candidiasis confirmed, more aggressive therapy indicated e.g. fluconazole 200-400mg PO day 1, followed by 100-200mg OD for minimum of 3 weeks)
- Intravenous/GJ tube feeding/rehydration if required

Stomatitis

- Baking soda oral rinse
- Xylocaine viscous 5-10 ml ac meals
- Sulcrafate 30 ml 4-6 times/day
- Nystatin/hydrocortisone
- Diphenhydramine (*Benadryl*) elixir 12.5 mg/5 ml 10 ml swish and spit qid
- NSAIDs/opioids as needed
- If frank oral candida, treat with higher dose nystatin, oral fluconazole, or other potent antifungal agent

Xerostomia

- Pilocarpine (*Salagen*) PO tid (ideally should start concurrent with radiotherapy). Continue for at least 3 months, or as long as needed
- Oral water sprays/saliva substitutes

Pruritis Ani

- Hydrocortisone/zinc sulfate (*Anusol-HC*) or hydrocortisone/framycetin sulfate (*Proctosedyl*) cream or suppository bid and with each bowel movement

Cystitis

- Treat UTI if present
- Phenazopyridine (*Pyridium*) 200 mg PO tid

Prostatitis

- Terazosin (*Hytrin*) 1 mg PO OD. Titrate up carefully (there is a max dose) until symptomatic relief obtained.

- Tamsulosin (*Flomax*) 1 tab PO OD (works very well, few side effects)

Pneumonitis

- If radiotherapy induced and not overly symptomatic, may not need treatment
- If symptomatic, prednisone 40-60 mg PO OD x 4-6 weeks, then slowly taper

Cytopenias:

Systemic antineoplastic therapy may cause anemia, thrombocytopenia, and/or leukopenia/neutropenia. If asymptomatic, this usually does not warrant therapy. However, if severe, bone marrow suppression can be life-threatening (e.g. febrile neutropenia). Therefore, prophylactic G-CSF is sometimes used (in regimens with expected febrile neutropenia rates of >20%, according to American Guidelines). G-CSF is also used in febrile neutropenia complicated by high-risk features (hypotension, cultures positive, cancer uncontrolled, change in level of consciousness, pneumonia, etc.) and to keep counts up in intensive regimens where avoiding treatment delays and dose reductions is important (e.g. adjuvant chemotherapy in Breast Cancer, Lung Cancer, Colon Cancer).

Febrile neutropenia: this a medical emergency - see chapter on emergencies for management guidelines

Anemia is treated with blood transfusions; there are erythropoietin analogues (darbopoeitin, EPO) however these have only found to be safe if the anemia is due to the chemotherapy itself (and not for Hb>120 or if anemia of chronic disease).

Platelet transfusions - local practices vary (no firm rules) but use if plts<10, or <20 if febrile, or <40-50 approx. and bleeding significantly. Downside: plt refractoriness may develop. If due to bone marrow infiltration low plts have poor prognosis.

Diarrhea:

Apply the usual differential diagnosis (bloody vs non-bloody, infectious-inflammatory-neoplastic-structural-vascular-exogenous for example). Only after considering and excluding the usual causes, attribute diarrhea in a cancer patient to the chemotherapy/radiotherapy if appropriate. Infection (C. Diff), neutropenia, and chemotherapy-induced diarrhea can co-exist and be life threatening.

If C.Diff or other infection is ruled out or at least highly unlikely, can consider symptomatic therapy of the diarrhea:

- Loperamide (*Imodium*) 2 tablets (4 mg) PO initially, followed by 1 tablet (2 mg) with each loose bowel movement up to a maximum of 12 tablets (24mg) per day
- Diphenoxylate HCl-Atropine Sulfate (*Lomotil*) 5mg PO tid or qid
- Consider octreotide 50-250 µg SC TID
- Consider hospital admission, imaging, IV therapy (?antibiotics empirically), electrolyte support if severe (accompanied by clinical dehydration, fever, neutropenia, pain, or bleeding or nausea/vomiting)

Constipation:

Very common, especially in patients with opioid medications. Get abdomen flat plate if suspect constipation and to r/o obstruction; DRE. Treat with laxatives if no obstruction:

Osmotic - milk of magnesia, or lactulose daily to start

Once having movements, and stool soft, can add irritant (Senna, cascara etc) daily for maintenance. Efficacy of stool softeners (Docusate sodium [Colace]) questionable and definitely not to be ordered PRN, but daily dose of 200-500 mg works for some patients in combination with other agents.

Dyspnea:

May be due to a variety of causes; do not forget the non-malignant ones. Approach: Heart - Lung - Blood [anemia]. Treat reversible causes (COPD exacerbation, infection, CHF exacerbation, anemia, effusion, etc.)

Treatment of dyspnea as a symptom (in addition to treating the cause of it):

oxygen (especially if hypoxic, although hypoxia and dyspnea are not always correlated!)

nonpharmacologic interventions: open window, fan blowing on face, decrease number of people and things around head of bed, etc.

opioids - increase baseline opioids by ~25% (titrate carefully). NB: one may at times be in a situation where consciousness level will be reduced for the sake of symptom relief; discuss with pt and family!!. Inhaled

opioids (e.g. 5 mg morphine in saline via nebulizer q1-2h prn) used by some. If opioid-naive try 5 mg morphine q1h SC prn to start, and adjust as needed

anxiolytics - Lorazepam 1 mg SL q6-8h PRN; Midazolam 1-2 mg SC q1-2h PRN if more severe (e.g. admitted to hospital). Can use alone or add to opioids.

dexamethasone - especially for lymphangitic carcinomatosis or radiation pneumonitis. 8 mg IV/SC/PO twice a day for a few days then taper down as tolerated

Skin Reaction to radiation:*Mild*

- Aloe vera gel topically prn
- *Biafine* applied sparingly topically tid
- Hydrocortisone 1% cream apply sparingly tid

Severe (including moist desquamation)

- Silver sulfadiazine (*Flamazine*) applied generously topically OD
- Framycetin dressings (*Sofra-Tulle*) bid

ANCILLARY SERVICES

Supportive Care

The Supportive Care department consists of social workers, dietitians, pain and symptom management nurses, an education co-ordinator and the co-ordinator of the SCOPE program.

Supportive Care is: The provision of necessary services as defined by those living with or affected by cancer to meet their physical, informational, psychological, social and spiritual needs during prediagnostic, diagnostic, treatment and follow-up phases, encompassing issues of survivorship, palliation and bereavement. The Supportive Care Department members are integral members of the patient care teams contributing their expertise to help provide holistic care for oncology patients and their families.

Social workers and pain and symptom management nurses work both in the Center and on the inpatient oncology floor. There is a referral form for supportive care with which you can request intervention from the Pain and Symptom Management Team (which includes a social worker) or Social Work. There is a separate referral for Dietitian intervention. The social workers and dietitians work on site-specific teams to provide individual, couple and family counseling. Social workers are involved in discharge planning for inpatients and all members of the Supportive Care Department are aware of community resources available to patients and their families. The Pain and Symptom Management Team have weekly pain and symptom management clinics.

A variety of other programs are also provided through the Supportive Care Program:

Patient and Family Library	Monday to Friday 9:00 am - 4:00 PM
Prostate Cancer Information and Support Group	4th Monday of the month 7:00 PM - 9:00 PM
Look Good Feel Better: Workshop for Women Living with Cancer	2nd Wednesday of the month 6:30 PM - 8:30 PM (must preregister) 4th Tuesday of the month 2:00 PM - 4:00 PM
Relaxation Program	First four Wednesdays of month 10:30 am - 11:45 am
Relaxation Practice Session	2nd Tuesday of the month 10:30 am - 11:45 am
Bereavement Group Coping Skills Group	Three times a year – must preregister Periodically

Guidelines for Referrals to Social Work

1. Patient or Family Request
2. Problems with Patient or Family Reaction to illness
 - anxiety or fear
 - depression
 - anger
 - limited support system
 - difficulty with decision-making
 - cultural or lifestyle barriers to receiving care
 - case management

3. Problems with Other Issues for Patient or Family
 - physical or sexual abuse
 - impaired relationships
 - multi-problem family
 - difficulty caring for patient/self at home
 - bereavement
 - job loss
 - substance abuse

4. Problems with Practical Assistance
 - finances
 - drug coverage
 - community resources, i.e. placement, transportation, equipment, volunteers, occupation, education
 - referrals to other professionals
 - legal matters

Community Care Access Centre

Community Care Access Centre (CCAC) is a Ministry of Health funded program available throughout the province of Ontario. CCAC has case managers and placement co-ordinators on staff that conduct patient assessments. CCAC contract service providers to provide professional services in the community such as visiting nursing, complex care nursing, physiotherapy, occupational therapy, speech therapy, social work, and dietician services. Supplementary services include home support services, drug coverage, equipment rental, dressings and payment of emergency transportation costs. As an added service in London/Middlesex, CCAC in-home IV therapy is available and blood transfusions at home are currently being implemented.

In general, a referral to CCAC can be made through anyone by calling the local CCAC office. For London, the number is (519) 434-2222. An intake case manager will assist the caller. More specifically to the London Regional Cancer Centre and the adult oncology unit at Westminster Campus of the London Health Sciences Centre, any health care professional can make a referral to CCAC. An on-site case manager completes assessments for in-home services. Due to the high workload, early referrals are requested to better facilitate discharges. To speak to a case manager directly, one can call pager 13429 or leave a voice mail at extension 51095.

Many patients receiving cancer treatment require services through CCAC. Some examples include:

- patients who are having pain management difficulties
- patients with ADL difficulties
- patients requiring IV antibiotics or hydration at home
- patients with central lines
- patients with wound care
- patients with repeated neutropenic episodes
- patients learning how to administer self-injections
- palliative patients

Physiotherapy/Occupational Therapy

When a person has been diagnosed with cancer, his or her physical functioning, emotional well-being and quality of life can be severely impacted by the disease and treatment. Occupational Therapy and Physiotherapy play a supportive role for many persons with cancer if the effects of cancer have impacted his or her daily activities of life. A physician's referral for Physiotherapy and/or Occupational Therapy consultation is required to activate one or both of these services prior to active involvement on behalf of the therapists. Once the therapist receives notification of a written consult, he or she will then independently assess, treat, educate and progress the patient to optimize his or her level of functioning within a holistic framework. The following summaries will identify those signs, symptoms, or issues that may necessitate a referral to the respective therapies.

Indications for Physiotherapy

- physical deficit(s) that inhibits safe and/or independent mobility (e.g. decreased range of motion, decreased strength, balance, endurance, co-ordination or sensation). Physiotherapy assesses and prescribes appropriate ambulatory aids and progresses mobility as tolerated.
- Risk of cardiopulmonary compromise or difficulty clearing secretions secondary to immobilisation, surgical intervention or disease.
- Risk of developing or presence of musculoskeletal dysfunction secondary to illness or treatment.
- Need for complex discharge planning

Following assessment, physiotherapists may incorporate therapeutic exercise, education, manual techniques, modalities (e.g., TENS, ultrasound, heat, ice, etc.) to achieve client goals. There is close collaboration with other members of the health care team especially Occupational Therapy so the gains in physical status may be incorporated with functional activities. Each patient receives individualized treatment and is progressed as tolerated. People with cancer represent a patient population where quality of life and safety are central to the therapy provided.

Indications for Occupational Therapy

Occupational Therapy is indicated when a patient/client exhibits impairments in their ability to maintain daily activities of living to a maximal level within the limits of the disease process. Cancer can impair a person's strength, range of movement, cognitive status, endurance, energy levels, and emotions. Many of these factors can have significant impact on a person's ability to live in his/her home environment safely and independently. Occupational Therapists can assist persons and/or family members in managing some of daily living tasks through education about strategies and techniques, demonstration, routine practice, provision and trial of adaptive aids/equipment. The Occupational Therapist can then recommend and assist the individual on how to locate the aids that are needed for optimal functioning.

Some of the goals of Occupational Therapy include:

- *Maintain or increase a person's ability to perform activities of daily living such as dressing, bathing, grooming, eating, cooking, reading or shopping.*
- *To ensure home safety*

- *To facilitate individual interpersonal adjustments to the disease process.*
- *To optimise personal comfort and ability to mobilise independently*

Registered Dietician

Nutritional care of the oncology patient is designed to provide maximum nutrition support for the prevention of malnutrition-induced complications, the prevention of further nutritional deterioration and the maintenance or improvement in quality of life outcomes^{1, 2}. Individuals at all stages of disease may require nutritional counselling. Many interventions must be individualised, giving consideration to both the theoretical and practical issues relevant to the patient.

With respect to patients who receive radiation therapy, many of them have some degree of malnutrition before they even start treatment; many others develop malnutrition secondary to radiation therapy side effects³. Specific measurements, such as weight loss and serum albumin, can be useful prognostic indicators. For instance, a weight loss of 10% or more of usual pre-illness body weight at any time in a person with cancer is considered significant, and an indicator of poor survival and response to treatment^{4, 5, 6}. Johnson, et al found a mean weight loss of 10% in head and neck cancer patients undergoing radiotherapy, and that odynophagia, dysgeusia, xerostomia and dysphagia were more common and of longer duration among the patients with weight loss⁷.

Likewise, if laboratory values are available, hypoalbuminemia may be used to identify patients with an increased risk of morbidity and mortality from cancer and its treatment⁸. Arnold randomised 50 ambulatory head and neck patients to oral nutrition supplements or no nutrition supplements during their course of radical radiotherapy⁹. The patients who received no nutrition supplements had a significant reduction in serum albumin compared to the supplemented patients. Both groups lost weight during treatment and although there was no significant difference, the patients supplemented had a lower percentage of weight loss, even though they did not consume 100% of the recommended volume of the supplement. This study suggests that more aggressive feeding regimens are needed for head and neck cancer patients. In accordance with this, the need for enteral or parenteral nutritional support should be considered for patients who are no longer able to maintain an adequate oral intake, even with medical nutritional supplements².

Patients who receive radiation therapy to the abdomen, thorax central nervous system or pelvis are also at nutritional risk from treatment side effects^{3, 6, 10}. These effects may develop during or after treatment is completed. Examples of acute symptoms that have nutritional consequences include nausea, vomiting, anorexia, mucositis, odynophagia, dysphagia, and dysosmia. Chronic effects, such as dental caries, osteonecrosis, esophageal fibrosis, intestinal fistula formation, fibrosis/stricture formation, obstruction, perforation or hemorrhage can develop months or years after treatment is done and may be symptoms requiring long term, significant dietary change¹⁰. Other symptoms can be both acute and chronic, including xerostomia, colitis, enteritis/malabsorption, GI ulceration, dysgeusia/hypogeusia and trismus.

As poor nutrition can lead to interruption or discontinuance of potentially curative therapy, patients who are able to maintain or achieve a reasonable nutritional status during treatment are better able to maintain their immunologic integrity and withstand any further cancer treatment³. A summary of typical nutritional management strategies for the most common symptoms is attached. One-on-one counselling allows patient-specific goals to be developed as part of a nutrition care plan. This reduces the burden on the patient and caregiver of not

knowing how to decide on priorities/strategies, while increasing the likelihood of successful symptom management and improved patient and family satisfaction.

Another important factor for quality of life of some cancer patients is their need to explore complementary or alternative therapies for cancer, which often include a nutritional component (e.g. diet therapies, vitamin/mineral or other nutritional supplements)¹¹. As a health care provider, patients need to know you have an honest concern for their situation, as well as the time and knowledge to address their needs. It is a time consuming process to discuss unproven nutritional therapies for cancer, but oncology dieticians and pharmacists often have valuable resources that enable patients to make the most informed choices possible. These resources can also provide the physician with a basis for talking with a patient about the pros and cons of specific therapies.

In conclusion, it is important to consider the nutritional status of patients undergoing radiation therapy. Anticipation of the nutritional consequences of treatment, or intervention for pre-existing malnutrition can help to improve radiation treatment outcomes and reduce patient morbidity and mortality. Referrals to oncology dieticians can be an important part of this process, and can provide patients with the support they need to effect changes at any time in the cancer care continuum.

Pharmacy

Oncology practice is a specialized area of pharmacy. Chemotherapy medications have narrow therapeutic indices and dose limiting toxicities. Pharmacists in oncology practice review each patient's order for appropriate regimen, dose calculations, appropriate dose reductions, and adequate anti-emetics. They also oversee the preparation of chemotherapy. They assist in the management of chemotherapy induced side effects: nausea/vomiting, diarrhea, mucositis/stomatitis, neutropenia, and pain management.

As part of the multi-disciplinary team, pharmacists have a significant role in providing drug information to patients and health care professionals. In addition to information on doses, drug interactions, side-effects/adverse drug reactions, new drugs, compatibilities, pharmacists are also involved in monitoring a patient's therapeutic plan and have a role in supportive care management. Pharmacists counsel patients on their medication to maximise compliance and advise patients on the use of complementary and alternative therapies, especially the use of herbal products.

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RADIATION ONCOLOGY AS A CAREER

Typical Radiation Oncologist's Work Day

2-3 days/week: outpatient clinics
1-1 ½ days/week: simulation/treatment planning
½-1 ½ days/week: research/administration

Other Considerations

- Typical work day runs from 8 am to 5 pm
- Call tends to be lighter than other specialities and relatively infrequent
- Treatments are rarely given after midnight
- Lots of research opportunities in clinical (retrospective, prospective) and basic sciences (radiobiology, radiation physics, genetics, molecular biology) are available. The patient workload in Canada unfortunately does impinge upon time available for research.
- Radiation Oncologists hold salaried positions within Cancer Centres in Canada. The Cancer Centres tend to be located in larger towns/cities
- There are lots of jobs forecasted and currently available in Canada for Radiation Oncologists
- Most patients are outpatients
- Radiation Oncologists practice in a “multidisciplinary” setting; that is patients are often seen in conjunction with other cancer specialists. Treatment plans are often reviewed by a tumour site-specific multidisciplinary “team” consisting of Radiation Oncologists, Medical Oncologists, Surgical Oncologists, Pathologists, Radiologists, Oncology nurses, and other Supportive Care staff.

Training

- 5 years, consisting of 12 months of rotating through various specialities (surgery, paediatrics, gynaecology, etc), at least 6 months of Internal Medicine, and 3 ½ years of core Radiation Oncology
- Further fellowship training available but optional
- Training available in Nova Scotia/New Brunswick (Dalhousie), Quebec (Laval, Montreal, McGill), Ontario (UWO, U of T, Queens, U of O, McMaster), Manitoba (U of M), Alberta (U of A), and British Columbia (UBC)

MEDICAL ONCOLOGY AS A CAREER

Typical Medical Oncologist's Work Day

3-4 days/week: outpatient clinics
1-2 days/week: research/administration/teaching

Other Considerations

- Typical workday runs from 8 am to 5-6 pm
- Proportionately more patients are inpatients than Radiation Oncology
- Many job opportunities throughout North America
- Most Medical Oncologists are split between salaried positions within Cancer Centres in Canada, and community practice, often as part of a provincial Alternate Funding Plan . About fifty per cent of chemotherapy in the province is delivered outside the eleven cancer centres in Ontario. Some physicians in private practice do a combination of medical oncology, haematology and internal medicine, though the latter are becoming rare.
- Lots of opportunities for research in clinical or basic science settings
- The role of chemotherapy is expanding into the treatment of tumour sites such as head and neck, early breast cancers, cervical cancer, G.I. cancers, prostate cancer, etc.
- Newer, more effective treatments provide exciting improvements in survival and quality of life.
- Exciting opportunities to explore biological therapies.
- Practice environment is “multidisciplinary”, like Radiation Oncology
- Call for staff people is still relatively light, although is somewhat busier than Radiation Oncology because of more potential emergencies (febrile neutropenia, tumour lysis syndrome, etc.). Since Medical Oncologists have Internal Medicine certification, they will often take the ‘lead’ in very ill patients cared for by a team including Surgeons and Radiation Oncologists.

Training

- 3 years of general Internal Medicine, and 2 years of Medical Oncology
- Fellowship training available but optional
- Training available in Nova Scotia (Dalhousie), Quebec (Laval, Montreal, McGill), Ontario (UWO, U of T, U of O, McMaster, Queen's), Manitoba (U of M), Alberta (U of A, U of C), and British Columbia (UBC)

SURGICAL ONCOLOGY AS A CAREER

Typical Surgical Oncologist's Work Day

1 - 1.5 days/week: OR

1-1.5 days/week: clinic

0.5 days/week: admin or teaching

1.5 days/week: research or personal time

Other Considerations:

- There is extreme variability within surgical oncology depending upon which area of surgery you have trained with regards to hours and lifestyle issues
- Typical work day runs from 8am to 5pm, often have 1-2 days per week with 7 am rounds or meetings
- Call frequency depends on number of faculty on staff, typically one night/week - often covering general surgical emergencies during call (surgical oncology emergencies are rare)
- Able to provide immediate impact on patients with cancer with curative surgery or improving quality of life with palliative surgery
- Often able to assist medical and radiation oncologists by providing diagnostic biopsies in difficult cases
- Extensive sub-specialty opportunities from general surgical oncology, neurosurgical, urological, gynaecological, head and neck, thoracic and orthopaedic with opportunities to sub-specialize within each of these to a particular niche or area of interest
- Great demand for surgical oncologists at present for employment throughout Canada
- Salary is typically fee-for-service with base salary stipend linked to University appointment, however most surgical departments are heading toward an Alternate Funding Plan.
- Able to gear practice to family-friendly outpatient surgery or in-patient type practice depending on interest
- Focus on multi-disciplinary approach: can consult with other oncologic specialties and within surgical specialties for multi-team surgical resections
- Lots of research opportunities - Surgical oncology is just beginning to expand into research forum, thus great need for research leaders in the field for the advancement of knowledge and improved patient outcomes
- Able to practice surgical oncology in large centres or in smaller centres depending on personal choice as most surgical resections do not require highly technical equipment or fancy operating rooms

Training

- 5 years of surgical specialty training (general surgery, urology, gynaecology, ENT, orthopaedics or 6 years neurosurgery) at any of 13 training universities in Canada
- Additional 1-2 years of recognized surgical oncology fellowship (available fellowships typically posted through Society of Surgical Oncology (SSO) in US or Canadian Society of Surgical Oncology (CSSO))

COMMON ONCOLOGY TERMS AND ABBREVIATIONS

- Adjuvant** In addition to a primary treatment in the absence of any gross residual disease (e.g. adjuvant radiotherapy after lumpectomy in breast cancer)
- Anemia** Decreased hemoglobin concentration, a common adverse effect of advanced cancer or of cancer treatment. Usually requires intervention when the hemoglobin level drops below 80 g/l
- Apoptosis** “Programmed cell death”, thought to be a major component of cell death in neoplasms
- Alopecia** Loss of hair
- AFP** Alpha-fetoprotein (marker for liver, ovary, and testicular tumours). Elevated in some benign conditions
- Bolus** Tissue equivalent material (e.g. wax) used to bring the maximum dose of radiotherapy closer to the surface
- Boost** Further radiotherapy given to the primary tumour or residual tumour volume alone after a larger volume treatment. Usually indicated for close or positive surgical margins, or gross residual disease

Brachytherapy

Radiotherapy at a short distance, e.g. intracavitary insertion, interstitial insertion, mould applicator (associated terms: brachy, HDR, LDR)

- CA-125** A tumour marker used to monitor ovarian cancer; also elevated with some tumours involving the pleural or peritoneal space as well as some benign conditions

CADD Pump A pump used to deliver a continuous parenteral infusion of medication

- CEA** Carcinoembryonic Antigen associated with colorectal and ovarian tumours, also elevated with some benign conditions. Occasionally elevated with breast, lung and other adenocarcinomas.

Cachexia Unintentional weight loss/wasting secondary to malignancies

Centigray Measure of absorbed radiation dose, given in terms of energy per unit mass (1 Gray = 1 Joule/kg = 100 centigray = 100 rads)

Chemotherapy Regimens (some examples of common regimens)

- **AC** adriamycin (doxorubicin) and cisplatin (*breast*)
- **CAF/CEF** cyclophosphamide, adriamycin/epirubicin, and 5-FU (*breast*)
- **CAV/EP** cyclophosphamide, adriamycin (doxorubicin), and vincristine alternates with etoposide and cisplatin (*small cell lung*)
- **CHOP** cyclophosphamide, adriamycin (doxorubicin), vincristine, prednisone (*non-Hodgkin's lymphoma*)
- **CMF** cyclophosphamide, methotrexate, and 5-FU (*breast*)
- **CV (Dillman)** cisplatin and vinblastine given prior to radiotherapy (*non-small cell lung*)

- **FOLFIRI** 5-FU and folinic acid and irinotecan (*colorectal*)
- **FOLFOX** 5-FU and folinic acid and oxaliplatin (*colorectal*)
- **MOPP/ABVD** nitrogen mustard, vincristine, procarbazine, and prednisone alternates with adriamycin, bleomycin, vinblastine, dacarbazine (*Hodgkin's lymphoma*)
- **PCV** procarbazine, CCNU, and vincristine (*oligodendroglioma*)

Cobalt-60 A radioactive isotope; has been incorporated into a machine to allow delivery of highly penetrating collimated megavoltage radiation beams to deep seated tumours. Incidentally, the first treatment of a patient using Cobalt-60 teletherapy, which revolutionised modern radiotherapy, occurred in London, Ontario on October 27, 1951

Collimator Defines edges of radiation field

Concurrent Treatments given simultaneously, as opposed to sequentially (usually refers to "concurrent" chemoradiation)

Couch The bed upon which the patient lies during radiotherapy treatment. This can be rotated to aim the radiation beam

3D-CRT "Three-dimensional conformal radiotherapy". A relatively new technology using 3D imaging (e.g. CT, MRI) to localize the target, and precise radiotherapy treatment delivery equipment to maximize dose delivered to the target, and minimise dose delivered to normal tissues

Cytology A technique to examine small numbers of cells (e.g. PAP smear, sputum sample, pleural fluid, fine needle aspiration, etc)

DNAR "Do not actively resuscitate", e.g. no invasive interventions, such as advanced cardiac life support, intubation, or ICU admission in the event of severe cardiopulmonary compromise or arrest. This is written as an order on the hospital chart as an order with the patient's permission

DCIS Ductal carcinoma in situ, a pre-malignant condition of the breast

Desquamation (dry and moist)

A sloughing of the skin epidermis associated with radiotherapy

Dosimetry A Radiation Oncology-related field dealing with the dose distribution of radiotherapy beams

Electrons A type of radiation beam used to treat relatively superficial tumours. Electrons deposit dose primarily in the superficial tissues, after which the dose falls off rapidly

Emetogenic Treatment is associated with nausea and vomiting

Gantry A rotatable component of a linac or other radiation generator from which the radiation beam is delivered

Hickman catheter

A type of central line, with external ports on the chest wall

Immunohistochemistry

Used by pathologists to identify cell surface markers (e.g.. CD 45, CD 20, ER, PR, etc.). Individual cells are stained with labelled antibodies to a specific antigen (eg CD 20), and then are run through a detector

IMRT “Intensity Modulated Radiotherapy”, a new technology used in conformal radiotherapy (see *New Radiation Technologies*)

Induction a chemotherapy term; chemo given with the intent of getting the patient into a first remission

Linear Accelerator (Linac)

A producer of high-energy photon beams. Some machines also have the ability to generate electron beams

MDT “Multidisciplinary Team”, consists of a site specific team of radiation, medical, and surgical oncologists, pathologists, radiologists, and ancillary health care staff, who review each new referred patient’s treatment plan

MLC “Multi-leaf collimator” (see *collimator*)

Mucositis Inflammation of the mucous membranes (e.g. oral cavity)

NPR “New patient Referral”; the department handling new referrals to the LRCC

Neoadjuvant

A cancer treatment given before the primary treatment (e.g. neoadjuvant hormones to treat locally advanced prostate cancer)

Neutropenic Decreased neutrophil count, associated with some cancer therapies. Considered critical when the ANC (*absolute neutrophil count*) is less than $0.5 \times 10^9/L$

Palliation To alleviate symptoms but not to cure

PICC line Peripherally inserted central catheter (another type of central line) inserted in the brachial vein

Photon An electromagnetic wave (e.g. light, X-ray, UV light, etc)

Portacath A central line with a subcutaneous port, usually on the anterior chest wall

Portal Imaging

An image is taken with the patient in the treatment position on the treatment machine. This is to verify correct patient setup, and is recorded with film, although some new technologies using electronic media (i.e. *on-line portal imaging*) are evolving

PR “Patient Review”; radiotherapy patients are assessed here while on treatment

PSA Prostate Specific Antigen (a tumour marker for prostate cancer)

Radical curative intent

4R's of Radiobiology (see also section on *Radiobiology*)

- **Reassortment** the reassortment of cells into radiosensitive phases of the cell cycle after having been “synchronised” into a radioresistant phase by ionising radiation
- **Reoxygenation** the increased delivery of oxygen to previously hypoxic cells after partial tumour kill by radiotherapy. These cells are made more radiosensitive by the increased oxygen concentration
- **Repair** the ability of the cell to repair potentially lethal or sublethal DNA damage by radiation
- **Repopulation** the repopulation of the tumour if too much time is allowed between fractions of radiotherapy

Simulation (*Sim*)

A process, which occurs before the start of a course of radiotherapy during which the target volume and critical organs to be spared are identified. Requires the use of diagnostic imaging modalities (eg fluroscopy, computerised tomography)

Stomatitis mucositis of the mouth

Thrombocytopenia

Decreased platelet count, commonly seen with oncology treatments. Critical value considered to be less than 10×10^9 platelets/l

TNM Primary tumour, lymph node, and metastasis staging of various cancers (e.g. $T_2N_1M_0$ carcinoma of the breast). Published by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC)

TPN “Total Parenteral Nutrition”, consisting of amino acids, lipids, carbohydrates, and micronutrients administered either peripherally (peripheral vein), or centrally (via PICC, Hickman line, etc)

Tumour An abnormal proliferation of cells. May or may not have the ability to invade adjacent tissues and/or spread to locoregional lymph nodes or distant sites (benign vs. malignant)

Xerostomia dry mouth secondary to impaired salivary gland function, commonly seen after irradiation of the salivary glands

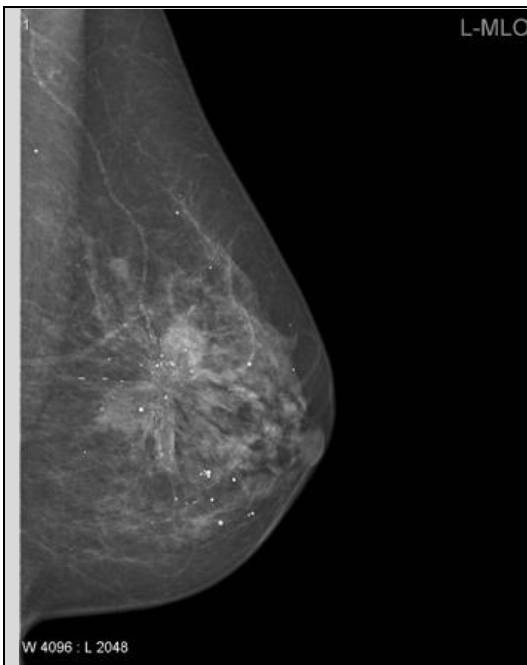
ONCOLOGY QUESTIONS FOR CLINICAL CLERKSHIP CASES FOR RESIDENT DISCUSSIONS

1. Breast Cancer Module

Clinical Case: Beth Williams is a 45-year-old woman who presents to the Ontario Breast Screening Program (OBSP) for assessment. She had been advised to start breast cancer screening at age 45, since her mother was diagnosed with breast cancer at age 55. Beth is a premenopausal, G2P2, otherwise healthy woman.

1. What is the purpose of a screening test in terms of disease prevention?
2. Discuss the components of a good screening test.
3. Other than breast cancer, what other cancers have screening tests that have been shown to reduce mortality?
4. What are the risk factors for breast cancer and which, specifically, would you ask about in this patient?
5. What is your approach on history, to a woman presenting with a breast mass?
6. What is your approach on physical exam, to a woman presenting with a breast mass?
7. What is your approach to a differential diagnosis for a breast mass?
8. What are some red flag findings for a breast mass?
9. What initial investigations would be important to work up a patient with a breast mass?

Case Continued: Beth undergoes a bilateral mammogram, which reveals a spiculated density in the upper outer quadrant of the left breast with associated calcifications. There is no palpable mass in this area nor does the patient have any skin changes or nipple discharge.



Case Continued: A tru cut biopsy reveals a diagnosis of infiltrating ductal carcinoma, no special type, Grade 1. You refer the patient to a general surgeon.

10. Given that this patient now has a confirmed breast cancer, how would you complete her staging investigations?
11. What surgical options are available for this patient?
12. What are the three components of TNM staging?

Case Continued: The patient undergoes a lumpectomy with sentinel lymph node biopsy. She is subsequently staged as a T1 (0.8 cm) N0 (0/2 sentinel nodes), M0. The rest of the breast cancer features are as follows: no lymphovascular invasion (LVI), grade 1, clear margins, ER/PR negative, Her-2-neu negative. Staging investigations are within normal limits.

13. What is the clinical significance of the following terms found on this patient's pathology report? Stage, LVI, Grade, Margin status, ER/PR and Her 2-neu status.
14. What adjuvant treatment is indicated for this patient and what are the potential side effects?
15. If the patient underwent mastectomy for a 2.5 cm tumor, clear margins, ER/PR positive, Her-2-neu positive, and positive lymph nodes (i.e. T2N1). What three adjuvant treatments would be indicated in this case (also discuss potential side effects)?

Case Continued: Two years later, the same patient presents to the emergency department with a two day history of reduced mobility. She also has had back discomfort for several weeks, which has only slightly been relieved with Tylenol.

16. What is your working diagnosis?
17. What are some important questions to ask about in a patient presenting with back pain in order to determine the underlying etiology of their pain? Think broadly.

18. What questions are important to ask on history with respect to a working diagnosis of spinal cord compression?

Case Continued: On examination CVS is normal, chest is clear to auscultation and percussion. Abdominal exam reveals a soft non-tender abdomen. Neurological exam shows normal fundi, and cranial nerve function within normal limits, no neck stiffness. Gait is wide based and awkward. Muscle strength and tone are normal in upper limbs but only 3/5 in proximal lower limbs and 4/5 in distal lower limbs. Sensation to pinprick is abnormal to the level of the umbilicus. Upper limb reflexes are symmetrical and 1+. Lower limb reflexes are symmetrical and 3+. Finger nose test is normal but heel to shin is inaccurate

19. What is your initial management plan and what investigations would you order?

20. What are the potential treatment options for spinal cord compression?

21. What is the prognosis in terms of neurological function and overall survival?

22. Other questions to consider:

What is the difference between invasive and non-invasive breast cancer? What is the importance of making the distinction between the two for the patient?

Explain the principle/procedure behind a sentinel lymph node biopsy?

Be able to explain the difference between treatment that is neo-adjuvant, adjuvant, palliative and curative treatment. Give examples of each.

Who might you consider referring for genetic counseling for breast cancer?

What does a palliative care physician do and when is it appropriate to refer a patient to palliative care?

2. Prostate Cancer Module

Clinical Case: Mr. Jones, a 68-year-old man presents with difficulty hesitancy and post void dribbling. He has had nocturia for the last 18 months, which has progressed to a frequency of 4-5 times per night. He has recently retired from an accounting firm and has otherwise been well. He has not seen a physician for many years.

1. What is your approach on history, to a man presenting with urinary hesitancy?
2. What is your approach on physical exam, to a man presenting with urinary hesitancy?
3. What is the differential diagnosis for this gentleman?

Case Continued: On digital rectal examination there is a moderately enlarged prostate with a firm nodularity on the left lobe.

4. What other investigations are required?

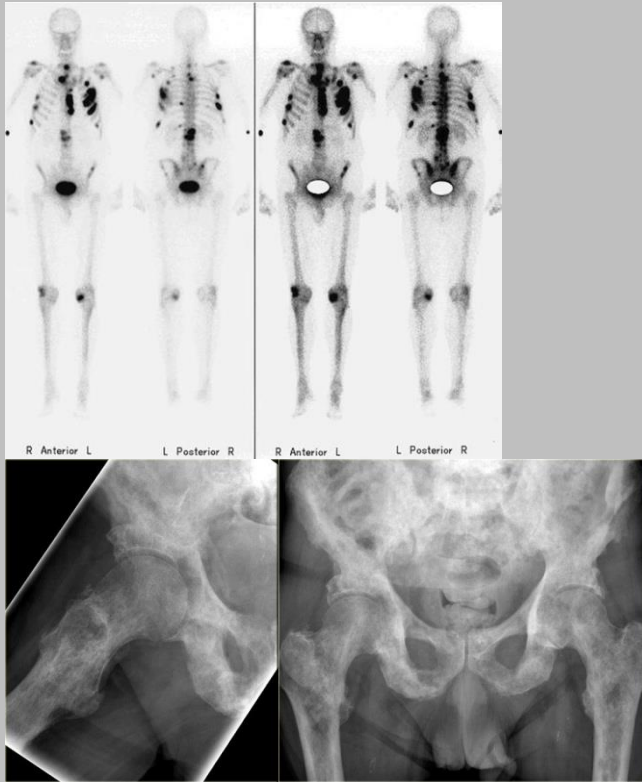
Case Continued: The PSA is 9ng/ml and the biopsies shows disease at the apex and middle zone of the left lobe of the prostate. The histology is adenocarcinoma with a Gleason score is 6. He is otherwise healthy.

5. What is the PSA? In your answer, consider where it is made, its function, how it's regulated and how the PSA value is used clinically,
6. What is the Gleason score?
7. What are the three components of risk classification and what risk category does this patient fit into?
8. What are his treatment options and the associated side effects of each (list four)?
9. What is a PSA failure after definitive treatment?

Case Continued: The patient does well after his prostatectomy. The final pathology revealed a Gleason score of 6 and the margins were clear with no extra-prostatic extension. The PSA dropped to negligible after three weeks. He presents to the local emergency department 2 years later with back pain. PSA is drawn but takes 7 days. He is also having worsening problems with urinary hesitancy.

10. What is your approach to a differential diagnosis of back pain?

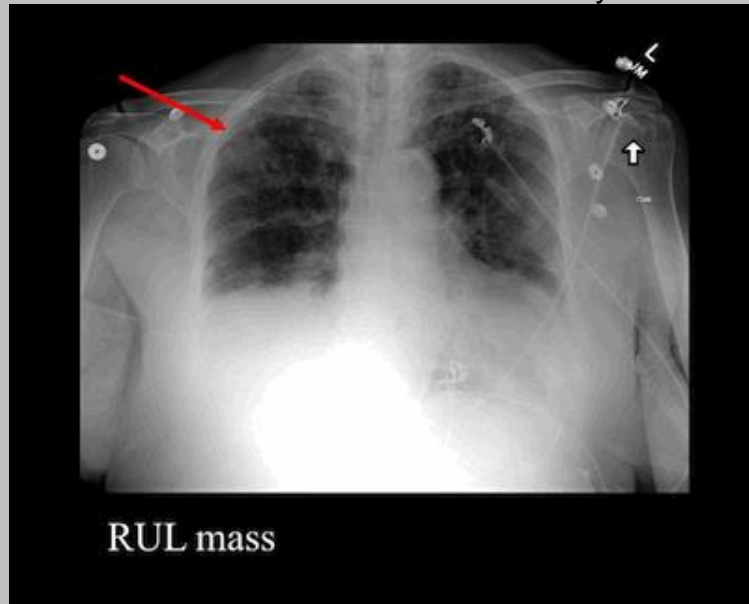
Case Continued: Xrays show no destructive changes. Bone scan however shows multiple areas of increased uptake as illustrated below. The image to the right is a plain film of bony metastasis in a patient with prostate cancer.



11. Assuming that these areas of uptake represent metastatic prostate cancer to bone, what is your initial medical management?
12. What oncology treatments are available?
13. How do hormones work and approximately how long do hormones keep prostate cancer under control?
14. What other options are available for treatment of painful bony metastases once the prostate cancer cells become resistant to the hormonal therapy?

3. Lung Cancer Module

Clinical Case: A 60-year-old man, with a 40 pack-year history of smoking, presents to the emergency department with cough and fever. On examination there were decreased breath sounds in the right upper and right lower lung zones. Laboratory investigations revealed an elevated WBC. His chest x-ray is illustrated below.



1. What is your approach to reviewing chest x-rays? Identify the salient features of the above image.
2. What is your approach to taking a history on a patient who presents with the above findings?
3. What is your approach to the physical exam in a patient presenting with the above history?
4. What is meant by the term Pan coast tumor and describe five possible clinical presentations associated with a tumor in this location.
5. What is the definition of a Paraneoplastic syndromes? Give at least 4 examples of paraneoplastic syndromes that are associated with lung cancer.
6. Briefly describe the classification of lung cancers and give the clinical relevance of determining the histology of the lesion.
7. What investigations would you order to further investigate this lesion? It will be useful to divide your answer into blood work, imaging/staging investigations and possible methods of obtaining a tissue sample?

Case Continued: A percutaneous FNA of the RUL mass is performed and the diagnosis is a squamous cell carcinoma (NSCLC)

8. Why is it important to know whether there are any positive mediastinal nodes prior to surgery?
9. Assuming that the patient does not have involved mediastinal nodes, what are the surgical options?

Case Continued: After your therapeutic intervention you are left with information that a 4.1 x 2.0 lesion consistent with a NSCLC has been identified. The margins of resection were clear. None of the sampled nodes demonstrated any tumour. The stage is therefore T2N0 (Stage IB).

10. What adjuvant therapy would you recommend to this patient?

11. What is the prognosis (5 year survival) of this patient?

Case Continued: The patient remained well for 18 months but at his last follow-up visit he complained of feeling progressively unwell. He was quite fatigued and became short of breath with minimal exertion. His appetite was low and he had lost twenty pounds since his last visit. He had also noticed some swelling of his right arm. On exam his neck and face were also swollen and his neck veins were distended. There was no overlying erythema or tenderness on palpation. In addition to the previously identified RUL lesion, his chest x-ray confirmed a right paratracheal fullness.

12. What is the most likely diagnosis?

13. List other physical findings related to the shortness of breath and facial edema that you would look for.

14. What further investigations would you order?

15. Assuming the most likely diagnosis, what is the management (both initial medical management and oncologic management)?

4. Colon Cancer Module

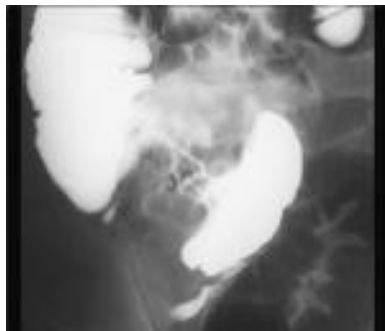
Clinical Case: A 55-year-old man comes to your office for routine renewal of his blood pressure medications. The patient casually mentions that he has recently starting using Metamucil for constipation. You ask further about this change in bowel habits and find out that he has also been passing small amounts of blood mixed with his stool. He is convinced that the bleeding is “hemorrhoids”.

1. What is your approach to a patient presenting with a change in bowel habits and blood in his stools?
2. Identify some specific risk factors for colon cancer?
3. What is your differential diagnosis for a lower GI Bleed?
4. What is your approach to the physical exam in a patient presenting with the above history?

A complete history and physical was performed and the examination was normal aside from some mild conjunctival pallor. The DRE was normal. Initial blood work is outlined below;

Hemoglobin	105 g/L (normal 136-172)
MCV	76 f/L
WBC	$5.6 \times 10^9/L$
Platelets	$256 \times 10^9/L$
Sodium	142 mMol/L
Potassium	4.6 mMol/L
Chloride	98 mMol/L
Bicarbonate	24 mMol/L
Alkaline Phosphatase	180 U/L
GGT	79 U/L
AST	67 U/L

5. What abnormality is identified in the above blood work? What is the next test you would order?
6. Describe the abnormality identified in the image shown below? What is the next step?



7. What further investigations would be done to complete the staging?

Case Continued: Colonoscopy was done and identified a large, necrotic mass in the right colon. Biopsy revealed adenocarcinoma. You refer him to a surgeon who does a right hemicolectomy. The pathology shows a 3.2 cm, moderately differentiated adenocarcinoma penetrating through the bowel wall. 2/15 positive lymph nodes with clear margins.

8. Describe how the T stage of colon cancer is determined? What is this patient's stage of cancer?

9. Given that this is a T3N1 tumour (Stage IIIB), would this man need any adjuvant treatment?

10. What are the side effects of this chemotherapy treatment?

11. How would you follow this patient?

Case Continued: The patient's 25-year-old daughter attends a follow up appointment with her father. She is concerned about what her risk of colon cancer might be and what she should do about it.

12. What are the Canadian colorectal screening guidelines and what would your recommendations be to this patient's daughter?

13. Other things to consider:

What is a tumor marker? Why do we use tumor markers? Give examples?
Pros and cons of tumor markers?

5. Testicular Cancer Module

Clinical Case: A 24-year-old man presents to your office complaining of a swelling in his right scrotum. On exam you find a hard mass 3 cm in diameter replacing his right testicle. On further questioning he tells you it has been there about a month and has been increasing in size.

1. What is your approach on history, to a man presenting with the above history?
2. What is your approach to the physical exam in a patient presenting with the above history?
3. What is your differential for a unilateral swollen scrotum?
4. What imaging investigations would you order for this patient?
5. Would you arrange for a testicular biopsy on this patient why or why not?
6. In addition to base line blood work are there any specific blood tests/tumor markers that would be helpful in this case?
7. In broad terms, how are testicular cancers categorized?
8. Assuming this is a testicular cancer, what will be the primary treatment modality for this patient? What are some of the important psychosocial issues that should be addressed with this patient at the time of his initial consult?

Case Continued; In keeping with the previous assumptions, the patient is referred to a Urologist and undergoes a unilateral inguinal orchiectomy. The diagnosis is consistent with a seminoma limited to the testis. The rest of the staging investigations are negative. The final diagnosis was Stage I seminoma.

9. Given these results, what would you tell him, in general, about his prognosis?
10. What are three adjuvant management options available to this patient?
11. What are the pros/cons of each treatment option you listed above?
12. How would his management differ if the patient had multiple pulmonary metastases at diagnosis?

Assume now a situation where the patient has pulmonary metastases and is being treated with chemotherapy. The patient calls you and tells you that he is feeling very tired and has a fever. He tells you his last chemotherapy treatment was two weeks ago.

13. What specific treatment related complication are you concerned about?
14. What investigations would you order?
15. Would you treat him as an inpatient or outpatient?
16. What is the management?

6. Head and Neck Cancer Module

A 55 year old man presents to his family doctor with a 4 week history of a small painless lump in the right side of his neck just below the angle of the jaw. He noticed the lump when he developed a sore throat he had a month ago. It was the size of a penny and had gradually increased to the size of a quarter. This prompted him to seek medical attention.

1. What is your approach, on history, to a patient presenting with a neck lump?
2. What are the established risk factors for the development of head and neck cancers?

The patient denied having any associated H&N related or systemic symptoms but did provide information that he has been smoking for the past 40 years and drinks six beers every night with more intake of alcohol on the weekends.

3. What is your differential diagnosis for a patient presenting with a neck lump?
4. What is your approach to a physical exam in a patient who presents with a neck mass?

On physical examination, he was found to have an enlarged mobile & firm right-sided Jugulodigastric (JD) lymph node (Level II Lymph Node). A routine head & neck examination carried out by his family doctor was normal. The patient was started on a two-week course of a broad-spectrum antibiotic & asked to report back on completing the course.

5. In simple terms describe the Lymph node levels in the neck?
6. How do you clinically describe an enlarged lymph node?
7. What are some red flags associated with lymph nodes? I.e. when should someone with an enlarged lymph node be investigated?

The patient calls his doctor back in 10 days informing him that the lump has increased in size. The family doctor sets him up to see an ENT surgeon in a week's time. The ENT surgeon conducts a detailed H & N exam, which includes a flexible fiberoptic Nasopharyngolaryngoscopy. He then proceeds to evaluate him further after Nasopharyngolaryngoscopy examination was normal.

8. Why did the ENT surgeon perform the Nasopharyngolaryngoscopy?
9. How would you proceed further with this patient?
10. Explain the difference between each of the following types of biopsies; excisional, incisional, FNA, core needle, stereotactic, US/ CT guided, endoscopic

The results of the FNAC come back as a Squamous Cell Carcinoma. The patient is then staged as having a Primary Unknown (PUK) with metastatic neck nodes TxN2aMx

11. What imaging tests would you order for the patient and why?
12. What is involved in a panendoscopy? Do you think this patient needs one?

The patient undergoes a Panendoscopy and is found to have no lesions detected visually & by directed biopsies of the Nasopharynx & base of tongue. The CT scans were negative with respect to detecting a primary lesion & thoracic pathology. The patient was seen by the Head & Neck MDT (multi-disciplinary team) and he commenced his treatment within a couple of weeks.

13. Explain the concept of multidisciplinary team as it pertains to the treatment of oncology patients?
14. What treatment do you think was recommended?
15. Why is the patient being administered chemotherapy along with his radiation?
16. What are the acute (within 3 months) and late side effects experienced by a patient undergoing Head & Neck radiotherapy?

The patient completed his treatment uneventfully and was subsequently seen on follow up six weeks after completion of treatment. He was found to have no evidence of lymphadenopathy or any other primary lesion. He was followed up at regular intervals without having any reappearance of disease.

7. CNS Cancer Module

A 49-year old man presents to the family doctor's office complaining of headaches. The headaches started around 3 months previously and are getting worse. Yesterday the headache was severe in the morning and was associated with vomiting.

1. What are the concerning features of this gentleman's history? New onset of headaches, which are getting worse.
2. What would be your approach to taking a history on a patient with the above history?
3. What is your differential diagnosis for a patient presenting with the above stated history?

The patient is otherwise well on history. You perform a physical examination and the cranial examination is normal. The motor examination reveals 4 + power for left upper and lower extremity muscle groups. The sensory examination DTR's plantar reflexes tone and cerebellar testing were normal.

4. What investigations would you order?

A CT scan reveals a ring enhancing mass with central hypodensity in the right frontal lobe measuring 2.0 x 2.5 cm.

5. What is your differential diagnosis of this ring-enhancing lesion?
6. What is your initial management?

You refer the patient urgently to a neurosurgeon at the local hospital. Your initial management relieves the patient's headache except for a mild morning headache. A subtotal resection is performed a couple days later. The pathology shows a glioblastoma multiforme (GBM). Post operative imaging is consistent with post operative changes as well as a small amount of residual tumour (0.8 x 0.5 cm).

7. What adjuvant therapies are indicated and list their side effects?
8. What would you tell the patient about driving and whom do you notify?
9. What is the patient's prognosis?

Two months later the patient presents to the emergency department complaining of feeling progressively unwell in the last several weeks. His appetite is diminished and he notes that he has lost some weight though his fluid intake has been adequate. He is more easily tired. In the last several days he finds himself quite generally weak. The neurological exam yields only mild generalized muscle weakness. No focal findings can be elicited. The patient is clinically euvolemic. Laboratory investigations show:

Hemoglobin	135 g/L
WBC	12.0 x 10 ⁹ /L
Platelets	527 x 10 ⁹ /L
Sodium	123 mMol/L
Potassium	3.8 mMol/L
Chloride	89 mMol/L
Bicarbonate	27 mMol/L
Calcium	2.10 mMol/L
Magnesium	.69 mMol/L
Albumin	32 g/L
Alkaline phosphatase	123 U/L
ALT	20 U/L
LDH	512 U/L

CT Head: The right frontal mass has slightly increased edema compared to a CT performed one month after completing cranial radiation.

10. What is abnormal with the bloodwork and what is your working diagnosis?
11. What other investigations would you order?
12. Assuming the patient does have the suspected disorder, what are the criteria for this and what is the management?

DICTAPHONE DICTATING INSTRUCTIONS

London Health Sciences Centre
London Regional Cancer Program

All dictators **must** have a **personal dictator ID number** obtained from Health Records Transcription, **call ext. 35131**.

TO ACCESS THE SYSTEM

Dial extension **66080** or **519-646-6080** from outside the hospital.
Enter your **5-digit** User ID number followed by #.
Enter the **LRCP site code** followed by # key, **5** for LRCP...
Enter the **work type** followed by # key (see below) .

WORK TYPES

- 32** Operative Report (or **39** for procedure report)
- 33** Discharge Summary (should be dictated on LHSC site Victoria Hospital =2)
- 34** Consultation (**City-Wide Work Type**)
- 38** Admission note (**City-Wide Work Type**)
- 70** Radiation Treatment
- 71** Letter
- 72** Social Work
- 73** GYN Snap Shot
- 74** Ovarian Progress Note
- 75** LRCP Clinic Note

Do not use Work Type 37. This is used for hospital in-patient Progress Notes

Enter the patient **MRN number** (***LRCP Chart Number**) followed by # key.

Enter 2 to begin dictation: * Please state your name, patient demographics, *LRCP Chart number, work type, and required copies at beginning of dictation (***Note that the LRCP Chart number is NOT the same as the HOSPITAL, LHSC number**).

KEYPAD FUNCTIONS

- 2** To begin, pause or resume dictation
- 3** Short rewind (3 to 4 seconds)
- 44** Fast forward to end of report
- 5** To end last report and dictation session
- 6** Priority dictation
- 77** Rewind to beginning of dictation
- 8** Go to next report
- 0** To open / interrupt report that cannot be finished during the current dictation session. When beginning a new session and after entering the site code, you will hear "you have an open report". To retrieve it, enter **1** and continue to dictate. To ignore it, enter **2**
- *** To go back to the previous prompt

Help Line: 53248

MUST READ:

When dictating, use site code "5" to ensure the notes are transcribed by the cancer clinic transcription service

EXAMPLES OF DICTATION NOTES:

HOW NOT TO DO A CONSULT NOTE: (This is an example of a real note)

PATIENT LOCATION: V-CL2

(This is a real note!!)

DATE OF CLINIC: October 15, ~~2007~~
(WRONG DATE)

DIAGNOSIS: Squamous cell carcinoma of the right lung, T3N2 or N3M0, most likely *why the question?*
Stage 3B.

I saw Mr. [REDACTED], a 74-year-old gentleman and retired farmer and gravel pit laborer, as a consult from radiation oncology, Dr. Yaremko.

too casual

Mr. ~~Prater~~ got a new GP in early 2007. That spring he experienced some shortness of breath and had a chest x-ray on July 31, ~~2007~~. This showed a large central mass in his right upper lobe as well as some enlarged mediastinal lymph nodes. On September 12, ~~2007~~, he received a transbronchial biopsy that ~~had~~ identified a squamous cell carcinoma. *underwent*

no timeline, no description

can't be seen on CXR

He does not experience any unusual headaches or fevers or chest pains. He gets short of breath on one flight of stairs, coughs on lying down (possible aspiration or reflux). He sounds hoarse, however he or his wife say that his voice has not changed. Also, he claims to feel something in his chest on coughing, no hemoptysis. He has lost 25 pounds over the last three months.

Physical!

ROS too brief!

interpretati not History

He lives in an apartment with his wife. His son lives in Byron, however they do not talk very often. He does not have many friends. *what? why? Too casual*

He does not drink more than one or two drinks per month. He smoked one pack per day from the age of 14 till 71 years old. In his youth he worked in a gravel pit and claims to have inhaled a large quantity of rock dust and diesel fumes.

His past medical history includes back surgery due to a trauma while working on a farm, some mole removal surgeries, and a motor vehicle accident that caused a large laceration across his right skull and amnesia.

Medications?

He is allergic to pollen and dust. He has medication allergies to Voltaren, Indocid, and Alka-Butazolidin. This medication allergy results in wandering, confusion and memory loss.

not an allergy describe reaction

On physical examination, he had dilated superficial chest veins spanning across his entire anterior chest. No descended neck veins. *??*

His lung fields were clear. No crackles or wheeze was heard. *were Percussion?*

On auscultation of his heart an S1 and S2 were heard. No S3 or S4 or murmurs.

He had no palpable nodes on examination of his head and neck.

He had bilateral resting tremor in both of his arms.

*Abdomen exam?
Hesit? Weight?
Neuro exam?*

Our plan is to have return on October 15 to decide upon a treatment plan.

*Investigations? pathology? Summary?
Thanks for referral?*

RADIATION TREATMENT NOTE

Dr. Mario Cureall, LRCP
Dr. Be Good, London - Batch Faxed

PATIENT LOCATION: V-CL2

DATE OF CONSULTATION: October 31, YEAR

DIAGNOSIS: Right lung squamous cell carcinoma. Tumor 5.3 cm located in the right upper lobe with local invasion of the posterior chest wall. Completed palliative radiation therapy 20 Gy in 5 fractions October 30, 2007.

Mr. X attended the London Regional Cancer Program today, accompanied by his friend Mr. Y. He describes a history of right chest pain made worse with activity which has been progressive over at least one year. Approximately a month ago, he had a fall which occurred secondary to pain as well as weakness. This fall prompted his niece to contact his Family Physician. Subsequent investigations included a chest x-ray, CT of the thorax and a referral to thoracic surgery for a lung biopsy. In addition, Mr. X was admitted to Palliative Care for pain management from October 12 to 23, 2007.

Mr. X describes mild cough which was productive for yellow green phlegm prior to a course of antibiotics. He continues to have mild cough which is now productive for clear phlegm. He denies any hemoptysis. He has not had any previous shortness of breath with the exception of some mild difficulty breathing immediately following his radiation therapy treatments. He completed five fractions of radiation therapy yesterday. This patient denies any fevers. He has had some fluctuation in his weight and he has lost approximately 40 lb over the last six months. His appetite has been good recently as long as he has good bowel function. He had had some difficulty with constipation after starting narcotic pain medication. He currently uses enemas every other night which results in bowel movements. Mr. X has had some hoarseness of his voice which is worse over the past three weeks. As well, he describes some intermittent coughing with swallowing.

Mr. X is using a Dilaudid pump for control of his right chest pain. This has been quite effective and he feels that he is currently able to maintain his regular daily activities with good pain control.

PAST MEDICAL HISTORY: This patient reports a previous diagnosis of asthma. He denies any cardiac disease or hypertension. His previous surgical history includes a right ankle fracture in a train accident with subsequent ankle pinning in 1979.

MEDICATIONS: This patient did not have a complete list of his medications with him today. He does relate the following:

1. Dilaudid pump.
2. Furosemide 60 mg od.
3. An antibiotic.
4. An inhaler.
5. Salbutamol puffer qid.
6. Lactulose.
7. Senokot.
8. Dexamethasone.
9. Enemas alternating days.
10. Ibuprofen prn.
11. Vitamins.
12. Ranitidine.

ALLERGIES: No known drug allergies.

SOCIAL HISTORY: Mr. X lives in an apartment within a house on Hamilton Road. This is a one floor apartment with no stairs. He currently friends over for support and assistance at home. Mr. X has retired as a locomotive engineer at CP seven years ago. This patient has a smoking history of smoking two packs a day for approximately 55 years. He drinks up to eight alcoholic beverages at social events but does not drink alcohol on a daily basis.

PHYSICAL EXAMINATION: On exam today, this patient weighed 81 kg. His blood pressure was 98/60, heart rate 96, oxygen saturation 93% on room air. Mr. X was using a walker today and stands with a somewhat kyphotic posture. He had no palpable lymphadenopathy of the cervical or supraclavicular areas. On respiratory exam, he had an expiratory wheeze of the right lower lung with decreased breath sounds of the right upper lung. The abdomen

was soft with mild tenderness in the right lower quadrant to deep palpation. There was no hepatomegaly nor any splenomegaly. On neuromuscular examination, there was decreased sensation of the right upper extremity in an ulnar distribution. As well, there was some antalgic weakness of the right arm in C7 and C8 distribution. There was some palpable tenderness to the distal right forearm. Reflexes were somewhat diminished in the right upper extremities bilaterally. There was right lower extremity weakness with 4/5 strength on hip flexion and knee extension. There was otherwise 5/5 muscle strength in the lower legs. Sensory exam of the lower extremity revealed some blunting distal to the mid lower leg. Patellar and ankle jerk reflexes were intact bilaterally. There was 2+ pitting edema of the lower limbs bilaterally. On examination of the back, there was some tenderness over the spine at approximately L3. There was minimal tenderness to palpation of the right posterior ribs.

INVESTIGATIONS: CT of the thorax from September 21, 2007, showed a 5.3 cm mass in the right upper lobe extending to the superior right lower lobe and as well some destruction of the posterior rib. In addition, there are multiple small mediastinal nodes including subcarinal lymphadenopathy. A lung biopsy was completed October 09, 2007 which shows poorly differentiated squamous cell carcinoma. An ultrasound of the abdomen on October 17, 2007 shows two hyperechoic liver lesions which may be a metastatic disease versus hemangiomas. A bone scan on October 15, 2007 shows abnormal uptake in the posterior right seven the eighth ribs. As well, there is an abnormal focus in the anterior left ninth rib which may correspond with a fracture. There is abnormal uptake of the legs bilaterally consistent with hypertrophic pulmonary osteoarthropathy.

Blood work was last done on October 18, 2007 including a white blood count of 16.5, hemoglobin 98 and platelet count of 506. Creatinine was 48, urea 2.8.

ASSESSMENT AND RECOMMENDATIONS: Mr. X is a 67 year old gentleman with a recent diagnosis of locally advanced squamous cell lung cancer. He has a tumor in the right upper lobe with extension into the posterior chest wall. Mr. X has had a recent admission to palliative care for pain control with discharge on October 23, 2007. He continues to use the Dilaudid pump for pain control. He has also undergone palliative radiation therapy to control pain secondary to bony metastatic disease.

Today we discussed palliative chemotherapy which may also be helpful in controlling metastatic bone pain as well as improving this patient's nutritional status. Mr. X is keen to proceed with chemotherapy as soon as possible. He has been made aware that chemotherapy can have side effects including decrease in blood counts which increases the risk of infections. We have advised him to obtain a thermometer for home temperature monitoring.

Mr. X's recent hoarseness along with history of difficult swallowing and previous pneumonia is concerning for recurrent laryngeal nerve paresis. We have asked Mr. X to inform us should he experience further episodes of coughing with swallowing. At that time we would submit a referral to Otolaryngology for investigation and consideration of vocal cord stenting.

We will proceed with Carboplatin/Gemcitabine chemotherapy to start next week. We have also requested a CT of the head to complete staging, particularly in light of abnormal neuromuscular findings including right arm sensory changes and right leg weakness.

A return to clinic appointment has been made for repeat assessment in four weeks' time.

Thank you for involving us in the care of this patient.

Sincerely,

E. Helpall, MD
3rd Year Clinical Clerk for
M. Cureall, MD, FRCPC
Medical Oncologist



Elena B. Wolf Award

The Department of Oncology offers the **Elena B Wolf Award** to two students each year for the best essays in the field of cancer research or treatment. This award was endowed in 1972, in the memory of Mrs. Elena B. Wolf. Eligible candidates must be enrolled in the third year clinical clerkship at the Schulich School of Medicine, The University of Western Ontario.

We encourage submissions are in essay format and should be of a reflective nature and emphasize a unique oncological patient-centred clinical learning experience or speak to an existential, social, ethical or humanistic aspect of oncology or oncology practice.

The essay will be graded according to content, originality, and thoroughness of the literature review, style and organization. If more than one author writes the paper, it must be made clear that the person applying for the award did most of the work.

Applications are now to be completed on the online process and questions can be submitted to awards.ume@schulich.uwo.ca. Submissions are not to surpass 1200 words, submitted online. Submissions will be adjudicated by the Department of Oncology of the Faculty of Medicine & Dentistry.

Prize

Two prizes in the amount of \$200 and \$250 will be awarded.

V Encourages students to follow up on learning with extra work (readings, presentations, etc.):

1 Never encourages extra learning 2 3 4 5 6 Always promotes learning 7

VI Communicates clear and reasonable expectations that are appropriate to the students' level of ability:

1 Never communicates expectations 2 3 4 5 6 Always communicates 7

VII Respects diverse talents and is flexible with students' different learning needs:

1 Not flexible at all 2 3 4 5 Actively tries to ensure students are accommodated 6 7

COMMENTS: Please describe why you believe this resident is an excellent teacher. All comments are reviewed and play an important part in the selection of the Award winner.

Please return this form to the Postgraduate Medical Education Office, Schulich School of Medicine & Dentistry, The University of Western Ontario (UWO, Medical Sciences Building, M103) at the end of your rotation. **Final Deadline for receipt of all nominations is August 31, 2014.** Thank you!

THE DR. ED BRECEVIC AWARD (ANNUAL AWARD)

This award is for any clinical clerk or resident who demonstrated an exceptional bedside manner and compassionate care and is nominated by any staff member, colleague or fellow student.

The winner of this award receives a personal engraved plaque during the annual Research & Education Day ceremony, normally held in June of each year. The award winner will also have his/her name engraved on a large plaque that is on display in the London Regional Cancer Centre.

Please submit names of nominations, and preferably a short statement about why the nominee is a good candidate for this award, and submit to Dr. Tracy Sexton (tracy.sexton@lhsc.on.ca) by May 1st each year.