ORIENTATION TO THE

ST. MICHAEL'S HOSPITAL NEPHROLOGY SERVICE

FOR RESIDENTS, FELLOWS AND STUDENTS

Fifth Edition

January 2023

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A. INTRODUCTION

1. Welcome!

Welcome to Nephrology at St. Michael's Hospital. This manual provides guidance on many of the practical issues relating to your time on the nephrology service at St. Michael's Hospital, including each of the following:

- The nephrology ward (8-Cardinal Carter South),
- The nephrology in-patient consult service
- The nephrology in-centre hemodialysis units
- The nephrology home dialysis unit
- The nephrology outpatient clinics.

There are additional printed resources available on the nephrology ward.

You will at any time mainly be working with the consult team, the ward team, or (in the case of the fellows) on a dialysis rotation. The consult and ward teams are briefly introduced below, and more detail is provided later in this manual.

2. Consult and Ward "Teams"

The consult team has an attending nephrologist and at least two nephrology fellows, as well as two or three residents, and a variable number of elective residents and elective medical students.

The ward team has an attending nephrologist and two nephrology fellows, and may have a urology resident.

3. "Geography" of St. Michael's Hospital and of the Nephrology Program

St. Michael's Hospital's address is 30 Bond Street. The hospital occupies an entire city block.

The boundaries are:

- To the west – Victoria Street
- To the north – Shuter Street
- To the east – Bond Street
- To the south – Queen Street

There are two other buildings nearby that are also important:

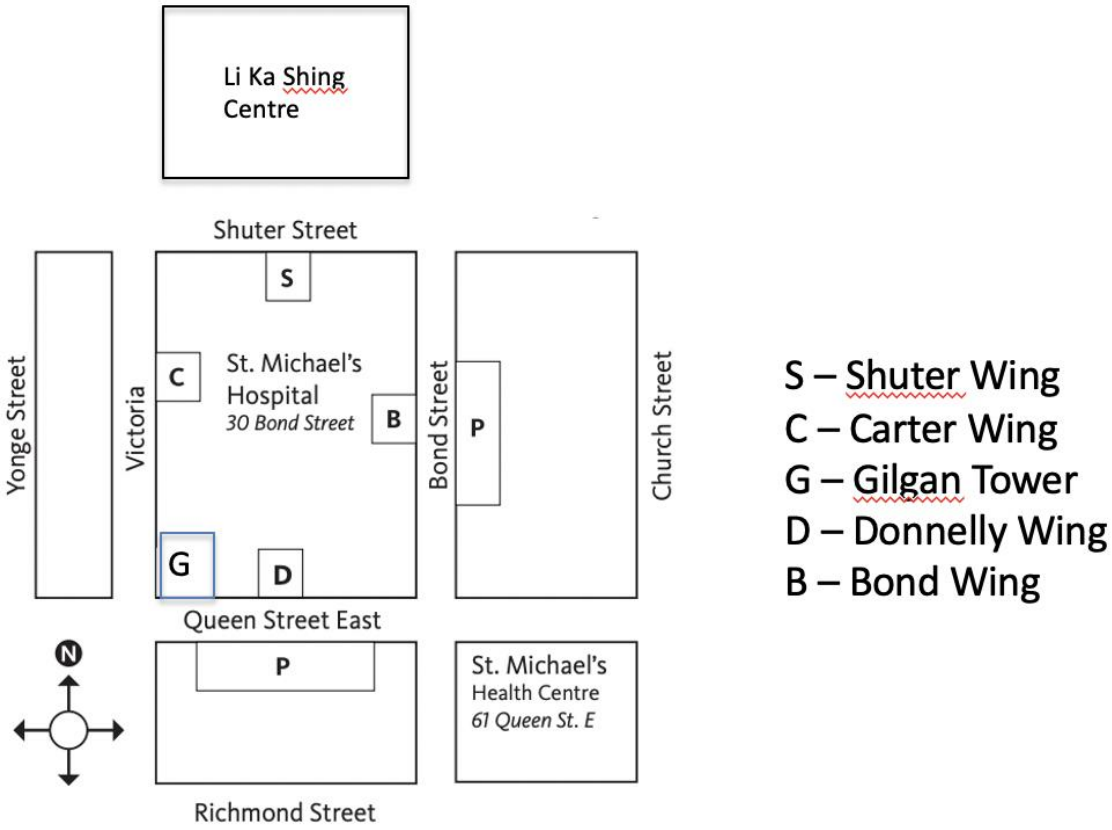
- Li Ka Shing Centre – this is north of the hospital, across Shuter Street. This is the location of a number of facilities, including:
    - The hospital library
    - The Student Centre
        - This is the administrative office for teaching activities at the hospital
    - Teaching rooms
    - Research activities
    - Simulation Centre

- 61 Queen Street East (St. Michael's Health Centre)
    - This is an office building on the south side of Queen Street East, just east of the hospital
    - This is where all of the staff nephrologists have their offices (mainly on the 9th floor)
    - This is where all of the ambulatory clinics in nephrology take place
    - Queen Street East is very busy. It is recommended that when walking between the hospital and 61 Queen Street East, one should cross Queen Street at the traffic lights at Church Street.

4. Map of St. Michael's Hospital (1)

Below is a schematic map of the hospital showing the hospital itself, the Li Ka Shing Centre to the north, 61 Queen Street East to the southeast.

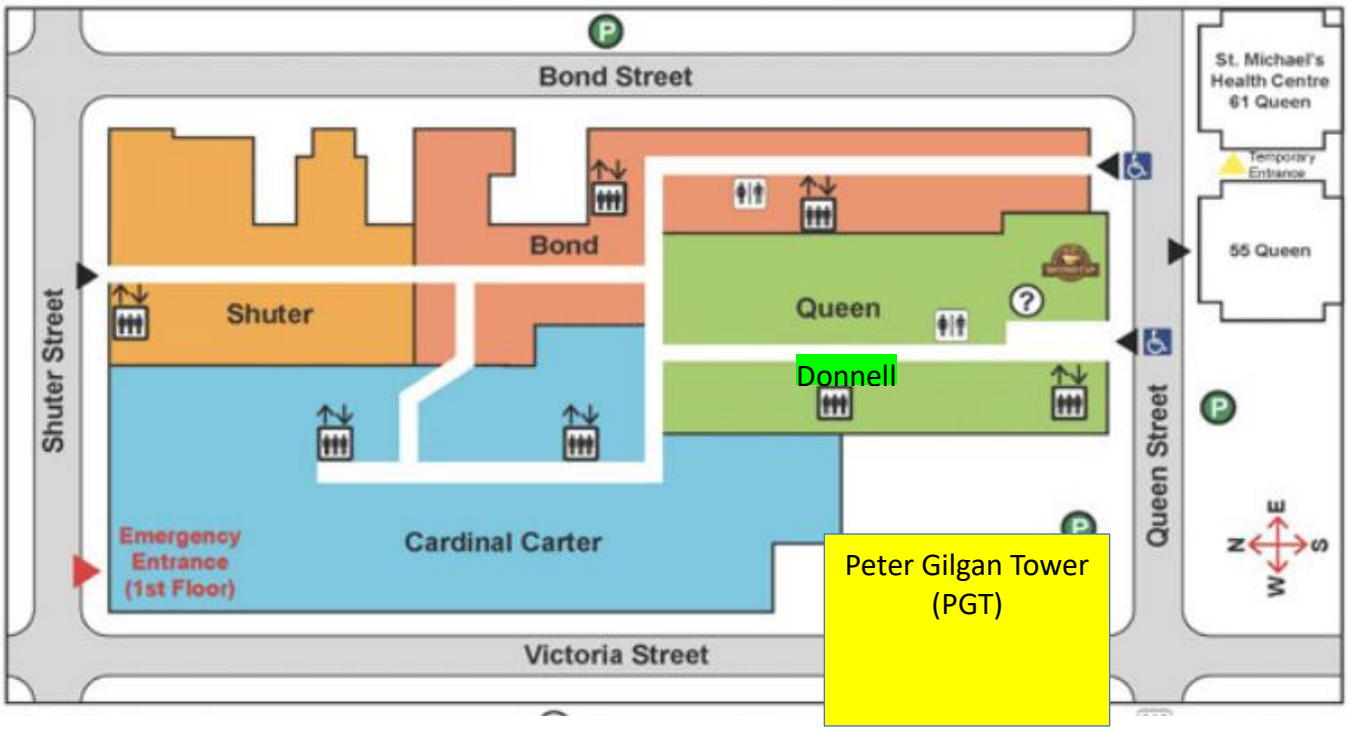
The major wings of the hospital are indicated by a single letter.



5. Map of St. Michael's Hospital (2)

Below is a more detailed map of the wings of the hospital, which are colour-coded.

Note that this map is rotated 90 degrees, so that north points to the left.



6. Important Locations within the Hospital pertinent to Division of Nephrology

Nephrology Ward – 8 Cardinal Carter South

The nephrology ward is described in detail below.

Nephrology Fellows and Residents Room – Room 8-073

This is an office dedicated with space to store belongings. The door is locked.
The room is located on 8 Cardinal Carter North. The room number is 8-073.
The code to enter the room will be provided to trainees at their orientation.

Washrooms

There is a staff washroom directly across from the Fellows' Room.
The room number if 8-074.
The code to enter the washroom is 8-6-4-2.
There are additional washrooms at the 8-Cardinal Carter South ward, at the corridor that leads south from the south elevators.

Elevators

- Carter Wing - There are 2 main banks of elevators in the Cardinal Carter wing (North and South). These are used most frequently when getting around the hospital.
- Donnelly Wing – There are also 2 sets of elevators in the Donnelly wing.
- Peter Gilgan Tower – There is a bank of elevators in the Gilgan Tower as well.

ICUs

There are 4 ICUs in the hospital:

- Medical Surgical ICU (MSICU)
    - There are 2 parts to this – PGT 4th floor and PGT 7th floor (shared with CICU)
    - Telephone 416-864-5286 (inside hospital, dial 5286)
- Cardiovascular ICU (CVICU)
    - This is the ICU for patients who have had cardiac or vascular surgery
    - This is located on the 4th floor Cardinal Carter Wing
    - Telephone is 416-864-5483 (inside hospital dial 5483)
- Trauma-Neuro ICU (TNICU)
    - This is the ICU for neurosurgical and trauma patients
    - This is also located on the 4th floor Cardinal Carter Wing
    - Telephone is 416-864-5816 (inside the hospital dial 5816)
- Cardiac ICU (CICU)
    - This is located on the Peter Gilgan Tower 7th floor

- Telephone is 416-864-5809 (inside the hospital, dial 5809)

Emergency Department

This is located in the Cardinal Carter wing, 1st floor.

Telephone number is 416-864-5094 (inside hospital dial 5094).

Access to the Emergency Department is via either:

- Cardinal Carter South elevator to 1st floor (use badge on the elevator to access the first floor)
- Bond Street wing access is also possible

7. Other key locations

LOCATION	WHAT UNIT IS FOUND THERE
1 Cardinal Carter (CC)	Emergency Department (enter from CC-South elevator)
2 CC	Labs
3CC	Medical imaging
4CC and 4PGT	ICUs (MSICU, CVICU)
5 CC	OR and PACU (only reach by CC-north elevators)
6 CC	Cafeteria, Tim Horton's
6 PGT	Respirology
7 CC - South	Cardiology
7 CC - North	CV and vascular surgery
7 PGT	Cardiac ICU
8 CC - South	Nephrology ward, main in-centre hemodialysis unit
8 CC - North	Home hemodialysis unit, north in-centre HD unit
8 PGT	Hematology/oncology
9 CC – North	Neuro-Trauma ICU
9 CC	Orthopedics, neurosurgery
14 CC and 14 PGT	GIM
15 CC	Ob-Gyn (only reach by south elevators)
16 CC	General surgery and GI (only reach by north elevators)
17 CC	Psychiatry (only reach by north elevators)

8. Key telephone numbers

Topic	**Telephone Number***
General SMH number	416-360-4000
Locating	416-864-5431
Nephrology ward	416-864-5097
In-patient pharmacy	416-864-5757
In-centre hemodialysis unit (main unit)	416-864-5228
In-centre hemodialysis unit (north unit)	416-864-5338
Kidney Care Centre (satellite unit)	416-867-3700
Home dialysis	416-864-5794
Emergency department	416-864-5094
MSICU	416-864-5286
Cardiac ICU	416-864-5809
TNICU	416-864-5816
CVICU	416-864-5483
Interventional radiology	416-864-5886
Dr. Schreiber's office	416-867-7454
Dr. Schreiber's cellphone	647-620-7904

* Most of these telephone numbers can be reached from within the hospital by just dialing the last 4 numbers.

B. DIVISION OF NEPHROLOGY AT ST. MICHAEL'S HOSPITAL

1. Administrative Structure

Nephrology is part of the Kidney and Metabolism Program of Unity Health Toronto (UHT).
UHT includes St. Michael's Hospital (SMH), St. Joseph's Health Centre, and Providence Healthcare.

The program director is Jonathan Fetros (X5791).
The Medical Director is Dr. Jeff Zaltzman, who is also the Division Head, Nephrology, at SMH.

2. Nephrologists

All are available through hospital locating (416-864-5431).
All are located at 61 Queen Street East, 9th floor, except Dr. Harel, who is on the 7th floor.

Dr. Ziv Harel	416-360-4000-x8462	Ziv.harel@unityhealth.to	61 Queen 7th floor
Dr. Kamel Kamel	416-867-7479	Kamel.kamel@unityhealth.to	61 Queen 9th floor
Dr. Philip Marsden	416-847-1736	Philip.marsden@unityhealth.to	Li Ka Shing
Dr. Philip McFarlane[1]	416-867-3702	Philip.mcfarlane@unityhealth.to	61 Queen 9th floor
Dr. Jeffrey Perl[2]	416-864-6016	Jeffrey.perl@unityhealth.to	61 Queen 9th floor
Dr. Ramesh Prasad[3]	416-867-3722	Ramesh.prasad@unityhealth.to	61 Queen 9th floor
Dr. Martin Schreiber[4]	416-867-7454	Martin.schreiber@unityhealth.to	61 Queen 9th floor
Dr. Ronald Wald[5]	416-867-3703	Ron.wald@unityhealth.to	61 Queen 9th floor
Dr. Jordan Weinstein	416-867-3703	Jordan.weinstein@unityhealth.to	61 Queen 9th floor
Dr. Ann Young		Ann.young@unityhealth.to	61 Queen 9th floor
Dr. Darren Yuen	416-867-3665	Darren.yuen@unityhealth.to	Li Ka Shing 5-059
Dr. Jeffrey Zaltzman[6]	416-867-7444	Jeff.zaltzman@unityhealth.to	61 Queen 9th Floor

1. Medical Director, Home Dialysis; Medical Director, Living Donor Program
2. Director, Multi-Care Kidney Clinic (MCKC)
3. Director, Transplantation
4. Director, Education
5. Director, Hemodialysis
6. Head, Division of Nephrology

C. COMPONENTS OF NEPHROLOGY PROGRAM AND KEY INDIVIDUALS

1. In-Patient Nephrology Ward

The nephrology ward is located at 8 Cardinal Carter South. This ward provides care to:

- Nephrology patients
- Urology patients
- Patients with kidney transplants (both newly transplanted patients, and patients with an existing transplant who is admitted with a new complication)

Telephone number for the ward is 416-864-5097

Manager: Dana Witham 416-864-6060 (extension 7436)

Care and Transitions Facilitator: Jumi Charles 416-864-6060 (extension 3429)

Other health professionals

- Dietitian – Karen Burleigh
- Pharmacist – Jenny Jong
- Occupational Therapist – Lisa Buenaventura
- Physiotherapist – Celia Rojas
- Social worker – Courtney Sas

Medical Director: Dr. Martin Schreiber (416-867-7454)

2. In-hospital Hemodialysis

At any time, between approximately 10 and 20 in-patients are receiving hemodialysis as inpatients. These patients are either admitted to the nephrology ward service, or they are being followed by the nephrology consult service while admitted to other services (e.g. ICU, general internal medicine, etc.).

For patients who receive chronic hemodialysis treatments, where possible, we aim to keep them on their existing schedules – Monday/Wednesday/Friday or Tuesday/Thursday/Saturday. This may need to be supplemented during their admission for a period of time; for instance, to provide an extra treatment to facilitate fluid removal in a patient who is fluid-overloaded.

The scheduling for in-hospital hemodialysis is managed by a specially designated “hemodialysis charge nurse”. This senior nurse is in the dialysis unit generally from 7:30 am to 3:30 pm daily from Monday to Saturday. After 3:30 pm, the duties transfer to the nurse in charge for the rest of the day and overnight.

It is essential to notify the hemodialysis unit charge nurse (generally can be found at extension 6131) of any patients newly admitted to hospital who will likely require hemodialysis.

The hemodialysis charge nurse meets with both the consult and ward teams on a daily basis to plan for hemodialysis: both early in the day to confirm the plans for that day's patients, and also at the end of the day to plan for the next day.

It is essential that orders are entered for at least 1/3 to 1/2 of each of the ward's and consult team's hemodialysis patients the day before, so that the hemodialysis nurses can start their dialysis work first thing in the morning (i.e. close to 7:00 am) and not need to wait for the medical team to write orders.

Patients identified as needing urgent dialysis must be brought to the attention of the following, depending on the time the need for dialysis identified:

Day of the week	**Time**	**Whom to notify**	**How to reach them**
Monday – Saturday	7:30 am – 3:30 pm	HD charge nurse	Call X 6131
Monday – Friday	3:30 pm – 7:30 am next day	In charge nurse in the hemodialysis unit	Call X5228
Saturday	3:30 pm – 11:00 pm	In charge nurse in the hemodialysis unit	Call X5228
Sunday	3:30 pm – 7:30 am next day	In charge nurse in the hemodialysis unit	Call X5228
Saturday night – next Sunday evening	11:00 pm Saturday to 7:00 pm following Sunday	On-call HD nurse	Call locating X5431

3. In hospital Peritoneal dialysis (PD)

There is generally a smaller number of patients on in-hospital PD at any one time – ranging from 2 – 5 typically.

PD patients admitted to the nephrology ward or to other units have their PD done by either the Home Dialysis nurses (during the day on weekdays, and they can be reached at X5794) or the in-charge ward nurse (X5097).

4. Hemodialysis Units - In-centre

These units are located on 8 Cardinal Carter and provide in-centre hemodialysis treatments to approximately 300 patients.

There are 2 units:

- Main (south) unit – 416-864-5228 (entrance located at 8-CC-south elevator lobby)
- Second (north) unit – 416-864-5338 (entrance is at room 8-086)
- In-charge nurse – 416-864-6060 (extension 6131)

Manager: Fiona Harrington 416-864-6060 (extension 2791)
Medical Director: Dr. Ron Wald (416-867-3703)

a) <u>In-centre hemodialysis schedules</u>

Patients are generally scheduled for in-centre hemodialysis either on a day shift schedule, or nocturnal.

Dayshifts – 3 times per week

Patients are scheduled in one of the following 6 shifts:

- MWF morning (7:30 am – 12:00 noon), MWF afternoon (12:30 – 5;00 pm), MWF evening (5:30 – 10:00 pm)
- TTS morning, TTS afternoon, TTS evening

There is no in-centre hemodialysis on Sunday during the day.

Extra dialysis shifts on day schedule

A small number of patients come for 1-3 more dialysis treatments per week, mainly to manage their tendency to fluid overload.

Nocturnal dialysis

Approximately 20 patients come for dialysis overnight. They generally arrive at 10:00 pm, and are on dialysis until 5:00 or 6:00 am.

The schedules are either Monday/Wednesday/Friday or Tuesday/Thursday/Sunday.

There is no overnight dialysis on Sunday night.

The nurses who are covering the nocturnal dialysis patients are also available to provide in-hospital hemodialysis to a small number of patients who urgently require dialysis overnight.

b) Vascular Access Coordinators

The vascular access coordinators are dialysis nurses who have advanced training in all aspects of vascular access, including:

- AV fistula and AV graft cannulation, monitoring and troubleshooting
- Tunneled line monitoring and troubleshooting
- Coordinating interventional radiology procedures for each type of access

The coordinators are:

- Kathleen McIntosh, Sadie Webster, and Elizabeth Petershofer

They can be reached as follows

- Telephone extension 416-864-6060 (extension 6258)
- Email – VACnurses@smh.ca
- Office address (just inside the 8-CC-south main hemodialysis unit)

c) Nurse Practitioners (NPs)

There are several nurse practitioners who are an integral part of the hemodialysis program. In collaboration with several of the staff nephrologists, they provide the bedside care for the chronic in-centre hemodialysis patients.

When a patient on chronic in-centre HD is admitted to the hospital, whether it is to the ward or consult service, it is essential to communicate with that patient's NP at the time of the patient's admission (to identify any recent issues affecting the patient's health), if necessary during the admission, and most importantly at the time of discharge, to ensure a smooth transition back to the outpatient in-centre dialysis setting.

The NPs are noted in the following table.

Nurse practitioner	Shifts covered	Email	Telephone number
Alison Thomas	MWF afternoon TTS morning	alison.thomas@unityhealth.to	416-864-6060 X6979
Leora Wanounou	MWF morning TTS afternoon	Leora.wanounou@unityhealth.to	416-864-6060 X2609

Samiksha Singh	Monday and Wednesday evening Nocturnal dialysis patients Satellite unit TTS2	Samiksha.singh@unityhealth.to	416-864-6060 X6517
Crystal Vanderwyk	Satellite unit	Crystal.vanderwyk@unityhealth.to	416-867-3700

d) Other health professionals
   - Dietitians – Sabrina Janes
   - Pharmacists – Lisa Liberatore, Triyu Vather, Elena Nazvitch
   - Social Worker – Asha Aggarwal

5. Kidney Care Centre (KCC)

This is St. Michael's Hospital's satellite dialysis unit, and also a site for ambulatory clinics, home dialysis training and other activities.

It is located at 45 Overlea Blvd. This is approximately 8 km northeast of St. Michael's Hospital.

The KCC can be reached by a direct telephone extension from inside St. Michael's Hospital, at X3700. From outside the hospital, the telephone number is 416-867-3700.

The NP for the KCC is Crystal Vanderwyk (crystal.vanderwyk@unityhealth.to) for most of the shifts. Samikha Singh covers the TTS shift at the satellite unit.

6. Home Dialysis

The Home Dialysis unit provides care to outpatients who do dialysis at home – both peritoneal dialysis and also home hemodialysis. The unit also provides support to these patients when they are admitted to hospital.

The location is 8 Cardinal Carter North.

Telephone extension is 416-864-5794 (call 5794 from inside the hospital).

Clinical Leader Manager: Elizabeth Anderson 416-864-6060 (extension 2721).
Medical Director: Dr. Philip McFarlane (416-867-3702)

Nurse Navigator: Mina Kashani 416-864-6060 (extension 2387).
Case Manager: Fatima Benjamin-Wong 416-864-6060 (extension 6977)

Other health professionals

- Dietitian – Carol Huang
- Pharmacist – Diane Chong
- Social Worker – Carmen Morris
- Pharmacist/Drug Navigator – Christa Brechin

7. Transplant Program

The kidney transplant program is managed from a set of offices on the 9th floor of 61 Queen Street East. There are 3 transplant nephrologists (Drs. Prasad, Zaltzman and Yuen), and several transplant nurses. Dr. Prasad is the Director of Transplantation.

Ambulatory clinics for post-transplant patients take place on:

- Monday mornings (Dr. Prasad)
- Wednesday mornings (Dr. Yuen)
- Thursday mornings (Dr. Zaltzman).

Each of the transplant nephrologists also has additional clinics in which they assess potential transplant recipients.

The transplant nephrologists are supported by a group of transplant nurses, who are integral to the full spectrum of transplant care, including assessment of potential recipients, assessment of potential living donors and care of transplant recipients after their procedures.

The transplant clinic telephone number if 416-867-3665.

All of the staff urologists do kidney transplant surgery:

- Dr. Kenneth Pace (416-867-3695) (kenneth.pace@unityhealth.to)
- Dr. Monica Farcas (416-867-3735) (monica.farcas@unityhealth.to)
- Dr. Michael Ordon (416-867-3705) (Michael.ordon@unityhealth.to)
- Dr. Robert Stewart (416-867-3686) (Robert.stewart@unityhealth.to)

8. Multicare Kidney Clinic (MCKC)

The MCKC provides comprehensive care to patients with advanced chronic kidney disease. Patients generally have eGFR below 30 (i.e., stage 4 or stage 5 CKD). Patients are seen in clinic by the whole team, consisting of a nurse, dialysis nurse navigator, dietitian, pharmacist, social worker and physician.

The clinic operates every Tuesday and Friday morning with various nephrologists.

Leadership

- Medical Director – Dr. Jeffrey Perl
- Clinical Leader Manager – Elizabeth Anderson (Elizabeth.anderson@unityhealth.to)
- Administrator – Katherine Harris (Katherine.harris@unityhealth.to)

Telephone number – 416-864-5707

Collaborating health professionals

- Dietitian – Carol Huang (carol.huang@unityhealth.to)
- Pharmacist - Muna Khan (muna.khan@unityhealth.to)
- Social Worker – Carmen Morris (carmen.morris@unityhealth.to)
- Dialysis nurse navigator – Mina Kashani (mina.kashani@unityhealth.to)
- MCKC Nurses
    - Zeineb Abdulkder (zeineb.abdulkader@unityhealth.to)
    - Hong Gao (hong.gao@unityhealth.to)
    - Melissa DeVera (melissa.devera@unityhealth.to)

9. Acute Kidney Injury Clinic (AKI Clinic)

The AKI Clinic follows patients recently seen in hospital with a diagnosis of AKI who recovered to the point where they do not need dialysis, but are judged to need comprehensive nephrology follow-up at

least for a period of time.

The clinic generally runs every 2 weeks on Monday afternoons.

The attending physician for 2022-2023 is Dr. Sara Wing (sara.wing@unityhealth.to)

Clinic administrator is Mickail Lawrence (mickail.lawrence@unityhealth.to)

Telephone number is 416-867-8209

D. KEY COLLABORATING UNITS AND TECHNIQUES

The nephrology services work closely with multiple other units in the hospital. In this section, we describe two of the most important: Interventional radiology, and pathology. We also briefly describe the use of urine microscopy, as this is something both nephrology services make use of.

1. **Interventional Radiology (IR)** X5886

a) Location

The IR suite is located in the Cardinal Carter wing, third floor, towards the north end.

The telephone number is 416-864-5886 (inside the hospital it can be reached by dialing 5886).

b) Interventional Radiologists

There are 4 IR staff radiologists:

- Dr. Andrew Common
- Dr. Danny Marcuzzi
- Dr. Vikram Prabhudesai
- Dr. Andrew Brown

c) Services provided by IR

The IR service provides critical support for the nephrology service, including in particular the following:

- Hemodialysis (HD)
    - Insertion and removal of tunneled HD catheters
    - Declotting of clotted AV fistulas and AV grafts and related procedures such as angioplasty
- Peritoneal dialysis (PD)
    - Insertion of PD catheters (and removal of PD catheters that were inserted in IR)
    - Manipulation of PD catheters that may have migrated with their tip out of the pelvis
- Kidney biopsies (for both transplant and native kidneys)
- Nephrostomy tubes and related procedures
- PICC line insertion

Inser

tion of tunneled hemodialysis lines

d) To order any of these procedures

- Open Soarian, and select Orders
- Search for IR using “Interventional Radiology”
- The digital request form automatically enters the patient’s most recent INR and aPTT
- In the comments section, please include:

- Whether the patient is able to give informed consent
    - If the patient is not able to give consent, then consider obtaining consent from a substitute decision-maker (SDM) ahead of time, or arranging for the SDM to accompany the patient to the IR unit
- Whether the patient is isolated, and if so what kind of isolation
- Whether the patient has i.v. access already
    - If the patient does not have i.v. access, please ensure this is arranged prior to the patient going to IR
- Any other special issues or instructions

2. Renal Pathology

a) Renal Pathologist

The renal pathologist at SMH is Dr. Adriana Krizova.

She can be reached via email at Adriana.krizova!@unityhealth.to

She can be reached by telephone at the Pathology lab at 416-864-6060 (extension 2921)

Please ensure Dr. Krizova is aware that a kidney biopsy is coming, either via email or telephone, particularly if a result is needed urgently (i.e. the same day).

b) To organize a kidney biopsy

- *Review rationale for the biopsy and the risks with the patient*
    - The major risk of kidney biopsy is bleeding, both into the urine and around the kidney
    - Different staff nephrologists may quote somewhat different risk levels
        - Gross hematuria – approximately 10%
        - Bleeding sufficient to require a blood transfusion varies from 1-5%
        - Bleeding sufficient to require intervention such as angiographic embolization from 0.1-1%
        - Death – exceedingly rare

- *Review the patient's risk factors for increased peri-biopsy bleeding, and try to minimize the risk as much as possible*
    - Uncontrolled hypertension
        - BP should be normalized prior to the kidney biopsy to below 140 systolic and

below 90 diastolic

- Ideally, it should be normal for several days prior to the procedure

- Increased bleeding tendency
  - Antithrombotic therapy
    - Any antithrombotic agents should be discontinued for a sufficiently long period of time that their effect has worn off at the time of the biopsy
      - Antiplatelet agents, including ASA, NSAIDs, Clopidogrel, Ticagrelor – ideally should be discontinued for at least 7 days
        - Patients at particularly high risk of thrombosis if they stop ASA (e.g. patients post PCI) may continue ASA at the time of biopsy, but this requires a detailed risk-benefit discussion with the patient, cardiologist and the attending staff nephrologist
      - Anticoagulants
        - DOAC – consult guidelines for each agent
          - UpToDate suggests holding DOACs for 5 days before the biopsy, and using bridging UFH for those at high thromboembolic risk
          - Other references suggest a shorter period of omission
        - Warfarin – ensure INR is below 1.4 before the biopsy is done
        - Low molecular weight heparin should be stopped on the day prior to the procedure and the day of the procedure, and can be resumed 48-72 hours post procedure provided there is no evidence of bleeding
      - Patients may require “bridging” with unfractionated heparin (UFH) if they are at particularly high risk of thrombosis, in which case the UFH is stopped prior to the biopsy for at least 6 hours to ensure its effect has worn off
    - The antithrombotic therapy should only be resumed
      - when it is clear there is no post-procedure bleeding
      - generally not sooner than 7 days post biopsy
        (unless absolutely required, in which case UFH may be resumed earlier, as early as 12-24 hours post procedure)
  - Coagulopathy

- Patients with a prolonged INR and/or aPTT need to have the cause for the abnormality investigated and corrected, with the help of hematology consultation if needed

▪ Thrombocytopenia
- Platelet count should be at least 100 x 10(6)/L, and preferably over 140x10(6)/L

▪ Platelet dysfunction
- Uremia
  - Desmopressin (DDAVP) can be administered in the hope of reducing the risk of bleeding in patients with reduced renal function, since the uremic milieu reduces platelet function
    ▪ Its use is controversial
    ▪ There is no consensus on the level of kidney function at which DDAVP ought to be considered
      - Common thresholds are serum creatinine over 150 umol/L or eGFR below 45 ml/min/1.73m2
    ▪ The dose is 0.3 ug/kg i.v. over 30 minutes when the patient is called for the biopsy procedure
    ▪ The major risks are a theoretical concern about causing thrombosis, and hyponatremia (so the patient should have free water restriction)
- Other platelet function abnormality such as von Willebrand's disease
  - Hematology consultation should be requested

o Small, scarred kidneys
▪ Small (< 9cm) scarred kidneys increase the risk of post-biopsy bleeding, and the finding on ultrasound of such small, scarred kidneys should prompt reconsideration of whether the biopsy is truly indicated

o Hydronephrosis
o Possibility of renal infection
o Multiple renal cysts
o Solitary kidney
o Skin infection near the proposed biopsy site
o Uncooperative patient

- *Reach out to Dr. Krizova*
  - Dr. Krizova's contact information is above
  - If possible, please complete the pre-biopsy form available on 8-CC south, as a means

of providing the pathologist with clinical background information

- *Enter the order for biopsy in Soarian*
    - This is an Interventional Radiology procedure
    - See comments above for Interventional Radiology

- *If the biopsy result is needed urgently (i.e. the same day)*
    - Then the biopsy needs to be done before 10 am
    - Alert the IR unit of the urgent request for biopsy by telephone or visit to the IR suite either the day before (preferable) or first thing in the morning

3. Division of Urology

The Division of Nephrology works closely with the members of the Division of Urology, including the 4 staff urologists (Drs. Pace, Farcas, Ordon and Stewart), and the residents and fellows. The staff urologists' coordinates are summarized above under "Transplant Program". The 2 divisions share the 8 Cardinal Carter ward. Many of the urology outpatient clinics are held on the 9th floor 61 Queen Street East.

The collaboration is especially notable in the areas of kidney transplant care (both for new transplants, and for complications occurring later), kidney stone management, and management of obstructive uropathy.

4. **Microscope For Urinalysis**

There is a microscopy room on 8CC-south. It is across the hall from the nursing station, in room 8-015. The entry code for the lock on the door is 5244. The room has necessary supplies for urine microscopy (slides, coverslips, dipstick test strips), a centrifuge, and the microscope. The microscope has a camera linked to it which allows the projection of the slide on to a computer screen so that other members of the team can also see what is being looked at.

There is also a centrifuge and microscope on the 9th floor at 61 Queen St. East, where most of the nephrologists have their offices.

<u>Preparing a slide for microscope</u>

- Take 10 cc of urine and place it in a conical centrifuge tube
- Take 10 cc of water and place it in a second conical tube for balance
- Place the 2 tubes on precisely opposite sides of the centrifuge
- Close the centrifuge, and set it to spin for 3 minutes, at 2000 RPM
- While the centrifuge is spinning, dip a urinalysis dipstick into the urine in such a way that all of the squares on the stick are covered
    - Match the colour change on each square to the nearest corresponding colour on the dipstick container to determine the level of blood, protein, leukocytes, glucose, pH, and specific gravity
- After the centrifuge has finished spinning, remove the conical tube with urine and pour off the supernatant into the sink in the urinalysis room used to discard fluids
- Resuspend the urine; this can be done either by tapping it gently on the counter, or running it across the metal centrifuge tube stand on the countertop
- Then pour off a drop of resuspended urine on to the slide; one can use a pipette to do this, but this is not necessary
- Cover the drop of urine with a coverslip; preferably, place the edge of the coverslip onto the slide at the edge of the drop of urine to spread it out, and then slowly lower the coverslip on to the slide to spread the urine out into an even layer, without capturing any air that would cause bubbles

<u>Examine the slide</u>

- The eyepiece is 10x magnification
- The low power objective (yellow colour) is also 10x, so together with the eyepiece this will give 100x magnification
- Start with the low power objective – make sure you are at roughly the right height with the stage by focusing on the edge of the coverslip
- Then use both hands to move around the slide and to focus up and down

        - The right hand is used to move the slide on its “stage” side-to-side and forward and back
        - The left hand is used to focus up and down
    - Take your time – it often takes a while to find significant abnormalities
    - If you spot something via low power, focus on it, and then swtich to the higher power (either the green 20X or the blue, 40x) objective to characterize it better

E. IN-PATIENT WARD NEPHROLOGY EXPERIENCE

1. Location of the In-patient Nephrology Ward

The in-patient nephrology ward is located on 8 Cardinal Carter South. The main telephone number is 416-864-5097 (inside the hospital, dial 5097).

Patients admitted to the nephrology service are in the large majority of cases admitted to this ward. At times, if it is especially busy, patients may be bed-spaced to other wards, and also may be admitted to the emergency department for a period of time ranging from a few hours to a few days.

Most of the rooms are 2-bed rooms.

Room 828 has 4 beds and this is the room where generally patients are admitted for the several days immediately after kidney transplant.

2. Composition of the Medical Ward Team

The ward team has an attending nephrologist and two nephrology fellows, and may have a urology resident.

3. Categories of patient admitted to the nephrology ward

- Patients who are on *chronic in-centre hemodialysis* experiencing a *complication of dialysis* (e.g. dialysis catheter associated sepsis; dialysis catheter malfunction; fluid overload; electrolyte disturbance)
- Patients who are on *chronic home hemodialysis or chronic home peritoneal dialysis* (PD) and experiencing a *complication of dialysis* (e.g. PD-related peritonitis; PD catheter malfunction)
- Patients receiving a *new transplant*
- Patients with an *existing kidney transplant admitted with transplant-related issues* (e.g. acute kidney injury, kidney transplant rejection, or transplant pyelonephritis)
- Other patients who have a *complex issue related to acute or chronic kidney disease that is judged by their staff nephrologist to require in-patient care*; a common example would be a patient who needs an urgent kidney biopsy, and/or who has a relatively high risk of post-biopsy bleeding, and so needs closer monitoring post-biopsy

These patients may be admitted from a nephrologist's office, from clinic or via the emergency department.

4. Most "renal" patients will be not be admitted to the nephrology ward on 8CC-S.

- *Admissions to the nephrology ward should be reserved for those patients with primarily nephrologic issues as identified above.*

- For example, a hemodialysis patient with a *medical* illness such as an acute stroke or GI bleed should (generally) be admitted to the general internal medicine service and followed by the nephrology consult team.
- A hemodialysis patient with a *surgical* problem such as a hip fracture or ischemic foot needing revascularization will be admitted to the appropriate surgical service, and followed by the nephrology consult service

- *Procedures to follow if the GIM service reaches its census*

  In addition to the principles above, there is a system in place designed to ensure that the workload for various in-patient services at St. Michael's Hospital is shared.
  - This means in particular that if the GIM service is getting overloaded, while the nephrology in-patient ward is relatively quiet, then patients on either HD or PD can be admitted to the nephrology ward service for management of general medical issues such as pneumonia or a GI bleed.
  - Each day, the Chief Medical Resident (CMR) reviews the census numbers of patients on GIM and on nephrology. (The plan for the weekend is determined on Friday morning according to that day's census.)
  - The CMR uses a previously-agreed algorithm to determine if a dialysis patient with a general medical (i.e. non-dialysis-related) problem will be admitted to GIM (which is the default); to nephrology (if GIM is over its census limit, and nephrology is under census limit); or alternating (if both services are over census).
  - The nephrology ward census limit is 13 patients.

5. Patients admitted to the ward are admitted to the attending ward nephrologist

All ward admissions are under the attending nephrologist for that period (or under the weekend attending nephrologist if the patient is admitted over the weekend while the consult attending nephrologist is covering the service). The patient will be transferred to the care of the regular ward attending at the end of the weekend or holiday.

6. Discharges

a) <u>Timing of discharge</u>

Discharges should as much as possible be planned the night prior to discharge with notification of patient and nursing staff, and the goal is for the discharged patient to leave by 11:00 am.

b) <u>Discharge summaries</u>

It is essential that discharge summaries be completed online at the time of discharge, with copies sent to family physicians, referring physicians and the attending ward nephrologist, and appropriate components of the discharge summary given to the patient.

Notes regarding Transplant, Hemodialysis, and Peritoneal Dialysis patients are to be copied to the relevant attending nephrologist, and for in-centre hemodialysis patients to the responsible nurse practitioner.

Patients who are discharged sometimes require urgent attention from either the in-centre hemodialysis unit, home dialysis unit, or the transplant clinic. This might include for instance follow-up of blood cultures or imaging, or continuing medications that must not be interrupted. In such a case, an email must be sent separately to the responsible health care provider by the physician completing the discharge summary, to avoid a potentially dangerous interruption of care.

Details about discharge summaries are provided below, under “Documentation”.

7. **The schedule of daily activities on the ward service**

a) Weekdays

9:00 am handover

The ward team members, including the fellows and resident, meet each morning shortly after 9:00 am to get handover from the fellow on-call the night before about any new admissions and any issues addressed overnight for already admitted patients. There may separately be information provided by the SCT resident who was on-call the night before.

The Hemodialysis Charge Nurse generally meets with the ward team early in the morning after 9:00 am to review the patients who will be receiving hemodialysis that day.

The attending staff nephrologist may also attend.

9:45 – 10:15 am Multidisciplinary team meeting ("Bullet rounds")

Bullet rounds with the ward medical team and 8CC-S nursing and other health care team staff occur from 0945-1015 every weekday morning to highlight the plans for the day for each in-patient. This is an opportunity for the medical team to update other team members on the medical progress of each patient, and for the other health team members to provide the medical team with their perspectives. A shared plan is then developed and modified for the whole team.

10:15 am – approximately 2:30 pm – Time to see patients

During this middle part of the day, the fellows and resident go to see the ward patients, arrange any consults and tests, communicate further with other members of the health care team, document their daily notes, and admit any new patients, among other tasks.

Approximately 2:30 pm – Attending rounds

On most (if not all) weekdays, the attending staff will meet the team to review the patients' progress in the middle of the afternoon, and to comprehensively review any new patients. During these attending rounds, the staff nephrologist provides case-based teaching related to the ward patients, and any other related issues.

Approximately 5:00 pm - Signover

We aim to conclude the workday each day by 5:00 pm. This is, of course, not always possible, as there may be a large number of patients to see, and some of them may be particularly ill.

One of the ward fellows will be designated to call the on-call SCT ward resident. The fellow needs to

signover *all* of the ward patients with at least a brief summary of each patient's issues, and a more detailed description of patients who are particularly ill and a clear outline of any tasks the on-call SCT ward resident needs to do.

Weekend days on the ward

The major differences on Saturdays and Sundays (and Holiday Mondays and Good Friday) are that there are no bullet rounds, and there is only one fellow on-call. The on-call ward fellow will generally meet with the on-call nephrologist each morning on the weekend to review patient progress and outline priorities for the day, and to review any newly admitted patients. They will meet again towards the end of the afternoon to again review patient issues. Because there is only one fellow on-call on the weekends, the review of the admitted patients will of necessity be more focused, but all ward patients should be seen each day. If it is particularly busy, the staff nephrologist is expected to help with seeing ward patients.

8. Expectations for documentation – Nephrology Ward Service

a) Daily notes via Digital Dictation

Generally, most residents enter notes – both the initial admission notes and notes for follow-up visits – using Digital Dictation. The notes can either be typed in, or they can be dictated using the Dragon app on one's cellphone. (Notes can, if preferred, also be entered into the physical chart by hand.)

A useful feature of the Digital Dictation application is the "Quicksave" button near the top left of the screen, to ensure that even without finalizing the note, one's work can be quickly saved while creating the note, to avoid inadvertent loss.

A second useful feature is the copy and paste button, that allows the note that was most recently entered by the nephrology service to be copied and pasted into the current note. This can save time in that one does not need to retype information such as the patient's demographics, reason for admission, other health issues, etc. The risk of such copying and pasting is that one may leave points in the new note that are no longer relevant. Accordingly, if one chooses to use this feature, it is *essential* to carefully proof-read the note before submitting it, to ensure that any points that are no longer relevant have been removed.

It is also important to select the correct service (i.e. "Nephrology") for each of the consult note, admission note and the daily note.

All patients on the ward service should have a daily note entered every day.

b) Signout Sheet Updates

The "census" for the nephrology ward is maintained via the Signout Sheet. This is found in the "edischarge" application. The edischarge application is most conveniently located via Soarian.

It can be accessed via the blue Menu Bar, by clicking the button between the finder icon (magnifying glass) and the printer icon.

Select "eDischarge – Not patient specific".

Then click "eSign-out" (upper right corner)

Then choose either "Nephrology – Consults" or "Nephrology – Consults".

It is essential to:

- Enter every new patient on to the census sheet as soon as one becomes aware this patient has been admitted
- Update the signout sheet regularly so that it will be clear to any physician covering the service what the background history of the patient is, and what active issues are being followed
- Avoid ambiguous words such as "tonight" or "tomorrow" (use dates instead)
- Remove issues from the signout sheet that have been addressed
- Remove the patient from the active signout sheet once they have been discharged

c) Discharge Summaries – Steps in Preparation of the Discharge Summary

All patients discharged from the nephrology ward must have a discharge summary completed prior to their actual discharge from hospital.

The contents of the discharge summary should be discussed with the attending staff nephrologist prior to the patient's discharge (especially any plans for follow-up care) so that there is consistency in the instructions given to the patient at the time of discharge, particularly in relation to discharge medications and follow-up appointments.

The discharge summary application is identified initially via the same steps as the signout sheet:

- It can be accessed from Soarian via the blue Menu Bar, by clicking the button between the finder icon (magnifying glass) and the printer icon.
- Then from the dropdown menu - Select "eDischarge – Not patient specific".
- Then click "eDischarge Summary" (upper right corner)
- Then, find the patient using either their medical record number (MRN), or their name, using

the appropriate dropdown menu.

- Then click “Create”.

This starts the process of creating a structured discharge summary that is in 7 sections:

1) Patient information
    a. this is demographic data that is entered automatically by the system
2) Diagnoses
    a. Discharge diagnosis (or “most responsible diagnosis” (MRD)
        - This is the major condition that led to the patient’s hospitalization
        - If possible, select this from the dropdown menu, otherwise enter this free text
    b. Other conditions impacting length of stay
        - Identify all of the other conditions that may have had an impact on the patient’s length of stay – doing so is very important for hospital funding
    c. Other conditions
3) Course in hospital
        - This is the main section where one has the opportunity to comprehensively but succinctly describe the patient’s hospitalization
            - The presenting illness
            - The course of the presenting illness
            - Therapeutic interventions
            - Any other complications that developed during the hospitalization
4) Investigations
        - The results of major investigations (e.g. imaging, biopsy) can be summarized here
5) Discharge
        - The first section needs to indicate where the patient is being discharged
        - The second section provides the space for a comprehensive but succinct summary of the follow-up plan – investigations, therapies, need for follow-up visit for other physicians and other health care providers
        - The final section provides instructions to the patient
6) Medications
    a. All of the medications the patient will be taking need to be included in this section
    b. This requires medication reconciliation, such that it is clearly indicated to the patient
        i. Whether any medications they were taking prior to admission have been stopped
        ii. Whether any new medications have been started

        The pharmacist can assist with this
    c. The medication section of the discharge summary can be used to generate a

prescription

d. It is not necessary to provide a new prescription for medications the patient already has

7) Cc list
   - It is essential to ensure all relevant physicians and other healthcare providers are copied on the discharge summary
   - This includes
     - Family doctor
     - Outpatient nephrologist
     - Other consultants involved in the patient's care
     - Other health care providers – e.g. nurse practitioner

Finalizing the Discharge Summary

This will be done by the attending staff physician who will read the draft discharge summary prepared by the resident or fellow, edit it as needed, and then finalize it.

This final step should be completed within 24 hours of the patient's discharge.

F. NEPHROLOGY CONSULTATION EXPERIENCE

The Nephrology Consult Service assesses and follows patients admitted to other services who have renal and/or fluid-electrolyte disorders.

1. Composition of the Consult Team

The consult team has an attending nephrologist and at least two nephrology fellows, as well as two or three residents, and a variable number of elective residents and elective medical students.

2. Categories of patients followed by the consult service and related considerations

- a) Hemodialysis (HD) or peritoneal dialysis (PD) patients admitted to hospital to another service
    - Admitted for surgery
    - Admitted to general internal medicine or a medical subspecialty service because of a "non-dialysis" clinical problem (e.g. GI bleed, pneumonia, atrial fibrillation)

  These patients must be assessed and followed regularly to ensure they are receiving appropriate dialysis treatment. Dialysis needs often change when patients are acutely ill and/or have had surgery. For instance, they may eat less, or they may be catabolic, necessitating a reduction in their target weight. As a second example, due to their illness, they may need to avoid anticoagulation during the dialysis treatment.

  Some patients on HD or PD who are in hospital for a prolonged period of time (e.g. waiting for long-term placement, waiting for transfer back to their base hospital after surgery) may be quite stable, and thus may not require daily assessment by the nephrology consult team. This determination needs to be made in discussion with the attending staff nephrologist.

- b) Kidney transplant patient admitted to hospital to another service
    - Admitted for surgery
    - Admitted to general internal medicine or a medical subspecialty service because of a "non-transplant" clinical problem (e.g. GI bleed, atrial fibrillation, MI). Most kidney transplant patients with infection should be admitted to the nephrology ward service.

  These patients need to have their immunosuppression carefully managed while in hospital. Examples of frequent considerations include:
    - *Patients may need "stress steroid" coverage*. This is because almost all

kidney transplant patients are on long-term corticosteroids, and so they will generally not mount an adequate corticosteroid response to stress. If their illness is mild-to-moderate, it is sufficient to double their baseline steroid (usually prednisone) dose. If they are severely ill, they should receive coverage for adrenal insufficiency, generally Hydrocortisone i.v. 100 mg q8h, which is then tapered once they are stabilized.

- *Patients need to have their level of calcineurin inhibitor monitored.* Both cyclosporin and tacrolimus interact with many medications and levels may change during illness. It is therefore important to monitor their serum levels:
  - For tacrolimus – "trough" levels are drawn before the morning dose
  - For cyclosporin - "C2 levels" are drawn 2 hours *after* the morning cyclosporin dose.
- *Vigilance for infection.* Owing to their immunosuppression, transplant patients are obviously at higher risk for infection, and may not mount a typical response to an infection; for instance, they may not have a fever. Transplant patients who do develop an infection while in hospital often have an adjustment made in their immunosuppression. The most frequent of these is to stop the antiproliferative agent (in most cases this is Mycophenolate Mofetil) until the patient has started to improve. This should be reviewed with the attending staff nephrologist.

- <u>c) Patients with acute kidney injury</u>
  - This is the commonest reason for nephrology consultation, apart from managing patients on HD, PD or with a transplant
  - It is essential early on in the consultation process to identify patients with emergencies (e.g., hyperkalemia, fluid overload causing pulmonary edema) that may need to be managed even before the consult assessment has been completed
  - It is almost always useful to get a renal ultrasound to rule out obstructive uropathy, confirm there are two kidneys, and assess kidney size
  - It is almost always useful to get a urine sample for review via the microscope on 8-CC-south. A useful strategy is to ask the nurse on the ward where the patient is admitted to get a urine sample in a labeled specimen container, and leave this with the patient (i.e. not to send it to the lab) for the nephrology team to retrieve.
  - It is very important to review prior serum creatinine measurements as part of the patient's "History of presenting renal illness". This can be done via Soarian and, if necessary, through the ConnectingOntario database.

- d) Patients with apparent parenchymal renal disease
    - These patients typically present with hematuria and/or proteinuria and/or impaired renal function.
    - They also need a urinalysis to be done.
    - In some cases, they may require a kidney biopsy.

- e) Patients with an electrolyte disorder
    - *Hyponatremia*
        - This is very common
        - It may lead to morbidity due to both the disorder itself but also if there is overly rapid correction, as this may lead to osmotic demyelination in a patient with chronic hyponatremia
        - It is essential to involve the fellow and/or attending staff very early in the care of a patient who is correcting too rapidly (i.e., more than 8 mmol/L/24 hours) or is at risk of doing so due to an increased rate of urine flow (i.e. more than 100 mL/hour) in the setting of severe hyponatremia (i.e. serum sodium < 120)
        - It is essential to monitor the electrolyte levels frequently (sometimes as often as every 4 hours or even every 2 hours), and follow-up to ensure this is being done and the results appropriately responded to.
    - *Hyperkalemia*
        - This is also a quite common electrolyte disorder
        - In the immediate workup of the patient, it is essential to
            - Get an ECG to determine if there is any immediate risk to the patient with regard to cardiac rhythm disorders
            - Check for hemolysis and order a repeat potassium level, as a very common cause of a measured elevated serum potassium level is an error in specimen handling or processing, either due to hemolysis in the tube, vigorous fist clenching, or possibly delay in transport of the sample to the lab
            - Be prepared to administer emergency therapy, including
                - Calcium gluconate 1 g iv
                - Humulin R 10 units IV
                - Dextrose 50% at a dose of 50 cc iv
                - Capillary blood glucose every 30 minutes for 4 hours

- f) Other reasons for consultation
    - There are of course multiple other reasons for patients to be referred for nephrology consultation, including but not limited to:
        - Pregnancy-associated complications such as preeclampsia
        - Intoxication with substances that can be removed via dialysis
        - Hypertension
        - Hematologic disorders like thrombotic microangiopathy

3. Schedule of daily activities on the consult service

Weekdays

9:00 – 10:00 am Handover and Plan for the Day – Generally in the Conference Room 8 CC-North

The consult team receives handover from the previous night from the fellow on-call, and sometimes also from the SCT Consult resident who was on-call the night before.

The consult team (fellows, residents, students, and often attending staff) then meet to review new consults, and to assign existing patients to team members.

Major issues needing attention are addressed at this time in planning the day's activities, including:

- Patients requiring dialysis
- Patients requiring specific investigations (imaging, biopsy, etc.)
- Patients requiring special communication with the primary team
- Patients who may be signed off

The Hemodialysis Charge Nurse will meet with the consult team to confirm the hemodialysis plans for patients on the consult team.

9:30 am – 2:30 pm – Time to see existing and new consult team patients

The middle part of the day is the time when existing patients on the service are reviewed, and any new consults are seen. It is essential for the team members to stay in close contact throughout the day so that the fellows are kept up-to-date on any significant developments affecting existing patients, and so that the whole team is aware of any new consultations, and who has been assigned to see the patients.

Approximately 2:30 pm – Rounds with the Attending Staff – Nephrology conference room

Around the middle of the afternoon, the team will generally be joined by the attending staff nephrologist. During the rest of the afternoon, the goal is to:

- Review major issues affecting the existing patients
- Review new consults
- Go to the bedside to see new consults and also any patients with specific issues to be reviewed

Approximately 5:00 pm

We aim to conclude the working day at approximately 5:00 pm on most days, and certainly by 6:00 pm. It is of course possible that there will be particularly busy days on which this may not be possible due to the need to attend to the safe patient care of a large number of potentially very sick patients, but this should be unusual.

4. Expectations for documentation

a) Daily notes via Digital Dictation

Generally, most residents enter notes – both initial consultation and follow-up visits – using Digital Dictation. The notes can either be typed in, or they can be dictated using the Dragon app on one's cellphone.

A useful feature of the Digital Dictation application is the "Quicksave" button near the top left of the screen, to ensure that even without finalizing the note, one's work can be quickly saved while creating the note to avoid inadvertent loss.

A second useful feature is the copy and paste button, that allows the immediately prior note from the nephrology service to be copied and pasted into the current note. This can save time in that one does not need to retype information such as the patient's demographics, reason for admission, other health issues, etc. The risk of such copying and pasting is that one may leave points in the note that may no longer be relevant. Accordingly, if one chooses to use this feature, it is *essential* to carefully proof-read the note before saving it, to ensure that any points that are no longer relevant have been removed.

It is also important to select the correct service (i.e. "Nephrology") for both the consult note and the daily note.

Most patients on the consult service should have a daily note entered every day. The major exception to this expectation is for stable patients (e.g. a patient awaiting placement with no recent health issues), in whom it may be sufficient to enter a daily note perhaps twice per week.

b) Signout Sheet Updates

The "census" for the nephrology consult service is maintained via the Signout Sheet. This is found in the "edischarge" application. The edischarge application is most conveniently located via Soarian.

- It can be accessed via the blue Menu Bar, by clicking the button between the finder icon (magnifying glass) and the printer icon.
- Select "eDischarge – Not patient specific".
- Then click "eSign-out" (upper right corner)
- Then choose "Nephrology – Consults"

It is essential to:

- Enter every new patient on to the census sheet as soon as one becomes aware this patient is being seen by the consult service, even before the consult has been completed
- Update the signout sheet regularly so that it will be clear to any physician covering the service what the background history of the patient is, and what active issues are being followed
- Avoid ambiguous words such as "tonight" or "tomorrow" (use dates instead)
- Remove issues from the signout sheet that have been addressed
- Remove the patient from the signout sheet once they have been discharged or signed off

5. Interactions with referring services

It is critical for members of the nephrology consult team to regularly interact with the patient's primary team (i.e., with the team that requested the nephrology consult in the first place). This communication can of course occur via several means:

(i) The note on Digital Dictation
(ii) An order handwritten on the green order sheets in the physical chart
(iii) A telephone call or page to one of the team members.

This is particularly important in the following circumstances:

- For patients on hemodialysis, the dialysis procedure is a time-consuming activity. If a patient in hospital needs another procedure (such as endoscopy, coronary angiography, etc.), then the potential exists for a conflict between the dialysis procedure and the other procedure. This may require coordination of timing to avoid such a conflict.

- The nephrology service often is addressing acute issues in sick patients, and it may be important to alert the primary service of suggestions or interventions from the nephrology consult team. It may not be sufficient to simply leave a note in the Digital Dictation and assume the primary team will see this in a timely manner. Instead, it may be necessary to call

or page a member of the primary team.

G. NEPHROLOGY FELLOWS ASSIGNED TO DIALYSIS ROTATION

This is a 4-week rotation completed by PGY4 nephrology trainees.

The faculty education lead for this rotation is Dr. Ziv Harel.

During each week, trainees spend time as follows:

- They round in the hemodialysis unit 2 or 3 times on a given daytime shift (MWF1, MWF2, TTS1 or TTS2) for a half-day with the staff nephrologist and/or the nurse practitioner assigned to that shift
- They attend the Multicare Kidney Clinic (MCKC) on Tuesday and /orFriday mornings
- They take part in Home Dialysis activities
    - Tuesday afternoon Home Dialysis clinic
    - Thursday morning Home Dialysis rounds
    - Home dialysis clinic/drop-ins for 2-3 half-days per week
- They attend their longitudinal clinic

The precise timetabling of this block is worked out between the trainee and Dr. Harel.

H. NEPHROLOGY HOUSESTAFF ASSIGNMENT AND ON-CALL RESPONSIBILITIES

1. Residents and Elective Students

a) Core Internal Medicine Residents, Elective Residents and Elective Students

The Nephrology rotation for (core) internal medicine trainees (and for residents on elective, and elective medical students) is a predominantly in-patient consult experience, in addition to providing some ambulatory clinic exposure. The blocks are generally 4 weeks in length.

There are scheduled teaching sessions each morning from 8:00 – 9:00 am on Mondays, Tuesdays, Wednesdays and Thursdays, and sometimes on Fridays. A teaching schedule is provided prior to the rotation.

Core internal medicine residents each have a mandatory academic half-day that they attend: PGY1 residents on Thursday afternoons; PGY2 on Wednesday afternoons; and PGY3 on Tuesday afternoons.

b) Urology Residents

Urology residents are assigned to the ward team for their 4-week block of nephrology, in order to provide substantial exposure to both kidney transplantation and to the management of end-stage renal disease. Urology residents also have exposure to the kidney stone prevention clinic. They attend the same teaching sessions as the core internal medicine residents. They also attend their Tuesday morning surgical skills teaching, and Friday morning urology school.

c) On-Call Duties for Junior Residents

The *core internal medicine residents* take part in the "SCT" ("subspecialty consulting team") on-call process. The residents for the SCT team come from the nephrology, endocrinology, gastroenterology, hematology-oncology, infectious disease, respirology, allergy/immunology, medical consults and rheumatology services. They provide coverage overnight and on weekends for:

- the emergency department for patients needing admission to these services
- the in-patient wards for patients already admitted to these services, including intial assessment of post-operative renal transplant recipients
- urgent in-patient consultations (in collaboration with on-call fellows and attending staff) for these services

The *urology residents* are assigned to cover the nephrology in-patient ward for a small number of overnight calls during their 4-week block.

2. Nephrology Subspecialty Trainees and Internationally Trained Fellows

We refer to all of these trainees as "fellows".

a) PGY4 Trainees in the Royal College Nephrology Training Program

These fellows are assigned to the following nephrology services at SMH:

- 1 or 2 blocks of Consult
- 1 block of Nephrology Ward
- 1 block of Dialysis
- 1 Half-day each week of ambulatory nephrology clinic at SMH, UHN, or Sunnybrook

b) PGY5 Trainees in the Royal College Nephrology Training Program

These fellows are assigned to SMH for a variety of experiences, based on their choice and their educational needs. They may participate in clinics (including transplant clinics), dialysis, and/or the ward and consult services in a "Junior Attending" capacity

They each have a half-day clinic each week in ambulatory nephrology at SMH, UHN, or Sunnybrook.

c) Internationally Trained Clinical fellows

These fellows are generally assigned to SMH for a 6-block (24 weeks) or 7-block (28 weeks) period.

Their time is generally divided between in-patient nephrology ward service and the consult service.

They are generally assigned to a 2-week period in ambulatory clinics.

They take part in a half-day per week of ambulatory nephrology clinic with designated SMH Nephrologist

d) Ambulatory clinics for fellows

Fellows also attend a single half-day clinic each week.

- For the nephrology subspecialty trainees, these clinics may be at St. Michael's Hospital (SMH), Toronto General Hospital, or Sunnybrook Health Sciences Centre.
- Internationally trained fellows will have their clinics at SMH, and may also be assigned to a 2-week ambulatory clinic block.

e) Academic half-day teaching sessions for fellows

Fellows have mandatory teaching sessions Wednesday afternoons, generally from 3:00 – 5:00 pm. The sessions usually originate from Toronto General Hospital, and are broadcast to a viewing room at SMH on 3 Shuter. Since the onset of the pandemic, most of these have been delivered via Zoom.

f) Requests related to time on-call and for vacations

Requests for call and vacation must be sent at least 6 - 8 weeks ahead of the requested time to Michelle Job (michelle.job@unityhealth.to)

g) First call during the day for ward and consult services

One of the fellows on each of the ward and consult services is designated to be "first call" during the day.

- The fellow who is first call for the *ward service* will receive calls from locating related to patients needing admission to the ward, and also from the ward for urgent patient-care issues
- The fellow who is first call for the *consult service* will receive calls from locating for new consults, and also for issues related to patients already being followed. This fellow will triage the calls, and in collaboration with the rest of the consult team decide which team member will be assigned a new consult, and which team member will be asked to address any issues related to patients already on the service.

h) On-call responsibilities

Nephrology fellows are assigned on-call as follows:

- *Weeknights*

  Fellows take call from home. The on-call frequency is approximately one weeknight per week.

  They provide "second call" coverage for both the ward and consult service. They mainly provide backup to the "SCT" (senior consulting team) residents – there is an SCT ward resident, and an SCT consult resident. The SCT ward resident provides overnight and weekend ward coverage to inpatients admitted to nephrology, respirology, gastroenterology and hematology-oncology. The SCT consult resident provides overnight and weekend coverage for emergency department admissions and urgent in-patient consultations to nephrology, endocrinology, gastroenterology, hematology-oncology, infectious disease, respirology, allergy/immunology, medical consults and rheumatology services.

  - The SCT *ward* resident takes first call to the nephrology ward. The SCT ward resident may review with the on-call fellow any nephrology in-patients whom they have seen while on-call if a significant problem is identified or if they need any advice whatsoever.
    - Any new direct admissions *to the ward* (where the patient bypasses the ED to a pre-arranged ward bed) will be done by the SCT ward resident. Please

correspond with this resident to provide background patient details that you are provided with.

- The SCT *consult* resident takes first call for nephrology to the emergency department, and if necessary for urgent in-patient consults.
    - Any new consult requests *for inpatients* that are made overnight are (as during the day) first triaged by the on-call fellow to determine if the patient needs to be assessed overnight, or if the consult can wait until the next morning. If an urgent inpatient consultation is needed, please call the SCT consult resident with the details.
    - New consultations referred from the ED for admission will be seen directly by the SCT consult resident without fellow triage.
    - Any new direct admissions *to the ED* (where a St Michael's Hospital nephrologist sends their patient to the ED for admission to the Nephrology service) will be done by the SCT consult resident. Please correspond with this resident to provide background patient details that you are provided with.
    - Any consults (ED admissions or inpatient consults) seen by the SCT resident are reviewed with the on-call fellow in real-time, generally by telephone.

- There is a staff nephrologist assigned to be on-call each weeknight, who provides support to the on-call fellow and SCT residents.

- *Weekends*
    - Each fellow will be on call for 1 weekend on-call per 4-week block; occasionally, a fellow will need to do 2 weekends in a 4-week period. (The PARO contract specifies that fellows must have 2 weekends off out of every 4 weeks, and may not be asked to work 2 consecutive weekends.)
    - There are two fellows assigned to be on-call each weekend.
        - One fellow is assigned to round on the nephrology ward patients.
        - One fellow is assigned to round on the consult patients who need to be seen during the weekend, according to Friday afternoon signover.
    - There is an attending staff nephrologist also on-call who will take part in rounding on the ward and consult services depending on the number of patients and their complexity, to ensure safe patient care and a reasonable workload for the fellows.
        - When rounding on the nephrology ward patients is complete, please provide handover to the SCT ward resident. Prior to handover, the fellow is expected to respond to ward issues and nursing concerns.

- One of the fellows will be on-call overnight on Friday and Sunday; the other fellow will be on-call Saturday night.
    - Fellows should keep track of who is doing Friday/Sunday nights call (heavier call) and who is doing Saturday night call, so that over their time at SMH, this aspect of the weekend workload evens out across the fellows
    - For long weekends that include a holiday Monday, the fellow who is on-call Saturday night will also be on-call Monday night.
    - For the long weekend that includes the Good Friday holiday (and that therefore starts at 5:00 pm on the Thursday afternoon), the fellow who is on-call Saturday night will also be on-call Thursday night.

- Hemodialysis shift coverage
    - Attending staff on weekends covers first and second and overnight HD shift for urgent issues,
    - Renal fellow covers evening (3rd shift) for urgent issues only

- There is an attending nephrologist on call each weekend, generally the one covering either the ward or the consult service at that time
    - The attending nephrologist reviews
        - All newly admitted ward patients
        - All new consults
        - All ward patients at least once per weekend
        - All complex or particularly sick consult patients
    - The attending nephrologist will help with the weekend workload, depending on the volume and complexity of cases, including (if necessary) seeing patients on the ward and/or consult services on their own

- The SCT residents (ward and consult) provide coverage on the weekends similar to on weeknights.
    - The fellow on-call receives requests for new consults and to triage the consult.
        - There are 3 individuals able to do new consults on the weekend
            - The SCT consults resident
            - The consults fellow
            - The attending staff nephrologist

- The decision as to who will actually do the consult needs to consider the urgency of the clinical problem, how busy the SCT consults resident is and how busy the consult fellow and attending staff are
    - It is always appropriate for these individuals to share the workload in a reasonably equitable way

- *New transplant patients*
    - As described in the Kidney Transplantation section of this manual, patients who have just received a kidney transplant need to be seen by a member of the nephrology team. In most cases, this will be one of the ward nephrology fellows (during the day) or the on-call nephrology fellow overnight.
    - When the patient comes to the "Post-anesthetic care unit" (PACU, the name for the post-operative recovery room at SMH), the appropriate fellow will be paged to come and assess the patient
    - The SCT ward resident can also be asked to assess the patient if the patient has completed their surgery in the middle of the night, but the SCT ward resident must review the case with the on-call fellow, and if there are any concerns, then the on-call fellow must be able to come in to assess the patient personally.

3. Need for periodic cross covering between ward and consult services

Residents and fellows may be away from their team for a variety of reasons, including: vacation, being post-call, at clinic, illness, and academic sessions such as half-day teaching, among others.

We strive to ensure that there is sufficient coverage every half-day on both the ward and consult services, but there will be times when these various factors leading to absences coincide such that one of the services may be left with only 1 or even zero housestaff.

At such times, it will be necessary for one of the housestaff on the better-staffed service to move to the short-staffed service either for the half-day or the full day.

It may also be necessary for a member of the housestaff to miss attending an outpatient clinic to ensure minimally adequate staffing of the in-hospital services.

The attending staff nephrologists will also help in providing frontline patient care at these times.

I. OUTPATIENT CLINIC EXPERIENCE

Every week there are Outpatient Clinics that have been organized to facilitate resident participation.

Most clinics are held in the office building at 61 Queen St. East, 9th Floor. (This building is on the south side of Queen Street, just across the street from the hospital.) A schedule of clinics is available from Muchelle Job.

The following are the clinics:

- Transplant clinics
- Multicare Kidney Clinic
- Acute Kidney Injury Clinic
- Kidney Stone Prevention clinic
- Home Dialysis Clinic

In addition, most of the staff nephrologists have private office clinics, also mostly held on the 9th floor.

Each resident will be sent an e-mail from Michelle Job (Dr. Schreiber's assistant) asking them when they will not be available in terms of (a) holidays, (b) other days off, (c) academic half-days. Once this is available, a clinic schedule for the rotation will be distributed on the first day of the rotation. We aim to schedule 2 clinics for each internal medicine resident during their 4-week rotation.

J. SCHEDULED TEACHING ACTIVITIES

1. **Didactic Teaching rounds at SMH: Most days, from 8am - 9am**

During the Covid-19 pandemic, most of the scheduled teaching sessions have been done via Zoom.

As the pandemic eases, we will likely return at least partially to in-person teaching.

A schedule of teaching for the upcoming block is sent out ahead of time via email by Dr. Schreiber's assistant Michelle Job.

Monday – Case Rounds

- These are led by either one of the renal fellows or one of the staff (schedule will be available ahead of each fellow's rotation)
- The focus is on presenting a case to stimulate discussion of pathophysiology, diagnosis, investigation and management
- The presenter will often review one aspect of the case in more depth, including a brief review of at most 1 or 2 references

Tuesday – Divisional Academic Rounds

- These rounds generally involve a staff nephrologist or invited speaker
- Once per month, there is a renal pathology rounds, with generally 2 cases presented together with the kidney biopsy slides
    - The renal fellows may be asked to provide a brief clinical summary with 2-3 PowerPoint slides if they are familiar with the case
- These rounds are held from the beginning of September until the end of the following June
- In July and August, Tuesday morning teaching sessions are led by one of the attending nephrologists assigned to either the ward or consult service

Wednesdays and Thursdays

- There are rounds on these mornings organized specifically for fellows, and a separate set of teaching sessions organized for the core internal medicine and urology residents

Friday

- During some weeks, we use the 8:00 – 9:00 am slot for additional teaching

2. Wednesday afternoon teaching for fellows

- This takes place on Wednesday afternoons, generally from 3-5 PM

- 3 – 4 pm – Dedicated core teaching for nephrology trainees
- 4 – 5 pm - Citywide nephrology rounds

During the Covid-19 pandemic, these sessions have been delivered via zoom.

Even when they were delivered in-person from a lecture room at Toronto General Hospital (TGH) prior to the pandemic, they were broadcast to a viewing room on 3-Shuter so that fellows did not need to travel to TGH to attend the sessions. We anticipate a similar strategy in future.

K. ADMINISTRATIVE EDUCATIONAL ASPECTS OF THE ROTATION

1. Core internal medicine trainees

a) Rotation Objectives: Core Internal Medicine Trainees

At the end of the nephrology rotation, the resident should be able to:

1.	Perform an accurate and detailed history and physical examination to elicit details of common renal disorders.
2.	Correlate relevant pathophysiology to the ordering and interpretation of laboratory and imaging investigations commonly used in the assessment of renal disorders, including urinalysis and arterial blood gas analysis.
3.	Demonstrate a cost-effective, patient-centred approach to and evidence-informed rationale for the management of common chronic renal disorders.
4.	Effectively manage acute renal disorders.
5.	Apply knowledge of medications commonly used in the management of renal disorders including indications, renal dosing adjustments, potential side effects, and contraindications.
6.	Collaborate effectively with interprofessional health team in the care of patients on dialysis treatment.
7.	Educate patients regarding lifestyle modifications relevant to renal disease.

b) Feedback and Evaluations

In-training assessment report (ITAR)

At the end of the rotation, the residents will receive summary feedback from the rotation coordinator both in writing (in the form of the ITAR on the POWER platform) and also verbally.

Periodic feedback during training

Each attending with whom the trainee interacts should provide the trainee with formative feedback at the end of their time with the trainee, as well as periodic feedback on their day-to-day work.

EPA Assessments

Residents are encouraged to ask faculty members and nephrology fellows to complete these for them, both in the in-hospital and the ambulatory clinic settings.

2. Nephrology Fellows

Rotation Objectives: Nephrology PGY4 Trainees – In-patient nephrology ward

Rotation Objectives: Nephrology PGY4 Trainees – Nephrology Consult Service

Rotation Objectives: Nephrology PGY4 Trainees – Dialysis Rotation

Rotation Objectives: Nephrology PGY5 Trainees – Junior Attending

In-training assessment report (ITAR)

At the end of the rotation, the fellows will receive summary feedback from the rotation coordinator both in writing (in the form of the ITAR on the POWER platform) and also verbally.

Periodic feedback during training

Each attending with whom the trainee interacts should provide the trainee with formative feedback at the end of their time with the trainee, as well as periodic feedback on their day-to-day work.

EPA Assessments

Fellows are encouraged to ask faculty members to complete these for them, both in the in-hospital and the ambulatory clinic settings.

L. RESEARCH OPPORTUNITIES

During the rotation, trainees are encouraged to take advantage of the opportunity for discussions with staff that have expertise in the different areas of nephrology. Indeed, there are numerous opportunities to get involved in various research projects of all sizes. This may involve patient centered clinical research, case reviews and chart audit type studies, basic physiology or bench type research.

The nephrologists encourage residents to participate in research activities and are happy to supervise a project. These projects could be presented at the annual St. Michael's Resident Research day (Higgin's Day) or oftentimes at national and international meetings. Special areas of interest and expertise amongst the staff are detailed below:

Dr. Harel - Quality improvement
Dr. Kamel - Acid-base and electrolyte physiology and renal stones
Dr. Marsden - Molecular medicine and hypertension
Dr. McFarlane - Diabetes, hypertension, dialysis, clinical epidemiology, health economics
Dr. Perl - Peritoneal dialysis, general nephrology
Dr. Prasad - Transplantation
Dr. Schreiber - Medical education/renal physiology
Dr. Wald - Acute kidney injury, hemodialysis, general nephrology
Dr. Weinstein - Medical education, e-Learning and web development
Dr. Yuen - Kidney fibrosis
Dr. Zaltzman - Transplantation

HEMODIALYSIS AT ST. MICHAEL'S HOSPITAL

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Hemodialysis (HD) Units

Hemodialysis Units at St. Michael's Hospital

The hemodialysis units are located on 8CC. Both units are locked, and require the physician's badge to be able to enter the unit.

- The main (south) unit has room for 23 patients. The entrance is accessible from the foyer of Cardinal Carter South elevators. The main unit on 8CC is open from Sunday 22:00 until Saturday 23:00.
- The second (north) unit has room for 12 patients. It is accessible from the hallway headed to the 8th floor Cardinal Carter North. It is open from Monday to Saturday, from 07:00-23:00.

Satellite Unit

St. Michael's Hospital has an out-patient chronic hemodialysis facility located at 45 Overlea Blvd.

Home Dialysis

Location: 8CCN
Internal Extension: 3848
Hours: Monday to Friday 8:00am – 4:30 pm
Clinic: Tuesdays 12:00 noon - 4:00pm in Home Dialysis Unit
Post Clinic Rounds/Review: Thursdays 9:15-10:30
Focus: Training for Peritoneal and Hemodialysis at home with ongoing follow up post training.

Hemodialysis Nurses

Charge Nurse

There is a charge nurse who manages the schedule for hemodialysis for both outpatients and inpatients, including those maintenance HD patients who are hospitalized and individuals with acute kidney injury who need HD. The charge nurse can be reached at extension 5228 or 6131. The charge nurse meets every day from Monday to Saturday with one or more representatives of both the ward team and the consult team to plan dialysis treatments for all inpatients. If a patient develops a need for HD during the day, the charge nurse must be notified as soon as possible.

Nurses providing HD care

- For outpatients, one dialysis nurse is responsible for the dialysis treatment for up to 4 patients.
- In the inpatient setting, if the patient requires hemodialysis in hospital, provided they are stable and there is space in the dialysis unit, then the patient may be dialyzed in the dialysis unit.
- If the patient is not stable enough to come to the dialysis unit, hey will have to be dialyzed in their room. In such a case, the nurse looks after the patient in a 1:1 nurse: patient ratio.

Dialysis in the evening or overnight

If a patient requires urgent dialysis in the evening or overnight, the charge nurse should be notified. He/she will assign a nurse who is in hospital to provide the HD treatment.

The only time when there is no HD nurse in the hospital is from Saturday 22:00 to Sunday at 19:00. During this time, the on-call HD can be reached via locating.

Vascular Access Coordinators

There are three HD nurses who serve as vascular access coordinators. They can be reached either by telephone (extension 6353) or by email (VACnurses@smh.ca). They can facilitate the investigations and management of all vascular access issues.

Hemodialysis schedules

Conventional

Most patients are dialyzed 3 times per week: either on a Monday, Wednesday, Friday (MWF) schedule, or Tuesday, Thursday, Saturday (TTS) schedule. The dialysis “shifts” are either morning (starting at ~ 7:30 am), afternoon (starting at ~ 1:00 pm) or evening (starting at ~ 5:30 pm). The typical duration for conventional, 3 times per week HD is 4 hours.

Intensive

Some St. Michael's Hospital dialysis patients are receiving higher than conventional doses of HD. Examples of intensive HD include:

- short daily in-centre (4 or 5 times per week for 2.5 to 3.5 hours)
- nocturnal in-centre (3 times per week for 7- 8 hours overnight)
  - ➢ These shifts happen at St. Michael's Hospital, and the patients come on one of the following schedules:
    - Tuesday, Thursday, Sunday, OR
    - Monday, Wednesday, Friday
- short daily home (5 or 6 times per week for 2.5 to 3.5 hours)
- nocturnal home (5 to 7 times per week for 6 - 8 hours overnight)

Nocturnal dialysis involves the patients coming to hospital at ~ 10:00 p.m., and dialyzing for 7-8 hours overnight while they sleep.

Patients receiving intensive hemodialysis may have a different dialysate composition compared to patients on a conventional schedule. This is because they have a greater clearance of solutes compared to conventional dialysis, and therefore they may develop excessive reductions of plasma solute levels for substances such as phosphate. For example, their dialysate may have a potassium concentration of 3 or even 4 mmol/L; and, they may have phosphate (in the form of a Fleet® enema, which contains sodium phosphate) added to the dialysate.

As a result of receiving such additional dialysis, these patients often have a more liberal diet and fluid intake. If an intensively dialyzed patient is admitted to hospital and converted to a conventional dialysis dose (4 hours 3 times per week), their entire dialysis prescription should be reassessed, and dietary restrictions should be started as appropriate. In general, it is preferable to keep a patient who normally performs an intensive form of HD on an intensive form (e.g. in-centre intermittent nocturnal HD) while they are admitted, but this is often not possible as the patients may be too sick to be safely dialyzed in the HD unit on the nocturnal shift.

Home Hemodialysis

While the majority of HD patients are on in-centre HD three times weekly, there is a subset of patients who are trained to do HD at home. For these patients, there is no universal HD prescription, as patients have more flexibility to individualize their treatment. Some common examples of home dialysis prescriptions include short daily HD (3 hrs, 5-6 days per week) and nocturnal HD (7-8 hours, 3-6 nights per week). Patients are generally seen in clinic at 2-month intervals, or sooner if necessary.

For any home HD issue, it is important to consult with the multidisciplinary team in the Home Dialysis office on the 8th floor of the Cardinal Carter wing (416-864-5794 or extension 3848 or Case Manager extension 6977).

Resident responsibilities for patients on chronic in-centre HD

Residents do **not** provide first line care for the out-patient dialysis patients as there are nurse practitioners, nephrology attending staff and often nephrology subspecialty trainees who oversee the care of these patients.

Residents are responsible for HD orders for:
- patients admitted to the nephrology service
- patients on the consultation service receive chronic maintenance HD and therefore require close supervision irrespective of the main reason for admission
- patients on the consultation service with acute kidney injury who require HD

Residents are sometimes needed to:

- Respond to acute issues for in-centre hemodialysis patients if the nurse practitioner or the attending nephrologist is not available.
- Help complete admissions from the dialysis unit

Any acute dialysis needs and any changes to a patient's routine HD schedule should be brought to the attention of the charge nurse in the hemodialysis unit preferably the night before or at the latest first thing in the morning to facilitate planning for nursing resources. This includes entering the orders into Soarian.

When a patient is being discharged home from hospital and will need ongoing HD as an outpatient, *it is critical that there be a signover to the nurse practitioner and the attending staff nephrologist who will be looking after the patient in the outpatient setting.* The signover needs to provide a summary of events during the patient's hospital stay, and of issues for follow-up in the outpatient setting, including specific plans for problems that were addressed while in hospital. For example, if a patient was being treated for an infection as an inpatient, the plan for future antibiotic management and other aspects of care must be clearly communicated.

Vascular Access for Hemodialysis

Protect the arm veins of patients with advanced CKD or ESRD

IVs and BP measurements must be avoided in the limb that has an AV graft or fistula or one in which a graft or fistula is being planned.

Types of HD Access

Three types of vascular access are available for HD:

- Arteriovenous fistula (AV fistula)
- Arteriovenous graft (AV graft)
- Central venous catheter (CVC)

1) *Arteriovenous (AV) Fistula*

The preferred form of chronic access for HD is an AV fistula. This involves creating a surgical anastomosis of one of the patient's arteries to one of their veins. This is done by a vascular surgeon. This can be done on either arm, either in the forearm (most commonly end-to-side anastomosis of radial artery to cephalic vein) or upper arm (side to side anastomosis of brachial artery to cephalic vein). The high arterial pressure from the artery is then transmitted to the vein, whose wall hypertrophies ("arterializes"), which permits the vein to be repeatedly cannulated without being injured. The arterialization of the vein usually requires about 6-8 weeks; this is called "maturing". Having arterial flow to the vein allows for the high blood flow to enter the dialysis circuit which is needed for the dialysis treatment.

The AV fistula may occasionally become thrombosed, in which case patency can often be reestablished in the interventional radiology (IR) department, using a combination of thrombolysis and mechanical clot disruption, often followed by angioplasty. Patency of the AV fistula can be confirmed by feeling a thrill and/or hearing a bruit over the fistula site.

2) *AV Graft*

This is a connection of an artery to a vein using a PTFE (Teflon®) vascular graft. These are usually in the forearm, upper arm or sometimes thigh. The AV graft can be in a straight configuration, or in the form of a loop.

An AV graft is often created when a patient does not have sufficiently large veins available to permit the creation of an AV fistula, but has large enough veins to allow a connection from artery to vein via a graft. The dialysis needles are inserted into the graft. The graft

can be used earlier than a fistula after creation (within 1 week) but has a higher risk of thrombosis and infection. If an AV graft becomes thrombosed, it can often be recanalized in the IR department via a combination of thrombolysis and mechanical clot disruption, often followed by angioplasty.

3) *Central venous catheters (CVCs)*

All CVCs used for HD have 2 lumens in parallel with each other:

- One lumen is (somewhat confusingly) called the "Arterial" lumen. It is red in colour. The holes in the wall of the catheter that permit the entry of blood for this lumen are on the sides of the catheter. This lumen generally is used to take blood away from the patient and towards the dialysis machine. It is for this reason that it is called the "arterial" lumen – i.e., it is *arterial* to the machine. (The blood is of course venous blood in this lumen, and it is also venous blood in the "venous" lumen.)
- The other lumen is called the "Venous" lumen. It is blue in colour. The hole for this lumen that permits the return of blood from the catheter to the patient is at the tip of the catheter. This lumen takes blood *away* from the machine and back to the patient, and for this reason it is called "venous".

Temporary central venous catheters (CVCs)

Temporary dialysis catheters are placed by housestaff and fellows, under staff supervision as needed. These are double lumen catheters placed in either the femoral vein or internal jugular vein. They are used when dialysis is urgently required.

- Informed consent for CVC insertion must be obtained from the patient or from a substitute decision-maker if the patient is incapable of giving consent. The possible complications that should be mentioned include:
    - Infection
    - bleeding
    - injury to adjacent structures
        - Femoral vein cannulation
            - Femoral artery
        - Internal jugular vein cannulation
            - Carotid artery

    - Pneumothorax
- Bleeding tendency: Before CVC insertion is attempted, it is important to ensure the patient does not have any major bleeding diathesis by checking their medication list (for antiplatelet agents and anticoagulants), and checking the platelet count, INR and aPTT. As much as possible, any bleeding tendency should be corrected before attempting the CVC insertion – e.g., giving vitamin K or prothrombin complex concentrate for a patient treated with warfarin who has an elevated INR; or, a platelet transfusion for a patient with severe thrombocytopenia.
- Location of CVC insertion cart: The CVC insertion/removal cart is located at the Nursing Station on the 8 Cardinal Carter South ward. It is in the back room of the station. The cart must be signed out in the book attached to the cart and must be returned to the same location after the procedure has been completed. The cart is checked and stocked at least once per week.

- Equipment on the cart: The following equipment can be found on the Central Line Insertion Cart:

    - Central line Bundle – sterile towels, sterile gowns, sterile gloves, hair bonnet
    - Central line insertion kit
    - Dialysis lines – sizes available 15cm, 20cm and 24cm
    - Ultrasound Machine
    - Sterile ultrasound gel
    - Sterile ultrasound probe cover
    - Sharps Disposal Bin
    - Sterile 4x4 gauze
    - Sterile gloves
    - Guide Wire (45cm for IJ placement, 60cm for femoral line placement)
    - Surgical Skin Prep 2% Chlorohexidine gluconate w/ 70% Alcohol (Item T900021)
    - CHG gel
    - Tegaderm dressings

- Length of line: Generally, use the following catheter lengths:
    - Internal jugular line
        - Right IJ – 15 cm
        - Left IJ – 20 cm
    - Femoral line – 24 cm

- Procedure for CVC insertion

There is a very helpful New England Journal of Medicine video that demonstrates internal jugular vein cannulation, which can be accessed here:

https://www.nejm.org/doi/full/10.1056/NEJMvcm055053

Procedure cart

- It is stocked with all the required materials needed for CVC insertion

Find the vein with portable ultrasound

- Use a portable ultrasound machine to localize the vessel before doing the sterile preparation so that the location and patency of the vein is confirmed

Ensure sterile procedures

- Perform hand hygiene before starting
- Put on non-sterile mask and face shield and cap, then sterile gown and finally sterile gloves
- Clean the skin with Chlorhexidine 2%-Isopropyl Alcohol 70% cleaning solution
    - Use swab sticks dipped in the solution
    - Clean a large area (~ 20 x 30 cm) of the skin around planned entry sit
    - Use a side-to-side motion, as opposed to a circular motion
    - Scrub for 2 minutes
    - Antiseptic solution must be allowed to dry before proceeding with the CVC insertion.
- The drape for the CVC is then placed over the site, with the opening in the drape placed over the CVC entry site. Drape widely so that the patient's entire body is covered. This reduces the risk of infection and ensures there is a large sterile field available for all of the equipment needed

Prepare all necessary materials for CVC insertion

- The assistant applies ultrasound gel to the ultrasound probe, and then the sterile ultrasound probe cover is slipped over the ultrasound probe with the help of the assistant, taking care to ensure that the sterility of the outside of the cover is maintained.
- Prepare a syringe filled with 10 cc of 1% Lidocaine. (Note that 10 cc of a 1% solution is 100 mg of Lidocaine. The dose of Lidocaine administered to the patient should be limited to no more than 4 mg/kg to avoid Lidocaine toxicity, so in a patient with e.g. weight 60 kg, this would be a total dose of 240 mg.)
- Ensure all of the needed equipment is available and within easy reach, preferably in front of you on the sterile dressing:
    - Syringe with Lidocaine with 25G needle attached
    - Finder needle
    - Guidewire
    - Scalpel for skin incision
    - Dilator
    - Dialysis CVC itself
    - At least 4 syringes prefilled with normal saline for flushing the CVC
    - At least 2 empty syringes for aspirating from the lumens of the CVC
    - 2 syringes filled with Citrate 4% for locking the lumens of the CVC
    - Suture material (2-0 chromic) and needle
    - Materials for dressing – CHG gel, Tegaderm

Access the vein

- Locate the vein again with the ultrasound.
- Instill 5-10 cc of Lidocaine into the skin and subcutaneous tissues to ensure adequate anesthesia in the area of the proposed CVC insertion.
- While visualizing the vein with the ultrasound probe, insert the finder needle at 45 degrees to the skin with negative pressure applied to the plunger, until the vein is entered, identified by a flash of blood entering the syringe.
    - The depth at which the vein is entered varies according to the site being used, and the amount of adipose tissue.
    - The depth can be estimated using the ultrasound probe.
    - A typical depth is 1.0 – 3.0 cm.
    - Sometimes, the flash of blood only happens when withdrawing the needle slightly. This is because the tip of the needle has compressed the vein and gone through both the superficial wall of the vein and then through the deeper wall of the vein.

Insert and keep control of the guidewire

- The needle is now in the lumen of the vein. Taking care to maintain the tip of the needle in the vein, insert the guidewire through the hole in the top of the plunger, and gently push the guidewire well into the vein.
    - If an ordinary syringe is being used, then one needs to remove the syringe from the needle, while keeping the needle in the vein, taking great care to not move the needle so that it stays well within the vein.
- There should be no resistance encountered when inserting the guidewire through the needle into the vein. If resistance is encountered, remove the guidewire and then the needle, and repeat the procedure for entering the vein.
- Feed the guidewire through the needle, well into the vein – at least 10 cm from the skin entry site.
- NEVER LET GO OF THE GUIDEWIRE, during the entire procedure, to avoid the risk of the guidewire disappearing into the vein.

Make a small nick in the skin with the scalpel blade

- With the scalpel blade, make a small cut in the skin where the guidewire enters the skin. This is to make room for the dilator, and then the CVC itself. The cut should be ~ 3mm in length, and ~ 3mm in depth. To avoid cutting or nicking the guidewire, the scalpel blade should be directed so that the sharp part of the blade is away from the guidewire.

Insert the dilator

- Insert the end of the guidewire that is protruding from the skin into the “distal” end (i.e. the “tip”) of the dilator. Feed the dilator over the guidewire, while taking care to ensure the guidewire is not being removed from the vein. When the guidewire tip emerges from the other (“proximal”) end of the dilator, grasp that end of the guidewire between thumb and fingers. Then, insert the dilator over the guidewire through the skin and then the subcutaneous tissue and into the vein. The dilator should pass easily into the vein. It is often helpful to apply a rotary movement to the dilator as it passes through the skin and subcutaneous tissues.
- The dilator needs to enter into the vein, but should not be placed too far into the vein. A reasonable limit is to feed the dilator through the skin down to the vein (generally not more than 3 cm) plus another 2-3 cm for a total of not more than 6 cm from the skin surface.
- Remove the dilator while ensuring the guidewire remains in the vein. There are 2 potential problems here:

  (1) There is a risk of removing the guidewire along with the dilator. To avoid this:

  - Keep the guidewire “stationary” within the vein the whole time that the dilator is being inserted and then removed.
  - As soon as the end of the dilator emerges from the skin, grasp the guidewire *at the skin entry site* between thumb and fingers to keep it stationary as the dilator is removed from the guidewire.

  (2) A larger hole in the skin and subcutaneous tissue and in the vein itself will have now been created by the dilator. This may lead to some bleeding when the dilator is removed, which needs to be limited by tamponading the area with sterile gauze.

Insert the catheter, remove the guidewire

- Take the dialysis catheter. Clamp the “red” (“arterial”) lumen, as the guidewire will come out through the blue (“venous”) lumen.
- Follow a similar procedure with the dialysis catheter as with the dilator.
  - The end of the guidewire protruding from the skin is introduced into the tip of the catheter (the “distal” end), while always maintaining a hold of the guidewire.
  - The catheter is passed over the guidewire, until the end of the guidewire emerges from the other (“proximal”) end of the catheter.
  - The wire is then grasped at that proximal end, as the catheter is inserted along the guidewire through the skin and subcutaneous tissue into the

vein. As with the dilator, it may be helpful to use a rotating motion applied to the catheter as it is inserted over the guidewire. There should not be significant resistance as one inserts the catheter into the vein.
        - Blood should appear in the proximal end of the blue ("venous") lumen.
        - The CVC is inserted as far as it will go, with the proximal end at the skin entry site.
- The guidewire is then removed by pulling it out, ensuring that the dialysis catheter is kept stationary. The guidewire should come out easily, without resistance. If significant resistance is encountered while attempting removal of the guidewire, it may have become significantly bent or kinked, and there is a risk of blood vessel injury. In such a case the CVC and guidewire will both need to be removed, and the procedure will have to be restarted.

Flush both lumens; confirm both lumens permit aspiration; fill both lumens using 4% citrate; apply caps to the catheter

- Confirm patency of both lumens
    - First, aspirate blood from each lumen using the empty syringes by pulling back on the plunger in the syringe. Blood should promptly and easily fill the syringes. Return the blood to the patient through the lumen, and clamp each lumen, and remove the syringes.
    - Then attach the saline-filled syringes, and flush both lumens. There should be no resistance to the flushing.
- Fill both lumens with the appropriate amount of Citrate 4% solution. The volume to be instilled in each lumen (generally 1.2-1.3 cc) is printed on the side of the catheter at the hubs This serves to prevent blood clot formation within the lumen of the catheter, and is referred to as a "locking solution".
- Apply the caps that are supplied with the CVC to the ends of the catheter lumens.

Suture and apply a dressing to the catheter

- The catheter needs to be sutured securely in place. This may require additional lidocaine infiltration into the skin, as the sutures generally enter the skin somewhat distant from the actual catheter insertion site.
- Cover the site with a Tegaderm impregnated with Chlorhexidine Gluconate (CHG) that has had a slit cut in it to accommodate the exit of the catheter.

Dispose of sharps

- Carefully dispose of the scalpel blade, all needles, and suture needle in an appropriate sharps container.

Obtain a Chest X-ray for an IJ CVC insertion

- If an internal jugular catheter is inserted, a CXR is needed to rule out complications of insertion, such as pneumothorax, and to check that the tip of the IJ catheter is in the SVC or the right atrium.

Write a procedure note in the chart (or enter into Daily Notes online)

- The procedure note should include:
  - Name of the procedure that was performed
  - Who performed it
  - That informed consent was obtained
  - Number of punctures of vein required for cannulation
  - Any complications
  - Result of Chest X-ray (if catheter is an IJ catheter)

Tunneled central venous catheters

Tunneled CVCs are placed by the interventional radiology staff with fluoroscopy guidance.

The catheter is introduced into the internal jugular (IJ) vein, through a small incision made superficial to the IJ just superior to the clavicle. The radiologist then creates a subcutaneous tunnel that is about 8-10 cm long and extends from the entry point in the IJ vein to the exit site anterior to the shoulder and about 5 cm inferior to the clavicle. This can be on either the right side (preferred) or, if necessary, the left side. This is the preferred method for central venous catheter insertion.

The CVC that is inserted through the tunnel has a Dacron cuff located about 2 cm from the hub of the catheter. (The “hub” is the part of the CVC that sits right at the skin exit site.) The cuff elicits an inflammatory and then fibrotic reaction with surrounding tissues, which serves to anchor or cement the CVC in place. This both prevents it from falling out of the patient, and also provides a barrier to the spread of bacteria from the skin surface through the tunnel and down into the vein.

The two main advantages of the tunneled IJ CVC compared to a regular IJ CVC therefore are:

- It is more comfortable for the patient to have the CVC exiting the skin anterior to the shoulder, rather than at the superior part of the neck
- There is a lower risk of infection. This is largely due to the tunnel itself and the above-described cuff, and partly due to the way the CVC sits on the chest wall; it does not pull away from the skin and expose the exit site, in the same way as tends to happen with a non-tunneled IJ CVC.

In many cases, it is possible to arrange for a tunneled catheter insertion to be done either on the same day as when the need for the catheter is identified, or on the next day.

The IR team can be reached by telephone at 5886.

The requisition for the CVC insertion is entered into Soarian as follows:
- Select “Orders”
- Type in “Interventional radiology” into the search window
- Find and select “Interventional Radiological Procedure Request”
- In the text box under “Reason for Request”, type in the patient’s diagnosis, and then “Please insert tunneled 2-lumen hemodialysis catheter, preferably into right internal jugular vein”

A tunneled IJ catheter access is quite common among patients on chronic HD. Notwithstanding, in most cases one prefers an AV fistula or AV graft.

The major *advantages of a tunneled catheter* compared to AV fistula or AV graft are:
- A tunneled IJ catheter can be used immediately after insertion
- A tunneled IJ catheter can be inserted in the IR suite, so does not require time in the operating room
- A tunneled IJ catheter can be inserted in patients who do not have sufficiently large veins to permit creation of an AV fistula or AV graft

Tunneled IJ catheters do have significant risks and side effects:
- They may become thrombosed
- They may become infected
- They may be associated with inadequate dialysis

Many patients who have been on chronic HD for many years experience repeated episodes of thrombosis and stenosis of their central veins, and in some cases are not

able to have either upper limb AV fistulas or AV grafts or even tunneled internal jugular CVCs on either side. In these cases, the options for chronic HD access are:

- An AV *femoral* graft
- A tunneled femoral venous CVC
- A tunneled translumbar CVC, in which case the tunneled dialysis CVC is inserted into the inferior vena cava, and the tunnel and exit are along the abdominal wall

Problems with Central Venous Dialysis Catheters (1): Mechanical Problems

(1) Migration of a *non-tunneled* catheter:

If a CVC has come out from the patient's body, this is referred to as "CVC migration". The segment of the catheter that used to be inside the body (i.e. inside from the exit site) has now been exposed to the outside environment so there is a high likelihood that it has become colonized with bacteria or fungi on the surface of the skin. There is also the possibility that the CVC is no longer in the vessel. YOU MUST NOT PUSH THE CVC BACK IN. If one tries to push the CVC back in, there is a significant risk of infection and/or damage to local tissues. If there is sufficient catheter length remaining in the central vein so that one can easily aspirate blood from the "arterial" (i.e. red) lumen, and return blood without resistance through the "venous" (i.e. blue) lumen, the dialysis can be continued and plans made to replace the catheter before the next dialysis. If it is a temporary catheter and there is good flow through the venous port, the catheter can be changed over a guidewire. If there is no flow through the venous port, a new catheter insertion is required.

(2) Migration of a *tunneled* catheter

If a tunneled IJ catheter has migrated out, the "cuff" may be exposed. The cuff is a structure made of Dacron that surrounds the catheter. It is about 1 cm in length and is about 5 cm from the point where the two limbs of the tunneled CVC join together. It is located along the tunnel between the skin exit site and the site where the CVC enters the jugular vein. The cuff causes a fibrotic reaction under the skin and this leads to the catheter being adherent to the tissues and therefore the CVC is protected from falling out.

If the cuff is exposed, the CVC must be secured to the skin firmly with tape and a dressing. The CVC then needs to be changed as soon as possible in interventional radiology.

(3) Cannot aspirate from the *arterial* port (the holes in the catheter for the arterial lumen are on the side of the catheter):

(a) If you *can* infuse without resistance but cannot aspirate, the arterial port is likely against the wall of the vein (recall that the holes of this lumen are on the sides of the catheter) or the patient is intravascularly volume-depleted. In such a case, place the patient in slight Trendelenburg or "reverse the lines". ("Reversing the lines" means using the "venous" line to send the blood from the patient to the machine, and then using the "arterial" line to return the blood to the patient from the machine.)

(b) If you *cannot* infuse without resistance, the arterial lumen is blocked. In such a case, one should instill TPA (tissue plasminogen activator) in an attempt to lyse the thrombus. We use Alteplase (brand name is Cathflo®), and the dose is 2 mg. The HD should be restarted in 1 hour to see if the clot has been lysed.

(4) Cannot aspirate from the *venous* port (the hole in the catheter for the venous lumen is at its tip):

(a) Check to see if the CVC is kinked if so, the CVC should be changed and then carefully sutured so as to minimize the risk of kinking.

(b) If you can infuse without resistance but cannot aspirate, either the patient is volume-contracted or there is a "ball valve" thrombus at the tip of the catheter. Try positioning the patient in a supine position or in the lateral decubitus position (line side up), or try a dose of TPA as described immediately above.

- If it is a left sided CVC, perhaps the tip is against the superior vena cava and a longer CVC may be necessary. Ensure there is no pain on infusion as in a very rare instance, the tip could have migrated through the wall of the vein.
- Otherwise, if the patient is not volume-contracted, and if TPA fails to correct the problem and the CVC is not against a wall, then the CVC should be changed.

(5) CVC started out working well, but now when blood pump speed (BPS) above 200 mL/min there is arterial insufficiency (i.e. excessively high negative arterial pressures):

The initial good function rules out kinks and thrombi and suggests a mechanical problem (CVC sucking on vein wall) due to circulating volume contraction. Note that patients with hypoalbuminemia may have intravascular volume contraction yet still

have peripheral edema. Use tilt stretcher with patient head down and remove volume slowly. Support stockings or wrapping the legs with tensors often are helpful.

(6) Both ports aspirate well but it is not possible to get blood pump speed >200:
Does patient have intravascular volume contraction? If you cannot be sure, place head down on tilt stretcher and give 250500 cc normal saline and evaluate impact. If JVP is clearly elevated, do not give the saline, just place head down.

- If all efforts fail, check Xray position of CVC to see if a longer CVC will be beneficial and then have CVC changed.

(7) Cannot aspirate from, nor infuse into, either port:

- Ensure the clamps have not left the silastic tubing compressed
- Check for kinking and clotting
- If no obvious kinking, try to lock the catheter with TPA as described above, and try the HD procedure again in 1 hour.
- Check CXR to confirm the CVC position is appropriate.
- The patient may require a new CVC.

Problems with Central Venous Dialysis Catheters (2): Infections

There are 3 potential types of infections related to the dialysis CVC: (i) Exit site infection; (ii) Tunnel infection; (iii) Catheter-related blood stream infection (CRBSI)

1) Exit site infection

This is characterized by: hyperemia, induration, and/or tenderness *within 2 cm* of the catheter's exit site from the skin. This is external to the cuff. There may or may not be purulent drainage, and there may or may not be associated bacteremia.

Any purulent drainage should be sent for culture and sensitivity testing. Blood cultures should be obtained if the patient has a fever.

Treatment should consist of:

- Empiric systemic antibiotic treatment (oral or i.v.) which covers gram positive bacteria, adjusted according to results of culture and sensitivity testing.
- Topical antibiotic (e.g. Mupirocin) should also be applied.
- Treatment duration is for 7-14 days.

The catheter should be removed if:

- There is coexisting CRBSI
- There are signs of systemic infection (i.e., fever and/or leukocytosis)
- There is significant purulent drainage that can be expressed from the track of the catheter
- If signs of exit site infection persist despite antibiotic therapy, or recur after a course of antibiotics

Otherwise, the catheter can often be salvaged just with antibiotic therapy.

2) Tunnel infection

This is characterized by hyperemia, induration, and/or tenderness that extends for *more than 2 cm* from the exit site and along the subcutaneous tunnel. There may or may not be purulent drainage, and/or bacteremia. Purulent drainage should be sent for culture and sensitivity testing.
The patient should be treated with antibiotics as if they have a CRBSI (see below). The empiric choice of antibiotics will need to be modified according to results of culture and sensitivity.

In the case of a tunnel infection, it is not possible to cure the infection while the catheter is left in place. Therefore, the catheter will need to be removed. Also, it should not be replaced by exchange over a guidewire, since if the tunnel is infected the new CVC would simply be seeded by the bacteria in the tunnel. A new site for the new CVC will be required, ideally on the other side of the body; or, if this is not possible, then at a site removed from the previous tunnel on the same side.

3) Catheter-related bloodstream infection (CRBSI)

A patient with CVC and fever may have CRBSI
A patient treated by HD who has a chronic dialysis catheter (tunneled or non-tunneled) who develops a fever may have a CRBSI, and must be evaluated for this. However, CRBSI should be a diagnosis of exclusion after other potential infectious foci (e.g. pneumonia, cellulitis, UTI, diabetic foot infection) have been considered.

Pathogenesis of CRBSI

- Routes of infection. This can happen via at least 3 routes:
    - The infection is introduced via the catheter hub, due for instance to improper hand hygiene

- The infection travels from the skin surface down through the subcutaneous tunnel and into the bloodstream
- The infection enters the blood stream at a site removed from the CVC, but then the bacteria or fungi adhere to the catheter

- Colonization of the catheter
  - Bacteria may adhere to either the lining of the CVC on its inside, and/or to the outer surface of the catheter. The bacteria may secrete a protein matrix referred to as biofilm, which forms a protective coating inside which the bacteria may be sheltered and therefore antibiotics will not be able to sterilize the infection – i.e., the antibiotics will not be able to kill all the bacteria, and the only way to cure such an infection may be to actually remove the catheter.
  - A particular challenge is that a "fibrin sheath" may envelop the catheter. This can lead to catheter dysfunction as the fibrin plugs the side holes and/or CVC tip. In addition, if the fibrin sheath incorporates bacteria, then this further complicates the CRBSI. Even catheter removal will not necessarily cure the CRBSI, as the fibrin sheath may remain intact when the catheter is removed. The management of such a situation is uncertain. Some advocate for the interventional radiologist to actively disrupt the fibrin sheath at the time of CVC removal but there are risks of worsening acute bacteremia with doing so.
- Associated exit site and/or tunnel infection
  - An exit site and/or tunnel infection may or may not be present together with the bacteremia associated with a CVC.
  - Either of these make it more difficult to cure the infection without catheter removal and insertion of a new catheter.
- Risk of metastatic infection
  - This is particularly likely to occur with *Staphylococcus aureus* infections.
  - The major sites for metastatic infection are:
    - Endocarditis
    - Discitis
    - Osteomyelitis, particularly in vertebrae
- Patients may first become symptomatic during the dialysis procedure
  - At the time that the dialysis procedure begins, blood flow through each lumen of the catheter may be as high as 400 cc/minute.
  - If bacteria are adhering to the CVC, then the very high blood flow will serve to transfer the bacteria and their toxins into the bloodstream. This may then trigger chills, rigors and fever, and possibly also septic shock and related complications.

The major causative organisms are:

- Gram-positive aerobic cocci (40-80%)
  - Coagulase negative staphylococci
  - Staphylococcus aureus
    - Methicillin-sensitive *Staphylococcus aureus*
    - Methicillin-resistant *Staphylococcus aureus*
  - Enterococci
- Gram-negative aerobic bacilli (20-30%)
  - Various species, including Pseudomonas
- Fungi
  - Various species, including *Candida albicans*

Investigation of a patient with CVC and fever

- Examine a patient with CVC and fever for evidence of exit site and tunnel infection
  - If a patient with a CVC gets a fever, it is essential to examine the exit site and tunnel for evidence of exit site and/or tunnel infection.

- Send purulent exudate for gram stain, and send 2 sets of blood cultures
  - Swab any purulent exudate from the exit site and send for gram stain and culture.

- Send blood in 2 sets (i.e. 4 total bottles) of blood culture bottles.
  - 1 set from the catheter
  - 1 set from the circuit

Management of suspected CRBSI

There are 2 general aspects to the management of suspected CRBSI:

(1) Antibiotic therapy

(2) Catheter management

(1) Antibiotic therapy

Antibiotic therapy is initially chosen empirically to cover both gram-positive and gram-negative bacteria. This is subsequently adjusted according to results of blood culture and sensitivity testing.

- *For gram-positive coverage,* the 2 major choices are Cefazolin (Ancef®) IV and Vancomycin. Each of these is administered i.v. near the end of the dialysis treatment. There is little removal from the body of these medications other than via dialysis, and so one does not need to give either one of them on non-dialysis days. The gram-positive coverage is discontinued if the blood culture shows a gram-negative organism.
- The dose of *Cefazolin* is generally 2 g with each dialysis. (An alternative dosing regimen

of 20 mg/kg with each dialysis may be used for smaller patients.)

- *Vancomycin* should be used in place of Cefazolin in any of these situations:
  - If the patient has a serious beta-lactam allergy
  - If the patient has suspected or proven methicillin-resistant *Staphylococcus aureus* bacteremia
  - If the gram-positive infection is found to be resistant to Cefazolin
  - Vancomycin dosing is as follows:
    - Loading dose 20-25 mg/kg IV in the last hour of dialysis
    - Maintenance dose is usually 1 gram at the end of each dialysis. (Alternatively, a dose of 10-15 mg/kg in the last hour of dialysis may be used for smaller patients.)
    - One can check Vancomycin levels prior to each dialysis, and adjust the maintenance dose to achieve a pre-dialysis vancomycin level to be between 15-20 mg/L

- *For gram-negative* coverage, the 2 major options are Ceftazidime or Tobramycin. Both of these are given during the last hour of dialysis. As with Cefazolin and Vancomycin, there is little non-dialytic removal, and so these agents do not need to be given on non-dialysis days.
  - For Tobramycin, the loading dose is 2 mg/kg IV load (maximum 100 mg), and then 1 mg/kg IV at the end of each dialysis; this is discontinued if the blood culture indicates a gram-positive organism.

  - An alternative to Tobramycin is Ceftazidime, 1 g IV with each dialysis treatment. This can be used if the patient has significant residual renal function (and therefore one wishes to avoid aminoglycoside nephrotoxic injury to the remaining functioning nephrons), and/or there are concerns about aminoglycoside ototoxicity.

- *Treatment duration*

Treatment is generally for 3 weeks and is adjusted at the next dialysis treatment pending culture results and antibiotic sensitivities. If the cultures are negative, the patient is reviewed before simply stopping the course of antibiotics. The duration is extended to 4 weeks if the infection is due to Staphylococccus aureus, and as long as 6 weeks if there is endocarditis or metastatic infection.

(2) Catheter management

<u>Rationale for removal</u>

In a patient with a CVC and bacteremia, in addition to antibiotics, one needs to determine if the CVC should be removed. This should be done in most cases of CRBSI. This is because the CVC is often colonized with the infecting bacteria (or fungus). As a result, the patient may not respond adequately to antibiotic treatment alone. Alternatively, the patient may *initially* improve in response to antibiotic therapy (i.e. resolution of fever and other presenting findings) only to have the fever and symptoms recur once antibiotics are discontinued, as the bacteria may then re-emerge from the biofilm lining the CVC. The only way to avoid this happening is to actually physically remove the catheter, and thereby remove the reservoir of bacteria.

<u>Factors that influence decision-making about CVC removal and insertion of a new catheter</u>
If the catheter is removed, the next decision to be made is when and where should a new CVC be inserted. The variables that affect this decision-making are the following:

(i) What *alternatives for vascular access* does the patient have? One is more likely to use the same vein for future CVCs if the patient has few or no alternatives for another site for CVC insertion.

(ii) *What was the infecting organism*? The most dangerous organisms are S. aureus, pseudomonas species, and fungi. These generally cannot be cured without catheter removal, and generally it is preferred to have a "holiday" (i.e. a period of time of approximately 48 hours) without any intravascular devices. This "holiday" serves to prevent the infecting organism that was adhering to the old CVC then infecting any subsequent CVC.

(iii) *Has the patient responded to the initial antibiotic therapy*? If yes (i.e. patient is afebrile and feeling well), then one is more likely to try change the catheter over a guidewire with the same tunnel and exit site; or, at least preserve the vein currently used for access while creating a new tunnel with a new exit site.

(iv) *Are the conditions right to consider "salvage" of the existing catheter?* The word "salvage" in this context means that the existing catheter is left in place and the CRBSI is treated only with antibiotics. Attempts at catheter salvage are associated with a significant risk of recurrent bacteremia for reasons mentioned above. This is particularly likely to be the case with CRBSI due to S. Aureus, pseudomonas species, and Candida. The settings in which one is more likely to consider CVC salvage are the following:

- If the CRBSI is due to other organisms, particularly coagulase-negative staphylococci, enterococci, or gram negative aerobic bacilli other than pseudomonas

- If the patient has very limited options for vascular access, and there is a concern that removing the CVC from the patient's veins may lead to immediate thrombotic occlusion, so that one would not be able to recannulate the vein even if the CVC were being changed immediately over a guidewire
- If the patient declines to have a change in CVC

If one decides to pursue salvage of the CVC, then strong consideration should be given to the administration of antibiotics into the catheter lumen in between HD sessions. This is referred to as "antibiotic lock" therapy, and involves the instillation of the following into the lumen in an attempt to further treat the bacterial infection by having the antibiotic in place and diffusing into the biofilm lining the catheter.

The table below (page 21) presents options for this. The choice of antibiotics for antibiotic lock therapy depends on the same factors as those that guide the choice of systemic antibiotics: results of culture and sensitivity, and presence of any allergies.

(v) *Is there evidence of metastatic infection?* The commonest of these are the following:
- Osteomyelitis, particularly in the spine
- Discitis
- Endocarditis

If one of these is present, it makes cure of infection considerably more challenging, and leads to a need for a longer duration of antibiotic therapy, and makes removal of the CVC more urgent, since it becomes even more critical to remove the source of any future bacteremia.

(vi) *Is there an associated infection of the exit site and/or tunnel*? If yes, the catheter should be removed, and a new exit site created.

If there is a *tunnel* infection, the CVC generally should be removed on the same day as the febrile illness is identified. If the patient needs immediate dialysis (e.g. for severe hyperkalemia and/or pulmonary edema) then the patient can be dialyzed once through the existing CVC before it is removed.

If there is *exit site* infection, but the patient is otherwise stable, the existing CVC can generally be left in place for 2-3 days while the patient is treated with antibiotics. The CVC will need to be changed and the new CVC cannot simply be changed over a guidewire and left to exit through the same exit site as it is highly likely to get infected. Therefore, the 2 options for management are:

(a) Remove the CVC, and place a new CVC in a different vein with a different tunnel and exit site. (For instance, if the old CVC was in the right internal jugular (IJ) vein, one might remove this CVC, and place a new CVC in the left IJ and create a new tunnel and exit site on the left side.
(b) Use the same IJ vein for the new line but create a new tunnel and exit site. (see option (2) below.)

The key options for catheter management are:

(1) Remove the CVC and have a CVC-free period. Blood cultures should be repeated once the CVC is removed. Once one is certain that the cultures are negative after 48 hours incubation, one can insert a new CVC through a different vein. This approach is appropriate if:
- the patient has CRBSI due to S. aureus, pseudomonas species, or fungi
- the patient is septic with persistent hemodynamic instability
- the patient has gross purulence from the exit site and/or obvious tunnel infection
- the patient has evidence of metastatic infection
- the patient is not responding to the initial antibiotic therapy (e.g. with persistent fever)

(2) Change CVC over guidewire through the same tunnel and same exit site. The interventional radiologist dissects the cuff from the tunnel to free the CVC and then inserts a guidewire through the existing CVC (i.e. through the same exit site and same tunnel), removes the CVC, and inserts a new CVC over the guidewire. This is appropriate when the infection is due to organisms other than S. aureus, pseudomonas species or fungi, for instance due to Staphylococcus epidermimidis or gram-negative aerobic bacilli other than pseudomonas, and provided there is no tunnel infection nor exit site infection.

This is particularly a consideration if the patient has very limited vascular access options and hence one wishes to avoid a catheter-free interval out of fear that the internal jugular vein currently being used may become occluded if the catheter is removed altogether.

(3) Change CVC over a guidewire and make a new tunnel and exit site. The interventional radiologist will dissect the cuff from the tunnel to free the CVC. They then make an incision over the vein entry site and pull the CVC out of the tunnel. They then insert a guidewire through the old CVC, then remove the CVC while leaving the guidewire in the internal jugular vein, and then insert a new CVC over the guidewire. They then create a new tunnel, and a new exit site for the new CVC.

This is a consideration for patients with limited vascular access options with CRBSI if there is an *exit site infection*, provided the patient is responding well to initial antibiotic therapy, and provided the CRBSI is due to organisms *other than* S. aureus, pseudomonas species and fungi.

(4) Leave the current CVC in place and attempt to cure the infection with antibiotics alone. This is referred to as "catheter salvage". This is most often considered when the patient has the criteria alluded to in # (2) above, and has limited vascular access options, and/or if the patient refuses to have the CVC changed.

Summary: Catheter Management in CRBSI

Indications for *immediate* CVC removal (i.e., when CVC infection is first suspected)
Consider CVC removal at the onset of the infection if:
- Patient is very toxic (i.e. acutely ill, hypotensive).
- There is grossly purulent drainage from the exit site or obvious tunnel infection.

Otherwise, the decision for CVC removal is deferred until the next HD treatment.

Indications for catheter change later in treatment course
Catheter change is *definitely* appropriate if:
- Fever persists after 48 hours of appropriate antibiotic therapy
- There is tunnel infection
- There is metastatic infection (e.g. vertebral osteomyelitis)
- There are recurrent infections
- Infection is with fungi, pseudomonas species or S. aureus

Catheter change is *generally* appropriate for all patients with CRBSI, unless one or more of the following is present:
- There are resource constraints
- The patient refuses to have the CVC changed
- There is very difficult vascular access, and a concern that removing the catheter may lead to a complete lack of vascular access
- The infection is due to Coagulase negative staphylococci

Whether this is done with a 48-hour catheter-free "holiday", or over a guidewire depends on the factors identified above.

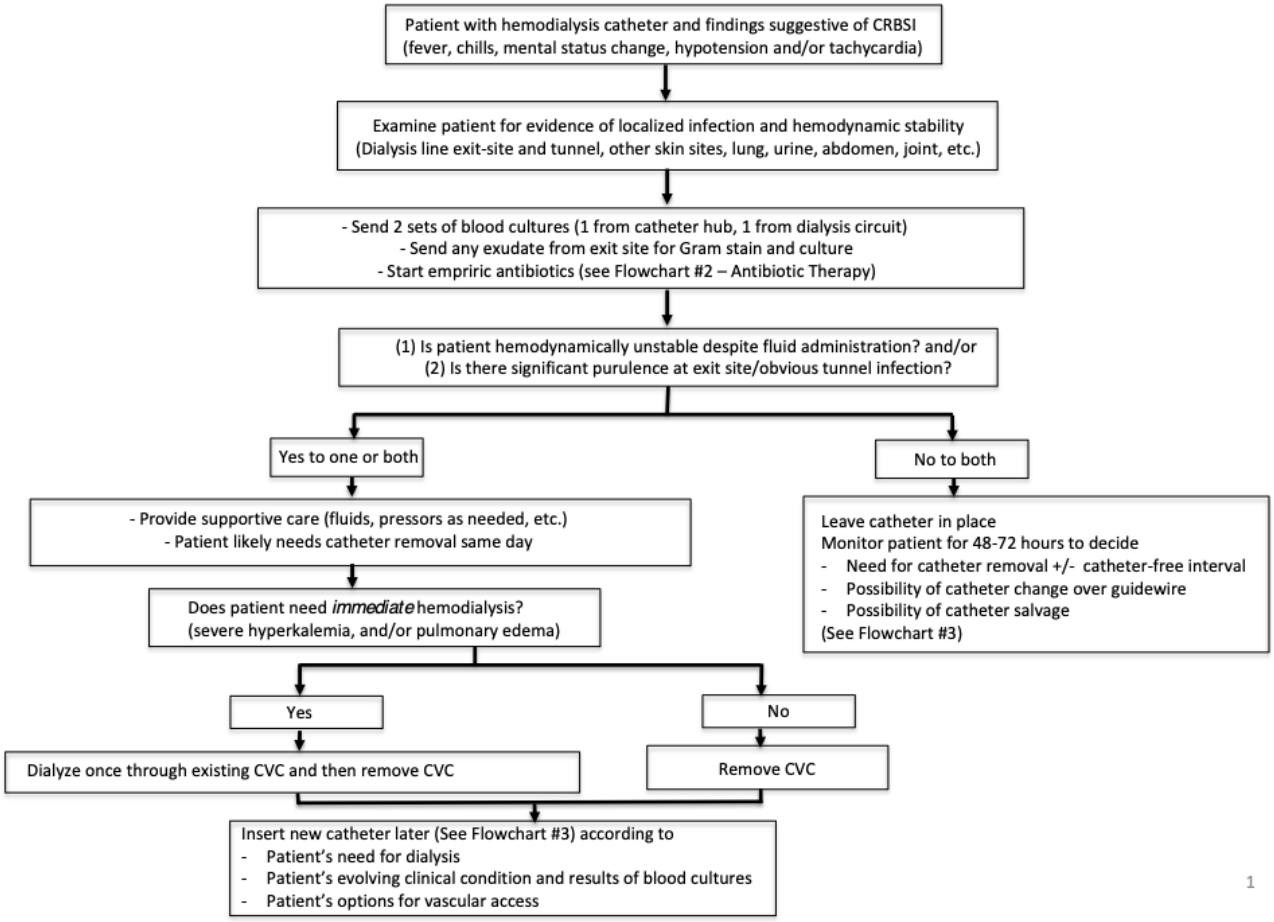
The flowcharts in Figures 1,2 and 3 summarize the approach to CRBSI.

The table on the next page summarizes use of antibiotic lock therapy.

Use of Antibiotics for CVC Lock Therapy (Courtesy of Dr. Charmaine Lok)

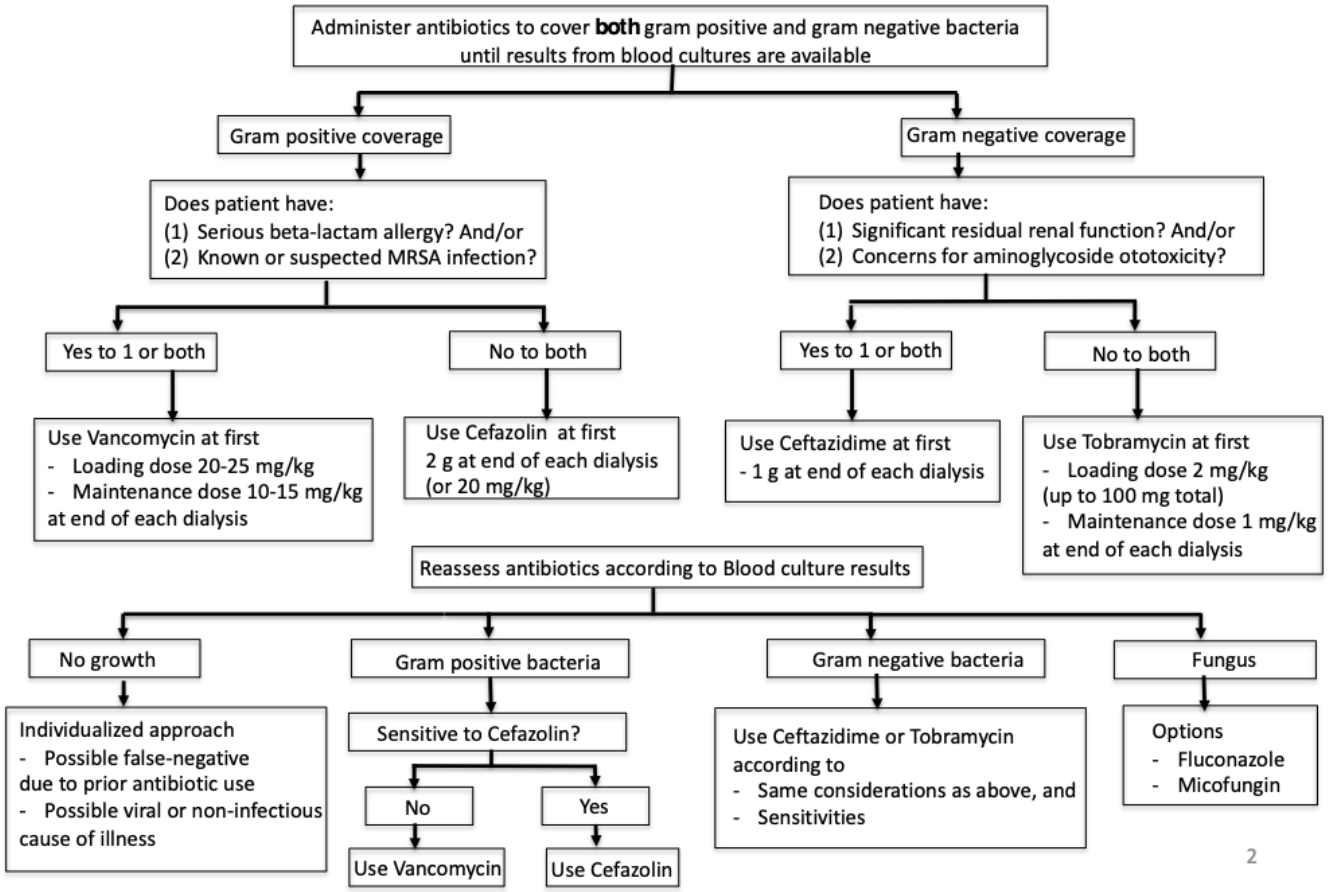
Antibiotic	**Anticoagulant**	**Comments**
Vancomycin 50 mg/ml Reconstitute 500mg vial of Vancomycin with 10mL water for injection (to give concentration of 50mg/mL) Draw up 1 mL (50 mg)	**Citrate 4.67%** (1 ml)	Draw up 1 mL of Trisodium Citrate 46.7 % and add to 1 mL of Vancomycin 50 mg/mL and 8 mL of Sodium Chloride 0.9% to give a total volume of 10 mL. Final concentration: 5mg/ml Vanco and 4.67% citrate in total vol 10 ml
Gentamicin (1 mg/mL) Draw up 0.25 mL (10 mg) of Gentamicin 40 mg/mL.	**Citrate 4.67%** (1 ml) Draw up 1 mL of Citrate 46.7 % and add to 0.25 mL Gentamicin 40 mg/mL and 8.75 mL of Sodium Chloride 0.9% to give a total volume of 10 mL.	Final concentration: Gentamicin 1 mg/mL Citrate 4.67% in a total volume of 10 mL
Vancomycin 5 mg/mL+**Ceftazidime** 10mg/mL	Heparin 1000 U/mL	Final concentrations: 2.5 mg/ML vancomycin 2.5 mg/mL ceftazidime 250U/mL heparin
Vancomycin 5 mg/mL	Heparin 1000 U/mL	Final concentrations: 2.5 mg/ML vancomycin 500U/mL heparin
Ceftazidime 10mg/mL	Heparin 1000 U/mL	Final concentrations: 2.5 mg/mL ceftazidime 500U/mL heparin
Cefazolin 10mg/mL	Heparin 1000 U/mL	Final concentrations: 2.5 mg/mL cefazolin 500U/mL heparin

FLOWCHART #1 - IMMEDIATE MANGEMENT OF PATIENT WITH HEMODIALYSIS LINE AND SUSPECTED CRBSI

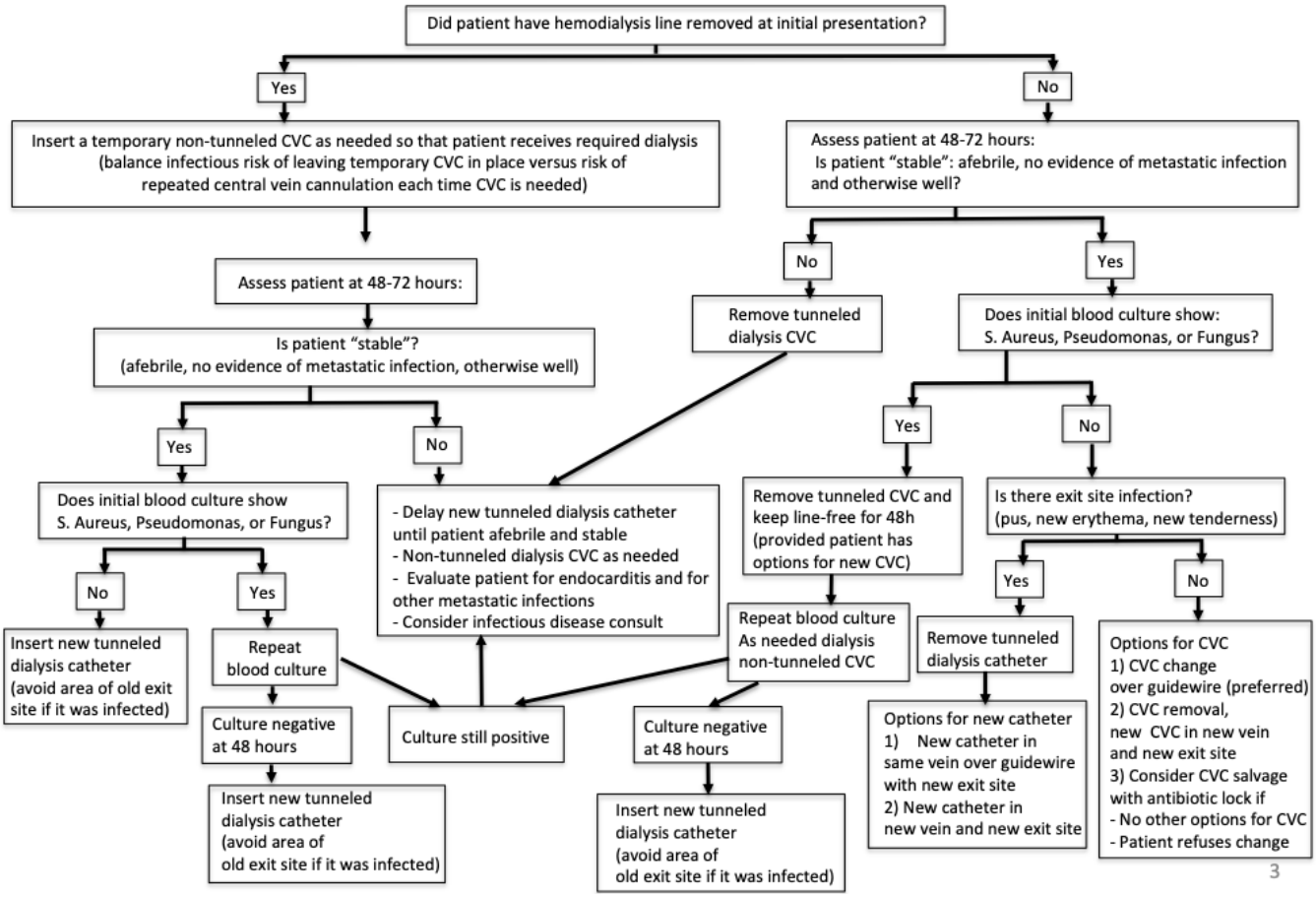


1

FLOWCHART #2 – EMPIRIC INITIAL AND SUBSEQUENT ANTIBIOTIC THERAPY FOR HEMODIALYSIS PATIENT WITH CVC AND SUSPECTED CRBSI



FLOWCHART #3 - DECISION-MAKING RELATED TO CATHETER REMOVAL AND REPLACEMENT IN HEMODIALYSIS PATIENT WITH SUSPECTED CRBSI



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Other complications during hemodialysis

Intradialytic Hypotension (IDH)

Definition and consequences

This is generally defined as a systolic BP falling to below 90 mm Hg at some point during the HD treatment. This is associated with significant morbidity including acute symptoms (muscle cramps, headache, reduced level of consciousness) and also increased long-term mortality.

Pathophysiology

There are 3 expected reasons for blood volume to fall during the dialysis treatment, each of which can contribute directly to IDH: (i) ultrafiltration of fluid from the plasma faster than the plasma refills from the interstitial space; (ii) translocation of water from ECF to ICF due to urea disequilibrium; (iii) loss of blood volume into the dead space of the extracorporeal circuit.

(i) Ultrafiltration of fluid. During the dialysis treatment, isotonic fluid is ultrafiltered from the bloodstream via the dialyzer. This leads directly to a reduction in blood volume and therefore in intravascular pressure. The reduced intravascular pressure in tissue capillaries favours the movement of isotonic fluid from the interstitial space of body tissues (muscle, skin, liver, etc.) into the plasma compartment of the bloodstream, a process called “refilling”. The net change in blood volume during dialysis is primarily due to the balance between volume lost through ultrafiltration (UF) and that added to the plasma from tissues via refilling.

(ii) Movement of water from ECF to ICF due to urea disequilibrium. A second factor which can lead to a reduction in plasma volume is the movement of water from the ECF into body cells. This is an extension of the process related to dialysis disequilibrium. During dialysis, there is diffusive removal of urea from the extracellular fluid (ECF) leading to a reduction in ECF urea concentration. This happens faster than the rate at which the intracellular fluid (ICF) urea concentration falls, since there is a period of time required for urea to diffuse from ICF to ECF. This leads to urea “disequilibrium” – in other words, ICF [urea] > ECF [urea]. This creates an osmotic force for water to move into cells: this can cause cerebral edema (dialysis disequilibrium syndrome), and also more widely lead to movement of water from ECF to ICF, including for instance into muscle cells. This can lead to further reduction in ECF volume.

(iii) Blood needs to fill up extracorporeal circuit. A third factor is that the extra-corporeal circuit has a volume of 250-300 cc, which needs to be filled with blood, and this may also contribute to hypovolemia.

In response to these stresses, in addition to the refilling mentioned above, the body responds via several compensatory mechanisms, each triggered by the sympathetic nervous system:

- Increased cardiac output due to tachycardia and increased contractility
- Increased venous tone to increase venous return
- Increased arteriolar tone

Patients who nevertheless experience IDH typically have one or more of the following contributing factors:

- High need for fluid removal due to large gain of fluid in between dialysis sessions
  - A high rate of ultrafiltration is generally defined as greater than 15 mL/kg/h, or 1 litre in a patient who weighs 70 kg.
  - This means the patient may need to remove say 4 L of isotonic fluid to get back to their target weight, and this may exceed their capacity to compensate via refilling and other mechanisms
  - A related issue is a patient requesting to come off dialysis early, thereby shortening their time, necessitating excessively rapid fluid removal
- They may have gained flesh weight, and their target weight may be inappropriately low
- They may have impaired vasoconstriction due to one or more of the following:
  - Excessive antihypertensive medications on board
  - Autonomic neuropathy due to DM, amyloidosis, or uremia itself
  - Temperature of dialysate is too warm
  - Eating during dialysis (which causes vasodilatation of the splanchnic circulation)
- They may have impaired capacity to increase cardiac output
  - Ischemic heart disease
  - Arrhythmia – e.g. new onset atrial fibrillation reducing cardiac output
  - Valvular heart disease – e.g., aortic stenosis
  - Pericardial disease
- Cause for hypotension is unrelated to dialysis procedure
  - Bleeding
  - Sepsis
  - Anaphylaxis or dialyzer reaction
  - Pericardial tamponade
  - Air embolism

Evaluation and Management

Presenting symptoms

- In addition to the fall in BP, patients with IDH often present with other findings, including the following:
    - Lightheadedness or dizziness
    - Fatigue
    - Muscle cramps
    - Yawning
    - Reduced level of consciousness
    - Dyspnea

Immediate management

- In most cases, IDH is due to excessive ultrafiltration. Therefore, the first steps in response to IDH is to:

(i) Stop the ultrafiltration

(ii) Place the patient supine or, if necessary, in a Tredelenburg (head down) position.

(iii) If the BP remains low, administer i.v. isotonic fluid (most commonly normal saline) 250-500 mL, as needed to restore BP to over 100 mm Hg systolic.

(iv) Administer oxygen to ensure oxygen saturation is at least 92%

Evaluation for serious causes if above measures fail to restore BP

- If BP remains low despite the above initial measures, it is important to address the possibility of a serious underlying cause of hypotension. The major disorders to search for are the following:

(i) Bleeding, particularly GI bleeding (search for evidence of this on history, physical exam, and on CBC)

(ii) Cardiac problems (search for these with ECG and measurement of Troponin levels)
   a. Myocardial ischemia
   b. Arrhythmia

(iii) Pericardial tamponade (search for this by noting quiet heart sounds, tachycardia, elevated JVP, and/or pulsus paradoxus (this requires a manual BP cuff))

(iv) Sepsis (check temperature, order CBC for WBC, and blood cultures and other cultures as appropriate)

(v) Dialyzer reaction (search for this via history of chest or back pain, and search for signs of an allergic reaction such as urticaria or other skin rash, wheezing, stridor, cough)

(vi) Air embolism (this is discussed below under “Air Embolism”)

Prevention

There are several measures that might be taken to prevent recurrent episodes of IDH. They range from straightforward to more elaborate:

(i) *Ensure target weight is not too low* by reassessing this regularly. This is done via:

a. Clinical exam for conventional signs of volume depletion (low JVP, orthostatic hypotension and orthostatic tachycardia), and careful review of previous dialysis run sheets.
b. If necessary, the dietitians can assist in determining target weight with the help of body composition monitoring (BCM). This involves the use of bioimpedance spectroscopy and is a simple bedside measure that takes only a few minutes.
    i. Two electrodes are applied to the patient – one to her hand, and the other to her foot
    ii. A high-frequency current (to measure total body water) and a low-frequency current (to measure extracellular water) are applied.
    iii. The BCM then uses these measurements and the patient's present weight via advanced software to calculate the patient's lean tissue mass, adipose tissue mass, and overhydration (OH) volume. The OH volume is then used to arrive at a new, suggested target weight. For instance, if the patient's current weight is 72 kg, and the OH volume is 2 L, then the suggested new target weight would be 72 – 2 = 70 kg.
c. Point of care ultrasound can also assist with target weight determination.
    i. B lines in the lung suggest fluid overload.
    ii. A collapsing IVC below 2 cm in diameter suggests volume contraction.
d. Measurements of relative blood volume during the dialysis treatment while ultrafiltration is taking place can be of some help in avoiding excessive fluid removal and therefore IDH.
    i. This technique involves the HD machine doing constant, online measurement of hematocrit.
    ii. As plasma water is removed via ultrafiltration, the hematocrit rises. If the hematocrit rises quickly, it suggests that the water being removed via UF is not being replaced by fluid from the interstitial space of tissues.
    iii. The ratio of the hematocrit at the start of the treatment to the hematocrit at any time during the treatment (the "measurement time") is equal to the ratio of the blood volume at the measurement time to the initial blood volume.
    iv. For instance, if the initial hematocrit is 30%, and the hematocrit at 2 hours into the treatment is 40%, this means that the blood volume at 2 hours is

30%/40% = 75% of the initial blood volume. This is called the “relative blood volume” (RBV).

v. The HD nurses monitor the RBV during the treatment, and generally slow down ultrafiltration if the RBV is approaching 85%.

(ii) *Minimize gain of fluid weight in between dialysis treatments*. This can be assisted by:

a. Dietary counseling to reduce intake of salt and fluid

b. If there is residual renal function, prescribing a diuretic to increase urine output

(iii) *If possible, increase dialysis time per week.* IDH seems to be triggered by an overly rapid rate of fluid removal. This is made worse if a patient attempts to shorten her treatment time, and can be mitigated by increasing the patient’s treatment time. This means sticking to a 4-hour treatment time whenever possible, and if recurrent IDH remains a challenge, considering either nocturnal dialysis or more sessions per week (e.g. 4 times or 5 times per week).

(iv) *Avoid eating during dialysis*. Eating during HD causes splanchnic vasodilatation which can worsen the tendency to IDH.

(v) *Avoid taking antihypertensive medications* prior to the HD session, and give these in the evening after HD instead.

(vi) *Consider sodium ramping.* A high sodium dialysate may be used in an attempt to mitigate IDH. This causes sodium in the dialysate to diffuse into the patient’s plasma, causing a degree of hypernatremia. This in turn leads to the translocation of water from ICF (especially from muscle cells) into the ECF. This opposes the loss of water from ECF to ICF due to the urea disequilibrium described above. The problem with this approach is that while it may be effective *during* the dialysis treatment session, it will leave the patient hypernatremic and therefore thirsty at the end of the session. This in turn triggers more fluid intake after dialysis, leading to more *inter*-dialytic weight gain, a need for more ultrafiltration, and paradoxically more risk of IDH.

For this reason, the notion of sodium ramping was developed, whereby the dialysis fluid removal timetable involved removing the bulk of fluid in approximately the first half of the treatment session, at which time the sodium level in the dialysate is at its highest. Then, the sodium in the dialysate is progressively reduced until it reaches a nadir level that is typically ~ 140 mmol/L. This means the patient has had the opportunity for fluid removal but is not so hypernatremic at the conclusion of the HD session. In contemporary practice, such sodium ramping is relatively rarely used.

(vii) *Enhance vasoconstriction*. This can be achieved by:

a. *Cooling the dialysate* to 0.5-1.0C below the patient's body temperature
    i. This is generally fairly well tolerated, although some patients do experience uncomfortable chills.
    ii. This works by causing vasoconstriction of cutaneous blood vessels.
b. *Prescribing Midodrine*.
    i. This is an oral, alpha-1-receptor sympathetic agonist. It stimulates widespread vasoconstriction and raises BP, or at least prevents it from falling excessively.
    ii. Typical doses are 2.5-10 mg po taken 30-60 minutes before the HD session. It can be repeated once during dialysis.

<u>Intradialytic Hypertension</u>

Intradialytic *hyper*tension is much less common than intradialytic hypotension, but it does occur in some patients. Towards the end of the HD session, the BP may rise, and sometimes quite significantly, which is paradoxical since one expects the blood pressure to fall in response to fluid removal during the dialysis treatment. This affects only certain patients on HD, and is inconsistent even in these patients.

The basis for this phenomenon is not clear, but may be related to abnormalities in the ratio of the vasoconstrictor endothelin-1 to the vasodilator nitric oxide, or other endothelial abnormalities, triggered by the HD treatment.

Treatment is challenging. Options include:

- Attempting to lower the target weight
- Using Carvedilol 12.5 – 50 mg bid, as carvedilol reduces endothelin release

<u>Muscle Cramps</u>

Muscle cramps are not uncommon during HD treatments, and can be very severe. They seem to occur most commonly in relation to fluid removal, and so are more common when patients have one or more of the following:

- Hypotension during dialysis
- Hypovolemia
- A high rate of ultrafiltration
- Low sodium dialysate

The basis for the muscle cramps may be muscle hypoperfusion due to reflex arteriolar vasoconstriction that occurs in response to hypovolemia.

Muscle cramps are more likely if the patient has hypocalcemia, hypomagnesemia, or hypokalemia.

Treatment of muscle cramps in the first instance involves the treatment of associated hypotension, which often leads to resolution of the cramping.

If muscle cramping persists, then the patient may be given hypertonic glucose (e.g. 50% dextrose), and attempts should be made to stretch the cramped muscle.

Prevention of muscle cramps involves:

- the same measures used to prevent IDH
- ensuring a dialysate magnesium of 0.5 mmol/L, and avoiding hypokalemia and hypocalcemia
- considering use of one or more of the following pharmacologic approaches:
    - Vitamin E (400 units daily)
    - Oxazepam (5-10 mg 2 hours prior to dialysis)
    - Biotin 1 mg daily
- Although formerly recommended (and quite efficacious) for prevention of muscle cramps, Quinine should **not** be used, as it is associated with thrombocytopenia and QTc prolongation.

<u>Nausea and Vomiting</u>

These are relatively common complications of the dialysis procedure, and may be due to one or more of the following:

- Associated IDH
- Early manifestation of dialysis disequilibrium
- Dialyzer reaction
- Gastroparesis due to diabetes mellitus and/or uremia itself
- Any other unrelated cause of nausea and vomiting, such as new medication, gastroenteritis, pancreatitis, etc.

Treatment focuses first on addressing IDH, and then using antiemetics.

Generally, one begins with Dimenhydrinate (Gravol®), 25-50 mg i.v.

Ondansetron 6 mg i.v. or Metoclopramide 5-10 mg i.v. can also be used.

<u>Headache</u>

Headache is also quite common in patients with ESRD during the HD treatment.

It may be due to:

- A subtle manifestation of dialysis disequilibrium
- Caffeine withdrawal as caffeine is rapidly removed from the bloodstream during the dialysis treatment
- Migraine, which may be triggered by the HD treatment
- Intracranial hemorrhage, triggered by dialysis-associated anticoagulation

Management of dialysis-associated headache focuses on analgesia (generally with Acetaminophen), and then treatment of any identified underlying causes.

Chest pain

Chest pain can occur during a HD treatment for any of the usual reasons that patients get chest pain.

A major consideration, of course, is chest pain due to *myocardial ischemia*, related to the increased myocardial oxygen demand entailed by the dialysis procedure. (The cardiac output needs to increase to deliver 400 cc/min of "extra" blood flow to the dialysis machine.) Therefore, the patient who presents with chest pain during HD needs to be investigated for the possibility of myocardial ischemia with ECG, troponin levels, and often an empiric trial of nitroglycerine. Chest pain that is suggestive of myocardial ischemia that does not resolve should lead one to consider stopping dialysis, and sending the patient for further assessment to the emergency department.

Other well-known causes of chest pain also need to be considered, including but not limited to the following:

- Aortic dissection
- Pericarditis
- Pulmonary embolism
- Pneumonia
- Pneumothorax
- Gastroesophageal reflux
- Peptic ulcer disease, gastritis, cholecystitis, pancreatitis
- Chest wall disorders

Dialysis Dysequilibrium Syndrome (DDS)

The pathogenesis and prevention of this are described above.

The manifestations of DDS include:

- Headache
- Nausea and vomiting
- Confusion
- Seizures
- Reduced level of consciousness including coma
- Respiratory arrest

The *treatment of mild-moderate suspected DDS* involves:

- reduction in blood pump speed to reduce the efficiency of dialysis
- increasing dialysate sodium level
    - This causes a modest degree of hypernatremia, which opposes the movement of water from ECF to ICF caused by the rapidly falling ECF urea level
    - This can be done either with:
        - Sodium ramping, starting with a [Na+] that is 15 mmol/L higher than the patient's initial serum [Na+] and progressing down to finish dialysis with a [Na+] 5 mmol/L higher than the initial serum [Na+]
        - Simply using a dialysate [Na+] that is 10 mmol/L higher than the patient's serum [Na+] throughout the treatment

The *treatment of severe DDS* (e.g. seizures, coma) involves the following:

- Stopping dialysis
- Administering hypertonic fluid to rapidly raise ECF osmolality with either of these approaches:
    - Hypertonic (3%) NaCl at a dose of 50 – 100 cc, repeated every 10 minutes up to a total of 300 cc, as one does in treatment of acute symptomatic hyponatremia
    - Mannitol – This is available as a 20% solution (20g/100cc). A reasonable dose is to give 0.25 g/kg. In a patient who weighs 80 kg, this would be 20 g, or 100 cc.

<u>Dialyzer Reactions</u>

A "dialyzer reaction" involves the dialyzer or associated aspects of the dialysis procedure triggering various immune-related phenomena, with a range of complications. These are generally grouped into 2 categories, Type A and Type B. To understand the basis for these, it is helpful first to review properties of dialyzers and their sterilization, and then Type A and B reactions are described.

- *General properties of dialyzers and sterilization*

- Dialyzers can be categorized according to their composition:
  - *Organic* dialyzers are comprised of cellulose, a derivative of cotton, which makes them quite likely to activate complement, and therefore "bioincompatible"
  - *Semi-synthetic* – comprised of cellulose with acetate added, which makes it less likely to activate complement, i.e. more biocompatible),
  - *Synthetic*
- Synthetic dialyzers are used almost exclusively currently
  - They are much more biocompatible - i.e., much less likely to activate complement and therefore less likely to trigger immune-mediated phenomena
  - Constituents of these are
    - (1) Polymethylmethacrolyte
    - (2) Polyether sulfone
    - (3) Polysulfone
    - (4) Polyacrilonitrile (PAN) and AN
  - At St. Michael's Hospital, we are currently almost exclusively using the Elisio 21H dialyzer, which is a Polyethersulfone dialyzer, sterilized with gamma irradiation
- Sterilization is either chemical or with irradiation
  - The major chemical sterilizer has been ethylene oxide, but this is rarely used now since it used to cause Type A reactions with significant frequency
  - Irradiation used for sterilization is either gamma or beta irradiation

- Type A reactions
  - Pathogenesis
    - This is essentially an anaphylactic (IgE-mediated) or anaphylotoxic (complement-mediated) reaction to one of the following:
      - The dialyzer
        - Most dialyzers used currently are synthetic, in contrast to the older cellulose, or semi-synthetic (cellulose with acetate bound to it)
        - These synthetic dialyzers are considerably more biocompatible, meaning they are less likely to activate complement
        - PAN/AN69 membranes are more likely to cause a Type A reaction in patients treated with ACE inhibitor, since the ACE

inhibitor reduces breakdown to bradykinin, and the resulting higher levels of bradykinin interact with the PAN membrane and may trigger an inflammatory reaction

- The sterilizer or disinfectant used to sterilize the dialyzer
- Chlorhexidine or other agent used to clean the skin
- Heparin
- Blood transfused during the dialysis treatment
- Other medications administered during dialysis treamtent (e.g. antibiotics, iron)

- It most commonly occurs when a patient encounters a new kind of dialyzer for the first time
- It is more common in patients with a history of atopy and/or eosinophilia

- Manifestations:
  - Presentation is within the first 5 - 20 minutes of dialysis
  - Cutaneous – itch, urticaria and other skin rashes
  - Eye and nasal - Itchy eyes, nasal stuffiness, sneezing
  - Gastrointestinal – abdominal cramps, diarrhea
  - Respiratory - Dyspnea, wheezing (bronchospasm), stridor (laryngeal edema)
  - Cardiovascular - Hypotension, shock, cardiac arrest
- Management:
  - Stop dialysis, clamp the blood lines, and do not return the blood to the patient
  - Provide supportive care for airway, breathing and circulation
  - Treat the anaphylaxis with medications according to the severity of the reaction
    - Antihistamine – Diphenhydramine (Benadryl) 25-50 mg IV in most cases
    - Corticosteroid – Methylprednisolone 100 mg IV in most cases
    - Epinephrine 0.3 mg IM if reaction is very severe
- Prevention:
  - Rinse the dialyzer and very thorough priming
  - Sterilization with gamma irradiation
  - Avoid PAN membranes in patients on ACE inhibitors

- Type B reactions
  - These are considerably less severe than Type A reactions
  - They occur later after the start of a HD session, typically 20-40 minutes
  - The major consequences are

        - chest pain and back pain
        - nausea and vomiting
    - The cause is unknown, but may involve complement activation
    - Management involves:
        - Rule out and address other causes of chest and back pain
        - May proceed with dialysis
        - Provide oxygen as needed
    - Prevention
        - Consider switching to a different dialyzer

<u>Hemolysis</u>

Breakdown of red blood cells can occur during HD treatments.

The major causes are:

- Related to dialysate
    - Contamination with heavy metal (Cooper, zinc)
    - Contamination with disinfectant added to city water supply (nitrate, chloramine)
    - Hypo-osmolar dialysate
    - Overheated dialysate (extremely rare since HD machine alarms if dialysate is warmer than 39.5C)
- Related to the extracorporeal circuit
    - Kink in dialysis tubing
    - Partial occlusion of CVC
- Related to the patient
    - Any cause of hemolytic anemia

The manifestations of intra-dialytic hemolysis are:

- Nausea and vomiting
- Chills and fever
- Abdominal pain and back pain
- Acute hypertension

Laboratory findings include:

- Fall in hematocrit
- Pink discolouration of the serum
- Fall in haptoglobin, rise in LDH

Management of hemolysis during HD:

- Stop the blood pump. This is done to avoid infusing plasma with hemolyzed blood back to the patient. The danger of infusing this blood is that the lysis of red blood cells causes leakage of potassium from the RBC interior into plasma, and infusing this plasma could lead to life-threatening hyperkalemia.
- Review course of other patients to ensure there is no systemic problem affecting dialysate or tubing, nor that that there are contaminants
- Monitor patient for hyperkalemia and treat as needed

Air Embolism

This is, fortunately, an exceedingly rare complication of modern HD, but it can still happen and is a potentially life-threatening complication.

How air can get into the dialysis blood tubing

Air can into the bloodstream at 1 of 4 possible entry points (see Clin J Am Soc Nephrol 2017; 12: 357–369):

(1) At the Luer lock between the arterial needle and the tubing, if there is a loose connection, inadequate clamping during connection or disconnection, or a broken bit of tubing. This is because the blood pump action causes a large, negative pressure inside the tubing, which will then suck air into the tubing from the Luer lock area.

(2) Through a hole in the arterial tubing. This can suck air into the arterial line, similar to what happens if there is a poor connection at the Luer lock described in (1).

(3) At the connection point for administration of heparin, saline, or other medications such as antibiotics.

(4) From the dialyzer or the dialysis tubing, due to inadequate “priming”. (The word priming here refers to the process of filling the dialyzer and the hollow fibres and blood tubing with saline prior to the dialysis procedure so that all of the air has been expelled.)

Note 3 additional points:

(i) A hole in the *venous* tubing will not cause air embolism, because there is positive pressure in this part of the circuit, which will prevent air from entering into the tubing.

(ii) There is a venous air trap located in the circuit distal to the dialyzer. If air has entered the blood tubing at any point, it will cause foaming in the chamber of the venous air trap. This will cause the blood in this chamber to drop in its vertical level, which will then trigger a sensor that stops the dialysis procedure.

(iii) Air embolism can also happen when a CVC is being inserted or removed, or if it is inappropriately left open to the air.

Consequences of air entering the dialyzer circuit

The volume of air entering the venous system that is considered to be fatal in humans is between 100-300 mL. The consequences of air embolism depend on the volume of air that enters, the patient's position, and the patient's underlying cardiorespiratory status.

(1) <u>If the patient is seated</u>

The air rises in the body, so it tends to travel superiorly from the arm and neck veins up into the head, where the air may occlude cerebral veins. This can lead to:

- Blurring of vision
- Loss of consciousness
- Seizures
- Death

(2) <u>If the patient is supine</u>

The air enters the heart, where it causes foaming in the right ventricle. It then enters the lung, where it can cause:

- Dyspnea
- Chest tightness
- Arrhythmias
- Hypotension and tachycardia, due to right ventricular overload

The air can cross through the pulmonary vasculature and enter the left ventricle, and then be pumped into the arterial tree, leading to occlusion of the arterial supply to organs such as parts of the brain, a limb or parts of the GI tract.

Suspecting and detecting air in the dialysis circuit and air embolism

- Air embolism may be suspected if the patient has one or more of the acute neurological and/or cardiorespiratory symptoms mentioned above
- Foam may be seen in the venous blood line and/or the chamber of the venous air trap
- A Doppler ultrasound of the heart may detect the air

Management of air embolism

(1) Clamp the venous blood line and stop the blood pump

(2) The patient is placed on their left side, head down. This is to encourage the air that is reaching the heart to stay in the right ventricle, since in the left lateral decubitus and head-down position, the right ventricle becomes the uppermost cardiac chamber. As a result, the air will tend to accumulate there rather than moving into the lungs, or from the lungs to the left ventricle and then into the arterial tree. (Supine position may suffice.)

(3) Administer oxygen 100% via face mask or endotracheal tube

(4) One may attempt to aspirate the air via a CVC if there is a CVC in place, since the tip of the CVC catheter is relatively close to the right ventricle.
(5) Attempts can be made to drain the air from the heart percutaneously by a cardiologist.

Preparing the patient for hemodialysis

Consent for Hemodialysis

A written consent must be obtained by the physician (resident, fellow or attending) or nurse practitioner for both:
- Dialysis CVC insertion, and
- Hemodialysis treatments

The signed consent forms must be added to the physical hospital chart (in the in-patient setting) or added to the physical hemodialysis unit chart in the hemodialysis unit.

Hepatitis B status

Patients who are positive for hepatitis B surface antigen (HBsAg) must be dialyzed in an isolation room in the hemodialysis unit, or in their hospital bed if they are an in-patient. This is to reduce the risk of transmitting hepatitis B to other patients. Therefore, *it is essential to know the HBsAg status of all patients who will need in-patient hemodialysis (as well as out-patients).*

Hemodialysis Orders

Order dialysis the day before the proposed treatment if possible

Dialysis orders for in-patients (both those receiving HD for AKI and for chronic HD patients admitted to hospital) need to be entered into Soarian in advance of their treatment, and if at all possible this should be done one day prior to the planned HD session.

Once-per-week orders for stable chronic in-patients may be appropriate

For in-patients who are on long-term HD and who are stable, orders can be entered just once for a whole week – i.e., for 3 HD treatments, although one must be prepared to adjust such “standing orders” if the patient’s condition changes.

Hemodialysis order set in Soarian

Orders are entered into an order set in Soarian. This can be found by searching in the orders section for “hemodialysis”. Each of the following sections has a prompt in the order set.

Orders for Conventional Hemodialysis

(see next section for comments on first and second treatments)

1) *Dialyser*

Usually, the Elisio-21H dialyzer is used.

2) *Time*

For patients on chronic HD, the usual duration is 4 hours.

3) *Blood pump speed (BPS, also known as Qb).*

(1) Generally, for patients on chronic HD, the nurses aim to use a BPS of 400 ml/min.

(2) Patients receiving nocturnal hemodialysis (with treatment times longer than 6 hours) may have a slower blood pump speed (200-350 mL/min).

(3) Acute and/or very uremic patients may need slower speeds (e.g. ~200 ml/min) initially to avoid the dialysis disequilibrium syndrome (see below).

4) *Dialysate flow (also known as Qd)*

This is generally 1.5 x Qb. For example, if the Qb is 400 mL/min., then the Qd will be 1.5 x 400 mL/min. = 600 mL/min.

5) *[Na^+] in dialysate*

a) Usual [Na^+] in the dialysate:

Usually, we use 140 mmol/L. In 2021, we are participating in a randomized trial of dialysate sodium concentration, and SMH has been randomized to dialysate sodium concentration of 137 mmol/L, so this will be the usual level used for our patients.

b) Sodium ramping.

Sometimes, one can use “sodium ramping”. The HD machine can be programmed to deliver a dialysate whose [Na^+] starts out higher than 140: this can be anywhere from 145 to 160 mmol/L. Subsequently, the machine then reduces the dialysate [Na^+] down to 140 over the first 3 hours of treatment.

Sodium ramping can be used when the patient is experiencing hypotension during dialysis (“intra-dialytic hypotension”) or when the patient is having difficulty reaching their target weight. It works by causing a degree of hypernatremia early during the HD treatment; this causes an osmotic gradient for water to leave body

cells and enter the extracellular fluid (ECF). This tends to increase intravascular volume even as excess ECF is being removed during the HD treatment via ultrafiltration, and reduces the likelihood of intradialytic hypotension.

c) <u>If the patient is significantly hyponatremic prior to HD:</u>
In such a circumstance, using a dialysate [Na^+] of 140 mmol/L may cause the serum [Na^+] to rise too quickly, and put the patient at risk of osmotic demyelination. In such a case, one should use a lower [Na^+] dialysate. The lowest dialysate [Na^+] that our HD machines are able to deliver is 130 mmol/L. This is suitable for patients whose plasma [Na^+] is as low as approximately 126 mmol/L prior to starting dialysis, since in such a case the HD treatment using a dialysate [Na^+] of 130 mmol/L would lead to a rise in plasma [Na^+] to a level somewhere between 126 and 130, and certainly not rising more than 4 mmol/L. This is a safe rate of correction, especially when starting at a level above 125 mmol/L. If the plasma [Na^+] is 125 mmol/L or less, then there is more concern about overly rapid correction. In such a situation, to avoid such overcorrection, the patient needs to be infused with D5W into the blood line at an appropriate rate to keep the plasma [Na^+] at a relatively steady level. A protocol for infusing D5W is available. Consult the attending nephrologist for advice.

6) *[K^+] in dialysate*
Most patients are dialyzed with [K^+] in the dialysate of 2.0 mmol/L or 3.0 mmol/L.
- if their pre-dialysis serum [K^+] is 4.5 mmol/L or higher, generally use dialysate [K^+] 2.0
- if their pre-dialysis serum [K^+] is 4.4 mmol/L or lower, generally use dialysate [K^+] 3.0

It remains possible to use a dialysate with a [K^+] of 1.0 mmol/L. One may be inclined to use this in a patient with severe hyperkalemia (e.g., plasma [K^+] over 6.5 mmol/L) in order to achieve more rapid and more complete removal of potassium. The risk of using this is that it may lead to an excessively rapid fall in plasma [K^+], which can then predispose the patient to serious cardiac (ventricular) arrhythmias. A compromise might be to use a dialysate [K^+] of 1.0 mmol/L for the first 2 hours of the HD treatment, and then switch to a dialysate [K^+] of 2.0 mmol/L for the final 2 hours, to avoid excessive total reduction in plasma [K^+].

7) *Calcium in dialysate*
The available options are 1.25 mmol/L and 1.55 mmol/L. In most cases, we use 1.25 mmol/L. Note that this is similar to the normal ionized calcium level in plasma since this is the calcium concentration that affects whether calcium diffuses across the dialyzer

membrane. This is because the calcium in plasma that is bound to albumin simply stays attached to albumin in the blood and is not "available" to diffuse across the dialyzer membrane, and therefore does not affect calcium movement across the dialyzer membrane.

In patients who have a tendency to hypocalcemia (e.g. patients who have had a parathyroidectomy), we may use the higher ionized calcium in the dialysate of 1.55 mmol/L.

8) *Bicarbonate (HCO_3^-) in the dialysate*

Generally, we use a [HCO_3^-] of 35 mmol/L. Note that this is higher than normal plasma [HCO_3^-], which is close to 25 mmol/L. This is one setting in which we expect a solute to diffuse *from* the dialysate across the dialyzer membrane *into* the patient's plasma. This is necessary since the patient with end-stage renal disease has kidneys which are no longer able to synthesize bicarbonate, and therefore need to have this administered to them.

9) *Phosphate in the dialysate*

Normally, there is no phosphate in the dialysate, as one is trying to remove as much excess phosphate as possible from the usual patient on HD, who is of course generally hyperphosphatemic.

The 2 settings where one might add phosphate to the dialysate in order to reduce the amount of phosphate removed are:

- Patients on intensive dialysis (i.e., nocturnal HD, or in-centre daily HD) who have more hours of dialysis per week, and therefore more time to remove phosphate and are therefore at risk of becoming hypophosphatemic
- Patients who are actually hypophosphatemic, for instance due to poor nutrition.

If a patient on HD is hypophosphatemic (phosphate level below 1.2 mmol/L), the following measures are appropriate:

- Reduce and eventually stop phosphate binders
- Liberalize dietary phosphate intake
- If the patient is still hypophosphatemic, then sodium phosphate from a Fleet® enema can be added to the dialysate as described below.
    - Fleet® enema has sodium phosphate at a concentration of 1.38 mmol/mL

- An appropriate volume of this should be added to the acid concentrate in order to achieve a final dialysate phosphate level that is appropriate for the patient's current serum phosphate level and expected ongoing dietary intake
- For instance: Adding 30 mL of Fleet enema to 4.5 L of acid concentrate adds 42 mmol of phosphate (30 mL x 1.38 mmol/mL = 42 mmol)
    - This will ultimately be diluted by the total dialysate volume during a 4-hour (i.e. 240 minute) dialysis treatment. If the dialysate flow rate (Q_D) is ~ 600 mL/min (0.6 L/min.), then the total dialysate volume will be 0.6 L/min x 240 minutes = 144 L
    - The resulting phosphate concentration will be 42 mmol/144 L = 0.3 mmol/L; this will remove less phosphate than dialysate that has no added phosphate
    - Adding 60 mL of the same solution would achieve a phosphate concentration of 0.6 mmol/L, which is close to the normal lower limit for phosphate in plasma (usual reference range is 0.7-1.1 mmol/L). This amount of added sodium phosphate will result in minimal removal of phosphate.
    - One can titrate the required amount of phosphate supplementation by sequential measurement of serum phosphate

10) Glucose in the dialysate

Glucose is routinely added to the dialysate in all patient to achieve a concentration of 5.3 mmol/L, in order to avoid having the dialytic removal of glucose from the patient's plasma into the dialysate, which could then cause hypoglycemia.

11)Ultrafiltration

This refers to the amount of net fluid removal required over the course of the dialysis treatment. The usual goal is to achieve the patient's "target" or "dry" weight. This is the weight that the patient would be at if they had no peripheral edema or excess ECF volume, while also avoiding excessive removal so that their blood pressure is not low in either the supine position or when they stand up.

The target weight is determined by clinical assessment of the ECF volume of the patient. This can be supplemented by information from lung ultrasound, and also in the chronic outpatient setting by determination of body composition.

Note that ultrafiltration removes fluid directly from the plasma in the intravascular space. Fluid then needs to translocate from the interstitial space into the plasma – this is called

refilling. This rate of refilling is generally slower than the rate of ultrafiltration. This means that the patient's blood volume falls during dialysis, and as a result they may experience a fall in blood pressure. Such a fall in blood pressure is more likely to happen under the following circumstances:

- The patient has had a large gain of fluid weight since their last dialysis treatment, and as a result they need to remove a large amount of fluid per hour of dialysis
- The patient starts the treatment with a relatively low blood pressure, perhaps because they have taken all of their antihypertensive medication prior to the dialysis treatment
- The patient has hypoalbuminemia, which means they have less of an oncotic pressure force attracting water into the plasma space from the interstitial space
- The patient has an autonomic neuropathy (due to e.g. DM, uremia, or amyloidosis), so they are unable to achieve sufficient vasoconstriction to maintain their BP as their intravascular volume falls
- The patient has significant heart disease, and so is unable to increase cardiac output via increased contractility and/or increased heart rate to maintain their BP as blood volume falls

In such situations, it may be preferable to have the patient dialyzed more frequently (e.g. short daily hemodialysis) with the ultrafiltration needs spread over a greater number of treatments.

Ultrafiltration orders can be entered in terms of either
(a) target weight; or,
(b) litres to be removed.

Using *target weight* is generally preferable.

However, under various circumstances, it may be necessary to enter a fluid removal order for a treatment in litres to be removed. These circumstances include:

- if the patient cannot be weighed
- if the patient has lost or gained "flesh" weight (i.e. change in their mass of muscle and/or fat) due to illness or a change in diet, in which case the target weight needs to be reassessed.

The amount of fluid to be removed when the target weight method cannot be applied requires careful volume assessment, and may benefit from point-of-care ultrasound,

determination of body composition with the help of one of the dietitians, and serial assessments as fluid is removed treatment-by-treatment.

During any given dialysis session, ultrafiltration may be “ramped” such that a greater proportion of the total fluid to be removed is removed earlier in the dialysis session (e.g., remove 40% over 1st hour, 30% over 2nd, 20% over 3rd and 10% over 4th). This is not done too often in contemporary practice.

12) BP support

This is especially important in the ICU setting. This can involve:

- ramping the dialysate [Na^+]
- ramping ultrafiltration
- infusing normal saline
- infusing albumin, or
- (in the ICU setting) giving inotropic support.
- Wrapping of legs with Tensor bandages to enhance shift of fluid from the interstitial to the intravascular space within the ECF compartment may be helpful.
- Cooling dialysate to 0.5C below body temperature. This causes vasoconstriction of cutaneous blood vessels, and may raise BP enough to permit further fluid removal.

13) Anticoagulation.

Anticoagulation is administered during the hemodialysis procedure in most cases, to reduce the risk of clotting of the extra-corporeal circuit.

This of course needs to be avoided if the patient:

- Has ongoing bleeding
- Is at risk for bleeding (e.g. has just had surgery)
- Has heparin-induced thrombocytopenia (in which case generally we use Argatroban as the anticoagulant).

At St. Michael’s Hospital, there are two options:

- Unfractionated heparin
- Low molecular weight heparin (Dalteparin)

(i) Unfractionated heparin (UFH)

This is the traditional modality and is still available, although it has largely been replaced by Dalteparin.

There are three rates of delivery for administration of heparin during the hemodialysis treatment:

a) Regular heparin: Most patients receive “regular” heparin. This involves using unfractionated heparin, with a 1000 unit bolus followed by an infusion of 1000 units/hour. The heparin is discontinued 60 minutes prior to the end of dialysis if the patient has an AV fistula or graft; in patients with central venous catheters, heparin is continued until the end of the treatment.

b) Tight heparin: This involves no bolus, and an infusion at 500 units/hour. This is used most commonly if a patient has had bleeding in the recent past but it is judged that some heparin can be given. In such a case, one may choose to use a small dose to make sure that the heparin will be tolerated without causing bleeding, before going on to regular heparin at a subsequent treatment.

c) No heparin. The nurse flushes the dialyzer every 30 minutes with normal saline to prevent clotting. The additional administered saline given with the flushes is then removed from the patient via ultrafiltration.

(ii) Dalteparin

In patients who are able to tolerate anticoagulation, in most cases at St. Michael’s Hospital we order Daltepain 2500 units i.v. at the start of the dialysis session. Occasional patients need a higher dose.

14) Other

It is possible to give some medications with dialysis. In particular, antibiotics are often prescribed at the end of a dialysis treatment.

Packed RBC transfusions, if required, are sometimes given while on dialysis. The advantage of doing this is that there is a risk of volume overload for a patient on dialysis when he or she receives a RBC transfusion; the chance of this can be reduced by ultrafiltration of fluid concurrently with the transfusion during dialysis.

The problem with transfusing during the dialysis treatment is that adding the packed RBCs to the dialysis circuit increases the viscosity of the blood and therefore increases the risk of thrombosis. As a result, it is important that the patient receive heparin during the treatment. The challenge with this strategy is that if the reason for the patient's anemia is bleeding, one (obviously) does not wish to give heparin. These competing considerations (desire to transfuse during the dialysis procedure to permit fluid removal and avoid the risk of fluid overload, but the need to avoid heparin) can be managed by transfusing via a peripheral intravenous line during the dialysis treatment, and concurrently ultrafiltering an appropriate volume of fluid.

Modifications of orders for the first two ever hemodialysis treatments to prevent dialysis disequilibrium syndrome

An important risk of hemodialysis that can occur with the first or second treatment is called dialysis disequilibrium. This is essentially the development of cerebral edema, similar to what can happen with acute hyponatremia, with a risk of headache, nausea and vomiting, depressed level of consciousness, epileptic-type seizures, and even, rarely, death. The pathophysiology involves a rapid reduction in the plasma level of urea during an aggressive hemodialysis treatment. Normally, urea is not an effective osmole since it achieves equal concentrations in the intracellular fluid (ICF) and the extracellular fluid (ECF). However, in the few hours of a hemodialysis treatment, the ECF urea level may fall rapidly but it takes time for the urea to diffuse from ICF to ECF, and until this happens there is a "disequilibrium" for urea with the ICF urea concentration considerably higher than the ECF urea concentraiton. This causes osmotic movement of water from ECF to ICF, in particular into brain cells, causing cerebral edema.

This can be avoided by ensuring that the first two HD treatments are relatively "gentle", and specifically, using a shorter duration, and slower Qb. One approach is as follows:

- First treatment – Duration 2 hours, Qb 200 cc/min, Qd 300 cc/min
- Second treatment – Duration 3 hours, Qb 300 cc/min, Qd 450 cc/min
- Third and subsequent treatments – Duration 4 hours, Qb 400 cc/min, Qd 600 cc/min.

A further preventative measure is to dialyze the patient with a dialysate that has a sodium concentration that is higher than the patient's serum [Na+]. This will cause a mild degree of hypernatremia, and cause water movement from the patient's cells to the ECF, which opposes water movement from ECF to ICF induced by the rapid reduction in urea concentration in the ECF. A reasonable approach is to use a dialysate [Na+] that is 5-10 mmol/L higher than the patient's serum [Na+].

Management of chronic HD patients admitted to hospital

When chronic dialysis patients are admitted to other services, the nephrology consult team will be consulted in order to manage dialysis-related issues. In addition to ordering dialysis, the consult team should monitor for co-interventions ordered by other teams that may require modifications in a dialysis patient.

1) **Medications**

   It is crucial to review the pre-admission medication list for all dialysis patients and ensure that these are continued or held (as appropriate) during the hospitalization. The patient's medication list may be found in Nephrocare. It should be reviewed at the outset of each hospitalization. At the time of discharge, it is important to identify dose adjustments to pre-existing medications, new medications started, medications that have been discontinued permanently and medications that need to be restarted after being temporarily held. This information should be conveyed to the patient's primary nephrologist.

   For all patients with acute or chronic kidney disease (including chronic dialysis patients), the medication list should be frequently reviewed to ensure that all medications that have been prescribed by the admitting service are not contraindicated in the setting of kidney disease. Furthermore, the consult service should verify if the medication dose and frequency is appropriate for the degree of kidney function. Note that some medications need to be given *after* dialysis and in some cases, supplemental doses are needed after dialysis.

2) Laxatives

   Magnesium, citrate, aluminium and phosphate containing bowel medications should be avoided. Fleet enemas (which have phosphate as a component), in particular, should always be avoided. If bowel preparation is required, the preferred solution is CoLyte or PegLyte. Although large volumes are typically required, these solutions (when used appropriately) are not absorbed and are not contraindicated in dialysis patients.

3) Maintenance IV solutions

The volume of delivered IV solutions should be monitored in dialysis patients. Standard "maintenance" orders (e.g. normal saline at 100cc/hour) could rapidly lead to volume overload in a patient with ESRD.

4) Dialysis dose and prescription

Patients who are acutely ill may require modification of their chronic dialysis prescription. For instance, If oral intake is reduced such that a patient may be consuming little or no potassium in their diet, then they may require a higher dialysate potassium concentration than usual. Similarly, they may require supplementation of calcium or phosphate.

Ultra-filtration requirements can be significantly altered during a hospital admission. If a patient is not eating and is losing flesh weight during a prolonged hospital admission, then their target weight will need to be adjusted downward, since continuing to use the same target weight when flesh weight is being lost will lead to extracellular fluid volume overload

Patients who are acutely ill may become uremic due to the increased metabolic stress and catabolism of the acute illness, despite continuing their formerly adequate dialysis prescription. If this occurs, then either more frequent treatment, longer treatments or both may be required.

Ultra-filtration, solute removal, and biochemical parameters should be monitored longitudinally, with adjustments of the dialysis prescription made as required.

Renal Replacement Therapy for Acute Kidney Injury

Renal replacement therapy for acute kidney injury (AKI) is frequently required when conservative measures fail to prevent or control life-threatening complications of AKI (e.g., congestive heart failure, hyperkalemia). In addition, severely ill patients with established AKI and no evidence of impending renal recovery are often started on renal replacement therapy. This criterion for renal replacement therapy initiation is more subjective and there is no consensus on the optimal time for commencement of renal replacement therapy in AKI.

Patients with AKI who require renal replacement therapy may be managed with intermittent hemodialysis (IHD), continuous renal replacement therapy (CRRT) or sustained low efficiency dialysis (SLED). The same patient may receive one or more of these modalities at different times of their course in hospital depending on the evolving clinical circumstances.

<u>Intermittent Hemodialysis (IHD)</u>

In intermittent hemodialysis (IHD), conventional dialysis machines and prescriptions (akin to those used in the chronic setting as described above) are applied to the setting of AKI. IHD may be administered anywhere in the hospital. IHD is typically reserved for patients with AKI who are hemodynamically stable, including patients who had received SLED or CRRT earlier in their admission and who have become hemodynamically more stable.

IHD is the most efficient form of dialysis and is the most effective way to manage life-threatening hyperkalemia (even if the patient is hemodynamically unstable) and intoxications (see below). The typical session duration is 3-4 hours at blood pump speeds of 300-400 cc/min. Anticoagulation is preferred but sessions may be feasibly administered with no heparin. Hemodialysis nurses administer IHD and sessions need to be arranged in coordination with the Hemodialysis In-Charge Nurse or the dialysis nurse on call.

Continuous Renal Replacement Therapy (CRRT)

Continuous renal replacement therapy (CRRT) provides 24-hour per day RRT using relatively slow blood flow and slow ultrafiltration rates. This is generally reserved for hemodynamically unstable patients.

CRRT may be administered as:

- Continuous veno-venous hemodialysis (CVVHD)
- Continuous veno-venous hemofiltration (CVVH)
- Continuous veno-venous hemodiafiltration (CVVHDF).

CRRT at St. Michael's Hospital is only available in the MSICU and CVICU and is administered using dedicated Prismaflex^{TM} machines. Critical care nurses are responsible for setup of the machines and administration of therapies. The Nephrology consult service is responsible for ordering, monitoring and adjusting the CRRT prescription.

Orders for CRRT are entered via Soarian. Search for "CCRT" to find the order sets.

One set of orders is employed for patients receiving heparin or no anticoagulation; another set is used for patients receiving regional citrate anticoagulation. **Completed orders must be reviewed with the Nephrology fellow and/or staff prior to finalizing them in Soarian.**

Clearance modes in CRRT

CVVH (see the 3 circuits on the left hand side of Figure 1):

This utilizes hemofiltration as the only mode of clearance. All solute removal is by convection (also known as “solvent drag”). Convection happens as follows:

- Using hydrostatic pressure gradients, a large volume of plasma is filtered across the dialyzer membrane (e.g. 2 litres per hour)
- The dialyzer membrane has very small diameter pores through which the water and small dissolved solutes are able to pass from plasma to the other side of the membrane
    - The smaller the solute (i.e., the lower the molecular weight of the solute), the more complete will be its transfer along with water across the dialyzer membrane
    - For instance, urea has a molecular weight of 60 daltons (60 g/mole), and is more completely transferred than creatinine, which has a molecular weight of 113 daltons, although even creatinine passes through quite well
    - Larger molecular weight solutes such as vitamin B12 (molecular weight 1350) pass through only partially; this is an example of a “middle molecule”
    - Proteins such as albumin (molecular weight 67,000 daltons) essentially do not pass through at all
- Consider the example of a patient who has CVVH at 2 litres per hour – this will be 2 x 24 = 48 litres/day
    - This volume might then be replaced by a similar volume of replacement fluid (often similar to dialysate) but will not include urea, creatinine and other undesirable solutes
    - The net effect of this is that the 48 litres of plasma water that were filtered are replaced by (e.g.) urea-free water, so there has been the *clearance* of 48 litres of fluid
    - Often, there is a desire for some net fluid removal, so in the above example one might be aiming to remove a net of 2 litres per day of fluid; therefore, one would replace 46 litres of fluid, having removed 48 litres
- Convection is a more effective way to remove middle molecules (those with a molecular weight of roughly 500-5000) than is dialysis.

<u>CVVHD:</u> (see Figure 1, right-hand column, top diagram)

This employs dialysis exclusively as the mode of clearance; all solute removal is by diffusion. This means the solute (e.g. urea or creatinine) *diffuses* from its high concentration in the plasma across the dialyzer membrane into the dialysate, where the concentrations of urea and creatinine are zero. The dialysate “washes away” the solutes that diffused in from the plasma, and fresh dialysate is brought into contact with additional plasma. (Pure CVVHD cannot be

delivered on the Prismaflex as there is, for technical reasons, an obligate 200 mL/hr of hemofiltration that must be given.)

CVVHDF: See Figure 1, right hand column, bottom diagram)
This involves a mixture of CVVHD and CVVH. Practically speaking, most patients will receive a combination of dialysis (diffusion) and hemofiltration (convection) in the form of continuous veno-venous hemodiafiltration (CVVHDF), often aiming for 50% of clearance via dialysis and 50% via hemofiltration. This serves to achieve a good balance of removal of small solutes and middle molecules.

Indications for CRRT

- *Hemodynamic instability*
  - Patients who require acute hemodialysis and are hemodynamically unstable to the point where conventional hemodialysis is judged to be too high risk. (This is of course requires judgement and discussion with the intensive care unit team; note that in very unstable patients, even CRRT may not be tolerated.)
  - Hemodynamic instability is suggested by a significant need for inotropic support:
    - High doses of Norepinephrine (Levophed®) – greater than 0.
    - Need for 2 or more inotropes (most commonly Norepinephrine and Vasopressin)
- *Very large, ongoing ultrafiltration requirements*
  - Patients with very large ultra-filtration needs, especially those with large IV infusion rates related to administration of, for instance, inotropes, TPN, etc.
  - In such cases it is unlikely that even daily intermittent hemodialysis will be able to keep up with the large daily fluid loads

Filter used for CRRT
In *hemodialysis*, blood and dialysate enter and interact inside an object called the “dialyzer”. In *CRRT*, the similar object is called a “filter”. This is consistent with the fact that one can use this filter for both dialysis but also exclusively for hemofiltration, without using any dialysate.

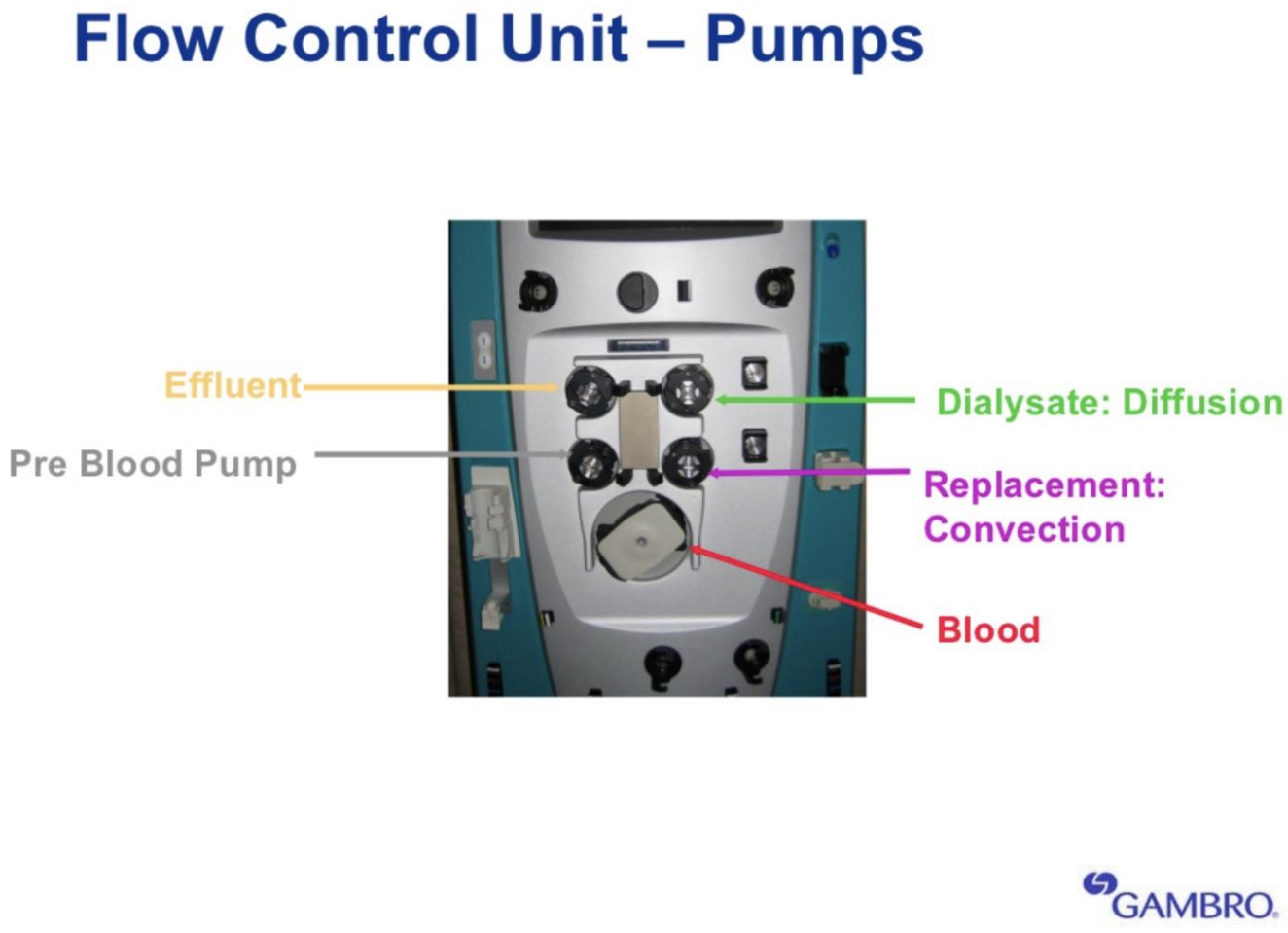
At St. Michael’s Hospital, we currently are using the filter known as ST-150.

Pumps on the CRRT Machine
There are 5 available pumps on the CRRT machine.

(1) Blood pump
(2) Preblood pump (for administration of infusion fluid, most commonly citrate for regional citrate anticoagulation)

(3) Dialysate pump
(4) Effluent pump
(5) Replacement fluid pump

See the diagram below. It is taken from a presentation in the Public Domain on Slide Share, found at:
https://www.slideshare.net/HammerheadNC/1-prismaflex-crrt-intro-seg-1-2007-7394701



Connections, bags and tubing in CRRT

The circuits and connections are quite complex in CRRT. The following is a brief overview of the setup. The description assumes one is looking at the front of the CRRT machine.

(1) The leftmost bag is connected to the filter via YELLOW tubing, and this is for the effluent draining from the filter.
(2) The second connection (and tubing) is GREY in colour, and this is for citrate administration which is connected to the blood line, prior to its entry into the filter. (This of course is only used if the patient is on regional citrate anticoagulation.)

(3) The third connection is GREEN in colour, and this is for dialysate to enter the filter in the dialysate compartment. This is not used if the patient is on exclusively CVVH.
(4) The fourth connection is PURPLE in colour, and this is for replacement fluid. Note that this can be connected to the blood tubing either prior to its entry into the filter (this is called “pre-filter” or “pre-dilution”), or it can be connected to the blood tubing after it has exited the filter (this is called “post-filter” or “post-dilution”). This is made possible by having Y-shaped connected in the tubing, with the option to plug this into the blood line prior to the filter, after the filter, or both.

<u>Dosage of CRRT</u>

- The dosage of CRRT is prescribed as the volume of “effluent” coming out of the filter
    - The “effluent” is all of the fluid that comes out of the filter, and is derived from 4 sources:
        - Dialysate
        - Replacement fluid that is then removed from the patient via hemofiltration
        - Actual ultrafiltration, which is the fluid removed from the patient beyond that added to the patient as replacement fluid
        - Any other fluid infused into the blood circuit, which is then removed via hemofiltration; most commonly, this is fluid administered along with citrate for regional citrate anticoagulation
- Generally, the total prescribed “effluent” dose should be 20-25 mL/kg/hour

As a practical example, consider a patient whose weight is 80 kg. Their total prescribed effluent would be 80 kg x 25 mL/kg/h = 2000 mL/h. This can be administered as any one of the following:

1. CVVHD – dialysate flow = 2000 mL/h
2. CVVH – hemofiltration rate = 2000 ml/h
3. CVVHDF – typically prescribed as 50% CVVHD and 50% CVVH, so the patient would receive
    - Dialysate flow 1000 mL/h
    - Hemofiltration rate = 1000 mL/h

There may also be additional effluent due to:

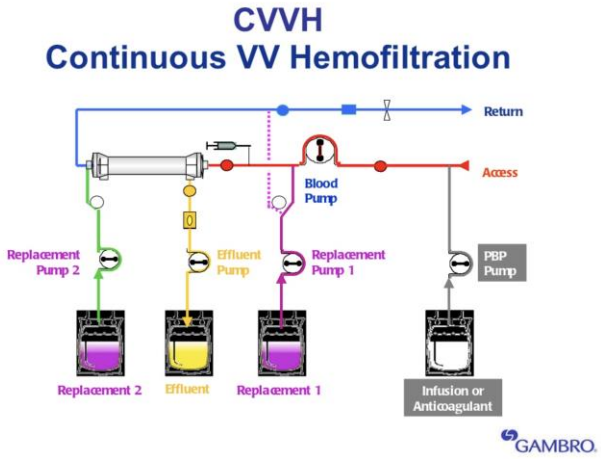
- Ultrafiltration

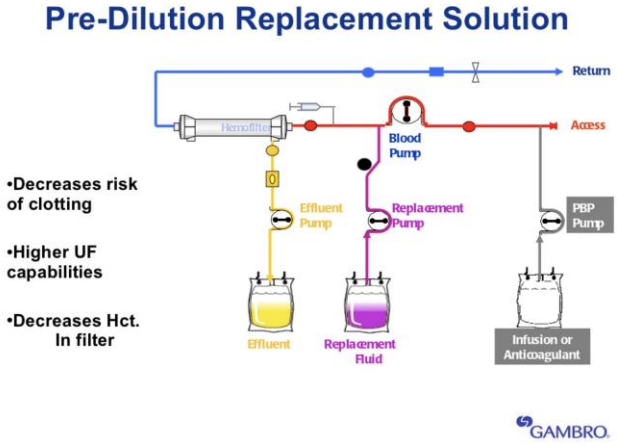
- Administration of fluid together with citrate (if the patient is receiving regional citrate anticoagulation), which is typically around 200 cc/hour

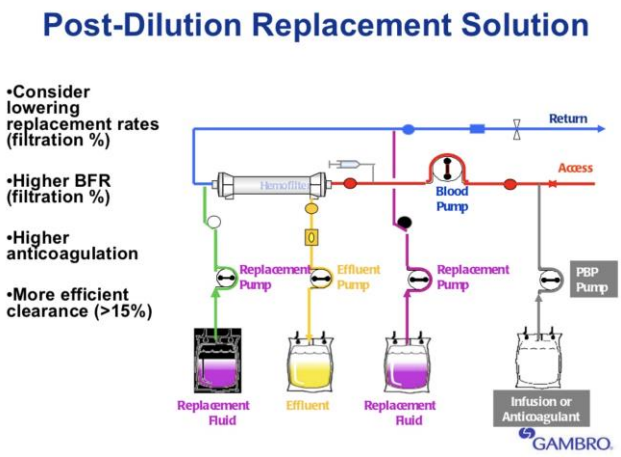
Figure 1. Circuit Diagrams for Continuous Renal Replacement Therapy

These figures are taken from a presentation in the Public Domain on Slide Share, found at: https://www.slideshare.net/HammerheadNC/1-prismaflex-crrt-intro-seg-1-2007-7394701

Below are illustrated circuits for CVVH in general, followed by CVVH with pre-dilution (pre-filter) replacement, and then CVVH with post-dilution (post-filter) replacemnt.

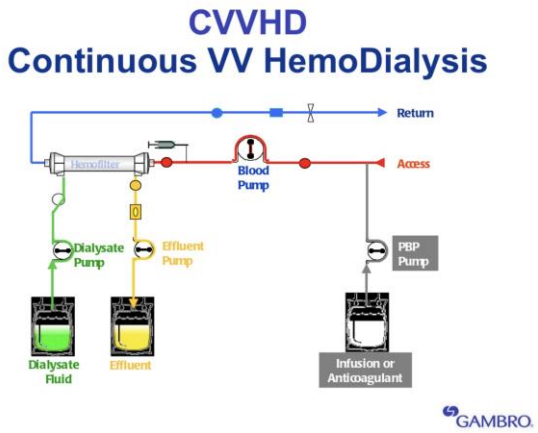




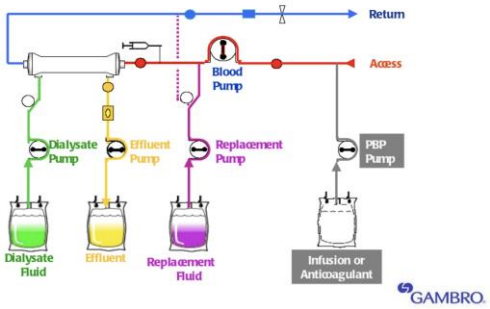


Below are illustrated circuits for CVVHD and CVVHDF.

Note that for CVVHDF, replacment fluid can be administered either pre-filter (solid purple line) or post-filter (dashed purple line), or both.



CVVHDF
Continuous VV HemoDiaFiltration



Filtration fraction monitoring

As the blood passes through the dialyzer, a proportion of the plasma is filtered across the dialyzer membrane. The proportion of the blood that is filtered across the membrane is called the "filtration fraction" (FF). The higher the FF, the more concentrated is the blood that emerges from the dialyzer, and as a result it will be more viscous and thus more prone to clotting.

This is mainly an issue when one uses CVVH to a significant extent, because hemofiltration involves the filtration of a very significant volume of plasma water to remove solute. The removed water is then replaced. A key issue is whether one provides the replacement fluid prior to the dialyzer ("predilution") or after the dialyzer ("post-dilution"). If the replacement fluid is provided in the predilution mode, then the blood is diluted before the plasma is filtered in the dialyzer. This will avoid excessive hemoconcentration and reduce the risk of clotting.

One should aim to avoid a filtration fraction greater than 25%. If the FF rises above this level, the following measures may be taken:

- Increase blood flow to the circuit
    - This delivers more blood and therefore more plasma and therefore more plasma water to the dialyzer
    - If the total amount of ultrafiltration does not change, then the ratio of ultrafiltration to delivered plasma water (i.e. the FF) will fall if there is more plasma water delivered
- Ensure the replacement fluid is being administered "pre-filter"
    - The impact of this is described above
- Reduce the rate of hemofiltration
    - This may necessitate some of the total dose of CRRT being delivered via CVVHD – i.e., more diffusive removal of solute, and less convective removal

Transmembrane Pressure (TMP) Monitoring

The CRRT machine measures the pressure difference across the dialysis filter, from the blood compartment to the dialysate/effluent compartment. The goal is to keep this at 150 mm Hg or lower. A higher pressure difference results from "fouling" of the filter due mainly to prolonged use as plasma proteins and blood cells adhere to the filter and lead progressively to interference of movement of smaller molecules across the filter. As the TMP approaches and exceeds 150 mm Hg, this is a signal that it is time to replace the filter.

Anticoagulation for CRRT

Anticoagulation is generally required in CRRT although under some circumstances, CRRT may be attempted with no anticoagulation. Two basic options for anticoagulation exist: regional citrate anticoagulation and heparin.

The order of preference for these 3 options is as follows:

(1) Regional citrate anticoagulation
(2) Heparin anticoagulation
(3) No anticoagulation

(1) Regional citrate anticoagulation

- Regional citrate anticoagulation provides isolated anticoagulation in the extracorporeal circuit through the chelation of free or ionized calcium by exogenous citrate, while avoiding anticoagulation of the patient.
- *Indications:* Regional citrate anticoagulation is indicated for patients:
  - In whom systemic anticoagulation is contraindicated (e.g. patients at high risk of bleeding such as those who have had recent surgery, who have active or recent bleeding, or those with thrombocytopenia)
  - With another contraindication to heparin such as heparin-induced thrombocytopenia.
  - Generally, citrate is more effective with less filter clotting than occurs with heparin
- *Mechanism of action.*
  - The chelation of calcium by citrate “paralyzes” the coagulation cascade since multiple coagulation reactions require calcium as a cofactor. This is achieved by administration of citrate into the blood line just before it reaches the dialyzer. This causes the concentration of ionized calcium in the blood that enters the dialyzer (and therefore the blood that returns to the patient) to fall; the goal is to achieve an ionized calcium concentration of 0.25 – 0.45 mmol/L; note that the normal range for ionized calcium is 1.15-1.35.
  - Systemic anticoagulation and hypocalcemia are avoided by the concurrent administration of exogenous calcium (as calcium chloride) intravenously through an i.v. line located in a different vein than the one through which the blood is returning to the patient from the dialyzer.

- *Monitoring of efficacy and toxicity*

- Both the blood returning to the patient from the dialyzer and the blood in the patient are sampled every 4 hours to ensure that the circuit blood calcium level (goal is 0.25-0.45) and the patient's calcium level (goal is 1.1-1.35) are appropriate.
- There is a sliding scale in the order set for adjustment of the citrate infusion rate according to the circuit ionized calcium level
- There is a second sliding scale in the order set for adjustment of the calcium chloride infusion rate according to the patient's ionized calcium level
- To maximize citrate effectiveness and to minimize the amount of citrate used, a Ca^{+2} free dialysate is used (Prismocal™)

- This process adds citrate-rich plasma to the patient. The expectation is that this citrate is delivered to the liver via the bloodstream, and the liver metabolizes the citrate to carbon dioxide and water. This reaction generates a bicarbonate anion as a byproduct, and this is added to the patient.

- *Risks of providing citrate:*
  - *Metabolic alkalosis.* This addition of bicarbonate means that patients with this modality may develop metabolic alkalosis. If the patient's HCO_3 level is over 30 and the pH is over 7.5, then a proportion of the replacement fluid should be changed from a bicarbonate-rich fluid to normal saline. Typically, this is done by providing 200 cc/h of replacement fluid as normal saline, and then the remainder of the treatment dose is provided as dialysate.
  - *Citrate accumulation.* Because critically ill patients may have liver cell dysfunction, the added citrate may not be efficiently metabolized. This leads to the possibility that citrate will accumulate, and theoretically may cause citrate toxicity, which includes hypocalcemia and possibly metabolic acidosis. Such accumulation of citrate is more likely if the patient has elevated transaminase levels (i.e., > 1000 IU/L) and/or lactic acidosis (lactate > 8 mmol/L).
    - Citrate accumulation can be recognized if the ratio of measured total calcium to ionized calcium is greater than 2.5. (Note that the measured total calcium is used; in other words, one does not use the calcium concentration corrected for hypoalbuminemia in this calculation.)
    - For example, consider a patient with total measured calcium of 2.3 mmol/L, and ionized calcium of 1.0 mmol/L
      - The ratio of total calcium:ionized calcium is 2.3/1.0 = 2.3, which is below 2.5, and would suggest that significant citrate accumulation has not occurred.

(2) Heparin

Systemic unfractionated heparin may be administered to prevent clotting of the extracorporeal circuit. The aPTT is targeted to 60-85 seconds using a protocol that is found in the online order set. This is identical to the “high PTT nomogram” that is used in the hospital for patients receiving unfractionated heparin.

The heparin can be infused either into the dialysis circuit or it can be infused into a separate intravenous line. Infusing it into the circuit may be associated with a lower rate of circuit clotting.

(3) No anticoagulation

- In some cases – e.g. patients with liver failure who develop citrate toxicity (hence regional citrate anticoagulation is contraindicated) who also has a contraindication to bleeding - one may need to attempt CRRT with no anticoagulation
- This is obviously associated with a significant risk of clotting of the dialysis circuit and the goal is to minimize this by using a dialysis modality where there is a low “filtration fraction” (FF). The FF is the fraction of blood that is filtered during the dialysis treatment. The higher this fraction is, the more concentrated is the blood leaving the dialyzer, and therefore the higher is the risk of clotting.
- The FF will be higher with hemofiltration.
- Therefore, to minimize the filtration and thus the risk of clotting, the prescription should be almost entirely CVVHD, with only the minimum CVVH replacement fluid of 200 mL/h.
- The filter life is likely to be only 1-2 days, instead of the usual 3-5 days.

<u>Dialysate and Hemofiltration Replacement Fluid</u>

- There are 3 available fluids to choose from:
    - Prismocal
    - Prismasol
    - Normal saline
- The choice mainly depends on the type of anticoagulation
    - For regional citrate anticoagulation - use Prismocal (this has no calcium in it)
    - For heparin anticoagulation or no anticoagulation – use Primasol
- The same fluid is used in a given patient for both the dialysate, and for the replacement fluid for hemofiltration
- Normal saline can be used as a portion of the replacement fluid if the patient is developing metabolic alkalosis
    - If a patient has developed significant metabolic alkalosis (plasma bicarbonate level over 30 mmol/L along with pH over 7.50) then one can start by

administering 200 cc/h of the replacement as normal saline, and reducing the flow rate of Primasol or Prismocal by 200 cc/h

Sustained low efficiency dialysis (SLED)

Sustained low efficiency dialysis (SLED) utilizes conventional dialysis equipment (as in IHD) applied over a more prolonged treatment time and with a lower blood flow (as in CRRT). As such, SLED has been described as a hybrid therapy that captures the benefits of CRRT (ie, greater hemodynamic tolerability) and IHD (ie, lower material costs, option for no anticoagulation). SLED may be administered in any critical care unit (MSICU, CVICU, TNICU or CCU) by a hemodialysis nurse. Patients with hemodynamic instability (similar to those being considered for CRRT) should receive primary consideration for SLED. Treatment duration is 8 hours at a blood flow of 200 mL/min and a dialysate flow of 350 mL/min. SLED may be administered with no anticoagulation. Given the intensive nature of the dialysis provided by SLED, patients may become hypophosphatemic after 1-2 SLED sessions; phosphate may be added to the dialysate in such individuals for subsequent sessions. All aspects of the SLED prescription are found in the pre-printed SLED orders which should be completed for each session.

MANAGEMENT OF POISONINGS

The management of certain poisonings may include enhanced removal from the body via an extracorporeal treatment, most commonly hemodialysis.

General Principles of Management of Poisonings where Extracorporeal Treatment is a consideration

<u>Properties of drugs and toxins that make them suitable for extracorporeal treatment</u>

A drug or toxin is more likely to be effectively removed from the body with extracorporeal treatment such as hemodialysis if the drug or toxin has the following properties:

- Its *molecular weight is low* (below 15,000 daltons)
    - Hemofiltration and hemodiafiltration may be able to effectively remove molecules of higher molecular weight, up to ~ 25,000
- Its *volume of distribution is relatively small*
    - A reasonable cutoff for volume of distribution is < 1 L/kg body weight
    - This means that the drug or toxin is not heavily bound to adipose tissue or concentrated inside cells
    - The volume of distribution is significantly influenced by whether the drug or toxin is water-soluble (and therefore less likely to be extensively bound to adipose tissue), which tends to reduce the volume of distribution
- It is *not heavily protein-bound*
    - A substance with > 80% protein-binding will in general not be effectively removed via hemodialysis
    - Note that protein-binding of drugs can be quite different in an overdose setting, compared to a usual therapeutic context. In a therapeutic dose range, a drug may be extensively protein-bound. However, with an overdose, the available protein-binding sites may become fully saturated, and therefore a (much) larger fraction of the total drug may be free, i.e., not protein-bound. As a result, it may be more effectively removed via extracorporeal treatment than would have been predicted from a knowledge of its usual, therapeutic-context protein-binding. This is relevant in particular to ASA and valproate.
- Endogenous clearance is not high
    - If a drug has a high rate of endogenous clearance (renal, hepatic or both), then - even though there may be a significant overdose - extracorporeal treatment may not be needed, since the drug or toxin will be removed effectively by endogenous means
    - An example of this is Metformin, which has a very high endogenous clearance of ~ 600 mL/min if kidney function is normal, which is considerably higher than the

clearance rate of 240 mL/min. achieved by hemodilaysis; even though Metformin is dialyzable, the only time hemodialysis is likely to be needed in the context of an overdose is if there is significant impairment of kidney function.

Drugs and toxins that can be effectively removed by extracorporeal treatment

The following are the drugs and toxins that are generally regarded as being amenable to removal by extracorporeal treatment (adapted from Ghannoum M et al, Kidney International 2018;94:682-688.)

- Alcohols
    - Methanol*
    - Ethylene glycol*
    - Ethanol*
- Analgesics
    - ASA*
    - Acetaminophen*
- Medications with effects on the central nervous system
    - Lithium*
    - Barbiturates
    - Carbamazepine
    - Valproate
- Methylxanthines
    - Caffeine
    - Theophylline
- Metformin*

* These are the drugs and toxins for which extracorporeal removal techniques are most commonly used.

Intermittent hemodialysis is the appropriate modality for removal of drugs and toxins

The management of intoxication requires a high dose of high efficiency dialysis. Slow low-efficiency techniques such as PD or CVVHD should not be used unless there is no other option.

The decision to use extra-corporeal treatment for a poisoning is based on both clinical conseuqences and drug levels

Indications for extracorporeal treatment include very high levels of the drug or toxin, but such treatment may also be appropriate with lower levels if the drug or toxin appears to currently be causing harm.

For instance, in a patient with Lithium overdose (see below), indications for hemodialysis include anyone with a level over 5.0 mmol/L, but also include a patient with Lithium ingestion who is having seizure, reduced level of consciousness or arrhythmias.

Poison Control

The telephone number for Poison Control in Toronto is (416) 813-5900. They should be contacted in all instances of significant poisoning for their advice about management.

Examples of poisonings and their management

Methanol

Sources of methanol

- Industry solvent (e.g. windshield washer fluid, gas line antifreeze, carburetor cleaner, copy machine fluid, shellacs, perfumes, food warming fuel and other types of fuels)
- Consumed to get intoxicated, or as part of a suicide attempt, or in error
- Occasionally due to distillation using simple equipment with formation of methanol as by-product

Pharmacologic properties

- Molecular weight is 32 mg/mmol, water-soluble
- Rapidly absorbed from gastric mucosa, achieves peak levels in 30-90 minutes post ingestion
- Metabolism
  - oxidation from methanol via alcohol dehydrogenase to formaldehyde
  - then oxidation to formic acid via aldehyde dehydrogenase
  - Formate
    - Can be metabolized to CO2 and water with help of Folinic acid (folinic acid is derived from folic acid)
    - Can be excreted into the urine
- Elimination (in the absence of alcohol dehydrogenase inhibition) follows "zero-order kinetics" via hepatic metabolism
  - This means that each hour a constant amount of methanol is eliminated, irrespective of its plasma concentration
    - Each hour approximately 2.7 mmol/L is eliminated
  - If an alcohol dehydrogenase inhibitor is used then the pharmacokinetics changes such that methanol is now eliminated via lungs and kidney, and this follows "first order" kinetics

- This means that the rate of elimination is now proportional to the methanol concentration in plasma
- The mean half-life in the presence of ADH inhibition is ~ 54 hours

- Toxic doses
  - As little as 10 cc may cause blindness
  - As little as 30 cc may be lethal

Pathogenesis

- Ingestion of methanol leads to its conversion to toxic metabolites (formaldehyde, formic acid)
- Formaldehyde and particularly formic acid are toxic to cells, particularly brain cells and retinal cells
- In an acidic milieu, the formate anion is converted to uncharged formic acid, which is more likely to cross cell membranes into the cell interior, where it can exert its toxic effects

Clinical manifestations

- Early stage (< 6 hrs): non-specific symptoms; mild or transient: inebriation, drowsiness
- Delayed stage (6-30 hrs): Vertigo, nausea, vomiting, abdominal pain
- Kussmaul breathing (deep and rapid)
- Blurred vision (papilledema, disc hyperemia)→ blindness
- Seizures, opisthotonus, coma → death

- Laboratory findings:
  - High anion gap metabolic acidosis
  - High osmolar gap (OG)
    - OG = measured osmolality – calculated osmolality> 10 mosm/kg;
    - calculated osmolality = 2 x Serum [Na+] + serum [Urea] + serum [glucose]
  - High plasma methanol level
  - High lactate level
  - High amylase level (pancreatitis)

- Toxic levels
  - >6.2 mmol/L (20 mg/dL or 200 mg/L)
  - ANY level with increased anion gap metabolic acidosis

Prognosis

- Prognosis depends on
  - amount of methanol ingested and metabolized to toxic-by products
  - amount metabolized, which is determined by:
    - the time between ingestion and treatment

    - the amount of ethanol on board (as ethanol slows down metabolism of methanol)
  - the degree of acidosis
  - the extent of the visual disturbance.

Management:

There are 5 major components to the management:

(1) Supportive care
(2) Contact poison control for advice
(3) Hasten metabolism with folic acid
(4) Alcohol dehydrogenase inhibition (generally with Fomepizole)
(5) Hemodialysis

(1) Supportive care

- Appropriate attention to airway, breathing and circulation are of course required
- It is important to consider any co-ingestions that may have occurred
- There is no role for activated charcoal or syrup of ipecac in the management of methanol ingestion, largely because it is so rapidly absorbed
- If the patient has a significant acidosis, this causes conversion of formate to formic acid, which makes it more likely to penetrate into cells (brain cells, retinal cells) leading to greater toxicity
    - If pH is below 7.3, they should be given intravenous $NaHCO_3$
        - One should give a bolus and then an infusion
            - The bolus as a reasonable starting dose is to give 1 – 2 mEq/kg (typically 1 – 2 ampoules, with an ampoule containing 50 mEq in 50 mL)
            - The infusion is made up by adding 3 ampoules of $NaHCO_3$ to 850 mL of D5W to make an isotonic solution of $NaHCO_3$, and this is then infused at a rate of 150-250 mL/h, while waiting for more definitive therapy
- If the patient has a coexisting respiratory acidosis due to respiratory depression from the ingested methanol, they may require tracheal intubation and assisted ventilation

(2) Contact poison control for advice

- The telephone number for Poison Control is (416) 813-5900. They should be contacted in all instances of significant poisoning for their advice about management.

(3) Hasten metabolism of formate with folic acid

- The dose of Folate is 50 mg IV every 6 hours (or if available, give Folinic Acid 50 mg IV q6h).

(4) Alcohol dehydrogenase inhibition

- This can be done via either Fomepizole or Ethanol

- Indications for alcohol dehydrogenase inhibition in a patient with suspected or proven methanol ingestion
  - Methanol level measured and is above 6.2 mmol/L (20 mg/dL), OR
  - Recent history of toxic alcohol ingestion and osmolar gap is > 10, OR
  - Strong clinical suspicion of toxic alcohol ingestion and 2 or more of the following
    - Arterial pH < 7.3
    - Serum [HCO3-] < 20
    - Osmolar gap > 10
- *Fomepizole* (although quite expensive) is preferred over Ethanol
  - Dose of Fomepizole is 15 mg/kg IV, followed by 10 mg/kg every 12 hours
    - After 48 hours, the maintenance dose is increased to 15 mg/kg every 12 hours, due to Fomepizole's inducing its own metabolism
  - Fomepizole is a generally safe and well-tolerated medication
    - Most common side effects are headache and nausea
    - Others include: Dizziness, drowsiness, altered or metallic taste, anxiety, agitation
    - Rare side effects are bradycardia, hypotension, diarrhea, heartburn, vomiting, anemia, DIC, blurred vision
  - If the patient is also treated with hemodialysis, the Fomepizole will be removed via dialysis, so additional doses need to be given
    - If the time that the patient starts hemodialysis has been more than 6 hours since the last dose of fomepizole, a supplemental dose of Fomepizole 10 mg/kg should be given at the start of HD
    - As long as HD continues, the patient should receive 10 mg/kg every 4 hours
  - Fomepizole should be continued until the methanol level has fallen to less than 6.2 mmol/L (20 mg/dL)
    - If Fomepizole was started due to a *suspicion* of toxic alcohol ingestion, if the subsequent specific assay for methanol returns negative, then the Fomepizole can also be stopped

- Ethanol can also be used as an antidote, although this is now rarely done. It is given orally or by IV. One aims for a plasma level of 100 mg% (20 mmol/L). The alcohols are distributed across total body water.

- Oral Ethanol
  - Loading dose of 40 gm ethanol. (Absolute or 95% ethanol has SG of 0.8 g/mL.) This works out to 50 mL of absolute ethanol or 120 mL of 40% ethanol like scotch or whisky.
  - The maintenance dose is 12 mL of absolute or 30 mL (1 oz) of whisky per hour with frequent measurements to ensure levels as above.
- IV Ethanol
  - Prepare 10% infusion
    - Take a 1000 mL bag of D5W, remove 100 mL, leaving behind 900 mL
    - Add 100 mL of absolute (98%) ethanol, which creates a 10% volume per volume solution (100 mL per 1000 mL total)
    - Specific gravity of absolute ethanol is 0.8 g/mL
      - 100 mL of absolute ethanol contains 80 g ethanol
      - Therefore, the final 1000 mL solution (900 mL D5W plus 100 mL absolute ethanol) contains 80 g ethanol
      - 10 mL of the solution will have 0.8 g of ethanol
    - Loading dose is 10 mL/kg = 0.8 g/kg
    - Maintenance dose starts at 1 mL/kg/h = 0.08 g/kg/h
    - Monitor serum ethanol level and titrate rate of maintenance infusion to achieve ethanol level of ~ 22 mmol/L (which is level at which alcohol dehydrogenase should be saturated by ethanol and therefore inhibited)
    - Continue infusion even if dialysis is in progress to make up for metabolized ethanol
    - Ethanol should be added to the dialysate at a concentration of 20 mmol/L to prevent its removal via dialysis
    - Continue ethanol infusion until
      - Methanol level is undetectable (if patient has end-organ toxicity e.g. visual symptoms, acidosis)
      - Methanol level is < 6.2 mmol/L if the patient is asymptomatic and pH is normal

(5) Hemodialysis (HD)

- <u>Indications for hemodialysis in a patient with known or suspected methanol ingestion</u>
  - Different expert groups offer different suggested indications making definitive recommendations challenging
  - Generally speaking, HD should be provided if one or more of the following is noted

- Significant acidemia (arterial pH < 7.25-7.35)
- End-organ damage
  - Visual signs or symptoms
  - Coma, seizures
- Worsening vital signs despite intensive care
- Kidney failure
- Serum methanol > 50 mg/dL (500 mg/L, which is 16.2 mmol/L)
  - The 2015 Extracorporeal Poisoning Treatment Working Group suggested that in a patient receiving Fomepizole, a methanol level of > 70 mg/dL (> 22 mmol/L) should be the threshold for starting HD
- Serum anion gap > 24 mEq/L

▪ If methanol ingestion is even *suspected*, HD should be started if the patient has a severe, otherwise unexplained increased anion gap metabolic acidosis together with an increased plasma osmolar gap

- <u>Dialysis modality</u>
  - Dialyze at Qb of 300 cc/min or more (400 cc/min if possible)
  - Use dialysate flow rate (Qd) of 800 cc/min
    - With Qb 400 cc/min, Qd 800 cc/min, methanol clearance is 200 cc/min., leading to a half-life of about 2 hours, and a formate half-life of ~ 220 cc/min.
  - Anticoagulation should NOT be used
    - There is a risk of intracerebral hemorrhage due to methanol toxicity
    - Therefore, anticoagulation should not be prescribed during HD for methanol ingestion
  - Interaction of inhibitor used and dialysis
    - If fomepizole is inhibitor, and at the start of dialysis it is more than 6 hours since the last fomepizole dose, give another dose 10 mg/kg, and repeat every 4 hours while on dialysis
    - If ethanol is used as the inhibitor
      - ethanol is added to the dialysate – see above for one approach to this
  - Continue to dialyze until the methanol level is < 6.2 mmol/L (20 mg/dL).
    - This is generally when the osmolar gap is down to ~ 6 mosm/kg
    - One can estimate the required dialysis time using a complex logarithmic equation using: initial methanol level, patient's estimated total body water, and the dialyzer urea clearance. Online calculators are available for this.
    - By the time this final methanol level is back, actual level will be lower since dialysis has continued while waiting for the methanol level.
    - Stop dialysis and send a methanol level.

- Dialysis often needed for > 10 hours.

Ethylene Glycol

Ethylene Glycol

Sources of ethylene glycol

- Mainly found in antifreeze, some solvents

Pharmacologic properties

- Molecular weight is 62 mg/mmol, water-soluble
- Rapidly absorbed from gastric mucosa, achieves peak levels in 30-90 minutes post ingestion
- Metabolism
  - oxidation from ethylene glycol via alcohol dehydrogenase to glycoaldehyde
  - then oxidation via aldehyde dehydrogenase to glycolic acid then to glyoxylic acid then to oxalic acid
    - Glyoxylic acid can be metabolized to less toxic metabolites via pyridoxine and thiamine
- Elimination (in the absence of alcohol dehydrogenase inhibition) follows first-order kinetics with half-life of 3 – 9 hours via hepatic metabolism and renal elimination
  - If an alcohol dehydrogenase inhibitor is used then the pharmacokinetics changes such that ethylene glycol is now eliminated via kidney, and this follows "first order" kinetics with half-life ~ 14 hours
- Toxic doses
  - As little as 1-2 cc/kg may be lethal
- Ingestion of ethylene glycol leads to its conversion to toxic metabolites (glycoaldehyde, glycolic acid, glyoxylic acid, oxalic acid)
- These products are toxic to brain cells
- Oxalate can bind to calcium and obstruct the lumens of renal tubules, leading to renal failure
- In an acidic milieu, the toxic anions are converted to uncharged acids, which are more likely to cross cell membranes into the cell interior, where they can exert their toxic effects

Clinical manifestations

- Early stage (< 6 hrs): non-specific symptoms; mild or transient: inebriation, drowsiness
- Delayed stage (6-30 hrs): Vertigo, nausea, vomiting, abdominal pain
- Kussmaul breathing (deep and rapid)
- Seizures, coma, death
- Laboratory findings:
  - High anion gap metabolic acidosis

- High osmolar gap (OG)
    - OG = measured osmolality – calculated osmolality> 10 mosm/kg;
    - calculated osmolality = 2 x Serum [Na+] + serum [Urea] + serum [glucose]
    - Note that the OG is only high in a toxic alcohol ingestion early in the course of the illness, before the parent alcohol has been converted to the acid metabolite
- High plasma ethylene glycol level
- Falsely high lactate level on point of care blood gas machines, due to instrument reading ethylene glycol metabolites as lactate
- Urinalysis shows calcium oxalate crystals
    - Early – see calcium oxalate dihydrate crystals, which are envelope-shaped
    - Later – see calcium oxalate monohydrate crystals, which are dumb-bell-shaped

- Toxic levels
    - >3.2 mmol/L (20 mg/dL or 200 mg/L)
    - ANY level with increased anion gap metabolic acidosis

Prognosis

- Prognosis depends on
    - amount of ethylene glycol ingested and metabolized to toxic-by products
    - amount metabolized, which is determined by:
        - the time between ingestion and treatment
        - the amount of ethanol on board (as ethanol slows down metabolism of methanol)
    - the degree of acidosis
    - the extent of the renal function disturbance.

Management:

This is largely similar to management of methanol ingestion. An important distinction is that renal elimination of ethylene glycol can be quite substantial and therefore, provided there is Fomepizole on board, a patient with even a relatively large ethylene glycol ingestion may be managed without hemodialysis, provided they are otherwise stable and asymptomatic.

There are 5 major components to the management:

(1) Supportive care
(2) Contact poison control for advice
(3) Hasten metabolism with folic acid

(4) Alcohol dehydrogenase inhibition (generally with Fomepizole)
(5) Hemodialysis

(1) Supportive care

Details of supportive care are similar to that for methanol ingestion.

(2) Contact poison control for advice

- The telephone number for Poison Control in Toronto is (416) 813-5900. They should be contacted in all instances of significant poisoning for their advice about management.

(3) Hasten metabolism of glyoxylic acid to less toxic products with thiamine and pyridoxine

- The dose of Thiamine is 100 mg IV and of Pyridoxine is 25 mg IV.

(4) Alcohol dehydrogenase inhibition

- This can be done via either Fomepizole or Ethanol and the approach is identical to their use in management of methanol ingestion

- Indications for alcohol dehydrogenase inhibition in a patient with suspected or proven ethyelene glycol ingestion
  - Ethylene glycol level measured and is above 3.2 mmol/L (20 mg/dL), OR
  - Recent history of toxic alcohol ingestion and osmolar gap is > 10, OR
  - Strong clinical suspicion of toxic alcohol ingestion and 2 or more of the following
    - Arterial pH < 7.3
    - Serum [HCO3-] < 20
    - Osmolar gap > 10
- *Fomepizole* (although quite expensive) is preferred over Ethanol and its use for ethyelene glycol ingestion is similar to its use for methanol ingestion
  - Dose of Fomepizole is 15 mg/kg IV, followed by 10 mg/kg every 12 hours
    - After 48 hours, the maintenance dose is increased to 15 mg/kg every 12 hours, due to Fomepizole's inducing its own metabolism
  - Fomepizole is a generally safe and well-tolerated medication
    - Most common side effects are headache and nausea
    - Others include: Dizziness, drowsiness, altered or metallic taste, anxiety, agitation
    - Rare side effects are bradycardia, hypotension, diarrhea, heartburn, vomiting, anemia, DIC, blurred vision
  - If the patient is also treated with hemodialysis, the Fomepizole will be removed via dialysis, so additional doses need to be given

        - If the time that the patient starts hemodialysis has been more than 6 hours since the last dose of fomepizole, a supplemental dose of Fomepizole 10 mg/kg should be given at the start of HD
        - As long as HD continues, the patient should receive 10 mg/kg every 4 hours
    - Fomepizole should be continued until the ethylene glycol level has fallen to less than 3.2 mmol/L (20 mg/dL)
        - If Fomepizole was started due to a *suspicion* of toxic alcohol ingestion, if the subsequent specific assay for methanol returns negative, then the Fomepizole can also be stopped

- Ethanol can also be used as an antidote, although this is now rarely done. It is given orally or by IV. One aims for a plasma level of 100 mg% (20 mmol/L). The alcohols are distributed across total body water.
    - Oral Ethanol
        - Loading dose of 40 gm ethanol. (Absolute or 95% ethanol has SG of 0.8 g/mL.) This works out to 50 mL of absolute ethanol or 120 mL of 40% ethanol like scotch or whisky.
        - The maintenance dose is 12 mL of absolute or 30 mL (1 oz) of whisky per hour with frequent measurements to ensure levels as above.
    - IV Ethanol
        - Prepare 10% infusion
            - Take a 1000 mL bag of D5W, remove 100 mL, leaving behind 900 mL
            - Add 100 mL of absolute (98%) ethanol, which creates a 10% volume per volume solution (100 mL per 1000 mL total)
            - Specific gravity of absolute ethanol is 0.8 g/mL
                - 100 mL of absolute ethanol contains 80 g ethanol
                - Therefore, the final 1000 mL solution (900 mL D5W plus 100 mL absolute ethanol) contains 80 g ethanol
                - 10 mL of the solution will have 0.8 g of ethanol
            - Loading dose is 10 mL/kg = 0.8 g/kg
            - Maintenance dose starts at 1 mL/kg/h = 0.08 g/kg/h
            - Monitor serum ethanol level and titrate rate of maintenance infusion to achieve ethanol level of ~ 22 mmol/L (which is level at which alcohol dehydrogenase should be saturated by ethanol and therefore inhibited)
            - Continue infusion even if dialysis is in progress to make up for metabolized ethanol
            - Ethanol should be added to the dialysate at a concentration of 20 mmol/L to prevent its removal via dialysis

- Continue ethanol infusion until
  - Methanol level is undetectable (if patient has end-organ toxicity e.g. visual symptoms, acidosis)
  - Methanol level is < 6.2 mmol/L if the patient is asymptomatic and pH is normal

(5) Hemodialysis (HD)

- Indications for hemodialysis in a patient with known or suspected ethylene glycol ingestion
  - Different expert groups offer different suggested indications making definitive recommendations challenging
  - Generally speaking, HD should be provided if one or more of the following is noted
    - Significant acidemia (arterial pH < 7.25-7.35)
    - CNS toxicity
    - Worsening vital signs despite intensive care
    - Kidney failure
    - Serum ethylene glycol levels – thresholds for dialysis
      - In the absence of inhibitor therapy > 50 mg/dL (500 mg/L, which is 8.2 mmol/L)
      - If the patient is receiving Fomepizole, then it may be reasonable to withhold dialysis up to an ethylene glycol level as high as 300 mg/dL (48 mmol/L) provided no other criteria for dialysis are met because in the presence of inhibitor therapy, renal elimination of ethylene glycol is relatively rapid (and much faster than with methanol ingestion)
  - If ethylene glycol ingestion is even *suspected*, HD should be started if the patient has a severe, otherwise unexplained increased anion gap metabolic acidosis together with an increased plasma osmolar gap
- Dialysis modality
  - Dialyze at Qb of 300 cc/min or more (400 cc/min if possible)
  - Use dialysate flow rate (Qd) of 800 cc/min
    - With Qb 400 cc/min, Qd 800 cc/min, methanol clearance is 200 cc/min., leading to a half-life of about 2 hours, and a formate half-life of ~ 220 cc/min.
  - Interaction of inhibitor used and dialysis

    - If fomepizole is inhibitor, and at the start of dialysis it is more than 6 hours since the last fomepizole dose, give another dose 10 mg/kg, and repeat every 4 hours while on dialysis
    - If ethanol is used as the inhibitor
        - ethanol is added to the dialysate – see above for one approach to this
- Continue to dialyze until the ethylene glycol level is < 3.2 mmol/L (20 mg/dL).
    - By the time this final ethylene glycol level is back, actual level will be lower since dialysis has continued while waiting for the ethylene glycol level.
    - Stop dialysis and send an ethylene glycol level.
    - Send one final ethylene glycol level at 4 hours later to ensure there is no rebound in ethylene glycol levels as there may be refilling from extravascular sites
    - Dialysis often needed for > 10 hours.

Salicylates

<u>Sources of salicylate</u>

- Aspirin tablets
- Oil of wintergreen (topically)

<u>Pharmacologic properties</u>

- Molecular weight 180 mg/mmol
- Rapid absorption from upper GI tract
- Metabolism – ASA hydrolyzed to salicylic acid → glycinated to salicyluric acid in liver→ excreted via kidneys; urine pH > 7.0 enhances excretion
- Minimum lethal dose 10 g ASA; levels useful 6 hrs post ingestion
- Acute ingestion: 1 tab/kg = severe (1 tab = 325 mg)

<u>Clinical manifestations of salicylate toxicity</u>

- Chronic users of ASA
    - Tinnitus, hearing loss, dizziness,
    - Weakness
    - Nausea, vomiting,
    - Tachypnea
    - Confusion
- Acute/severe intoxications:
    - Above + fever, seizures, coma, ARDS
- Acid base disturbances:

- Early - Respiratory alkalosis
- Later – High anion gap metabolic acidosis
- pH is often normal or close to normal, given opposite effects of respiratory alkalosis and metabolic acidosis on final pH

- Salicylate levels
  - Therapeutic range is 0.7 – 2.2 mmol/L
  - Toxic range is above 2.9 mmol/L

Management

- *Supportive care*
  - Airway
    - Avoid intubation if possible) because
      - Brief period of apnea and paralysis when performing intubation may lead to acute acidemia, protonation of salicylate, and enhanced entry of toxic molecule into brain
      - It may be difficult to mechanically ventilate patient to the same extent as patient achieves via spontaneous breathing, leading to less respiratory alkalosis, and therefore more acidic plasma pH and therefore greater salicylate cellular toxicity
  - Breathing
    - Supplemental oxygen may be of help
  - Circulation
    - Volume resuscitation, unless patient has pulmonary or cerebral edema
  - If reduced level of consciousness, give glucose boluses (D50W at a dose of 50 cc) to keep glucose 5-6 mmol/L, even if serum glucose level is normal, due to possibility of neuroglycopenia
  - Prevent absorption of ASA from gut with activated charcoal doses (50 g/dose)
- *Systemic and urinary alkalinization:*
  - Impact of alkalinisation
    - Systemic - Keeps salicylate in uncharged form (protons dissociate from salicylate, since free proton concentration in body fluids is kept low) and therefore reduces entry of salicylate into brain and other cells, thereby reducing toxicity
    - Urinary – Keeps salicylate in ionized form, reducing its reabsorption from renal tubule and therefore enhancing urinary excretion
  - Dose
    - May give bolus 50 – 100 cc (1-2 ampoules) of $NaHCO_3$ (50 mmol/50 cc)
    - Infusion - isotonic $NaHCO_3$ solution (3 ampoules of $NaHCO_3$) in 850 cc D5W, administered at ~ 200 – 250 cc/h

- Goal for urine pH >7.5
- Avoid plasma pH > 7.55
- Correct hypokalemia before giving i.v. NaHCO3, since the NaHCO3 may lead to translocation of K+ from ECF to ICF, worsening hypokalemia

- *Hemodialysis Indications:*
  - HD can rapidly eliminate salicylate
  - Consider for very high levels and/or signs of severe toxicity, as follows
    - Salicylate level > 7.2 mmol/L (> 6.5 mmol/L if renal insufficiency)
    - CNS changes – Seizures, coma, suspected cerebral edema
    - Fluid overload/ARDS, which prevents administration of i.v. fluid
    - Renal insufficiency (creatinine > 176 umol/L) since this will impair urinary elimination of salicylate
    - Severe acidemia (pH < 7.2)
    - Especially if elderly, smoker, acute on chronic ingestion
    - Modality should be intermittent hemodialysis, with high Qb and high Qd, at least 4 hours
    - Continue HD until patient's clinical status has normalized, acid-base parameters are normal, and ASA level is below toxic range (< 2 mmol/L)

Lithium

<u>Pharmacologic properties</u>

- Monovalent cation, size and charge similar to Na^+
- GI absorption is rapid
  - Immediate release – peak level reached in 1-2 h
  - Sustained release – peak level reached in 4-6 h
  - In an overdose situation – may take 12 hours or longer to reach peak level
- Volume of distribution 0.6 – 0.9 L/kg (minimal protein binding)
- Excreted via kidneys
  - Via glomerular filtration
  - Significant and variable tubular reabsorption (similar to sodium)
    - Proximal tubule ~ 60%
    - Thick ascending limb of loop of Henle – paracellular
    - Distal tubule and collecting duct via eNaC
- Half-life 18h (up to 36h in elderly)
- Therapeutic level is 0.8 – 1.2 mmo/L (i.e. very narrow therapeutic range)

- Toxic dose - > 1 g elemental Lithium

Clinical manifestations

- 3 somewhat distinct syndromes
    - Acute toxicity
        - patient consumes large number of tablets, but not previously taking)
    - Acute on chronic toxicity
        - patient who chronically is taking lithium, but then takes a large amount quickly
    - Chronic toxicity
        - Usually occurs in patient who chronically takes Lithium who then develops diminished renal function (e.g. due to GI illness, diuretic therapy, ACE inhibitor, NSAID use, etc.)
- Acute, or acute-on-chronic toxicity
    - Neurologic (generally a late finding with acute toxicity) – Ataxia, confusion, agitation, tremors, myoclonus, seizures, coma, death
    - GI – nausea, vomiting, diarrhea (which can lead to volume depletion, and increased lithium levels)
    - Cardiac – prolonged QTc, bradycardia
- Chronic toxicity
    - Neurologic (common) – Ataxia, tremor, myoclonus, seizures, encephalopathy, coma, death due to neurotoxicity
    - Cardiac – prolonged QTc, bradycardia
    - Renal – Nephrogenic diabetes insipidus, chronic internstitial renal disease
    - Endocrine – thyroid disorders (hypo- and hyperthyroidism), hyperparathyroidism

- Lithium levels
    - Often do not correlate well with clinical toxicity
    - With chronic toxicity, may have significant manifestations while lithium level is in therapeutic range

Management

- Investigations
    - CBC
    - Electrolytes (serum Na to address possibility of nephrogenic DI)
    - Calcium profile (to address possibility of primary hyperparathyroidism)
    - Creatinine (if there is renal insufficiency, it will be more difficult to excrete Lithium)
    - TSH (is there evidence of thyroid disease?)
    - Drug screen to rule out coingestion

    - ECG (QTc, rule out bradycardia)
    - Lithium levels – repeat every 4-6 hours until < 1.2 mmol/L

- Supportive care and management of poisoning
    - ABC – intubation if significantly reduced level of consciousness
    - Consider reducing GI absorption if within 2-3 hours of ingestion and patient is awake and alert
        - Nasogastric tube, administer Polyethyelen glycol (PEG) 500 mL every hour until rectal effluent is clear
- ECF volume expansion with normal saline
    - Purpose is to increase renal lithium elimination by reducing stimuli for renal tubular sodium reabsorption, since this will also reduce renal tubular Lithium reabsorption
    - Give normal saline – bolus 1-2 L, followed by ~ 150 cc/h if cardiac function tolerates
        - Monitor serum and urine electrolytes and urine osmolality since patient may have nephrogenic DI, and excretion of hypotonic urine while giving i.v. isotonic fluid may lead to rapid onset hypernatremia
- Hemodialysis
    - Indications (EXTRIP working group CJASN 2015;10(5):875-887)
        - *Recommended* if:
            - Lithium level > 4.0 mmol/L AND reduced renal function
                - Reduced renal function is defined by 1 or more of the following
                    - eGFR < 45
                    - Serum Creatinine > 176 (adults) or > 132 (elderly, low muscle-mass)
                    - K-DIGO AKI stage 2 or 3
            - Lithium level is > 1.0 mmol/L, and there are severe manifestations of toxicity
                - Reduced level of consciousness
                - Seizures
                - Life-threatening dysrhythmias
        - *Suggested* if:
            - Lithium level is > 5.0 mmol/L
            - Lithium level is > 1.0 mmol/L and the patient is confused
            - Expected time to reach Lithium level below 1.0 mmol/L will be more than 36h (based on log-linear plot of serial Lithium levels)
        - *Considered (*as per Daugirdas, Handbook of Dialysis)
            - Lithium level is > 3.5 mmol/L
            - Lithium level is > 2.5 mmol/L and there is one or both of

        - Reduced renal function
        - Appreciable symptoms attributable to Lithium toxicity
    - Lithium level is 2.5 – 3.5 but expected to rise due to massive ingestion
- Modality
    - Intermittent hemodialysis is preferred (CRRT is an acceptable alternative)
        - Achieves a lithium clearance of ~ 100 mL/min (compared to endogenous clearance of only 10-40 mL/min)
    - There is a significant risk of rebound in Lithium levels after HD is finished, as Lithium exits from cells slowly via sodium channels and "refills" the extracellular fluid compartment
        - Can stop dialysis once Lithium level is < 1.0 mmol/L or patient's clinical status has improved, but need to keep monitoring level every 4 hours for at least 12 hours to ensure another session of HD is not required
        - Generally need to dialyze for 8-12 hours

Theophylline

Theophylline has been used as a bronchodilator in patients with asthma/COPD, and for apnea of prematurity. It is much less commonly used than formerly, but is still available, and is occasionally ingested in an accidental or deliberate overdose.

<u>Pharmacologic properties</u>

- This drug has a very narrow toxic to therapeutic ratio
- It works via antagonism of adenosine receptors leading to increased adrenergic activity, and also at toxic levels it is a phosphodiesterase inhibitor and further enhances beta-adrenergic effects
- Rapidly and fully absorbed
- Has a low volume of distribution (0.45 L/kg)
- ~ 50% protein-binding
- Mainly eliminated via liver metabolism, with first order kinetics
    - There is the potential for significant interaction with other drugs which are also metabolized via the same cytochromes
- With overdose and toxic levels, switched to zero order kinetics
- Toxicity varies according to whether exposure is acute or chronic
    - Toxicity correlates with drug level in acute poisonings, but not with chronic

<u>Clinical Manifestations</u>

- Toxic levels

    - Acute overdose > 448 - 560 umol/L
    - Chronic ingestion > 168 – 224 umol/L
- Acute intoxication is usually due to an intentional overdose
    - GI
        - Vomiting, abdominal pain
    - Metabolic
        - Hypokalemia due to adrenergic effect of increasing potassium entry into cells
        - Hyperglycemia
    - CNS
        - Tremor
        - Seizures
    - Cardiac
        - Sinus tachycardia
        - Ventricular tacchyarrhythmias
- Chronic intoxication – more severe clinical manifestations than acute and may have liver or renal involvement contributing to intoxication

<u>Management</u>

- Supportive care including for
    - Vomiting
    - Seizures
    - Arrhythmias
    - Hypotension
- Reduce absorption with activated charcoal
- Extracorporeal removal
    - Hemodialysis together with charcoal hemoperfusion
    -
        - Small vol of distribution + low rate of clearance - effectively cleared by HD and charcoal hemoperfusion (HP) (hemoperfusion approx 2x as effective due to removal of protein-bound drug)
        - Use two sites for venous catheters
        - HD – use max blood flow, minimum 4 hours
        - HP – use charcoal cartridge, saturates in about 2 hours and hence the cartridge must be changed q2h
        - Serial HD-HP delays saturation of HP cartridge
        - No guidelines re level to dialyze to, advisable to continue to < 100umol/L

PERITONEAL DIALYSIS

Jeffrey Perl, MD

The peritoneal membrane can be used to perform dialysis (PD). Dialysate is infused into the peritoneal cavity, and allowed to dwell for a period of time, during which toxins diffuse out of the blood into the dialysate. Ultrafiltration (UF) also occurs during this time, as fluid is drawn out of the circulation by the osmotic force of compounds such as dextrose in the dialysate. Once the dwell is over, the dialysate is drained from the peritoneal cavity, and fresh dialysate is instilled. The process of draining spent dialysate and reinstilling fresh solution is known as an "exchange". PD comes in a variety of forms, which are discussed below. For any peritoneal dialysis issue, it is important to consult with the multidisciplinary team in the Home Dialysis office on the 8th floor of the Cardinal Carter wing (416-864-5794).

Peritoneal Dialysis Subtypes:

CAPD (Continuous Ambulatory Peritoneal Dialysis)

CAPD involves manual exchanges performed either by the patient and/or caregiver at home. Patients performing CAPD typically perform four 2 L exchanges per day, usually upon awakening, at lunch, at dinner and prior to bed. Exchanges are done using a "twin-bag" system, consisting of an empty drain bag and a full dialysate bag connected by a Y connector. A CAPD exchange first involves connecting the Y connector of the twin-bag to the patient's PD catheter. Spent dialysate is then drained into the drain bag. Once the peritoneum is empty, fresh dialysate is instilled into the peritoneum from the dialysate bag. This process typically takes from 20 to 40 minutes.

When prescribing CAPD, order volume of exchange (usually 2L), frequency of exchanges (usually 4x/day), additives (usually none), target weight specifying whether or not this includes the exchange volume (e.g. "dry weight 75 kg empty").

Example: CAPD 2 L fill volumes qid, target weight 68 kg (when full with 2 L).

Note: PD patients who are in the emergency department for prolonged periods of time or any other hospital location where automated peritoneal dialysis (APD) may not be possible or readily available to set up, then routine CAPD exchanges may be used in place of the patients' usual APD prescription. This is continued until the APD ''cycler'' system may be set up. Exchanges would typically be ordered every three to six hours.

APD (Automated Peritoneal Dialysis)

An automated machine called a "cycler" can be used to instill and drain dialysate from the peritoneal cavity. Typically, such a machine is used at night, with the cycler performing the dialysis exchanges while the patient sleeps. However, in patients who are admitted to hospital, particularly those in a critical care settings who are bed-bound, it may be used during the daytime as well. Normally, a larger number of exchanges can be ordered than would be practical during the day (e.g. 4-5 exchanges over 9 hours). In some cases, the patient can tolerate a larger volume of dialysate at night as well (e.g. 2.5L) because of lower intra-abdominal pressure when supine. While CAPD bags are usually 2 or 2.5 L, APD bags are usually 5 L. APD can be performed in one of three ways depending on the desired dialysis dose, discussed below:

(1) NIPD (Nightly Intermittent Peritoneal Dialysis)

In this form of dialysis, the cycler is used to perform exchanges during the night. In the morning, as the dialysis program is ending, the cycler drains the patient, who then disconnects from the machine and remains empty through the day. The cycle begins again the next evening, when the patient hooks back up to the cycler. To order NIPD, specify the number and volume of exchanges, the total number of hours of the cycler program, and the dextrose concentration of the dialysate or the patient's target weight.

Example 1: NIPD, 5 exchanges over 9 hrs, 2L fill volume, no last fill, target weight 65 kg

Example 2: NIPD, 5 exchanges over 9 hrs, 2L fill volume, no last fill, 2.5% Dianeal for all exchanges

(2) CCPD (Continuous Cyclic Peritoneal Dialysis)

Continuous cyclic peritoneal dialysis is similar to NIPD, but rather than have the patient empty during the day, the patient carries dialysate for part or all of the day. This is performed using the "last fill" option of the cycler. In NIPD, at the end of the cycler program the cycler drains the patient until they are empty, at which point the patient disconnects from the machine. In CCPD, the patient is drained, and then is refilled from either the same dialysate solution that was used overnight, or from a separate dialysate bag, and the patient completes the cycle program with fluid in their peritoneal cavity. This fluid is either kept in for the whole day and drained at the start of the next night's cycle, or is drained at some point during the day.

The last fill usually comes from a standard CAPD-type dialysate bag. Icodextrin solution is a good choice if the last fill is to dwell until the late afternoon or evening in order to prevent fluid absorption and promote UF. (Icodextrin is a polymer of glucose that is not absorbed from the dialysate into the bloodstream, whereas the dextrose in dialysate will be absorbed, especially during a long period of time.)

Order CCPD as you would NIPD, but you must also specify the composition, volume and duration of the last fill. Note that CCPD patients will have a target weight "full'' and this must take into account the weight/volume of the daytime exchange. NIPD patients will have a target weight that is ''dry'' owing to no residual fluid in the peritoneal cavity during the day.

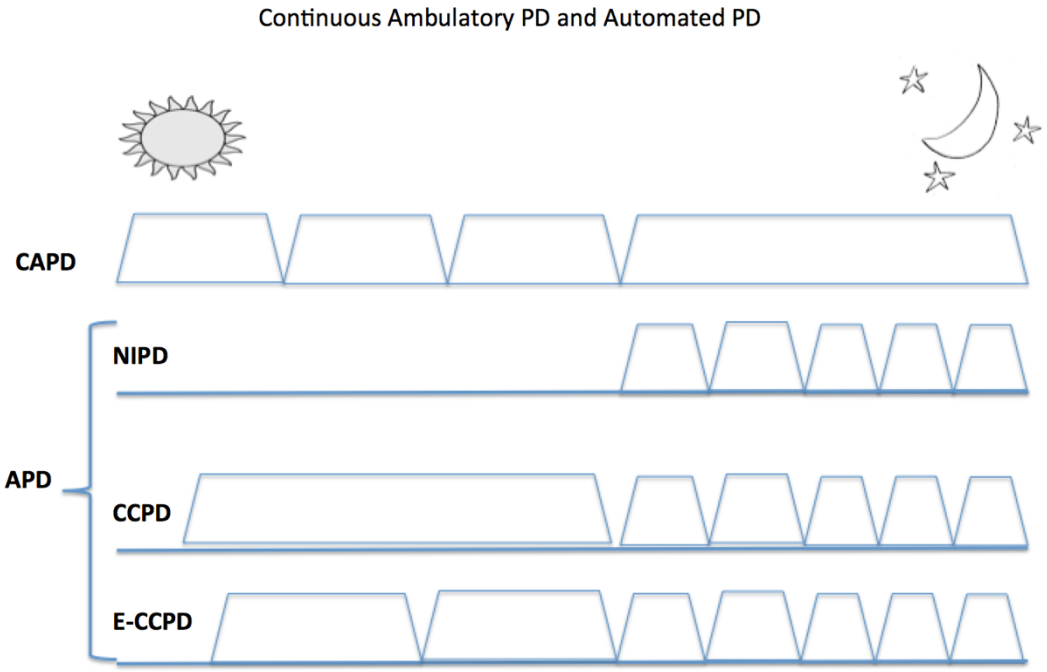
> Example: CCPD, 5 exchanges over 9 hrs, 10 L, 2 L fill volume, 1.5%/2.5% Dianeal. Last fill 2L Icodextrin. (In this example, since the total night volume is 10L, the 1.5%/2.5% means that the patient/nurse will use one 5L bag of 1.5% solution and one 5L bag of 2.5% solution).

(3) Enhanced CCPD

In patients who are not able to achieve adequate dialysis with CCPD, additional twin-bag exchange(s) can be added to the CCPD (night cycler and last fill) prescription. A CAPD twin bag is used for the daytime exchange. Order enhanced CCPD as you would standard CCPD, but you must also specify the composition, volume and timing of the additional exchanges, as well as any additives as required.

Example: Enhanced CCPD, 5 exchanges over 9 hrs, 10 L, 2 L fill volume, 1.5%. Last fill 2L of Icodextrin. Twin bag exchange 2L of 2.5% at 4 PM

For patients admitted to hospital, enhanced CCPD can also be delivered by continuous use of the cycler. This may meet the patient's medical requirements, as well as being more convenient for the nursing staff.



Inpatient PD Management

The general day-to-day management of the dialysis is done in conjunction with the Home Dialysis program. Check with home dialysis at extension 3848 with the desk nurse assigned for the week as to who to communicate with.

Ward PD: is managed by 8CCS Nursing Staff.

****For Consult/Off service PD: Home Dialysis Case Manager and nursing staff are responsible for setting up and administering the peritoneal dialysis Monday to Friday 8am-4pm for the Consult/Off service patients. For weeknights and weekends and holiday hours it is the 8CCS Unit Leader.

All dialysis orders should be completed by 1pm.

Peritoneal Dialysis Solution Types and Strengths

Standard dialysate (Dianeal™) comes in four dextrose concentrations, 0.5%, 1.5%, 2.5% and 4.25%. The higher the percentage of dextrose, the more likely UF will be achieved. As a rough guide:

- With a 1.5% solution, a 2 L 4-hour dwell should result in 0-100 cc of UF,
- A 2.5% solution should result in 150-250 cc UF
- A 4.25% solution should produce > 400 cc UF.
- A 0.5% bag is usually only used when the patient is hypotensive and volume contracted, as it typically results in a net negative UF (i.e. less fluid is drained out than instilled, with a net infusion of solution into the intravascular space).
- A 4.25% solution should only be considered in emergent settings (i.e. severe pulmonary edema) and is generally not recommended as part of a chronic peritoneal dialysis prescription.
- A more precise estimate of expected UF for a given dextrose concentration can be achieved by consulting the patient's log book from home.

On occasion, it is necessary to specify the concentration of dextrose in the dialysate, in order to give more precise instructions to the nursing staff. When a target weight is ordered and no specification is given regarding dialysate dextrose concentration, the nursing staff will consult a pre-made table that will provide them with guidance on how to select the dextrose concentration.

There are two *specialized* PD solutions available at St. Michael's:

(1) Extraneal™ (icodextrin) – uses a non-dextrose molecule to provide the osmotic force for UF. In contrast to dextrose-based solutions, Icodextrin is not readily absorbed into the bloodstream, so there is no dissipation of the osmotic gradient for UF. This solution is therefore ideal for a long dwell in order to prevent net absorption of fluid and to promote UF. Icodextrin should typically only be used for one long (6 to 16 hour) exchange daily (overnight exchange in CAPD patients/ day exchange in APD patients).

(2) Physioneal™ – a neutral pH, bicarbonate-buffered solution. All other bags use lactate as a buffer. Physioneal may be tried in patients with persistent abdominal pain during/after infusion as this pain may be due to the low pH of standard solutions. Others have suggested using Physioneal for long term preservation of the peritoneal

membrane, although supportive data is lacking. When used, Physioneal should replace all Dianeal exchanges.

It should be noted that all three specialty PD solutions are significantly more expensive than standard dialysate, and should therefore only be used when clinically indicated.

PD PERITONITIS

PD peritonitis means that the PD fluid has become infected but that this is not related to any secondary cause of peritonitis (e.g., bowel perforation, appendicitis etc).

PD peritonitis requires two of the following three criteria to be fulfilled:

1. Symptoms and/or signs of peritoneal inflammation (pain, tenderness, rebound, etc.)
2. Cloudy bags (or WBC count > 100 with >50% neutrophils (PMN's)
3. Positive dialysate culture or Gram stain

Initial Assessment

1) Clinical examination with particular attention to assessment of:
    - abdomen for symptoms and signs of peritoneal inflammation (e.g. rebound)
    - peritoneal catheter exit site; send swab for C&S if drainage or pus present; milk along tunnel of PD catheter if needed
    - rule out presence of incarcerated hernia
2) History- determine root causes – assess for breeches in sterile technique, assess if recent contamination of PD fluid, assess recent bowel habits.
3) Order first dialysate bag to be sent for Gram stain, C&S and cell count with differential. If patient is dry or recently completed the cycler, try to allow a dwell of at least 2 hours (can be as long as 4-6 hours) in order to get a meaningful sample.
    - Note PD fluid that has been left in the peritoneum for an extended period of time may have an elevated cell count but this will be largely monocytes and is not indicative of peritonitis. Similarly cell counts from shorter dwells may be falsely low and may required a timed 2-hour dwell. In such cases rely on

the percent neutrophil cell count criteria to initiate empiric antibiotics as indicated below.

4) Bloodwork on admission - CBC and differential, electrolytes, creatinine, urea, calcium, phosphate, protein, albumin.
5) Order antibiotics (see below and pre-printed order set for details)
6) Order dialysis prescription, including target weight. Antibiotic usually given IP once daily in 6-hour dwell
   - CAPD prescription usually does not need modification
   - Cycler patients should have antibiotics added to the longest dwell. For a cycler patient who normally does only NIPD, you can add a 6-hour day dwell (daytime exchange) on top of the usual nocturnal prescription. THE LAST FILL OPTION ON THE CYCLER CANNOT BE USED TO ADMINSTER ANTIBIOTICS IT REQUIRES A SEPARATE TWIN BAG EXCHANGE. Remember that the 6-hour antibiotic dwell is a minimum and can be in place longer
   - Patients may require higher % dialysate bags as peritoneal inflammation may lead to more rapid glucose absorption and therefore less UF
7) Order additional intraperitoneal additives:
   - Heparin 1000 u/L until effluent clears, then 500 U/L prn if fibrin still present
   - KCl, insulin as required
8) Order frequency for effluent sampling for inpatients (cell count daily until <100, and neutrophils < 50% and daily culture until total of 3 “no growths” and subsequently after the conclusion of antibiotic therapy.
9) For patients who are receiving vancomycin, check vancomycin levels at 48-72 hours post-initial dose.
10) Hold phosphate binders or calcium supplements if peritonitis is severe (due to risk of worsening constipation). Order appropriate diet and all other medications.
11) Patients on peritoneal dialysis who present with peritonitis are managed as out-patients, and CCAC usually assists in the delivery and administration of IP antibiotics unless it is a severe infection that requires hospital admission. Admission may be required for patients:
    1. With severe pain
    2. Who are frail or lack support at home
    3. Intractable nausea and vomiting
    4. Where concern exists regarding outpatient delivery and administration of intraperitoneal antibiotics.
    5. Where some degree of doubt exists over diagnosis (i.e. concern regarding other source of abdominal pain)

*** If no decrease in cell counts by day 5 or if count fell initially and then increased, repeat culture and consider:

(1) Inappropriate antibiotics for organism
(2) Associated exit site/tunnel infection
(3) Secondary peritonitis (e.g. ischemic bowel, cholecystitis, diverticulitis, appendicitis, pancreatitis). Management of non-resolving peritonitis after 5 days of appropriate antibiotics is catheter removal.

Peritonitis treatment guidelines

Initial therapy:

Urine output	No allergies	Beta lactam allergy
<100mL/24h	Cefazolin and Tobramycin	Vancomycin and Tobramycin
>100mL/24h	Cefazolin and Ceftazidime	Vancomycin and Tobramycin

*make sure to also cover for the most recent episode if within six weeks of presentation of current episode (i.e. vancomycin for recent MRSA peritonitis)

No allergies:

Patients with < 100 mL /24h urine:

If patient <50 kg: Cefazolin 1g in ONE exchange/day
Tobramycin 40mg in ONE exchange/day
Ideal dwell time of 6 hours (at least 3-4 hours).

If patient >50kg: Cefazolin 1.5g in ONE exchange/day
Tobramycin 60mg in ONE exchange/day
Ideal dwell time of 6 hours (at least 3-4 hours)

Patients with > 100 mL/ 24h urine:

If patient <50kg: Cefazolin 1g in ONE exchange/day
Ceftazidime 1 g in ONE exchange/day

Ideal dwell time of 6 hours (at least 3-4 hours)

If patient >50kg Cefazolin 1.5g in ONE exchange/day
Ceftazidime 1.5g in ONE exchange/day
Ideal dwell time of 6 hours (at least 3-4 hours)

Beta lactam allergy (regardless of urine output):

Replace Cefazolin with Vancomycin 30 mg/kg (round up to nearest 500 mg to a maximum of 2 g) in ONE exchange q3-5 days. Monitor Vancomycin levels q3 days, and repeat dose when level <15 mg/L. Follow dosing guidelines for Tobramycin above.

If presentation of peritonitis is within 4 weeks of previous episode, ensure antibiotic coverage addresses previous organisms antibiotic susceptibility.

Depending on C&S:

Treatment should be based on microbiological susceptibility test results. Commonly useful regimens are listed below but always check sensitivity results.

Enterococci:

Ampicillin 125 mg/L in EACH exchange X 21 days. (This may require conversion to CAPD for APD for some patients.) If lab reports high level Gentamicin sensitivity and urine output <100mL/24h, consider adding Gentamicin 2 mg/kg IV q48h for severe cases. Check Gentamicin trough prior to 3rd dose (should be < 1 ug/mL). Patients on NIPD or CCPD should be switched to CAPD for the duration of Ampicillin therapy. Ampicillin and Gentamicin cannot be mixed in the same bag due to chemical incompatibility.

If resistant to Ampicillin, use Vancomycin 30 mg/kg (round up to nearest 500 mg to maximum of 2 g) in ONE exchange q3-5 days. Monitor Vancomycin levels q3 days, and repeat dose when level <15 mg/L. Duration of antibiotic coverage would be 3 weeks.

Staphylococcus aureus:

	No allergies	Beta lactam allergy

Methicillin sensitive Staph aureus	Cefazolin	Vancomycin
Methicillin resistant Staph aureus	Vancomycin	Vancomycin

Methicillin-sensitive S. aureus: Cefazolin (according to previous dosing regimen) x 21 days. For severe peritonitis, consider adding Rifampin 300 mg po bid x 1 week. If there is an associated S. aureus exit site or tunnel infection, PD catheter should be removed.

MRSA: replace Cefazolin with Vancomycin 30mg/kg (round up to nearest 500 mg to maximum of 2 g) in ONE exchange q3-5 days. Monitor Vancomycin levels q3 days, and repeat dose when level <15 mg/L.

Coagulase-negative staphylococci:

Treat with Cefazolin (according to previous dosing regimen) x 14 days. If methicillin-resistant, replace Cefazolin with Vancomycin 30mg/kg (round up to nearest 500mg to maximum of 2 g) in ONE exchange q3-5 days. Monitor Vanco levels q3 days, and repeat dose when level <15 ug/mL.

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Single gram-negative bacillus:

Ceftazidime 1g (1.5g if >50kg) in ONE exchange/day x 21 days. If patient allergic to beta lactams, options include Tobramycin 40mg (60 mg if >50kg) in ONE exchange/day x 21 days or Cipro 500 mg po BID x 21 days (based on organism sensitivity).

Multiple gram negatives +/- anaerobes:

Ampicillin and Ceftazidime (according to previous dosing regimen), and add metronidazole 500 mg po BID x 21 days. Rule out perforated viscus (i.e. imaging via CT and/or general surgical consultation)

Pseudomonas:

Ceftazidime 1g (1.5g if >50kg) in ONE exchange/day x 28 days, and add a second antipseudomonal antibiotic: e.g. Ciprofloxacin 500 mg po BID (if sensitive). If there is an associated Pseudomonas exit

site or tunnel infection, PD catheter should be removed, and patient should be treated with IV antibiotics for 2 weeks after catheter removal.

Culture negative:

Continue empiric therapy for a period of two weeks if the cell count has normalized by day 5. If the culture is no growth but the patient is not improving and/or rising cell count consider abdominal imaging and speak to the microbiology lab and consider cultures for rare and usual organisms (i.e. mycobacterial species)

Nystatin therapy 500 000 u po qid (swallow not swish) is given for all PD patients receiving a course of antibiotics. Continue for 1 week post the cessation of the antibiotic course)

Definitions

Refractory peritonitis: failure of the effluent to clear after 5 days of appropriate antibiotics

Relapsing peritonitis: an episode that occurs within 4 weeks of completion of therapy of a prior episode with the same organism or a sterile episode

Recurrent peritonitis: an episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism

Repeat peritonitis: an episode that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism

Catheter-related peritonitis: Peritonitis in conjunction with an exit-site or tunnel infection with the same organism

Indications for PD catheter removal

- **FUNGAL peritonitis - remove immediately - this is an emergency even it the patient appears clinically well**
- Refractory peritonitis
- Relapsing peritonitis
- Refractory exit site/tunnel infection
- Pseudomonas or S. aureus catheter-related peritonitis

Consider catheter removal if not responding to therapy

- Mycobacterial peritonitis
- Multiple enteric organisms

*NOTE IF CATHETER REMOVAL IS REQUIRED THE SERVICE WHO FIRST INSERTED THE CATHETER I.E. UROLOGY OR INTERVENTIONAL RADIOLOGY IS RESPONSIBLE FOR ARRANGEMENT OF PD CATHETER REMOVAL. THE METHOD OF INSERTION SHOULD BE CAPTURED IN SOARIAN IMAGING AND/OR PROCEDURE NOTES . IF UNCLEAR, CONTACT MINA KASHANI PD ACCESS COORDINATOR AT EXTENSION 2387.

Reference: ISPD: PD-related Infections Recommendations: 2016 Update (www.ispd.org)

Antimicrobial prophylaxis for PD patients

PD catheter insertion and or manipulation of PD catheter via interventional radiology: Ancef 1 g IV 1 hour pre-procedure (or Vancomycin 1 g IV if beta-lactam allergy)

Dental procedures: Amoxil 2 g po 1 hour pre-procedure (or Clindamycin 600 mg po if beta-lactam allergy)

Colonoscopy:

If no allergies:

Ampicillin 2 g IV 1 hour pre-procedure
Ceftazidime 1.5 g IV 1 hour pre-procedure (1 g if < 50 kg)
Flagyl 500 mg po 1 hour pre-procedure and 500 mg 12 hours post

If beta-lactam allergy:

Vancomycin 1 g IV 1 hour pre-procedure
Tobramycin 1 mg/kg IV 1 hour pre-procedure
Flagyl 500 mg po 1 hour pre-procedure and 500 mg 12 hours post

On a course of antibiotics for any reason:

Nystatin 500 000 u po qid for duration of antibiotics + one week.

For daily application to the PD catheter exit site:

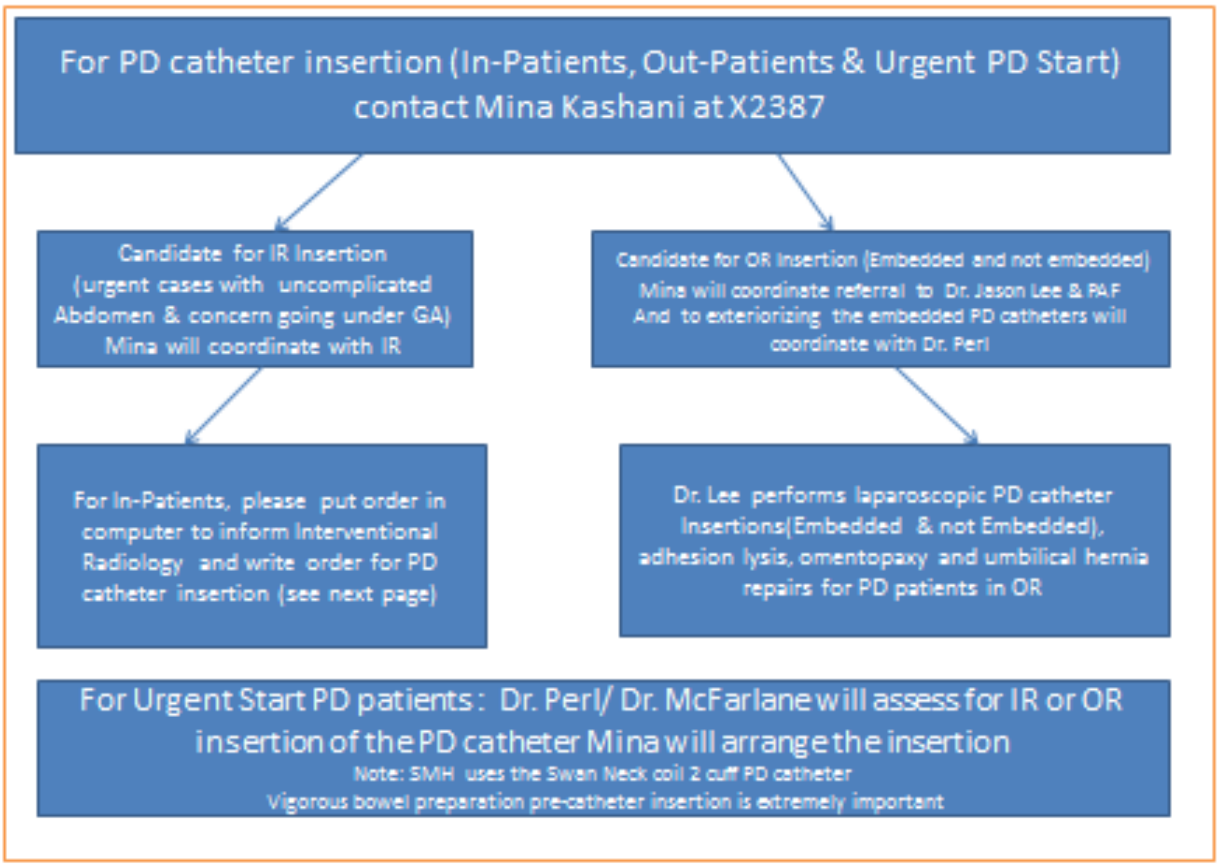
Mupirocin ointment

PD access program at St. Michael's

Mina Kashani – PD access coordinator Ext. 2387 cell 416-807-3067
Dr. Monica Faracas – PD access surgeon, Division of Urology
Interventional Radiology – ext 5886
Dr. Jeff Perl Ext. 6016 (PD catheter exteriorization for embedded PD catheters))

PD catheters are inserted in one of two methods at St. Michael's Hospital via interventional radiology under fluoroscopy, and in the OR by Dr. Monica Farcas using advanced laparoscopy. Each method has its advantages and disadvantages and for all PD access insertions consult the PD access coordinator Mina Kashani to determine the most appropriate method of insertion. The method is usually chosen using guiding principles as indicated in the pathway below

PD Catheter Insertion Pathway



1) **Pre-Insertion:** All patients going for PD catheter insertion should be given prophylactic antibiotics prior to insertion
2) Hold anticoagulants and antiplatelet therapies 1 week prior to catheter insertion (can individualize decision re. ASA/Plavix based on cardiac risk).
3) Hold calcium and iron for 2 days pre-insertion as they may predispose to constipation
4) Polythylene glycol with electrolyte (Klean-Perp) 250 cc po OD x 4 days prior to catheter insertion (can increase dose if necessary)

Prior to PD catheter insertion, please inform home dialysis unit. At St. Michael's Hospital, PD catheters may be inserted by interventional radiology (IR), or by urology in the OR (usually open surgical approach, with laparoscopy reserved for complex cases). PD catheters should be flushed by the nurse after insertion to ensure patency.

Short Term Management

1. Sterile PD dressing to cover exit site and catheter until site heals (about 2 weeks)
2. Flushes should be done for any patient with a new catheter. This is done to assess the catheter function and to remove fibrin and blood from the peritoneal cavity. Order 500cc volume "in and out" until the effluent clears.

Long Term Management

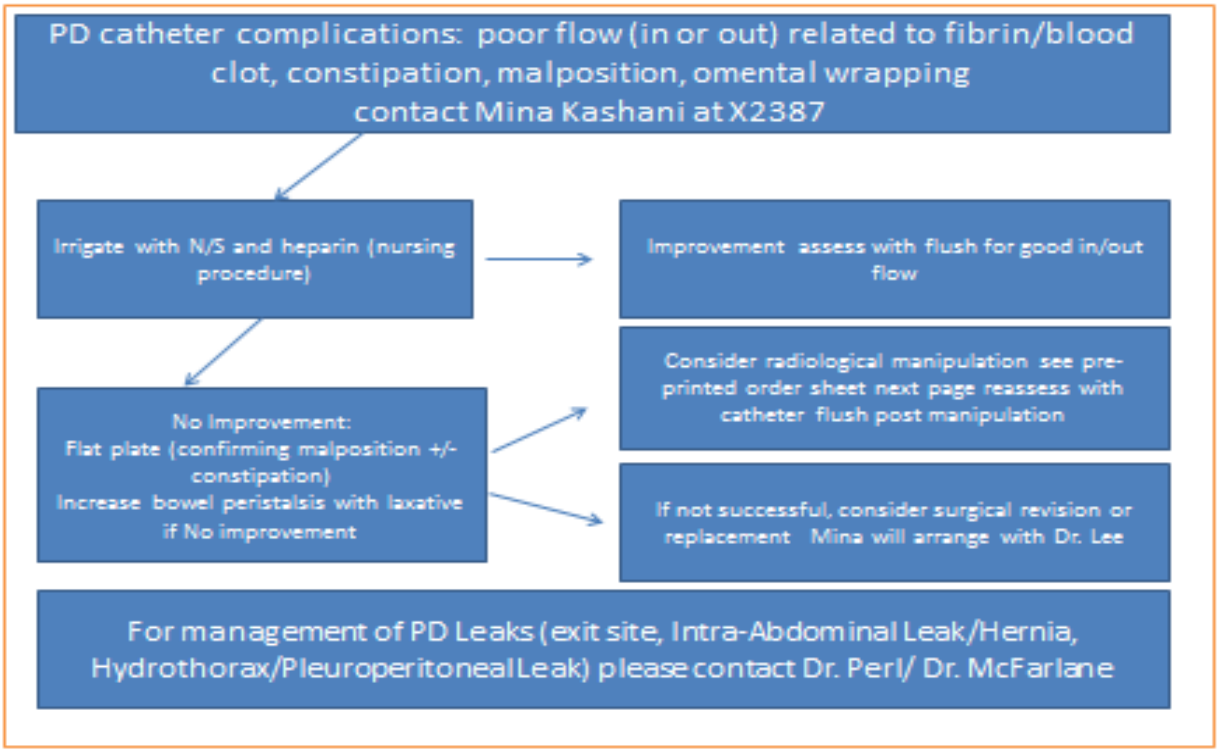
Standard nursing protocols for catheter exit care are used once the initial dressing is removed. Catheter care is every second day routinely with antibacterial soap and water followed by 2% chlorhexidine and a dry dressing. Twice weekly is the minimum frequency; exit site care should be increased for drainage or infected sites. Tobramycin ointment should be applied routinely by all PD patients with each dressing change.

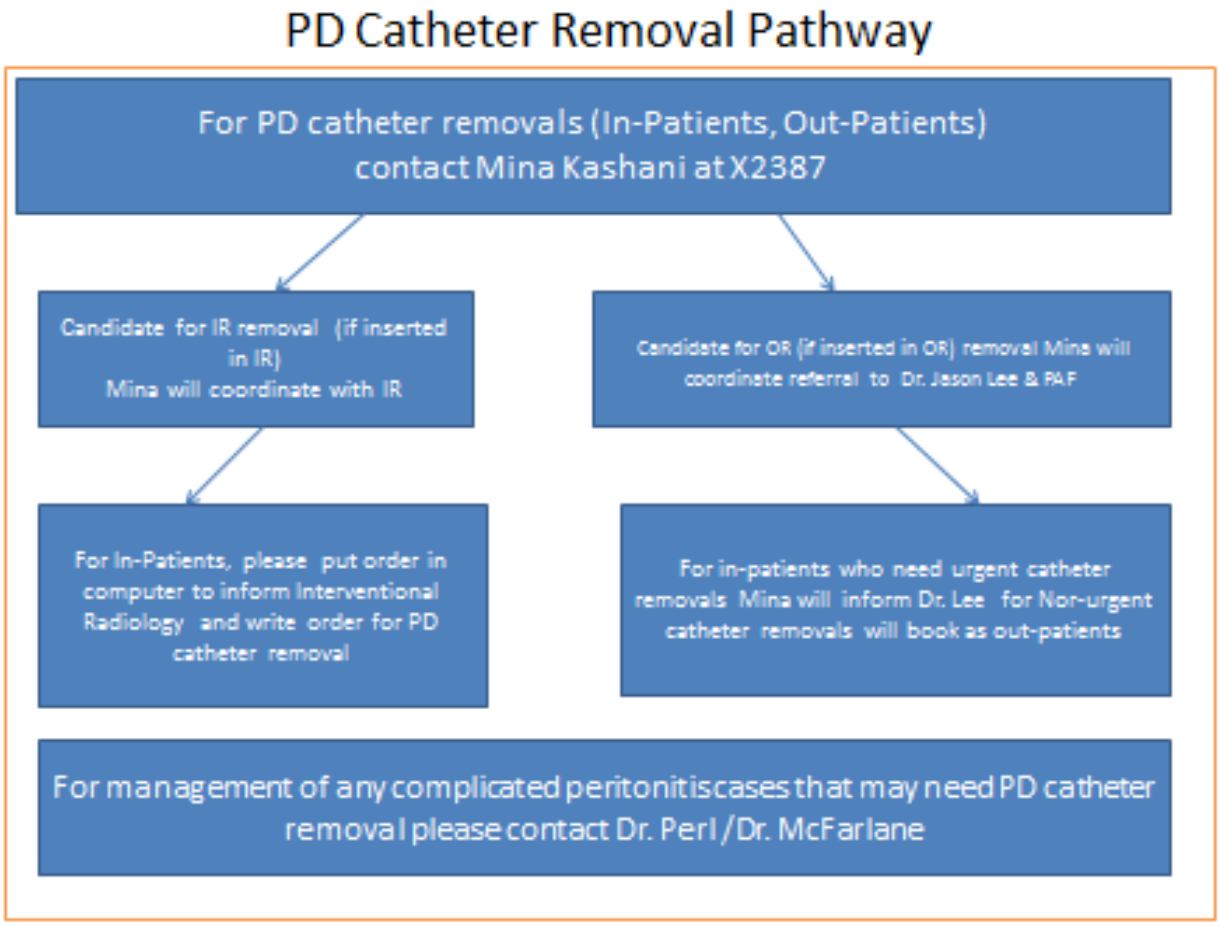
PD Catheter Dysfunction

If there is poor catheter flow, determine whether the difficulty is with outflow alone or both inflow and outflow. The most common cause of slow outflow is constipation.

- If there are problems with both inflow and outflow, consider mechanical obstruction of the catheter by fibrin/clot. Have the nurse irrigate with heparin and saline.
- Order abdominal X-ray to assess catheter position and presence of constipation. The PD catheter tip should be seen in the pelvis.
- If the catheter is in good position and there is evidence of constipation, increase bowel regimen and reassess in 2-3 days
- If the catheter tip has migrated out of the pelvis, refer patient for radiologic catheter manipulation (see below)
- If the catheter is in good position, there is no evidence of constipation and there is no improvement after catheter irrigation with heparin, the patient may have catheter dysfunction due to omentum wrapping around the catheter or adhesions (neither of which are visible on standard imaging techniques). Refer patient for radiologic manipulation (see preprinted orders after this section for PD catheter manipulation). If catheter dysfunction is recurrent, consider referral to Dr. Monica Farcas for laparoscopic PD catheter Revision +/- omentopexy/adhesiolysis discuss with PD access coordinator.

Pathway for PD Access Complications





Intraperitoneal (IP) medications

Heparin Indicated if fibrin is present in bags or for slow drainage. For CAPD, may be used in all bags or overnight bag only in relation to presence of fibrin.

Dose (Non-peritonitis): 500 units/litre

Dose (Peritonitis): 1000 units/litre until effluent clears

Potassium Chloride (FOR APD ONLY)

Intraperitoneal KCl is not usually added, but may be considered if alternatives such as increased dietary intake or oral potassium supplementation are not possible. It may be used for inpatients but is generally avoided in the outpatient setting.

Usual dose = 2 - 4 mEq/L. This dose will limit diffusive removal of K but will not supplement K to the patient. Max dose 10 mEq/L

PD Catheter Contamination (wet and dry contamination):

Occasionally after hours a PD patient will present to emergency having had a breech in technique which we refer to as a contamination. If the contamination has led to PD fluid visible on the outside of the catheter during an attempted exchange this is referred to as a 'wet contamination''

Wet contamination happens when the fluid filled tubing system is accidentally opened or unclamped. If this happens it may lead to a subsequent peritonitis.

Examples of when wet contamination may happen:

- There is a disconnection between the transfer set and the catheter at the titanium
- There is a small hole in the transfer set or the catheter
- Any time the **twist clamp on the transfer set is not closed** and fluid escapes due to poor technique

Procedure:

1. Examine the PD catheter for any damage cracks or wholes and the PD catheter transfer set
2. Have the PD or Ward Nurses Change the PD catheter transfer set
3. Arrange for a prophylactic dose of IP antibiotics with either cefazolin or vancomycin.
4. Inform the home dialysis nurse on call that this has occurred as the patient/caregiver may require technique retraining.

INTRODUCTION TO RENAL TRANSPLANTATION AT ST. MICHAEL'S HOSPITAL

Jeffrey Zaltzman, MD, FRCPC

A. Pre-op procedures

Living donor transplant (LD)

There are different categories of living donors:

1. Biologically related donors (siblings, parents, children)
2. Emotionally-related donors (spouse, friend)
3. Non-emotional directed donation
4. Kidney Paired Exchange (chains)

Living donors are admitted to Urology service day of surgery; you are not responsible for the donor. Recipient admitted to Nephrology service day prior to surgery; you are responsible pre-op and post-op.

1) The recipients' chart will be available on the ward. In addition, all pertinent letters will be found in Soarian. **There will be a recent note from the transplant physician outlining the plan for this recipient, including potential for participation in clinical research**

2) Brief history of any recent hospitalization, surgery, illness or blood transfusions that would preclude an elective procedure (e.g. recent MI)

3) Focused physical examination

4) If signs or symptoms of infection (fever, leukocytosis, etc.) are present, consider delaying the surgery

5) If patient is on dialysis, they are usually dialyzed the day prior to surgery. Assess the need for an additional run of dialysis:

- volume overload (clinical exam, CXR)
- hyperkalemia (K > 5.0)
- If patient is on nocturnal PD, ensure they get their usual dialysis overnight

6) ORDERS: All transplant order sets are on CPOE including transplant orders for pre-op, post-op, and medications (more on these later).

7) Ensure CXR and ECG are reviewed the evening of admission.

8) Consider beta-blockers for patients with medium and high cardiac risk

9) Patients with Type 1 diabetes (and some with Type 2) will need an insulin infusion started on the morning of their surgery

10) Can give required medications in morning of surgery

Deceased donor transplant (DD)

There are variations on the types and sources of deceased donors:

- How the donor dies
- Standard criteria or extended criteria
- Is there an exceptional distribution?

How The Donor Dies

1) Death by neurological criteria (NDD or Brain death)
2) Death by cardio-circulatory criteria (Donation after cardiac death (DCD))

Quality of kidney – Standard or Extended criteria

For each of these 2 categories, deceased donors can be subclassified by quality of kidney:

A) Standard Criteria Donor - Defined as a deceased donor with a KIDNEY DONOR PROFILE SCORE (KDPI) of < 80%
B) Extended Criteria Donor; Defined as a deceased donor with a KIDNEY DONOR PROFILE SCORE (KDPI) of 80-100%

*https://optn.transplant.hrsa.gov/resources/guidance/kidney-donor-profile-index-kdpi-guide-for-clinicians/

Exceptional distribution:

By Health Canada regulations, all organ donors are deemed either “safe” or “unsafe” for transplantation. There are many reasons for a donor being judged to be “unsafe”. For example, these reasons can include: the donor once resided in the UK (and therefore has a risk of mad cow disease); or, the donor is a current intravenous drug user.

Trillium Gift of Life staff obtains the medical and social history from next of kin. The attending staff will decide on donor suitability. “Unsafe” donors may still be used for transplantation, but are deemed by Health Canada as “EXCEPTIONAL DISTRIBUTION”. The use of such donors requires additional consent from the potential recipient.

Of note, donors who have an increased risk of infectious disease transmission are called “IRD”. All IRD donors are “Exceptional Distribution”, but only some Exceptional Distribution donors are IRD.

The actual risks are exceedingly low, as all donors are screened for infectious disease by serology and in the case of IRD “higher risk donors”, additional PCR Nucleic Acid Test (NAT) tests for HIV, Hepatitis B, and Hepatitis C are done.

Procedures when a potential deceased donor is identified
Trillium Gift Of Life (TGOL) calls the attending staff doctor on-call, and lets him/her know that a kidney has become available for transplant.

Potential recipients are identified based on points system and a negative virtual cross match. For allocation policies please visit:
https://www.giftoflife.on.ca/en/?gclid=EAIaIQobChMIrbLQx-_g6QIVCL7ACh1HvQ00EAAYASAAEgKs_PD_BwE

Recipients are called in by the on-call staff physician, or occasionally by the on-call nephrology fellow.

Urology resident is to be called early on in the process as they need to see the recipient, obtain surgical consent and book O.R.

DONOR INFORMATION IS GIVEN TO THE ATTENDING STAFF (by phone and usually also a PDF of the chart is emailed) and IS CONFIDENTIAL AND SHOULD NOT BE RECORDED IN RECIPIENT CHART

- age of donor
- NDD or DCD
- ECD or SCD
- National Highly Sensitized Patient Registry (HSP), donors can come from anywhere in Canada, for recipients with cPRA of 95% or greater
- EXCEPTIONAL DISTRIBUTION or not (see above)
- nature of injury/illness to donor
- amount of time on pressors
- baseline and most recent creatinine, eGFR and creatinine clearance of donor
- underlying comorbidities (diabetes, hypertension, etc.)
- anatomy of kidney (number of arteries and veins)
- time at which kidney was (or is expected to be) harvested
- blood type of donor

- serology of donor (CMV, EBV, HepB, HepC, HIV, HTLV)

For fellows; when you call in recipients:

- When speaking to recipient:
  - introduce yourself and reason for calling
  - ensure they are ready for transplant (not “on hold”)
  - ask brief history for: recent hospitalization, surgery, recent or ongoing illness, or recent blood products, and time of most recent dialysis
  - instruct them to hold all anticoagulants, stay NPO, and come directly to 8CC nursing station
  - if Recipient’s cPRA is >80%, may consider calling in a back-up
  - If donor is “Exceptional Distribution”, will need to let recipient know and obtain consent, together with attending staff.

Housestaff/Fellows: Review recipient chart from Soarian/Sovera:

1. Get patient’s MRN from recipient list on ward and logon to Soarian
2. In top right hand corner drop-down menu #3 choose “Sovera-Link”
3. In medical records, choose service “PRT” and click “view MRN”
4. In tabs click on “EXTERNAL” to get chart, scroll through scanned documents as you need (letters, lab, cardiac tests, other imaging)
5. Transplant physician, urologist and anesthesia letters on Soarian
6. In addition, all information (recent communications and notes) can be found in transplant EMR (See later for information on access to all post-transplant recipient data: labs, notes, meds, etc…)

Locate the DCCP database icon – either on the desktop of the hospital computer, or locate it by searching for it.

Transplant EMR:

Locate the DCCP database icon – either on the desktop of the hospital computer, or locate it by searching for it.

Access this using your username and password.

You open transplant data base, find patient by MRN, click on “clinical” to see notes from nurses regarding status updates.

You open transplant data base, find patient by MRN, click on “clinical” to see notes from nurses regarding status updates.

- When recipient arrives perform focused history and physical exam, obtain blood work
    - CBC, electrolytes, INR, aPTT
    - A STAT cross-match if needed
    - CXR,
    - ECG.
- If signs or symptoms of infection (fever, leukocytosis, etc.) are present, consider cancelling surgery and calling in another recipient
- Assess the need for urgent hemodialysis:
    - volume overload (clinical exam, CXR)
    - hyperkalemia (K > 5.0)
- Is recipient on Warfarin? - need to reverse
- Is recipient on a DOAC? (need to consult hematology)

Cross-match: (HLA lab : 416-340-4995)

a. All recipients will have a flow cross-match against potential donor
b. In the following cases the results of a STAT cross-match must be negative BEFORE beginning surgery:
    1. recent blood products
    2. cPRA > 80%
    3. Recipient has DP alloantibody against donor
    4. cPRA > 0% and fewer than 3 samples in HLA lab
    5. Most recent sample for virtual crossmatch is older than 3-4 months
c. All cross match results will be called in to the attending staff physician. Stat x-match results are available in approximately 6 hours

KEY TEACHING POINTS REGARDING CALCULATED PANEL REACTIVE ANTIBODY (cPRA);

1) cPRA [range 0-100%] is calculated based upon degree of HLA class l and class ll sensitization and Canadian organ donor pool. The cPRA indicates the percent of randomly selected blood donors against which the potential recipient has antibodies to HLA antigens.
2) (1-%cPRA) = likelihood of finding a donor against which that recipient does not have any antibodies (negative virtual cross-match or acceptable mismatch)
3) In the modern era, in the absence of donor specific antibody (DSA), the %cPRA has no correlation with the risk of rejection.
4) Kidney allocation in Ontario and Canada is based on finding a donor to which the recipient has no and has NEVER (historical) had “DONOR SPECIFIC ANTIBODIES” (NO DSA). This is the same as “ACCEPTABLE MISMATCH” OR “NEGATIVE VIRTUAL CROSS MATCH”. The allo-antibodies of the recipients are characterized and matching with a donor is done virtually. For the National highly sensitized registry (for Canadian recipients with cPRA of 95-100%), HLA class l : A, B and HLA class ll, DR, DQ, DP, must be acceptable. However, many, but not all class ll DP allo-antibodies, are of clinical importance. Thus, virtual cross match and allocation within Ontario does not exclude positive DP alloantibodies. This is to expand the donor pool. If TGLN informs the transplant program of positive DP, then a stat-cross match is required. (see above).

ORDERS

Use the online transplant order sets for pre-op, post-op, and medications (more on these later).

a. Consider beta-blockers for medium-high cardiac risk
b. Patients with T1DM will need an insulin infusion, as will some patients with T2DM
c. Any anticoagulants will have to be reversed:
    - Warfarin - Vitamin K, prothrombin complex concentrate (Octaplex, Beriplex)
    - If a patient is on DOAC, need to consult hematology

d. If the patient is on antiplatelet agents other than ASA (e.g. clopidogrel (Plavix)), let urology and anesthesiology services know)

e. Depending on immunological risk, the recipient may require additional therapy such as IV-Ig.

B. Post-operative management

You will be called from the recovery room - this is called the "post-anesthetic care unit" (PACU) at St. Michael's Hospital. You will be called immediately after the surgery. The patient will have a Foley catheter in place. Generally, the patients will not have an IJ line for monitoring. Urology service will continue to follow the patient for surgical issues. The pain service will provide patient controlled anesthesia and will provide advice on transitioning to oral analgesia.

1. Ensure that there is urine output.
    - No urine output means one or more of the following:
      - Foley catheter is obstructed
      - Ureter is obstructed
      - No blood flow to transplant kidney
      - Hyperacute rejection
    - Flush the Foley with saline to dislodge any clots. **If anuric despite this, obtain an URGENT renal ultrasound with arterial dopplers and resistive indices**, and call the urology service. This should be done in the PACU.
2. Watch for post-op hyperkalemia. This can be treated with insulin shift and furosemide diuresis, and if necessary one or more dialysis treatments.
3. The goal for the first 24-48h post-op is to maintain a slightly hypervolemic state to ensure kidney perfusion. This can be achieved by replacing urine volume 1:1 with IV replacement. ALWAYS START WITH NORMAL SALINE. However, if there is ongoing polyuria (>200 ml/hour) then to avoid abrupt changes in serum Na we match urine and IV tonicity. (Tonicity = [Na] + [K]).
4. If the patient is already hyponatremic and polyuric, we generally avoid hypotonic IV fluid. (see below for an example at "8:00 h").

Example:

Time Post-op	Serum Na	Urine Na	Urine K	IV Replacement
0:00 h 0:30 h 4:00 h 8:00 h	Pending 142 138 134	Pending 90 50 50	Pending 50 30 30	NS 1:1 for U/O NS 1:1 for U/O 1/2NS 1:1 for U/O NS 1:1 for U/O

IV solution	Tonicity
NS	154
1/2NS	77
50% 1/2NS + 50% NS	116

*RL: Na-130 mmol/l, Cl-110 mmol/l, lactate-28 mmol/l,
K- 4 mmol/l, Ca-1.5 mmol/l

5. Follow serum and urine lytes q6h. If the urine output is large, serum and urine lytes will have to be measured more frequently, e.g. q3h.
6. Fluid boluses of NS should be used to treat hypovolemia or reduction in urine output, provided the patient is not developing pulmonary edema. May consider using Ringers Lactate (RL), as emerging data has demonstrated that is safe and may have marginal benefits over NS in early post-transplant graft function.
7. At 24 hours post-transplant, the hourly IV fluid replacement can often be reduced to 50% of the urine volume.
8. Once the patient is tolerating clear fluids by mouth, the IV fluid can be stopped.
9. Routine post-op transplant ultrasound should be done on post-operative day (POD) 3.
10. Pharmacist will instruct transplant patient on their medication regimen.
11. Foley catheter is usually removed POD 5, but urology service must approve this.
12. Patient is discharged with follow-up in transplant clinic once renal function has stabilized and they are ambulating, eating, and voiding well.
13. Urology follow-up is required since most patients have a ureteric stent placed intra-op that will need to be removed.

C. Post-op medications

All transplant recipients require immunosuppression post-op. You must decide if the transplant recipient needs “low-risk” or “high-risk” treatment protocols based upon donor and recipient criteria (see below).

There may be ongoing research studies; ask your staff at the start of your rotation.

If there is an ongoing study, call Research Manager (Michelle Nash –pager 416-685-9775) to assess patient suitability and obtain consent; they will order immunosuppressive medications and enter other orders if patient is enrolled.

Immunosuppressive regimen

Class	Drug Name
Induction Therapies	Anti-Thymocyte Globulin (Thymoglobulin®) Basiliximab (Simulect®)
Calcineurin Inhibitors	Cyclosporine (Neoral®) Tacrolimus Extended Release (Advagraf®) Tacrolimus immediate Release (Prograf®)
Antiproliferative Agents	Mycophenolate Sodium (Myfortic®) Mycophenolate Mofetil (Cellcept®) Azathiporine (Imuran®)
mTOR inhibitors	Rapamycin, Sirolimus (Rapamune®)
Corticosteroids	Methylprednisolone (Solu-Medrol®) Prednisone
Infection Prophylaxis	PJP: - Sulfamethoxazole/Trimethoprim (Septra®) - Atovaquone - Dapsone CMV: - Valganciclovir (Valcyte®)
Supplementary	Proton Pump Inhibitor Iron Stool Softener

Induction Therapy:

Low Immunological Risk Transplant:

Basiliximab (Simulect®)

- Most recipients, regardless of cPRA
- no donor-specific anti-HLA antibodies
- no previous allograft loss due to acute rejection

Dosing:

20 mg IV x 1 on-call to OR and 20 mg IV x 1 on POD#4

A steroid sparing protocol may be utilized if the patient:

- has impaired fasting glucose or glucose intolerance
- known diabetes but not on insulin
- known history of GI bleed/Peptic Ulcers
- known osteoporosis
- history of steroid-induced psychosis

Discuss in advance with staff physician.

High Immunological Risk Transplant:

Anti-Thymocyte Globulin (Thymoglobulin®)

Indication:

1. Any chance of a missed or untested donor specific antibody (DSA)
2. Positive STAT cross match. (Need to reconsider doing the transplant, or choosing a back-up recipient.) In addition, would also need IVIg.
3. Previous allograft loss because of acute rejection

Dosing:

1. 1.5 mg/kg IV post-op when patient returns to the floor (< 6 hrs post-op).
2. Central line: in 250 mL 0.9% sodium chloride over 8 hours
   Peripheral line: in 500 mL 0.9% sodium chloride over 12 hours
3. Pre-medication prior to dose to prevent hypersensitivity reaction:
   - Diphenhydramine 50 mg IV x 1
   - Acetaminophen 650 mg PO/PR x 1
   - These pre-medications can be discontinued if no reaction after 2 doses

4. Cell counts should be monitored daily during thymoglobulin treatment.
    - Target for absolute lymphocyte count (ALC) < 0.2
    - Excessive drop in WBC and/or platelets requires decreasing or holding Thymoglobulin dose
5. **Daily order of thymoglobulin dose is required** based upon ALC, WBC, and PLT count
6. **Generally aim for 4 mg/kg total of thymoglobulin for induction**
7. Duration of Thymoglobulin depends on graft function, usually 5-7 days.

Calcineurin Inhibitor:

Tacrolimus Extended Release (Advagraf®) Dosing (preferred CNI):

- 0.15 mg/kg po daily starting evening of OR or on POD #1
- Trough levels daily starting on POD #2
- Goal trough level – see table below

- Use immediate release formulation (Prograf®) 0.075 mg/kg po bid if patient is unable to swallow by mouth/has NG tube

Cyclosporine (Neoral®) Dosing:

- Given to patients at high risk for developing new onset diabetes or those intolerant to Tacrolimus
- Cyclosporine 3 mg/kg po bid starting evening of OR or on POD #1
- C2 levels daily starting POD #2
- Goal C2 level – see table below

Cyclosporine (Sandimmune®) IV:

- IV Cyclosporine is used if the patient is unable to take oral cyclosporine or other oral immunosuppressant agents (i.e.: tacrolimus)
- Dose:
    - < 100 mg: dilute in 100 mL D5W or 0.9% sodium chloride
    - 100-500 mg: dilute in 250 mL D5W or 0.9% sodium chloride
- Administered by slow IV infusion over a period of no less than 2 hours, usual administration time is 4-6 hours.
- Can be given via peripheral or central vein
- IV Cyclosporine is associated with anaphylactoid reactions due to polyoxyethylated castor oil vehicle in the solution. Physician to remain on

the nursing unit for the first 30 minutes following the start of infusion. Keep anaphylaxis kit at bedside.

Anti-proliferative agents

Enteric Mycophenolic Acid (Myfortic®) Dosing:

- 720 mg po BID starting evening of OR or on POD#1

Mycophenolate Mofetil (Cellcept®) IV:

- Given to those patients unable to take oral capsule, tablet, or suspension
- Can be given for up to 14 days, patients should be switched to oral Mycophenolate once they can tolerate oral medication
- Dose: 1 gram IV bid in 140 mL of D5W administered by slow IV infusion over a period of no less than 2 hours. Final concentration is 6 mg/mL.
- Can be given via peripheral or central vein

Corticosteroid

Steroid Dosing:

- Methylprednisolone (Solumedrol®): 2mg/kg IV on-call to OR and then IV q12h x 48 hours

- Prednisone:
    - POD # 3-7: 1 mg/kg po daily
    - POD # 8-14: 0.5 mg/kg po daily
    - POD # 15 onward: 20 mg po daily until transplant clinic follow-up

Other medications:

- Iron: Ferrous Fumarate (Palafer®) 300 mg po daily
- Stool Softener: Docusate Sodium (Colace®) 100 mg po bid
- GI Symptoms (reflux, dyspepsia): Pantoprazole (Pantaoloc®) 40 mg po daily
- DVT Prophylaxis: Heparin 5000 units sc bid

Surgical Antimicrobial Prophylaxis

1. All transplant recipients receive surgical prophylaxis:
    - Patients less than or equal to 80 kg: Cefazolin 1 gm IV on call to OR

      OR
    - Patients greater than 80 kg: Cefazolin 2 gm IV on call to OR

OR

- Penicillin Allergic: Clindamycin 600 mg IV on call to OR

Infection Prophylaxis:

CMV or cytomegalovirus is a common pathogen seen in all organ transplant recipients. Although it can occur at any time, for renal transplant recipients it is most common within the first 12 months post-transplant or following treatment for acute rejection.

CMV viremia is characterized by fever, lassitude, and may have concomitant leukopenia. CMV tissue invasion can involve: lungs, allograft, stomach, colon, liver.

Any recipient with previous CMV exposure (+ serology) is at risk (reactivation, or primary infection), but the highest risk cohort are CMV seronegative recipients who receive an allograft from a seropositive donor, or those receiving induction or treatment with thymoglobulin. These patients all receive valgancyclovir prophylaxis. Suspected CMV infection should be confirmed by PCR testing for active virus. Counts of >10,000/ml require treatment.

Treatment involves a combination of reduction/cessation of anti-proliferative agent (MMF, mycophenolate) and treatment with oral valgancycovir or IV ganciclovir.

Dosing is based on renal function, and duration is based on response.

CMV Prophylaxis at time of transplant

RECIPIENT CMV	DONOR CMV	LOW-RISK (NO THYMOGLOBULIN)	HIGH-RISK (THYMOGLOBULIN)
+	+	None	**YES (VALGANCICLOVIR)**
+	-	None	**YES (VALGANCICLOVIR)**
-	+	Yes (Valganciclovir)	**YES (VALGANCICLOVIR)**

-	-	NONE	NONE

Start Valgancyclovir (Valcyte®) 450 mg Tablet POD #3. Dose is based on renal function (see below).

CREATININE CLEARANCE (ML/MIN)	CMV PROPHYLAXIS DOSAGE
60 OR GREATER	900 MG ONCE DAILY
40-59	450 MG ONCE DAILY
25-39	450 MG EVERY 2ND DAY
10-24	450 MG TWICE WEEKLY
< 10 (ORAL SUSPENSION ONLY)	100 MG THREE TIMES WEEKLY

Pneumocystis

All recipients receive Sulfamethoxazole/Trimethoprim 400/80 mg po daily (Septra® Single Strength) for PCP prophylaxis for 1 year. If patient is sulfa allergic, use Dapsone 100 mg po daily (need to ensure not G6PD deficient). May also use Atovaquone 1500 mg daily.

BK virus

BK is a ubiquitous virus that resides asymptomatically in the uroepithelium of ~ 75% of the population. Following renal transplant, owing to immunosuppression, ~ 30-40% of patients will shed BK virus in the urine (BK viruria). Of those, about one third will have BK viremia. High levels of BK in the blood (> 1000/ml) can lead to BK nephritis.

Unlike other infections, BK viruria, viremia and nephritis are completely asymptomatic. Transplant program surveillance for BK virus is by standardized PCR testing. At St. Michael's Hospital, patients are screened for BK at 1 month, 2 months and 3 months post-transplant, and then every 3 months for 2 years. From

years 2- 5 patients are screened annually. In addition, BK is sought when renal function deteriorates without any other obvious cause. There is no proven therapy for BK and management always involves reduction in immunosuppression.

Other Post Transplant Medications

1. Pre-op meds should be reassessed after transplant
    a) most medications should be resumed on POD #1
    b) NSAIDs, ACE inhibitors, and ARBs should be held until transplant recipient has stable GFR
    c) Most medications associated with ESRD (phosphate binders, calcitriol, erythropoietin stimulating agents) can be discontinued
2. Iron supplements are usually added for approximately 3-6 months post transplant

Therapeutic Drug Monitoring

Tacrolimus (Advagraf® & Prograf®):

- Draw Tacrolimus **trough** level immediately prior to the morning dose at 10 A.M
- Time to steady state after initiation of therapy or after change of dose = 2.5 – 3 days

Target Troughs

TIME OUT FROM TRANSPLANT	TARGET TAC LEVEL (UG/L)
0 – 14 DAYS (1ST 2 WEEKS)	**5-9**
14 – 90 DAYS (2 WEEKS – 3 MONTH)	**5-8**
> 90 DAYS (> 3 MONTHS)	**4-7**

Cyclosporine Oral:

Target C2 Level

- Draw cyclosporine **C_2** level exactly 2 hours after the morning dose at 8 A.M.

TIME OUT FROM TRANSPLANT	TARGET C_2 LEVEL (UG/L)
0 – 30 DAYS	**900 – 1000**
1 – 2 MONTHS	**800-1000**
2 – 3 MONTHS	**700-900**
3 – 6 MONTHS	**700-900**
6 – 12 MONTHS	**500 – 800**
> 12 MONTHS	**300 – 600**

Cyclosporine IV:

Target Trough

- Draw cyclosporine **trough** level immediately prior to morning dose at 8 A.M

TIME FROM TRANSPLANT	TARGET TROUGH LEVEL (UG/L)
0-1 MONTH	**350 – 450**
1 – 3 MONTHS	**300 – 350**
3 – 6 MONTHS	**250 – 300**
6 – 12 MONTHS	**200 – 250**
> 12 MONTHS	**100 – 200**

NOTE:

- **Cyclosporine Oral to IV dose conversion = 3:1**
- **Tacrolimus Oral to Cyclosporine Oral dose conversion = 1:75**

Example:

A patient is taking Advagraf (tacrolimus) 6 mg p.o. daily, but has intractable vomiting, so needs to switch to i.v. medication. There is no i.v. tacrolimus available. How much i.v. cyclosporine should she receive?

1. Convert oral tacrolimus to oral cyclosporin at 1:75, this means 75 x 6 = 450 mg/day
2. Convert oral cyclosporin to i.v. cyclosporin, at 3:1 this means 450/3 = 150 mg per day
3. Prescribe this total daily dose to be given in divided doses every 12 hours, i.e., in this case 150/2 = 75 mg i.v. q12h.

D. Delayed graft function

Common causes:

Pre-renal:

- hypovolemia
- post-operative complications (pulmonary embolus, MI, etc)
- tacrolimus/cyclosporine toxicity
- other meds: NSAIDs, ACE inhibitors
- renal artery embolus or thrombosis

Renal:

- post-ischemic reperfusion injury/ATN
- hyperacute or accelerated rejection

Post-renal:

- ureteric stricture
- lymphocele or urinoma
- hematoma

Investigations:

- assess volume status
- check tacrolimus or cyclosporine levels
- check pre-op cross-match

Obtain transplant ultrasound with dopplers and resistive indices
(ALWAYS DO ULTRASOUND and DOPPLER URGENTLY IF ANURIC)

Consider transplant biopsy

Management:

- ensure adequate effective circulating volume
- hold any nephrotoxic drugs if possible
- reduce tacrolimus/cyclosporine doses
- address any specific post-renal complication or rejection

Risk Factors for Post-Ischemic reperfusion/ATN

- prolonged cold-ischemia time
- prolonged (>30 min) warm ischemic time
- DCD donor (likelihood of DGF is 75%)
- increased donor age (including ECD donor)
- nephrotoxic agents (pressors, contrast dye) given to donor
- subarachnoid hemorrhage in donor
- vasculopathy in donor or recipient

E. Complications in transplant patients

General Care of Hospitalized Transplant Patients

1) Most transplant patients are on low doses of prednisone. Consideration must be given to the possibility of <u>relative adrenal insufficiency</u>:

   - severe stress (sepsis, ACS, major surgery)
     - hydrocortisone 100mg IV q8h
     - once stable change to prednisone taper (for example):
       - day 1 - 50mg
       - day 2 - 30mg
       - day 3 - 20mg
       - day 4 - 15mg
       - day 5 - 10mg

        - day 6 - 5mg

- mild to moderate stress (uncomplicated infection, day surgery)
    - double or triple baseline steroid dose for 3 days, then resume baseline dose

2) Patients who cannot take PO medications can receive some medications IV
    - Prednisone 1 mg PO = Hydrocortisone 4 mg IV (divide dose q8-12h)
    - Cyclosporine 3 mg PO = Cyclosporine 1 mg IV (use q12h dosing)
    - * IV TACROLIMUS is not available, so NEED TO USE IV CYCLOSPORINE
    - MMF 1 mg PO = MMF 1 mg IV (q12h dosing, no adjustment needed)

3) Nephrotoxic agents should be avoided as much as possible
    - Avoid radiocontrast dye when possible; if patient needs iv contrast dye, give IV fluid according to standard protocols (e.g. IV NS at 1 cc/kg/h for 12 hours prior to and 12 hours following contrast dye administration)
    - Avoid aminoglycoside antibiotics; use fluoroquinolones or cephalosporins instead
    - Avoid use of NSAIDs
    - Avoid use of RAAS blockade if any concern about renal perfusion

REMEMBER: Immunosuppressed patients have a reduced inflammatory response to infection and tissue damage. Therefore, it is important to have a high degree of suspicion for occult infection and to order appropriate imaging.

Acute Kidney Injury in Renal Transplant Patients

Common causes of AKI Weeks 1-12 post-transplant:

- Acute rejection
- Acute allograft pyelonephritis
- Tacrolimus/cyclosporine toxicity
- Hypovolemia
- Urinary tract obstruction (ureteric stricture or fluid collection)
- CMV infection
- Recurrence of primary disease (esp. FSGS and HUS/TTP)
- BK virus nephritis

Common causes of AKI beyond 3 months post-transplant:

- Acute allograft pyelonephritis
- Hypovolemia
- Tacrolimus/cyclosporine toxicity
- Acute rejection
- Recurrence of primary disease
- BK virus nephritis
- Post-transplant lymphoproliferative disorder
- De novo renal disease

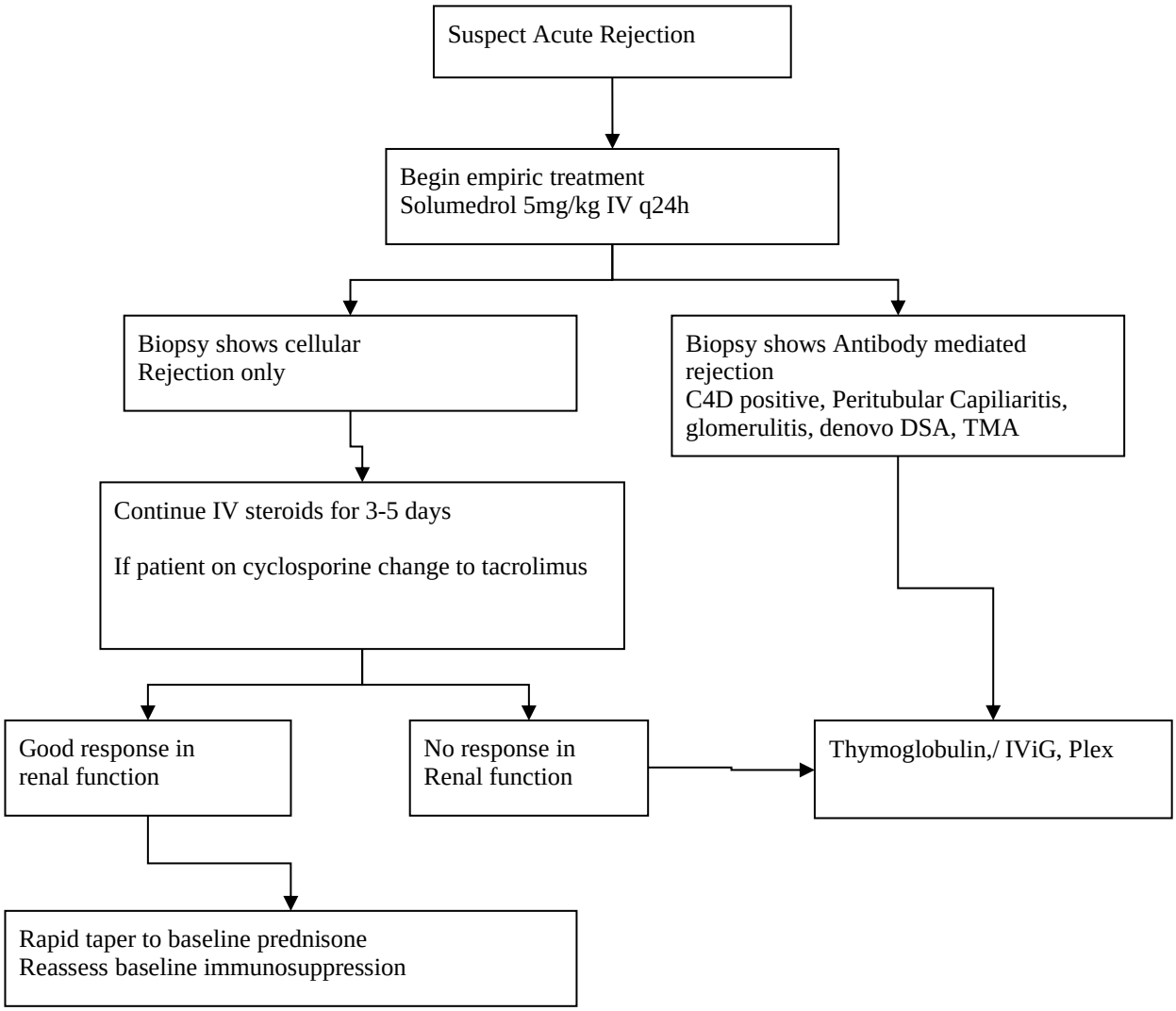
Investigations:

- history focusing on medication changes and adherence, history of CMV or EBV mismatch, and recent illness or volume loss
- physical exam focusing on volume status
- labs including
    - urine electrolytes, urine dip and microscopy for sediment
    - serum tacrolimus or cyclosporine levels
    - routine blood work
- transplant ultrasound with dopplers

Treatment Guidelines for Acute Allograft Rejection

1. Pulse steroids may be given in a patient suspected of acute rejection even before a kidney biopsy is done; this can be done without affecting the diagnostic yield of a transplant biopsy; dose is methylprednisolone 5 mg/kg daily for 3 days, followed by a prednisone taper
2. Thymoglobulin is given in the same way as for induction in high-risk transplants, but with a higher dose of 2mg/kg IV q24h – discuss with staff doctor. See flow chart below.
    a. Generally, the total dose to treat rejection is 8-12 mg/kg.
    b. Premedicate with diphenhydramine and acetaminophen for first 2 days
    c. Ensure gancyclovir IV prophylaxis is given
    d. Septra for PJP prophylaxis
    e. Nystatin mouthwash
3. Reason for rejection should be addressed
    a. Inadequate immunosuppressive regimen
    b. Decreased tacrolimus/cyclosporine levels
    c. Non-adherence to medications
    d. Drug interactions with immunosuppressants
4. Antibody-mediated acute rejections are suggested by the following:
    - Development of *de novo* donor-specific antibody
    - Pathological features on biopsy including:
        - C4D positive staining on biopsy
        - Findings of thrombotic microangiopathy
        - Peri-tubular capilliaritis

    Treatment: in addition to thymoglobulin and methylprednisolone, will require additional therapies such as plasmapheresis, IVIG, Rituximab.


Suspect Acute Rejection
Begin empiric treatment
Solumedrol 5mg/kg IV q24h
Biopsy shows cellular
Rejection only
Biopsy shows Antibody mediated
rejection
C4D positive, Peritubular Capiliaritis,
glomerulitis, denovo DSA, TMA
Continue IV steroids for 3-5 days
If patient on cyclosporine change to tacrolimus
Good response in
renal function
No response in
Renal function
Thymoglobulin,/ IViG, Plex
Rapid taper to baseline prednisone
Reassess baseline immunosuppression

POST-RENAL TRANSPLANT PATIENTS SEEN ANYWHERE IN HOSPITAL

- Obtain data via the Transplant Database Electronic Medical Record

- These are outpatients so clinical notes and lab results will not usually be in Soarian

- Transplant EMR

1) Locate the DCCP database icon – either on the desktop of the hospital computer, or locate it by searching for it.
2) Click on transplant data base, the FIND PATIENT
3) Find patient by name or MRN#
4) Database has: current lab values, current meds, inactive meds and all medical notes, encounters, history, demographics