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ST. MICHAEL'S HOSPITAL

A teaching hospital affiliated with the University of Toronto

INFORMATION PACKAGE

FOR INTERN/RESIDENTS

ON THE HEMATOLOGY AND ONCOLOGY
ROTATION

AT ST. MICHAEL'S HOSPITAL



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2. Introduction

Welcome to the **Hematology -Oncology** service at St. Michael's Hospital. This rotation is designed to provide a broad exposure to many areas of hematology and oncology (objectives and evaluation from the college of physicians and surgeons are outlined) At SMH internal medicine residents do 1-2 month rotation on hematology–oncology combined. However from July 2005 oncology rotation is mandatory therefore this rotation will be divided into one month on each Hematology Oncology. The rotation will consist primarily of ambulatory clinics, inpatients consultations, and formal teaching sessions. By the end of the rotation, trainees should be familiar with investigation and managing a wide variety of hematology and oncology problems.

This booklet will provide you with a practical guide to different aspects of the service. At the start of the rotation you will receive a brief orientation, much of which is covered in this booklet. **Objectives** of the rotation and learning goals of the of the trainee will be reviewed by Dr. Haq (divisional director of education) at the beginning of each rotation, at mid-point an interim evaluation will occur, and at the end of the rotation a written evaluation will be provided and discussed with the trainee. If any problems arise during the rotation please let Dr. Haq (416-864-5912) know as soon as possible , Any issues can be discussed at any point in the rotation, many problems are correctable, but only if we know about them. We are dedicated to working as hard as possible to ensure that you have a well-rounded educational experience.

3. Overview

The hematology- oncology rotation at St. Michael's Hospital will offer you opportunities for developing an understanding and approach to diagnose and manage common hematologic problems as an internist.

Internal medicine trainees have to do one month mandatory rotation on Oncology service. Cancer is on the rise and effects the population at large. Prevention and screening for early diagnosis of cancer is our top priority as an internist and in most subspecialties of medicine. Importance of Risk factors and genetic predisposition to cancer development is recognized in many cancers and will be emphasized during the rotation. On the oncology service management of patients with the diagnosis of different cancers will be addressed. The mandate is to provide the best care possible for each patient seen in terms of:

1. Diagnosis (history, physical examination, focused investigations for staging of cancer).

2. Multidisciplinary nature of cancer management (surgeons, medical, radiation oncologist and family physicians)
3. Understanding of the pathology of different cancers clinicopathologic correlation
4. Principles of cancer treatments. Adjuvant and palliative
5. Communication and support to the patient and families during treatments, complications and end of life issues.

These categories reflect a synthesis of the old style of practice (diagnosis & treatment) with the new requirement of the Royal College of Physicians and Surgeons of Canada (RCPSC), which is to promote a **patient centered** environment in which physicians are expected to be responsible to societal needs.

The Royal College of Physicians & Surgeons of Canada initiative for the new millennium, identifies seven essential skills for the specialist physician:

- (1) Medical expert
- (2) Communicator
- (3) Scholar
- (4) Manager
- (5) Collaborator
- (6) Health advocate
- (7) Professional

Objectives for Internal medicine trainees on Hematology-Oncology Rotation (UofT 2004)

1. Medical Expert

Hematology

- To efficiently diagnose patients presenting with undifferentiated anemia, leucopenia, thrombocytopenia, pancytopenia, erythrocytosis, leukocytosis and thrombocytosis
- To demonstrate an approach to the investigation of lymphadenopathy and splenomegaly
- To manage patients with suspected or known bleeding tendency
- To manage patients with known or suspected thromboembolic disease
- To manage patients with known or suspected hemoglobinopathies
- To diagnose, stage and refer for therapy patients with known or suspected lymphoproliferative diseases, myeloproliferative diseases, and plasma cell disorders
- To know the blood components and related transfusion products that are available in Canada, the clinical indications for their use and the side effects that they may produce. To understand the principles of therapeutic apheresis and appreciate its therapeutic benefits.
- To efficiently manage hematologic and oncologic emergencies including febrile neutropenia, hyperleukocytosis, severe thrombocytopenia, suspected TTP and DIC
- To recognize common blood film abnormalities including different types of anemia, megaloblastic and dysplastic changes and presence of blasts
- To perform a bone marrow aspirate and biopsy safely and with minimal discomfort and appropriately obtain informed consent for the procedure

Oncology

To be aware of common risk factors and have an evidence-based approach to screening for breast, colorectal, lung, prostate and gynecologic cancers

To understand the natural history, goals of therapy and approach to the therapy of breast, colorectal, lung, prostate and gynecologic cancers To understand the principals of cancer treatment and the general mechanism of action of common anticancer therapies including chemotherapy, radiotherapy, hormonal therapy, immunotherapy and stem cell transplantation

To recognize and manage common immediate and long term complication of chemotherapy including febrile neutropenia, cardiac dysfunction, neuropathy, nausea, emesis, mucositis and fertility

To efficiently manage oncologic complications including febrile neutropenia, spinal cord compression, obstruction of SVC, biliary tree or ureters, malignant hypercalcemia and tumor lysis syndrome.

To effectively manage pain in a patient with cancer and be aware of resources available

2. Communicator

To efficiently take and convey a history for suspected bleeding tendency, iron deficiency and suspected malignancy

To “break bad news” to a patient or family member in a professional and compassionate manner

To convey a verbal and written consult request in a clear and accurate manner and provide a consultant report in the same way

To initiate discussion of palliative care

3. Scholar

To be able to critically assess the literature in Hematology/Oncology and in particular to be able to appraise randomized trials of new cancer treatments

To understand the hierarchy of outcomes in cancer studies, including survival, relapse-free survival, response rates, toxicities and surrogate outcomes

4. Manager

To learn to appropriately allocate time within a busy ambulatory care setting

To balance competing commitments in the outpatient and inpatient (consult) settings

To understand the duty of physicians to practice responsibly within a cancer care organization

To develop an approach to practicing in an environment of limited resources and understand how policy decisions regarding funding of new agents are made

5. Collaborator

To function as part of a multidisciplinary team caring for the cancer patient

To collaborate effectively with other medical specialties

6. Health Advocate

To recognize the inherent tension between the physician's role as "gate-keeper" and patient advocate

To be aware of the community resources available to the cancer patient .

7. Professional

To demonstrate professional attitudes in interactions with patients and other health care professionals.

To complete assigned tasks and attend clinical and teaching commitments consistently and punctually.

Hematology/Oncology at SMH

The Hematology/Oncology rotation is a 2-month block in which residents will spend roughly half their time in both Hematology and Oncology. The nature of these two experiences will differ somewhat, but the core objectives to be covered are outlined below.

Residents will be exposed to a wide variety of conditions with emphasis on an approach to the diagnosis of undifferentiated conditions, cancer epidemiology and screening and a general understanding of the broad principles of therapy of common hematologic and oncologic conditions. As well a more detailed approach to the management of complications of these conditions and their treatment, especially medical emergencies and palliative care will be emphasized. These are reflected in the new ITERS, which are now mandated to be completed every month in order that any weaknesses may be quickly identified and addressed. During your hematology/ oncology rotation at SMH and the above assessment criteria will be addressed through:

- 1. Ambulatory clinics**
- 2. Consultation service**
- 3. Formal interactive teaching rounds**

Objectives for Trainees in Hematology Rotation at SMH

General objectives:

1. To be able to diagnose and manage common hematologic problems as an internist
2. For trainees from internal medicine (and other disciplines) the combination of learning consists of ambulatory care clinics, and consultation service coupled with regularly scheduled teaching sessions, case rounds and morphology rounds which enable the trainee to consolidate an understanding of hematology, focused on patient care.
At the end of the rotation, the trainee should expect to have an understanding of the diagnosis and treatment of the following common hematologic disorders thrombotic thrombocytopenic, bleeding disorders
3. The trainee should also have developed an approach to evaluating common hematologic problems anemia , thrombocytopenia ,lymphadenopathy,and splenomegaly

Specific objectives:

1. The ability to perform a full history and focused examination of hematology patients with confidence.
2. An approach to diagnose and manage common hematologic problems such as anemia, thrombocytopenia and others as listed above
3. Diagnosis and management of thromboembolic disease
4. Diagnosis and management bleeding disorders

Objectives for Trainees in Oncology Rotation at SMH

General Objectives:

1. To be able to perform a full history (risk factors and family history) and focused examination (metastases) of oncology patients with confidence.
2. To have an understanding of screening for different cancers breast, colon ect.
3. To understanding the clinicopathological correlation (sessions with the pathologist and cases)
4. To understand Multidisciplinary approach to cancer mangement
5. To understand the diagnose, staging and treatment of different cancers.
6. To understand the principles of chemotherapy and management of side effects of chemotherapy
7. To be able to provide Supportive care and Palliative care
8. To have the basic understand of principles of radiation therapy in oncology

Specific objectives:

1. To be able to prevent cancer by knowing the risk factors and genetic factors (breast and colon and ovarian cancer).
2. To understand the guidelines for screening of breast, colon, prostate and cervix.
3. To understand the multidisciplinary approach to cancer treatments ie the role of the oncologist, pathologist, surgeons and radiation oncologist in managing cancer patients in the new millinium for the best care.
4. To be able to diagnose and manage common oncologic problems as an internist and to be able to refer patients such as patients with breast lump, abdominal mass, anemia etc.
5. To have a good understanding of indications of chemotherapy and management of toxicity.
6. To be able to manage acute oncologic emergencies and to recognize the toxicities of treatment.
7. To be able to discuss bad news, treatment options, and toxicity in a supportive manner with patients and families.
8. To be able to provide supportive care such as pain control
9. To be able to critically review the evidence in oncology.

Ambulatory Care Clinics

It is in this setting that trainees see the majority of HEMATOLOGY- ONCOLOGY patients with a wide variety of problems.

Hematology and oncology clinics will give you the opportunity to evaluate, investigate, and manage the common ambulatory problems in these specialties. This is a critical part of

your rotation, as you will encounter these problems regardless of which branch of medicine you choose.

The resident will spend each morning in an outpatient clinic or office (**9-12AM**). A schedule of these clinics will be provided at the start of the rotation. You will be expected to attend all of the clinics, unless there is an emergency consult which requires your immediate attention. Non-emergency consults can be done in the afternoon. The focus will be on seeing new consults and selected follow-ups, which are deemed to be teaching value. There is a **General Hematology** teaching clinic on 4-Cardinal Carter each Wednesday starting at 8:00a.m. which all residents on hematology are expected to attend. All other **outpatient clinics** take place in Medical Day Care Unit (MDCU) on 2-Queen. Oncologic care is multidisciplinary and residents rotating through oncology will spend time on these **multidisciplinary clinics**. There will be multidisciplinary clinics from 9-12 pm on 3queen (CIBC Breast centre) and on 4 cardinal carter (colorectal cancer), 6 bond respirology clinic. Tumour board sessions are once a month.

Consultations

Hematology /oncology consultation service is provided to all patients at St. Michael's Hospital. The number of consultations is variable, ranging from 5- 12 plus per week. **Consultations** must be seen promptly, the same day if possible and reviewed with attending staff.

Urgent consultations must be reviewed immediately after assessment by the trainee.

Inpatients consultations are an important component of the hematology/ oncology rotation, as they provide learning material for problems in all aspects of acute hematology and oncology (diagnostic, management difficulties, supportive and palliative care).

Arrange a fixed time of the day to review consults with the attending staff. It is strongly suggested that all residents on the service be present when the consult is reviewed, so that everyone can learn from it. Hematology resident when on the service will supervise the junior housestaff,

Some hematology/oncology consults will come from the Emergency Department. If the patient has been cared for by a member of staff who is not on the consult service, there is the option of reviewing the case with that person rather than the attending staff member who is on the consult service. If the patient requires admission to our inpatient ward, please format your consult note as an admission note, and write the admitting orders.

Please keep the **consult list** up to date. This file is on the desktop of one of the computers at the 2-Queen nursing station.

Hematology Staff (4 weeks rotation)

Drs Teitel, Garvey, Dotter, Hicks and alternate staff coverage for hematology consults (you will be given the attending schedule at the start of your rotation).

Oncology Staff (4 weeks)

Drs Haq, Brezden and Schipper (schedule will be available)

Hematology –Oncology Teaching Rounds

One hour teaching seminars are scheduled for either Monday morning or Thursday afternoon, a schedule will be distributed. Check ahead with the staff to confirm the time.

The topics have been chosen to cover a wide range of key hematology and oncology problems, including morphology sessions at the microscope.

Morphology rounds are scheduled every Tuesday afternoon from 1:00 – 2:00 pm with Dr. Wahbi Hammouda in the main lab.

Seminars are scheduled for the second and fourth Wednesday of the month at 1:00p.m. immediately following grand rounds. All staff attend these seminars. All Residents will be asked to present a topic of their choice at one of these seminars during their rotation (please select a topic relevant to the objectives of the rotation) When there is no residents presentation scheduled, the staff will present interesting or difficult cases (schedule will be distributed).

You should make every effort to attend Medical Grand Rounds every Wednesday at noon in the Paul Marshall Lecture Theatre located on the ground floor (just inside the Queen St. entrance).

Ward Responsibilities

The inpatient service ward is on 2-Queen.

Hematology Rotation

Trainees will not have primary inpatient responsibilities but may admit or transfer patients to this ward from Emergency or the Medical Day Care Unit.

Attending staff and Dr. Dory Abosh (hospitalist) and assistants (nurse practitioners) cover the ward who will handle routine admissions and discharges. However, trainees may have an opportunity to assist in the management of selected patients with interesting hematologic problems (e.g. TTP, ITP, etc).

Oncology Rotation

In a 4 week rotation you may take the responsibility of inpatients admitted by you such as writing chemotherapy orders with the guidance of the oncologist and the pharmacist, or other oncologic problems.

Multidisciplinary rounds /bedside rounds on Wednesday at 9:30 am would be of educational value for oncology rotation.

Residents will be on the night call schedule for 2Queen. You may also occasionally be asked to assist with an acute medical problem on the ward if this is necessary, and will be expected to do so.

You will also have an opportunity to gain experience in doing hematology- oncology related procedures (bone marrows, intrathecal chemo, etc.), under direct or general supervision, depending on your familiarity with these procedures.

Night Call

You will have up to 5 hematology/oncology night calls per month during your rotation. You will be responsible for all patients on 2-Queen, a 20-bed unit which includes 5 beds designated for the HIV service (this excludes any off-service patients who may be on the unit at the time). You will also be responsible for ward and Emergency hematology/oncology consults, but not HIV consults. This is home call, not in house. You will be removed from the SAR call pool during this rotation. The staff physicians have a

weekend call pool but not a weekday pool. Therefore if you need to speak with a staff member when you are on call at night you should call the appropriate person. For patients on 2-Queen this will be the admitting staff. For emergency or ward consults, this will generally be the staff on either the hematology or oncology the consult service. However, if a patient in emergency is being followed by another staff member it will be more appropriate to call him or her, regardless of who is on consults; for example, all calls for emergency hemophilia management should go to Dr. Teitel, who is director of the hemophilia program. If you were on call the previous night and admitted a patient to 2 queen, or something significant occurred to an inpatient on our ward, please let the attending staff and ancillary staff know the following morning. If you are on call, it is also a good idea to get in touch with Dr. Abosh / nurse practitioner just before 5:00p.m. to obtain sign-out, particularly regarding any patients who may present a problem.

There are printed sign-out lists left on the 2 QUEEN every day (ON COMPUTER); you should pick these up before you go home in case you get called

PRACTICAL GUIDE TO COMMON PROBLEMS ON THE HEMATOLOGY- ONCOLOGY SERVICE

1. Transfusions:

You are reminded to always obtain an informed consent for transfusion and to document this on the chart. Patients transfused for the first time will need to sign a transfusion consent form after you have explained the risks and benefits of this procedure.

A. Red Blood cells – Usually given as at least 2 U packed RBC (there are very few indications for a an elective single Unit transfusion in an adult). The indication to transfuse should be based primarily on the patient's signs and symptoms and physiology rather than actual hemoglobin level. However, in patients who are pancytopenic post-chemotherapy (e.g. the acute leukemic), we usually transfuse to maintain the hemoglobin above 80 g/l. It is recommended to transfuse according to patient requirement however there has been good correlation of poor quality of life and low hemoglobin and therefore patients on cancer treatments are either transfused more frequently to keep hemoglobin higher or given erythropoietin.

B. Platelets – Generally given as five units pooled platelet concentrate. If you are ordering the platelets, you must also phone the blood bank (5084) to let them know. You may, while on call, also be called to approve a platelet transfusion from another ward. For patients who are pancytopenic post-chemotherapy, our usual policy, is to administer prophylactic platelet transfusions to maintain a platelet count $\geq 10 \times 10^9/L$. This is based on studies indicating that spontaneous blood loss from the GI tract increases below platelet counts of $10 \times 10^9/L$. However, in patients who are actively bleeding (not including petechiae) a higher level is usually maintained ($20-50 \times 10^9/L$ depending on the severity of the bleed). Superimposed platelet function defects or coagulopathies may also require transfusion at a higher platelet count. Normally a 5 unit platelet transfusion should raise the platelet count by $20-50 \times 10^9/L$. Since a normal platelet lifespan is approximately 10 days, a platelet transfusion ideally should last an average of about 3-5 days. Factors which may decrease platelet survival include fever, infection, DIC, certain drugs, hypersplenism or platelet antibodies. For platelet **autoantibodies** (autoimmune thrombocytopenia), platelet transfusions are not indicated as the platelets are rapidly

removed and no response is seen. **Alloantibodies**, i. e. antibodies to donor platelets, are a common cause of platelet refractoriness, particularly in multiply-transfused patients. If this is suspected on the basis of a suboptimal 1-hour post-transfusion platelet count on two occasions in the absence of factors known to cause platelet destruction such as splenomegaly, DIC, bleeding or infection, the Blood Transfusion Services should be contacted and blood sent through the Blood Transfusion Services to the Canadian Blood Services to test for alloantibodies. If alloimmunization is confirmed, HLA- matched single donor platelets collected by plateletpheresis may be requested

C. Transfusion Reactions: Febrile reactions are most commonly caused by leukocyte antibodies or leukocyte-derived cytokines in the blood product. They occur more commonly with platelet transfusions because platelets are stored at higher temperatures, causing more cytokine release. However, febrile reactions are seen less often than in the past, since all cellular blood products are leukodepleted by the Canadian Blood Services. A febrile reaction can be treated symptomatically with antipyretics and steroids if necessary (e.g. hydrocortisone 50-100mg IV), and patients with repeated febrile reactions may be premedicated with these for subsequent transfusions. Rigors, if severe, can often be rapidly abolished by IV Demerol 25-50 mg (the mechanism is unclear). For severe febrile reactions which do not respond adequately to premedications, or washing red cells (removing the plasma) can often be effective. These procedure are time-consuming for the Blood Transfusion Service and special request must therefore be made through Dr. Hammouda.

Urticaria due to limited-specificity anti-IgA antibodies can be treated with antihistamines such as benadryl. Another common preventable acute complication is fluid overload, particularly in elderly patients or those with CHF; in such patients, red cells should be given more slowly, with furosemide if necessary. A severe reaction should prompt a call to the Blood Transfusion Service to test for evidence of hemolytic transfusion reaction. In fact, all adverse reactions to transfusion should be reported to the Blood Transfusion Service

D. Plasma products: - Fresh frozen plasma is generally only for replacement of multiple clotting factor deficiencies (e.g. DIC, liver disease) with active bleeding or for prophylaxis for a surgical procedure. It should not be given for volume replacement. **Cryoprecipitate** should be given for fibrinogen replacement only.

For **hemophilia A and B**, specific factor concentrates are available. For **hemophiliacs with inhibitors**, alternative products include porcine Factor VIII, Factor VIIa and FEIBA. For information on specific factor concentrated, see the section on Hemophilia Care.

IVIg is given to selected patients with acquired or hereditary immunodeficiency states characterized by severe hypogammaglobulinemia and recurrent bacterial infections. It is also given for emergency treatment of severe ITP, to raise the platelet count in the setting of an acute hemorrhage or in preparation for urgent surgery. The total dose in this setting is 2 grams/kg divided over 2 or 5 days. The standard treatment of ITP is still prednisone. IVIg is sometimes used in other situations as well, not always supported by well-controlled studies.

E. Special requests: CMV negative blood products should be requested for patients who are CMV seronegative and are immunosuppressed (e. g. by HIV infection or early post-bone marrow transplant), or are potential candidates for marrow transplant. This is to prevent exposure to CMV which can reactivate post-BMT and cause a lethal infection.

Irradiated blood products should be requested for patients who have marked suppression of cell-mediated immunity. This is to prevent leukocytes in the donor product from mounting a graft-versus-host reaction in the recipient, which has a high mortality. This primarily applies to patients who have undergone bone marrow transplant within the past 90 days, as to selected other patients such as those with Hodgkin's disease or organ transplants.

2. Febrile neutropenia:

Severe neutropenia is usually defined as an absolute neutrophil count (ANC) $\leq 0.5 \times 10^9/L$. Below this level the body's ability to deal with bacterial pathogens is severely impaired. As a result, bacteremia, which may be of little consequence in someone with a normal neutrophil count, can produce septic shock and be rapidly fatal in a matter of hours. The first sign of such an infection is usually a fever. For this reason, fever in a severely neutropenic patient is a medical emergency.

If you are called to assess a severely neutropenic patient with a fever (defined as temp. $\geq 38.2^\circ C$), whether on the floor or in emergency, the steps to take are as follows:

1. Do a clinical assessment to look for an obvious source of infection.
2. Order two sets of blood cultures to be done immediately – if the patient has a central line, one set should be drawn through the line.
3. Order urine culture, other cultures (e.g. stool, sputum) as indicated by the patient's symptoms, and a chest x-ray.
4. As soon as the blood cultures have been drawn, **immediately** start the patient on IV broad spectrum antibiotics (see below). It is your responsibility to ensure that the first dose of antibiotics is given promptly.

The choice of initial empiric IV antibiotics in these patients varies from centre to centre (Febrile Neutropenia protocol at SMH attached in the end). However, the most important principle is to provide adequate coverage for gram negative bacilli, esp. Pseudomonas but also E. Coli, Klebsiella, etc. Our standard regimen is Tobramycin 5-7 mg/kg IV q24h (avoid tobramycin if patient is on cisplatin as risk of nephrotoxicity) plus cefazolin (Ancef) 1-2 gram IV q8h.

Order pre- and post-Tobra levels with the 3rd dose. For patients with mild renal dysfunction, the Tobramycin dosing interval should be increased, but the dose should be maintained (it is the trough level, not the peak, that determines renal toxicity). If severe renal dysfunction is present, or acute renal deterioration is occurring, piperacillin-tazobactam monotherapy with dose adjustment is an alternative. Concurrent therapy with G-CSF 5 microgram/kg (300 -480 microgram) SC shortens the duration of neutropenia and reduces risk of serious infection .

Subsequent measures depend on culture results. However, if cultures are negative and the patient remains febrile after 48 hours, we usually add a second antipseudomonal agent, Piperacillin 4 grams IV q6h. If a patient is allergic to penicillin, ciprofloxacin or ceftazidime are acceptable alternatives. However, piperacillin or ciprofloxacin do **not** provide adequate single agent gram negative coverage in these patients.

If the patient is still febrile another 24 hours, and has a central line, we often empirically switch Cefazolin to Vancomycin to provide additional coverage for coagulase negative staphylococcus, a frequent cause of central catheter infections. If such an infection is

strongly suspected and does not respond promptly to appropriate antibiotics, the central line may need to be removed.

If the fever persists after another 2-3 days, with negative cultures and persistent severe neutropenia, patients are usually started empirically on systemic **antifungal** therapy. Fungal infections, particularly candida and aspergillus, are a common cause of persistent fevers in patients with prolonged neutropenia, and are notoriously difficult to diagnose. It is important to re-evaluate febrile neutropenic patients on an ongoing basis, as infections can progress very rapidly in the absence of neutrophils. Common sites to examine at least once daily include the mouth, chest, central lines and perianal regions. If a perianal abscess is suspected, anaerobic coverage (metronidazole or clindamycin) should be added. Do **NOT** perform rectal examinations in neutropenic infections as this may lead to bacteremia.

Diarrhea is frequently caused by Clostridium difficile colitis and can be diagnosed by looking for toxin in the stool. Treatment is metronidazole; oral vancomycin is an alternative.

Antibiotics are usually continued until the neutropenia has resolved **and** the patient is afebrile for at least several days. Stopping antibiotics while the patient is still severely neutropenic has been associated with a high incidence of recurrent sepsis in previous studies, but may be considered if the patient has been afebrile for a prolonged period (at least 2 weeks), is stable and can be closely monitored. Do not stop antibiotics without first discussing it with the attending.

3. Chemotherapy :

Cancer chemotherapy drugs are used in several settings:

1. With curative intent (e.g. certain lymphomas and leukemias)
2. In an adjuvant setting, to reduce the risk of recurrence following surgery (e.g. localized breast cancer or colon cancer)
3. With palliative intent, i.e. to control symptoms by reducing disease (e.g. metastatic breast cancer, low-grade lymphoproliferative disorders etc)

With potentially curable malignancies, chemotherapy treatment tends to be more aggressive, usually involves combinations of agents at higher doses, and is often more toxic. In a palliative setting, quality of life is of greater importance and the treatment regimes are therefore less toxic, usually utilizing one or two drugs.

Many of our regimens are given in an outpatient setting, in the Medical Day Care Unit. Patients who are receiving complicated regimens requiring continuous infusions, dose-intensive regimens resulting in severe prolonged marrow suppression, or patient too ill to remain at home, are admitted to hospital for their chemotherapy. 2-Queen is the only ward where nursing staff is certified to give chemo. Patients on other wards who need chemo require transfer to this floor. If this is not possible (e.g. ICU patients), the physician usually has to administer drugs.

Booklets are available on the floor and in the MDCU which list the chemotherapy regimens we often use. Other regimens are in filing cabinets in the nursing station. For more detailed information about the individual drugs, the Cancer Chemotherapy

Handbook (Dorr & Fritz) is useful. A few protocols are on printed sheets where you only have to fill in the doses.

A. Chemotherapy Drug Toxicity:

1. **Nausea and vomiting** are among the most common complications of chemotherapy agents. However with 5HT3 ANTAGONIST (ondansetron and granisetron) chemotherapy can be administered as an outpatient. The likelihood and degree of symptoms vary widely with different agents and dosages. For emetogenic drugs, we generally premedicate the patient:

i: Mildly emetogenic drugs (e.g. moderate-dose cyclophosphamide, 5-FU) -

Prochlorperazine (Stemetil) 10mg PO + Decadron 10mg IV +/- Lorazepam 1mg SL, then Stemetil 10mg PO q6h prn i.

ii: Highly emetogenic drugs (e.g. high-dose cyclophosphamide, cisplatin, doxorubicin) –

Ondansetron 8mg PO + Decadron 10mg IV, then Ondansetron 8mg PO q12h X 3 doses.

2. **Mucositis** – Due to direct toxicity to cells lining the GI tract. It is more often seen with higher-dose regimens for ABMT/ or in regimens used for colon and breast cancer such as those used in with 5 fluorouracil/ adriamycin then is characterized by sore mouth, odynophagia.

Treatment is mainly symptomatic –sore mouth, with Tantum mouth rinses or 2% viscous Xylocaine. In severe cases, the patient may have constant throat pain and swallowing may be difficult. In these cases, an IV Morphine drip may be necessary until symptoms improve.

It is important to exclude other causes of these symptoms, e.g. infectious diarrhea or candida esophagitis or thrush

3. **Myelosuppression** – see section on Febrile neutropenia and Transfusion

4. **Diarrhea** – chemotherapy induced diarrhea is an acute emergency with` drugs such as irinotecan used for colorectal cancer. Prophylactic loperamide is used in all cases however if diarrhea persists after loperamide may need to be admitted for iv fluids and ciprofloxacin may be helpful. Stool to be sent for clostridia

B. Other Chemotherapy Issues:

1. **Tumour lysis syndrome** is caused by rapid lysis of tumour cells by (usually chemotherapy drugs, with release of intracellular products. The full blown syndrome is characterized by hyperuricemia, hyperphosphatemia and hyperkalemia. This can then lead to acute renal failure which, in the setting of massive K release, can be rapidly fatal. Tumour lysis syndrome is seen most often in patients with rapidly-dividing malignancies (acute leukemia, aggressive lymphomas, small cell lung cancer) with bulky tumours such as greater than 10 cm, although it is occasionally seen in lower-grade malignancies as well. In patients at risk for this, we routinely use measures **to prevent** or minimize tumour lysis. This includes **allopurinol, aggressive hydration +/- alkalinization of the urine.**

2. **Adjustment of chemotherapy** doses must sometimes be made for patients with hepatic or renal failure or myelosuppression. For example, the half-life of methotrexate is

significantly prolonged in patients with liver dysfunction (see page 14 for more details). It is a good idea to check with the pharmacist or attending regarding such patients prior to ordering these drugs.

3. **Intrathecal chemotherapy** is given in patients with established CSF leukemia/lymphoma, as well as prophylactically in certain situations (e.g. ALL, high-grade lymphomas) where the risk of meningeal spread is high. The usual drugs used are methotrexate 12 mg or Ara-C 50-70 mg. They should always be ordered in preservative-free NS. First an equivalent volume of CSF is withdrawn and sent for appropriate studies (cell count, cytology +/- others if indicated), then the drug is given by push. The drug can be given via the lumbar route or through an Ommaya reservoir (inserted by the neurosurgeon into the lateral ventricle of the brain). The latter is particularly useful if frequent treatments are needed or fixed leptomeningeal disease in the brain is present, as drug concentrations in this area are higher through an Ommaya.

C. Hematopoietic Growth Factors:

Granulocyte colony stimulating factor (G-CSF, Neupogen) is sometimes used to hasten neutrophil recovery in patients with severe neutropenia and life-threatening infections. It is also used to prevent neutropenic infections or chemotherapy dose reductions in patients receiving chemotherapy with curative intent. It is not generally used for this purpose with palliative chemotherapy. The usual dose is 5 ug/kg/day SC (rounded off to the nearest vial, either 300 or 480 ug). Neulasta is now available for patients with prolonged neutropenia despite neupogen. Need to accurately assess patients for neupogen as this drug is fairly expensive.

Erythropoetin (Eprex) is sometimes used for symptomatic cancer-related anemia, either on or off chemotherapy. In this setting it must be used at high doses (at least 150 U/kg 3x week), which is also expensive. It takes at least 4 weeks for its effects to be seen.

D. Coagulation problems:

Many hematology consultations relate to coagulation problems, e.g. prolonged PT/PTT in an ICU patient. Many of these patients will benefit from special clotting investigations performed in our laboratory. Such tests, including factor assays, generally require a hematology consult for approval. These tests are done on weekdays from 8:00-5:00.

If you are asked to see a consultation for a coagulation problem, please call the special coagulation lab (local 5123) immediately. They can obtain the necessary blood samples and work through the diagnostic routine while you are seeing the patient. You can then review the consult with the staff physician on consults and have the lab results available. Do not wait until late in the day before contacting the lab as the tests usually take several hours to perform.

Remember, blood samples for coagulation assays should never be drawn from arterial lines which contain even miniscule amounts of heparin as this seriously affects the coagulation results.

On evenings or weekends, the routine hematology lab can perform PT/INR, PTT, thrombin time, fibrinogen and D-dimers. More detailed investigations will not generally be

done until the following weekday unless approved by Dr. Garvey or the hematologist on call.

Special investigations for hypercoagulable states (e.g. antithrombin III, Protein C & S, factor V Leiden) also require a hematology consult. If you are asked to see such a consult and feel such a workup is indicated, please call the special coagulation lab and tell them what you would like done. Remember, it is best to draw blood for such investigations before initiating anticoagulation therapy as these drugs may interfere with some of the assays – for example, Protein C and S are Vitamin K-dependent and will therefore be affected by warfarin.

A. Heparin-induced thrombocytopenia (HIT): Guideline for approach to HIT

This condition usually occurs 5-10 days after initiation of heparin therapy and is characterized by a >50% drop in platelet count. It may in some instances be associated with venous or arterial thrombosis (HITT). Although clinical assessment is very important in evaluating whether HIT is present, laboratory confirmation is also important. At our centre we do an ELISA assay for confirmation. Requests for HIT assay will generally be batched and performed on the next available run.

“Urgent” HIT assays are rarely justified; the initial management should be based on the clinical *a priori* probability. The management includes immediate discontinuation of the heparin (including heparin used to flush arterial lines).

Alternative anticoagulants which can be used include danaparoid (orgaran), argatroban, and hirudin. Low molecular weight heparins should not be used in HIT as the cross-reactivity with regular heparin in HIT is high.

Orgaran (danaparoid) is a heparinoid compound (a mixture of glycosaminoglycans). It has an advantage of rapid onset but has a longer half-life than heparin (24-32 hours, longer in renal failure). There is also no specific antidote or reversing agent available.

Therapeutic dosing is as follows:

Bolus:< 60 kg 1500 U

60-75 kg 2250 U

75-90 kg 3000 U

>90 kg 3750 U

This is followed by 400 U/hr x 4 hours, then 300 U/hr x 4 hours, then a maintenance dose of 150-200 U/hr. Treatment can be monitored by measuring Factor Xa levels (therapeutic range is 0.5-0.8).

For DVT prophylaxis, Orgaran is usually given at a dose of 750 Units SC twice daily.

Hirudin (Lepirudin) is a direct thrombin inhibitor. It is a recombinant substance similar to the naturally occurring anticoagulant in leeches. It can be used as an alternative anticoagulant in heparin-induced thrombocytopenia as the HIT antibody does not cross-react with it. It has certain advantages over the above agents: (1) its half-life is shorter, about 90 minutes (longer in renal failure), and (2) the PTT can be used to monitor its anticoagulant effect.

It is usually given as a bolus dose of 0.4 mg/kg IV, followed by a continuous IV infusion at 0.15 mg/kg/hr. The PTT should be kept between 1.5-2.5 x baseline. Dose adjustment is needed in patients with hepatic impairment.

Argatroban is also a direct thrombin inhibitor with a short half life but not specific antagonist. It is infused at an initial rate of 2 ug/kg/min, adjusted according to the PTT.

Dose adjustment is needed in patients with hepatic impairment. (Guidelines for approach to Acute Heparin-Induced Thrombocytopenia 2005 Appendix B).

B. Emergency management of hemophilia

The Toronto and Central Ontario Comprehensive Hemophilia Clinic is a program of the Division of Hematology at St Michael's Hospital. If information is required on any registered patient, it may be obtained from Dr. Teitel (5128; pager 334-9961) or the hemophilia nurse (5129; pager 334-0404). Index cards containing diagnostic and therapeutic information specific to each registered patient are kept on file in the Emergency Department. Patients will also shortly be issued with wallet cards by the clinic with similar updated information. Most patients are trained to self-infuse factor concentrates at home. Such patients may appear in the Emergency Department if they have run out of product. They may be allowed to self-infuse factor product in the ER.

General Principles of Treatment

Useful ancillary measures for acute hemorrhage in hemophilia:

1. Local rest of affected part (eg. Splint, sling) or complete or modified bed rest.
2. Ice packs for intra-articular or intra-muscular bleeds.
3. Anti-fibrinolytic agents (Amicar or tranexamic acid) for oral bleeding or epistaxis only.
4. Short courses of acetaminophen + codeine compounds for analgesia.
5. Do NOT perform or allow intramuscular injections or arterial punctures.
6. Mild bleed may require only a single infusion of clotting factor. Experienced patients can often judge whether further treatment is necessary.

4. Hemostatic Therapy:

1. Early or non-threatening intra-articular or intra-muscular bleed, mucosal bleeds which does not threaten airway: target factor VIII or IX level is approximately 30%. Products of choice are usually recombinant factor VIII or concentrate 15-30 u/kg. Mild factor VIII deficient hemophiliacs (factor VIII > 3-5%) may be known to respond to DDAVP. This is given at 0.3 microgram/kg (maximum 20 micrograms) by slow IV (20-30 min). Hospital admission is usually not necessary.
2. Delayed treatment, or more severe intra-articular or intra-muscular bleeds (eg. Threatened compartment syndrome): factor VIII concentrate 30-50 u/kg, or factor IX concentrate 50-100 u/kg. Some patients should be admitted to hospital. Dr. Teitel or hematologist on call should be notified.
3. Life or limb threatening hemorrhage, intracranial hemorrhage, mucosal hemorrhage threatening the airway, GI hemorrhage, urgent surgery, multiple trauma: factor VIII concentrate 40-50 u/kg, or factor IX 75-100 u/kg. Most such patients should be admitted to hospital.

5. Other Circumstances:

1. Other factor deficiencies: concentrate of factor VII, XIII, and XI are available. The alternative is plasma. Dr. Teitel or the hematologist on call should be notified for discussion of options.

2. Inhibitors to factor VIII are anti-factor VIII antibodies which arise in 10-15% of treated classical hemophiliacs. Treatment options for acute hemorrhage include: human factor VIII, sometimes given after therapeutic reduction of antibody titre, activated prothrombin complex concentrates (APCC), porcine factor VIII concentrate if available or most often recombinant factor VIIa. Dr. Teitel or hematologist on call should be notified immediately if an inhibitor patient presents with an acute hemorrhage.

6. Central lines:

Central venous lines are often required by hematology-oncology patients. Patients receiving aggressive chemotherapy regimens often require multiple antibiotics, regular transfusion, IV electrolytes, morphine drips, etc. In addition, some chemotherapy drugs are damaging to veins, so that many patients have poor venous access after a number of treatment cycles. Patients are encouraged to get central lines

1. **Hickman line** double lumen. These are inserted through the chest wall and tunneled up under the skin to the subclavian vein. In addition to infusions, blood samples can be drawn through this line. However, because heparin is usually placed into the line to prevent clotting, clotting tests should be drawn through a peripheral vein.

2. **PICC line** ie peripherally inserted central catheters, like Hickman lines, are external catheters but are inserted into a brachial vein and are usually not tunneled. Although single lumens usually suffice, double lumen PICC lines are available. Beware, however, that transfusions of packed RBC are often difficult through double lumen PICC lines, as the lumens are very small.

3. **Passports** lines have a small reservoir implanted under the skin in the arm. Like PICC lines, Passports extend up the arm vein into the subclavian. Passport lines have the advantage of being entirely subcutaneous and do not require flushing as frequently.

4. **Port-a-Cath**, is a reservoir under the skin and is inserted in the chest wall.

The most frequent complications of these lines are clotting and infection. Although flushed with heparin, small clots may develop within the lumen. If this is suspected by an inability to infuse or withdraw blood through the line, the clot can often be dissolved by infusing 5000 Units of Urokinase into the lumen, waiting an hour, and then withdrawing. This dose does not generally cause any systemic bleeding problem. If the ipsilateral arm becomes swollen, a larger clot may be present and may require systemic anticoagulation – a venogram or Doppler ultrasound should be obtained.

Infections are very common and are a frequent cause of fever in these patients. Coagulase negative staphylococcus is a common organism; other bacteria as well as candida may also be seen. Local infections at the exit sites may produce local erythema +/- pus. However, infections at the catheter tip may produce no signs other than fever. Some of these infections may respond to appropriate IV antibiotics, but if they do not respond promptly, the line may need to be removed. Rapidly spreading infections involving the Hickman line tunnel require urgent line removal.

All central lines for hematology –oncology patients are inserted by the interventional radiology department. Please phone Radiology if you need to book a line quickly; they are usually very prompt and will often insert the line within one weekday if needed. Removal of a Hickman or implantable line is also done by Radiology.

If a patient is being discharged with a central Hickman or PICC line in place, it is important to inform Home Care at least 24 (preferably 48) hours before discharge. Unless the patient can learn to care for the line him/herself, a nurse will need to flush the line at least 3 times weekly, and change the dressing at least once weekly. Lines are flushed with Hepalean 3 ml of 100 U/ml – you will need to order this at discharge.

7. Miscellaneous issues:

A. Apheresis: This procedure permits removal of a single blood component (plasma, leukocytes or platelets), returning the other components to the patient. This is available at St. Michael's under the direction of Dr. Freedman. An apheresis technician is on call 24 hours a day, but only true emergencies are done outside of the normal day shift. Dr. Freedman should be contacted for any emergency procedure.

Plasmapheresis is performed to remove plasma components such as immunoglobulins. Indications include TTP/HUS, Waldenstrom's macroglobulinemia with hyperviscosity, Goodpasture's syndrome and Guillaine-Barre syndrome. Albumin is usually used as replacement fluid (an exception is TTP/HUS, where cryosupernatant plasma or fresh frozen plasma is given as replacement fluid).

Leukopheresis may be used for leukostasis (usually seen in AML) or stem cell collections for transplant. Plateletpheresis is usually done at the Red Cross as single donor collection for transfusion, but occasionally is done therapeutically for extremely high platelet counts with thrombosis.

B. Bone marrows: Bone marrow aspiration/biopsy is a common procedure on hematology service; you will likely do a number of these. These should be booked with the hematology lab (call 2138) at least one day in advance, and should be done in the mornings to allow the technician to process the sample. Diagnostic marrows should often include a biopsy as well as an aspirate, unless a major coagulopathy is present. Biopsies are better for detecting metastatic tumour or fibrosis while an aspirate is usually better for cell morphology. The aspirate slides are available the same afternoon and can be reviewed with the staff. Ancillary marrow studies may be requested. Cell surface markers (immunophenotyping) can be helpful in characterizing leukemias and lymphomas, and must be booked with the cellular immunology lab; the sample must arrive in the laboratory before noon and must be accompanied by a specific statement of why the test is being requested. Cytogenetics is useful in diagnosing CML and may be of prognostic value in acute leukemias; however, they are expensive and must be approved by hematology staff. You will need to tell the lab ahead of time if you would like one.

6. SUGGESTED READING LIST:

Text:

1. Cancer Principles and practice of oncology ,Vincent T Devita , Samuel Helman, Steven A Rosenberg (www.LWWoncology.com) disc in Dr. Haq's office
2. Principles of Internal Medicine by Harrison 16th Edition (hematology and oncology section)
3. Hand outs TNM Staging and Anatomical reference (Compliments of Bristol-Myers)

Squibb)

4. Principles & Practice of Oncology Review
5. Selected Schedules of Therapy for Malignant Tumors (Compliments of Baxter Oncology)
6. MKSAP 13 Hematology and Oncology section
7. BLOOD Principles & Practice of Hematology Edited by Robert I. Handin, Samuel E. Lux, Thomas P. Stossel
8. Fastfacts Breast Cancer Third Edition by Michael Baum & Harvey Schipper
9. ASCO Educational Book (available in the office)
10. Clinical Oncology Basic Principles & Practice Second Edition by Anthony J. Neal & Peter Hoskin.
11. Clinical Oncology a Multidisciplinary Approach for Physicians & Students 7th Edition by Philip Rubin

Websites:

www.asco.com

uptodate

www.adjuvantonline.com

www.oncologyrounds.ca

www.cancercare.on.ca

www.cancer.ca

www.cycleofhope.org Info. On screening different types of Cancer 877-717-4673

www.nccn.org

www.jco

www.nejm

www.lancet

www.octrf.on.ca/octpqi/

CLINIC AND ROUNDS SCHEDULE (Schedules will be distributed)

Monday 8:00 – 11:00 Seminars (Hematology/Oncology)

9:00 - 12:00 Clinics

1:00 – 4:00 Clinics

1630-1730 GI Tumor Board (1st Monday of the month)

1600-1700 GI Tumor Board

Tuesday 9:00-12:00 Clinics

1:00 – 4:00 Clinics

1:00 – 2:00 Morphology Rounds (Hematology Rotation)

Wednesday 9:00-12:00 Clinics
1:00 – 4:00 Clinics
12:00 Medical Grand Rounds
1:00 Resident Presentation (2nd & 4th Wednesday of the month)

Thursday 9:00-12:00 Clinics
1:00 – 4:00 Clinics
1:00 – 3:00 Seminars (Hematology/Oncology)

Friday 8:30 – 12:00 Breast Clinic (Oncology Rotation)
9:00-12:00 Clinics (Hematology Rotation)
12:00-1:00 Breast Tumor Board (Every Friday Oncology Rotation)