

**HANDBOOK**  
**of**  
**INTERNAL MEDICINE**

**COC(Medicine)**  
**Hospital Authority**

**6<sup>th</sup> Edition**  
**2011**



## **DISCLAIMER**

This handbook has been prepared by the COC (Medicine), Hospital Authority and contains information and materials for reference only. All information is compiled with every care that should have applied. This handbook is intended as a general guide and reference only and not as an authoritative statement of every conceivable step or circumstances which may or could relate to the diagnosis and management of medical diseases.

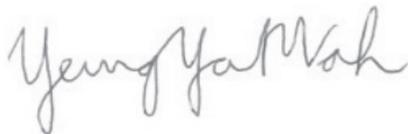
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## PREFACE TO 6<sup>th</sup> EDITION

Since the Handbook of Internal Medicine is published its popularity is rapidly gaining and has become an indispensable tool for clinicians and interns. Throughout these years we have received many requests for copies from other specialties and from doctors outside HA or even outside Hong Kong. However the purpose of this handbook is mainly for internal use as a quick reference. We have no intention to turn it into a formal guideline for internal medicine.

Again this new edition includes update guidelines on the major diseases. There is a new chapter on Medical Oncology dealing with emergency conditions encountered in this field. I would like to thank every one in the Editorial Board and all the specialists who have reviewed and update the various sections. Without their effort this handbook would not have been materialized. It represents a joint effort from our large family of physicians and I hope this spirit of fraternity can guide us to move ahead in development of our specialty.



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### ***Acknowledgement***



# Cardiology



## CARDIOPULMONARY RESUSCITATION (CPR)

1. **Determine unresponsiveness**
2. **Call for Help, Call for Defibrillator**
3. **Wear PPE:** N95/ surgical mask, gown, +/- (gloves, goggles, face shield for high risk patients)

**Primary CDAB Survey (Initiate chest compression before ventilation;** Ref: Field JM et al. Circulation 2010;122[Suppl 3]:S640-656)

### C: Circulation Assessment

- Check carotid pulse for 5-10 s & assess other signs of circulation (breathing, coughing, or movement)
- Chest compressions  $\geq 100/\text{min}$
- CPR 30 compressions (depth  $\geq 2$  inches) to 2 breaths

### D: Defibrillate VF or VT as soon as identified

- Check pulse and leads
- Check all clear
- Deliver 360J for monophasic defibrillator, without lifting paddles successively if no response; or equivalent 200J for biphasic defibrillator, if defibrillation waveform is unknown

### A: Assess the Airway

- Clear airway obstruction/secretions
- Head tilt-chin lift or jaw-thrust
- Insert oropharyngeal airway

### B: Assess/Manage Breathing

- Ambubag + bacterial/viral filter + 100%O<sub>2</sub> @ 15L/min
- Plastic sheeting between mask and bag
- Seal face with mask tightly
- Give 2 rescue breaths, each lasting 2-4 s

**Secondary ABCD Survey****A: Place airway devices; intubation if skilled.**

- If not experienced in intubation, continue Ambubag and call for help

**B: Confirm & secure airway; maintain ventilation.**

- Primary confirmation: 5-point auscultation.
- Secondary confirmation: End-tidal CO<sub>2</sub> detectors, oesophageal detector devices.

**C: Intravenous access; use monitor to identify rhythm.****D: Differential Diagnosis.****Common drugs used in resuscitation**

Adrenaline	1 mg (10 ml of 1:10,000 solution) <u>q3-5 min</u> iv
Vasopressin	40 IU ivi push
Lignocaine	1 mg/kg iv bolus, then 1-4 mg/min infusion
Amiodarone	In cardiac arrest due to pulseless VT or VF, 300 mg in 20 ml NS / D5 rapid infusion, further doses of 150 mg over 10 mins if required, followed by 1 mg/min infusion for 6 hrs & then 0.5 mg/min, to maximum total daily dose of 2.2 g
Atropine	1 mg iv push, repeat q3-5min to max dose of 0.04mg/kg
CaCl	5-10 ml 10% solution iv slow push for hyperkalaemia and CCB overdose
NaHCO <sub>3</sub>	1 mEq/kg initially (e.g. 50 ml 8.4% solution) in patients with hyperkalaemia
MgSO <sub>4</sub>	5-10 mmol iv in torsade de pointes

*Tracheal administration of Resuscitation Medications  
(If iv line cannot be promptly established)*

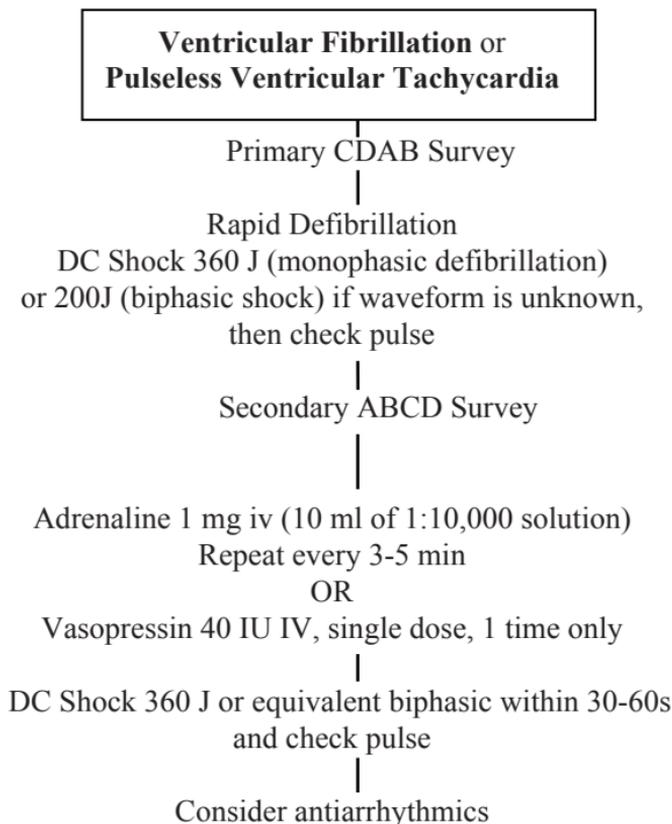
- Lignocaine, Atropine, Epinephrine, Narcan (**L-E-A-N**)
- Double dosage
- Dilute in 10 ml NS or water
- Put catheter beyond tip of ET tube
- Inject drug solution quickly down ET tube, followed by several quick insufflations
- Withhold chest compression shortly during these insufflations

***Post-resuscitation care:***

- Correct hypoxia with 100% oxygen
- Prevent hypercapnia by mechanical ventilation
- Consider maintenance antiarrhythmic drugs
- Treat hypotension with volume expander or vasopressor
- Treat seizure with anticonvulsant (diazepam or phenytoin)
- Maintain blood glucose within normal range
- Routine administration of  $\text{NaHCO}_3$  not necessary

## ARRHYTHMIAS

(I)



- Amiodarone 300 mg iv push, can consider a second dose of 150 mg iv (maximum total dose 2.2 g over 24 hr)
- Lignocaine 1-1.5 mg/kg iv push, can repeat in 3-5 minutes (maximum total dose 3 mg/kg)
- Procainamide 30 mg/min (maximum total dose 17 mg/kg)

(II)

**Pulseless Electrical Activity  
(Electromechanical Dissociation)**

Primary CDAB and Secondary ABCD

**Consider causes** (“6H’s and 6T’s) and give specific treatment

<b>Hypovolaemia</b> †	<b>Tablets</b> (drug overdose, accidents)
<b>Hypoxia</b> †	<b>Tamponade</b> , cardiac
<b>Hydrogen ion</b> (acidosis)	<b>Tension pneumothorax</b>
<b>Hyper / hypokalemia</b>	<b>Thrombosis</b> , coronary (ACS)
<b>Hypothermia</b>	<b>Thrombosis</b> , pulmonary (Embolism)
<b>Hyper/hypoglycaemia</b>	<b>Trauma</b>

Adrenaline 1 mg iv (10 ml of 1:10,000 solution)  
Repeat every 3-5 min

† Most common causes of PEA

(III)

**Asystole**

Primary CDAB and Secondary ABCD  
Consider causes\*

Transcutaneous pacing

If considered, perform immediately

**NOT** for routine use

Adrenaline 1 mg iv (10 ml of 1:10,000 solution)

Repeat every 3-5 min

Consider to stop CPR for arrest victims who, despite successful deployment of advanced interventions, continue in asystole for more than 10 minutes with no potential reversible cause

\* Consider causes: hypoxia, hyperkalemia, hypokalemia, acidosis, drug overdose, hypothermia

(IV)

**Tachycardia**

- |   |                             |
|---|-----------------------------|
| - Assess ABCs & vital signs                   | - Review Hx and perform P/E |
| - Secure airway and iv line                   | - Perform 12-lead ECG       |
| - Administer oxygen                           | - Portable CXR              |
| - Attach BP, rhythm & O <sub>2</sub> Monitors |                             |

Unstable?

(chest pain, SOB, decreased conscious state, low BP, shock, pulmonary congestion, congestive heart failure, acute MI)

*Yes*

Immediate Synchronized  
DC cardioversion 100J/200J/300J/360J  
(except sinus tachycardia)

*No or  
Borderline*

❶ Atrial fibrillation  
Atrial flutter

❷ Regular Narrow  
Complex Tachycardia

❸ Regular Wide  
Complex Tachycardia

- For immediate cardioversion

- Consider sedation
- Note possible need to resynchronize after each cardioversion
- If delays in synchronization, go immediately to unsynchronized shocks

## ① Atrial fibrillation / Atrial flutter

### 1. Correct underlying causes

- hypoxia, electrolyte disorders, sepsis, thyrotoxicosis etc

### 2. Control of ventricular rate

- Digoxin\* 0.25-0.5 mg iv over 5-10 min or  
in 50 ml NS/D5 infuse over 10-20 min or  
0.25 mg po, then q8h po for 3 more doses  
(total loading of 1 mg)  
Maintenance dose 0.125-0.25 mg daily  
(reduce dose in elderly and CRF)
- Diltiazem\* 10-15 mg iv over 5-10 min, then  
iv infusion 5-15 µg/kg/min
- Verapamil\* 5 mg iv slowly, can repeat once in 10 min  
Risk of hypotension, check BP before 2nd dose
- Metoprolol\* 5 mg iv stat, can repeat every 2 min up to  
15 mg
- Amiodarone 150 mg/100 ml D5 iv over 1 hr, then 150 mg in  
100 ml D5, infuse over 4-8 hr  
Maintenance infusion 600-1200 mg/day.

\* Contraindicated in WPW Sx

- In AF complicating acute illness e.g. thyrotoxicosis,  
β-blockers and verapamil may be more effective than  
digoxin
- For impaired cardiac function (EF < 40%, CHF), use  
digoxin or amiodarone

### 3. Anticoagulation

Heparin to maintain aPTT 1.5-2 times control or LWMH

Warfarin to maintain PT 2-3 times control (depends on general  
condition and compliance of patient and underlying heart disease)

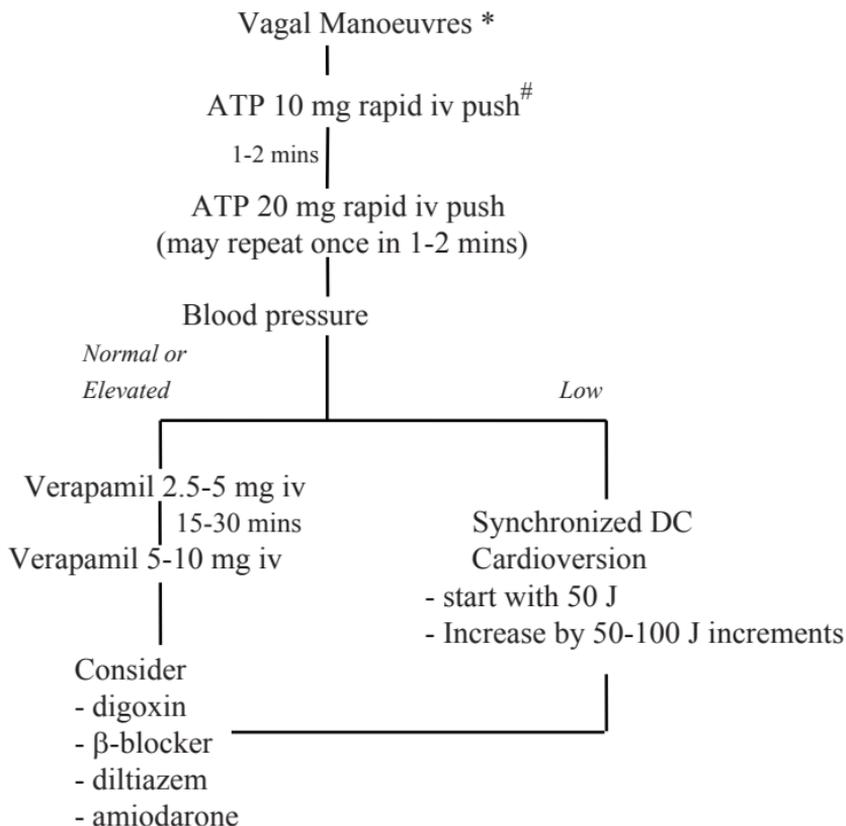
#### 4. *Termination of Arrhythmia*

- For persistent AF (> 2 days), anticoagulate for 3 weeks before conversion and continue for 4 weeks after (delayed cardioversion approach)
- Pharmacological conversion :
  - Procainamide 15 mg/kg iv loading at 20 mg/min (max 1 g), then 2-6 mg/min iv maintenance, or 250 mg po q4h
  - Amiodarone same dose as in C8
- Synchronized DC cardioversion
  - Atrial fibrillation 100-200J and up
  - Atrial flutter 50-100J and up

#### 5. *Prevention of Recurrence*

- Class Ia, Ic, sotalol or amiodarone.

## ② Stable Regular Narrow Complex Tachycardia



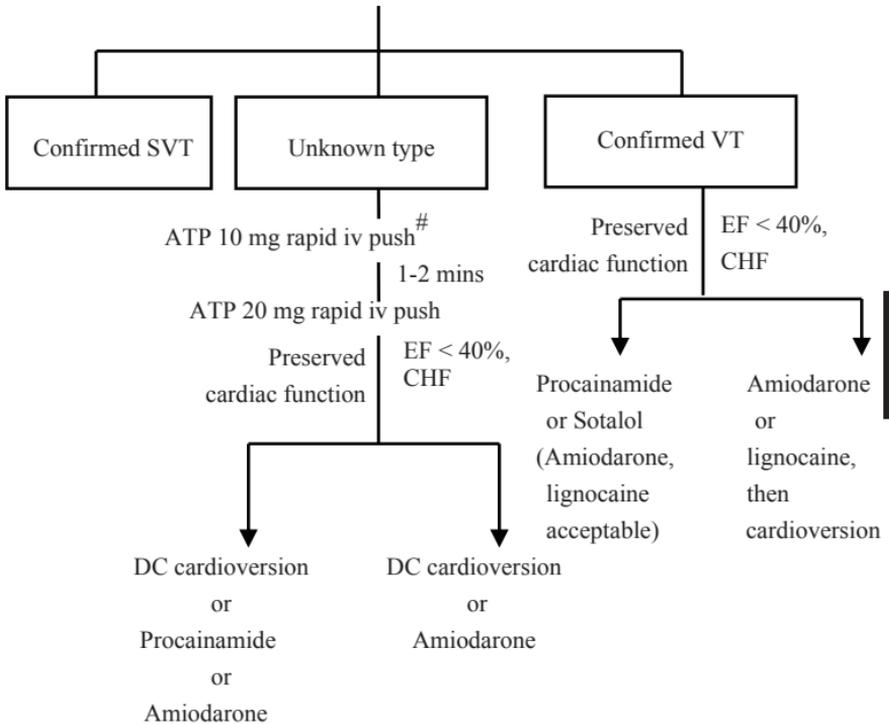
\* Carotid sinus pressure is C/I in patients with carotid bruits.  
Avoid ice water immersion in patients with IHD.

# contraindicated in asthma & warn patient of transient flushing and chest discomfort

③

**Stable Wide Complex Tachycardia**

Attempt to establish a specific diagnosis



Cardiology

**Dosing:**

- Amiodarone 150 mg IV over 10 mins, repeat 150 mg IV over 10 mins if needed. Then infuse 600-1200 mg/d. (Max 2.2 g in 24 hours)
- Procainamide infusion 20-30 mg/min till max. total 17 mg/kg or hypotension
- Lignocaine 0.5-0.75 mg/kg IV push and repeat every 5 to 10 mins, then infuse 1 to 4 mg/min (Max. total dose 3 mg/kg)

# contraindicated in asthma & warn patient of transient flushing and chest discomfort

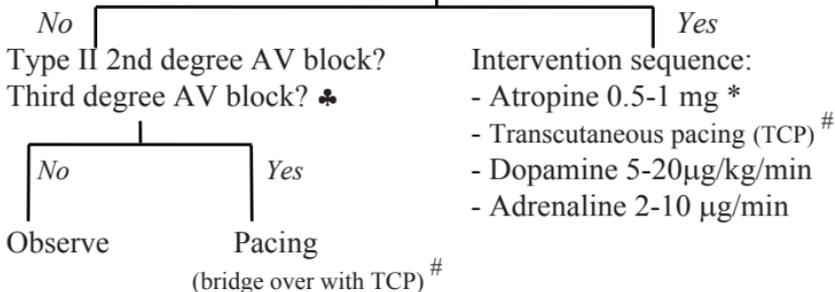
(V)

**Bradycardia**

- Assess ABCs & vital signs	- Review Hx and perform P/E
- Secure airway and iv line	- Perform 12-lead ECG
- Administer oxygen	- Portable CXR
- Attach BP, rhythm & O <sub>2</sub> Monitors	- Watch out for hyperkalaemia

Unstable?

(chest pain, SOB, decreased conscious state, low BP, shock, pulmonary congestion, congestive heart failure, acute MI)



- \* - Do not delay TCP while awaiting iv access to give atropine
- Atropine in repeat doses in 3-5 min (shorter in severe condition) up to a max of 3 mg or 0.04 mg/kg. Caution in AV block at or below His-Purkinje level (acute MI with third degree heart block and wide complex QRS; and for Mobitz type II heart block)

♣ Never treat third degree heart block plus ventricular escape with lignocaine

# Verify patient tolerance and mechanical capture. Analgesia and sedation prn.

## UNSTABLE ANGINA / NON-ST ELEVATION MI

Aims of Treatment: Relieve symptoms, monitor for complications, improve long-term prognosis

### Mx

1. Admit CCU for high risk cases\*.
2. Bed rest with continuous ECG monitoring
3. ECG stat and repeat at least daily for 3 days (more frequently in severe cases to look for evolution to MI).
4. Cardiac enzymes daily for 3 days. Troponin stat (can repeat 6-12 hours later if 1<sup>st</sup> Troponin is normal)
5. CXR, CBP, R/LFT, lipid profile (within 24 hours), aPTT, INR as baseline for heparin Rx.
6. Allay anxiety - Explain nature of disease to patient.
7. Morphine IV when symptoms are not immediately relieved by nitrate e.g. Morphine 2-5 mg iv (monitor BP).
8. Correct any precipitating factors (anaemia, hypoxia, tachyarrhythmia).
9. Stool softener & supplemental oxygen for respiratory distress.
10. Consult cardiologist to consider GP IIb/IIIa antagonist, IABP, urgent coronary angiogram/revascularisation if refractory to medical therapy

### Specific drug treatment:

#### Antithrombotic Therapy

- a. *Aspirin* (soluble or chewed) 160 mg stat, then 75 to 325 mg daily
- b. Clopidogrel 300mg stat, then 75mg daily if aspirin is contraindicated or combined with aspirin in high risk case
- c. Low-Molecular-Weight-Heparin e.g
  - Enoxaparin (Clexane) 1 mg/kg sc q12h
  - Nadroparin (Fraxiparine) sc 0.4 ml bd if <50 kgf BW,  
0.5 ml bd if 50-59 kgf BW, 0.6 ml bd if >60 kgf BW
  - Dalteparin (Fragmin) 120 iμ/kg (max 10000 iμ) sc q12h

## Anti-Ischemic Therapy

### a. *Nitrates*

- reduces preload by venous or capacitance vessel dilatation.
  - Contraindicated if sildenafil taken in preceding 24 hours.
- Sublingual TNG 1 tab/puff Q5min for 3 doses for patients with ongoing ischemic discomfort

IV TNG indicated in the first 48 h for persistent ischemia, heart failure, or hypertension

NitroPhol 0.5-1mg/hr (max 8-10 mg/min)

Isosorbide dinitrate (Isoket) 2-10 mg/hr

- Begin with lowest dose, step up till pain is relieved

- Watch BP/P; keep SBP > 100 mmHg

- Isosorbide dinitrate - Isordil 10-30 mg tds
- Isosorbide mononitrate - Elantan 20-40 mg bd or Imdur 60-120 mg daily

### b. $\beta$ -blockers (if not contraindicated)

- reduce HR and BP (titrate to HR<60)
- Metoprolol (Betaloc) 25-100 mg bd
- Atenolol (Tenormin) 50-100 mg daily

### c. *Calcium Antagonists* (when $\beta$ -blocker is contraindicated in the absence of clinically significant LV dysfunction)

- Diltiazem (Herbesser) 30-60 mg tds
- Verapamil 40-120 mg tds

## Other Therapies

### a. *Hydroxymethyl glutaryl-coenzyme A reductase inhibitor (statin)*

- Should be given regardless of baseline LDL-C level in the absence of contraindications.

### b. *Angiotensin- converting enzyme inhibitor (ACEI)*

- Should be administered within the first 24 hours in the absence of hypotension or contraindications.

- Angiotensin receptor blocker should be used if patient is intolerant of ACEI

**\*High risk features (Consider Early PCI)**

- Ongoing or recurrent rest pain
- Hypotension & APO
- Ventricular arrhythmia
- ST segment changes  $\geq 0.1$  mV; new bundle branch block
- Elevated Troponin  $> 0.1$  mg/mL
- High Risk Score (TIMI, GRACE)

## ACUTE ST ELEVATION MYOCARDIAL INFARCTION

**Ix** - Serial ECG for 3 days

- Repeat more frequently if only subtle change on 1<sup>st</sup> ECG; or when patient complains of chest pain

<u>Area of Infarct</u>	<u>Leads with ECG changes</u>
inferior	II, III, aVF
lateral	I, aVL, V <sub>6</sub>
anteroseptal	V <sub>1</sub> , V <sub>2</sub> , V <sub>3</sub>
anterolateral	V <sub>4</sub> , V <sub>5</sub> , V <sub>6</sub>
anterior	V <sub>1</sub> - V <sub>6</sub>
right ventricular	V <sub>3R</sub> , V <sub>4R</sub>

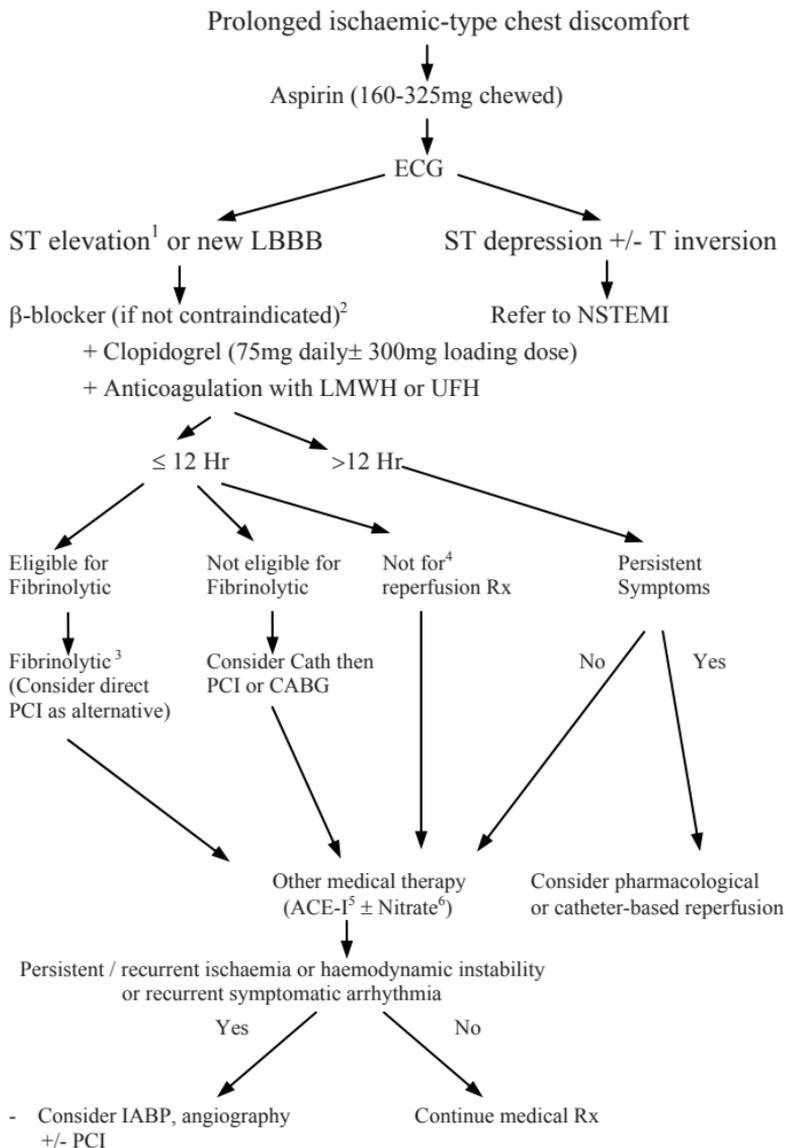
- Serial cardiac injury markers\* for 3 days
- CXR, CBP, R/LFT, lipid profile (within 24 hours)
- aPTT, INR as baseline for thrombolytic Rx

### **General Mx**

- Arrange CCU bed
- Close monitoring: BP/P, I/O q1h, cardiac monitor
- Complete bed rest (for 12-24 hours if uncomplicated)
- O<sub>2</sub> by nasal prongs if hypoxic or in cardiac failure; routine O<sub>2</sub> in the first 6 hours
- Allay anxiety by explanation/sedation (e.g. diazepam 2-5 mg po tds)
- Stool softener
- Adequate analgesics prn e.g. morphine 2-5 mg iv (monitor BP & RR)

\* CK-MB; troponin; myoglobin (depending on availability)

## Specific Rx Protocol



- <sup>1</sup> At least 1mm in 2 or more contiguous leads
- <sup>2</sup> e.g. Metoprolol 25 mg bd orally.  
Alternatively, metoprolol 5 mg iv slowly stat for 3 doses at 5 min intervals (Observe BP/P after each bolus, discontinue if pulse < 60/min or systolic BP < 100 mmHg).
- <sup>3</sup> See C22-23 under “Fibrinolytic therapy”
- <sup>4</sup> Not for reperfusion Rx if e.g. too old, poor premorbid state
- <sup>5</sup> Starting within the first 24 hrs, esp. for anterior infarction or clinical heart failure. Thereafter, prescribe for those with clinical heart failure or EF < 40%, (starting doses of ACEI: e.g. acertil 1 mg daily; ramipril 1.25 mg daily; lisinopril 2.5 mg daily)
- <sup>6</sup> Prescribe if persistent chest pain / heart failure / hypertension e.g. iv isosorbide dinitrate (Nitropohl/Isoket) 2-10 mg/h. (Titrate dosage until pain is relieved; monitor BP/P, watch out for hypotension, bradycardia or excessive tachycardia).  
C/I if sildenafil taken in past 24 hours

### **Detection and Treatment of Complications**

#### a. Arrhythmia

- Symptomatic sinus bradycardia
  - atropine 0.3-0.6 mg iv bolus
  - pacing if unresponsive to atropine
- AV Block :
  - 1st degree and Mobitz type I 2<sup>nd</sup> degree: Conservative
  - Mobitz Type II 2<sup>nd</sup> degree or 3<sup>rd</sup> degree: Pacing  
(inferior MI, if narrow-QRS escape rhythm & adequate rate, conservative Rx under careful monitoring is an alternative)
  - (Other indications for temporary pacing:
    - Bifascicular block + 1st degree AV block
    - Alternating BBB or RBBB + alternating LAFB/LPFB)

- Tachyarrhythmia  
(Always consider cardioversion first if severe haemodynamic compromise or intractable ischaemia)

*PSVT*

- ATP 10-20 mg iv bolus
- Verapamil 5-15 mg iv slowly (C/I if BP low or on beta-blocker), beware of post-conversion angina

*Atrial flutter/fibrillation*

- Digoxin 0.25 mg iv/po stat, then 0.25 mg po q8H for 2 more doses as loading, maintenance 0.0625-0.25 mg daily
- Diltiazem 10-15 mg iv over 5-10 mins, then 5-15 µg/kg/min
- Amiodarone 5 mg/kg iv infusion over 60 mins as loading, maintenance 600-900 mg infusion/24 h

*Wide Complex Tachycardia (VT or aberrant conduction)*

Treat as VT until proven otherwise

Stable sustained monomorphic VT :

- Amiodarone 150 mg infused over 10 minutes, repeat 150 mg iv over 10 mins if needed, then 600-1200 mg infusion over 24h
- Lignocaine 50-100 mg iv bolus, then 1-4 mg/min infusion
- Procainamide 20-30 mg/min loading, then 1-4 mg/min infusion up to 12-17 mg/kg
- Synchronized cardioversion starting with 100 J

Sustained polymorphic VT :

- Unsynchronized cardioversion starting with 200 J

b. Pump Failure

*RV Dysfunction*

- Set Swan-Ganz catheter to monitor PCWP. If low or normal, volume expansion with colloids or crystalloids

*LV Dysfunction*

- Vasodilators (esp. ACEI) if BP OK (+/- PCWP monitoring)
- Inotropic agents

- Preferably via a central vein
  - Titrate dose against BP/P & clinical state every 15 mins initially, then hourly if stable
  - Start with dopamine 2.5  $\mu\text{g}/\text{kg}/\text{min}$  if SBP  $\leq$  90 mmHg, increase by increments of 0.5  $\mu\text{g}/\text{kg}/\text{min}$
  - Consider dobutamine 5-15  $\mu\text{g}/\text{kg}/\text{min}$  when high dose dopamine needed
  - IABP, with a view for catheterization  $\pm$  revascularization
- c. Mechanical Complications
- VSD, mitral regurgitation
  - Mx depends on clinical and haemodynamic status
    - Observe if stable (repair later)
    - Emergency cardiac catheterization and repair if unstable (IABP for interim support)
- d. Pericarditis
- High dose aspirin
  - NSAID e.g. indomethacin 25-50 mg tds for 1-2 days
  - Others: colchicines, acetaminophen

### After Care (For uncomplicated MI)

- Advise on risk factor modification and treatment (Smoking, HT, DM, hyperlipidaemia, exercise)
- Stress test (Pre-discharge or symptom limited stress 2-3 wks post MI)
- Angiogram if + ve stress test or post-infarct angina or other high-risk clinical features
- *Drugs for Secondary Prevention of MI*
  - $\beta$ -blocker : Metoprolol 25-100 mg bd
  - Aspirin : 75-325 mg daily
  - ACEI (esp for large anterior MI, recurrent MI, impaired LV systolic function or CHF) :  
e.g. Lisinopril 5-20 mg daily; Ramipril 2.5-10 mg daily;  
Acertil 2-8 mg daily

- Angiotensin receptor blocker should be used in patients intolerant of ACEI and have heart failure or  $LVEF \leq 40\%$  or hypertension
- Aldosterone blocker should be used in patients without significant renal dysfunction or hyperkalaemia and who are already on therapeutic doses of ACEI and beta-blocker, with  $LVEF \leq 40\%$  + diabetes or heart failure
- Statin should be used in patients with baseline  $LDL-C \geq 100\text{mg/dL}$ .

**Fibrinolytic Therapy****Contraindications**

Absolute: - Previous hemorrhagic stroke at any time, other strokes or CVA within 3 months  
 - Known malignant intracranial neoplasm  
 - Known structural cerebrovascular lesion (e.g. AV malformation)  
 - Active internal bleeding (does not include menses)  
 - Suspected aortic dissection

Relative: - Severe uncontrolled hypertension on presentation (blood pressure > 180/110 mm Hg)<sup>†</sup>  
 - History of prior cerebrovascular accident or known intracerebral pathology not covered in contraindications  
 - Traumatic or prolonged (>10min) CPR  
 - Current use of anticoagulants in therapeutic doses; known bleeding diathesis  
 - Recent trauma/major surgery (within 2-4 wks), including head trauma  
 - Noncompressible vascular punctures  
 - Recent (within 2-4 wks) internal bleeding  
 - For streptokinase: prior exposure (>5days ago) or prior allergic reaction  
 - Pregnancy  
 - Active peptic ulcer

<sup>†</sup> Could be an absolute contraindication in low-risk patients with myocardial infarction.

**Administration**

- Streptokinase 1.5 megaunits in 100 ml NS, infuse iv over 1 hr
- Soluble Aspirin 80-300 mg daily immediately (if not yet given after admission)

If hx of recent streptococcal infection or streptokinase Rx in > 5 days ago, may use

- tPA\* 15 mg iv bolus, then 0.75 mg/kg (max 50 mg) in 30 mins, then 0.5 mg/kg (max 35 mg) over 1 hr or
- TNK-tPA iv over 10 seconds, 6ml (<60 kgf), 7ml (60-69 kgf), 8ml (70-79 kgf), 9 ml (80-89 kgf), 10ml (>90 kgf)
  - \* tPA to be followed by LMWH or unfractionated heparin (5,000 units iv bolus, then 500-1000 units/hr infusion for 48 hrs to keep aPTT 1.5-2.5 x control)

### **Monitoring**

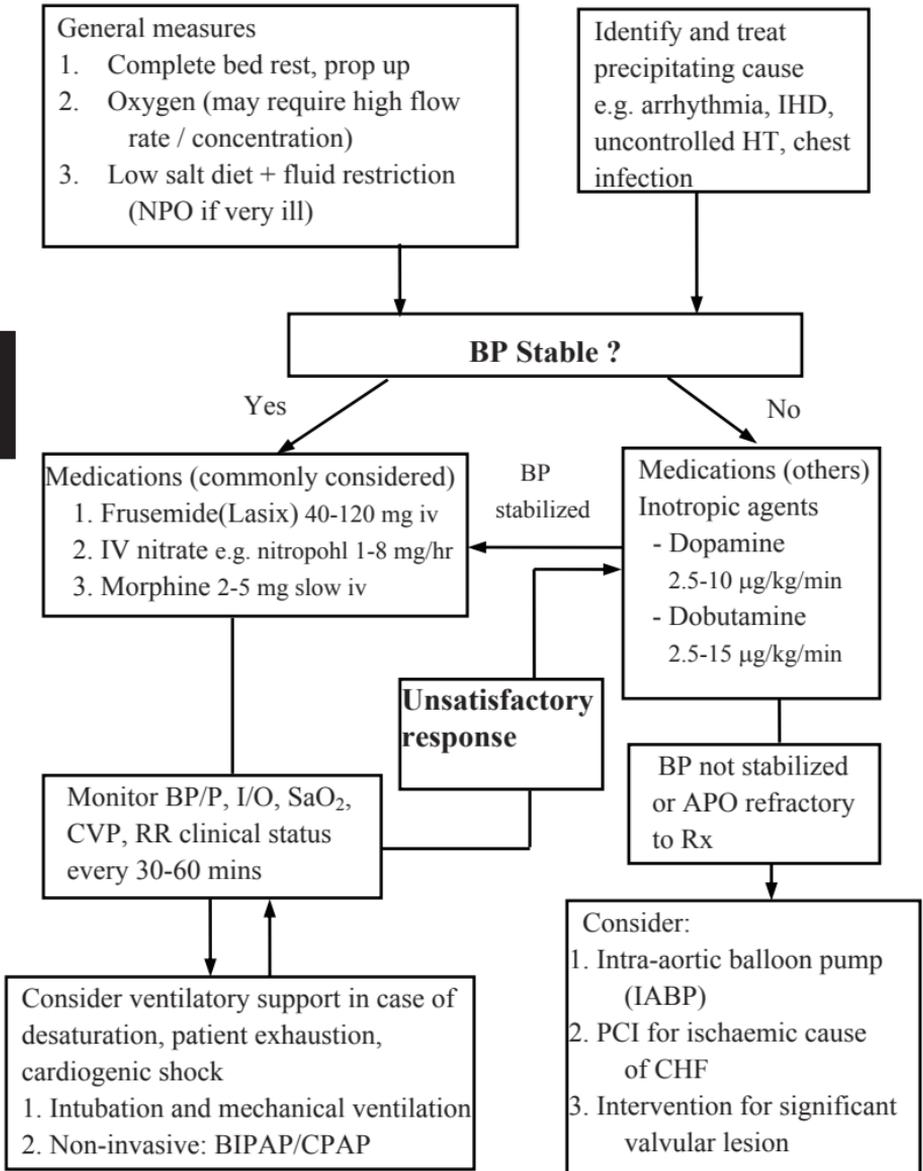
- Use iv catheter with obturator in contralateral arm for blood taking
- Pre-Rx: Full-lead ECG, INR, aPTT, cardiac enzymes
- Repeat ECG
  1. when new rhythm detected and
  2. when pain subsided
- Monitor BP closely and watch out for bleeding
- Avoid percutaneous puncture and IMI
- If hypotension develops during infusion
  - withhold infusion
  - check for cause (Rx-related\* vs cardiogenic)
    - \* fluid replacement; resume infusion at ½ rate

### **Signs of Reperfusion**

- chest pain subsides
- early CPK peak
- accelerated nodal or idioventricular rhythm
- normalization of ST segment / heart block

## ACUTE PULMONARY OEDEMA

Acute Management :



## HYPERTENSIVE CRISIS

- *Malignant* BP  $\geq$  220/120 mmHg + Grade III/IV fundal changes
- *Emergency* Malignant or severe HT + ICH, dissecting aneurysm, APO, encephalopathy, pheochromocytoma crisis, eclampsia (end organ damage due to HT versus risk of organ hypoperfusion due to rapid BP drop  
*Need Immediate reduction of BP to target levels*  
 (initial phase drop in BP by 20-25% of baseline)
- *Urgency*
  - Malignant HT without acute target organ damage
  - HT associated with bleeding (post-surgery, severe epistaxis, retinal haemorrhage, CVA etc.)
  - Severe HT + pregnancy / AMI / unstable angina
  - Catecholamine excess or sympathomimetic overdose (rebound after withdrawal of clonidine / methyldopa; LSD, cocaine overdose; interactions with MAOI)*BP reduction within 12-24 hours to target levels*

### Mx

1. Always recheck BP yourself at least twice
2. Look for target organ damage (neurological, cardiac)
3. Complete bed rest, low salt diet (NPO in HT emergency)
4. BP/P q1h or more frequently, monitor I/O (*Close monitoring in CCU/ICU with intra-arterial line in HT emergency*)
5. Check CBP, R/LFT, cardiac enzymes, aPTT/PT, CXR, ECG, urine x RBC and albumin
6. Aim: ***Controlled reduction (Rapid drop may ppt CVA / MI)***

	<u>Target BP (mmHg)</u>
Chronic HT, elderly, acute CVA	170-180 / 100
Previously normotensive, post cardiac/vascular surgery	140 / 80
Acute aortic dissection	100-120 SBP

### 7. Hypertensive urgency

- Use oral route, BP/P q15 mins for 60 mins
- Patients already on antiHT, reinstitute previous Rx
- No previous Px or failure of control despite reinstituting Rx for 4-6 hrs:

Metoprolol 50-200 mg bd / Labetalol 200 mg po stat, then 200 mg tds

Captopril 12.5-25 mg po stat, then tds po (if phaeo suspected)

Long acting Calcium antagonists (Isradipine 5mg/Felodipine 5mg)

If not volume depleted, lasix 20mg or higher in renal insufficiency

- Aim: Decrease BP to 160/110 over several hours

*(Sublingual nifedipine may precipitate ischaemic insult due to rapid drop of BP)*

### 8. Malignant HT or Hypertensive emergency

- Labetalol 20 mg iv over 2 mins. Rept 40 mg iv bolus if uncontrolled by 15 mins, then 0.5-2 mg/min infusion in D5 (max 300 mg/d), followed by 100-400 mg po bd
- Na Nitroprusside 0.25-10 µg/kg/min iv infusion (50 mg in 100 ml D5 = 500 µg/ml, start with 10 ml/hr and titrate to *desired BP*)

Check BP every 2 mins till stable, then every 30 mins

Protect from light by wrapping. Discard after every 12 hrs.

Esp good for acute LV failure, rapid onset of action.

Do not give in pregnancy or for > 48 hrs (risk of thiocyanide intoxication)

- Hydralazine 5-10 mg slow iv over 20 mins, repeat q 30 mins or iv infusion at 200-300 µg/min and titrate, then 10-100 mg po qid (avoid in AMI, dissecting aneurysm)
- Phentolamine 5-10 mg iv bolus, repeat 10-20 mins prn (for catecholamine crisis)

### 9. Notes on specific clinical conditions

- APO -Nitroprusside/nitroglycerin + loop diuretic, avoid diazoxide/hydralazine (increase cardiac work) or Labetalol & Beta-blocker in LV dysfunction
- Angina pectoris or AMI - Nitroglycerin, nitroprusside, labetalol, calcium blocker  
(Diazoxide or hydralazine contraindicated)
- Increase in sympathetic activity (clonidine withdrawal, pheochromocytoma, autonomic dysfunction (GB Syndrome/post spinal cord injury), sympathomimetic drugs (phenylpropanolamine, cocaine, amphetamines, MAOI or phencyclidine + tyramine containing foods) → Phentolamine, labetalol or nitroprusside  
Beta-blocker is contraindicated (further rise in BP due to unopposed alpha-adrenergic vasoconstriction)
- Aortic dissection - aim: ↓systolic pressure to 100-120mmHg and ↓cardiac contractility, nitroprusside + labetalol / propanolol IV
- Pregnancy - IV hydralazine (pre-eclampsia or pre-existent HT), Nicardipine / labetalol , no Nitroprusside (cyanide intoxication) or ACEI

10. *Look for causes of HT crisis, e.g. renal artery stenosis*

## AORTIC DISSECTION

Suspect in patients with chest, back or abdominal pain and presence of unequal pulses (may be absent) or acute AR

Dx - CXR, ECG, CK, TnI or TnT  
 - Transthoracic (not sensitive) +/- Transoesophageal echo  
 - Urgent Dynamic CT scan, MRA & rarely aortogram

### Mx

1. NPO, complete bed rest, iv line
2. Oxygen 35-40% or 4-6 L/min
3. Analgesics, e.g. morphine iv 2-5 mg
4. Book CCU or ICU bed for intensive monitoring of BP/P (Arterial line on the arm with higher BP), ECG & I/O
5. Look for life-threatening complication – severe HT, cardiac tamponade, massive haemorrhage, severe AR, myocardial, CNS or renal ischaemia
6. Medical Management
  - To stabilize the dissection, prevent rupture, and minimize complication from dissection propagation
  - It should be initiated even before the results of confirmatory imaging studies available
  - Therapeutic goals: reduction of systolic blood pressure to 100-120mmHg (mean 60-75mmHg), and target heart rate of 60-70/min

Intravenous Labetalol  
 10mg ivi over 2 mins, followed by additional doses of 20-80mg every 10-15 mins (up to max total dose of 300mg)

Maintenance infusion: 2mg/min, and titrating up to 5-20mg/min.

Intravenous sodium nitroprusside

Starting dose 0.25  $\mu\text{g}/\text{kg}/\text{min}$ , increase every 2 mins by 10  $\mu\text{g}/\text{min}$ , max dose 8  $\mu\text{g}/\text{kg}/\text{min}$

- Diltiazem and verapamil are acceptable alternatives when beta-blockers are contraindicated (e.g. COAD)  
*(Avoid hydralazine or diazoxide as they produce reflex stimulation of ventricle and increase rate of rise of aortic pressure)*

7. Start oral treatment unless surgery is considered
8. Contact cardiothoracic surgeon for all proximal dissection and complicated distal dissection, e.g. shock, renal artery involvement, haemoperitoneum, limbs or visceral ischaemia, periaortic or mediastinal haematoma or haemoperitoneum (endovascular stent graft is an evolving technique in complicated type B dissection with high surgical risk). Intramural hematoma should be managed as a classical case of dissection.

## PULMONARY EMBOLISM

### Investigations

Clotting time, INR, aPTT, ABG, D-dimer

CXR (usu. normal, pleural effusion, focal oligoemia, peripheral wedge)

ECG (sinus tachycardia, S<sub>1</sub>Q<sub>3</sub>T<sub>3</sub>, RBBB, RAD, P pulmonale)

TTE +/- TEE; lower limb Doppler (up to 50% -ve in PE)

CT pulmonary angiography (CTPA) or Spiral CT scan (sensitivity 91%, specificity 78%)

Ventilation-Perfusion scan (if high probability: sensitivity 41%, specificity 97%)

### Treatment

1. Establish central venous access; oxygen 35-40% or 4-6 L/min.

2. Analgesics e.g. morphine iv 2-5 mg.

3. a) *Haemodynamically insignificant*

- Unfractionated heparin 5000 units iv bolus, then 500-1500 units/hr to keep aPTT 1.5-2.5X control or

- Fraxiparine 0.4 ml sc q12h or enoxaparin 1 mg/kg q12h

- Start warfarin on Day 2 to 3: - 5 mg daily for 2 days, then 2 mg daily on 3<sup>rd</sup> day, adjust dose to keep INR 1.5-2.5 x control. Discontinue heparin on Day 7-10.

b) *Haemodynamically significant or evidence of dilated RV or dysfunction (no C/I to thrombolytic)*

- Book ICU/CCU,

- Streptokinase 0.25 megaunit iv over 30 mins, then 0.1 megaunit/hr for 24 hrs; or r-tPA 100 mg iv over 2 hours followed by heparin infusion 500-1500 units/hr to keep aPTT 1.5-2.5 x control

- Consider surgical embolectomy if condition continues to deteriorate, or IVC filter if PE occurred while on warfarin or recurrent PE, mechanical ventilation in profound hypoxic patient.

**Additional notes from Clinical Oncology:**

For PE in cancer patients, the duration of long term anticoagulation, if not contraindicated, is at least 3 to 6 months AND until the cancer resolved. LMWH is preferred to warfarin in malignancy-related thrombosis for lower rate of recurrent thromboembolism. Both have similar bleeding risks.

## CARDIAC TAMPONADE

### Common causes:

- Neoplastic
- Pericarditis (infective or non-infective)
- Uraemia
- Cardiac instrumentation / trauma
- Acute pericarditis treated with anticoagulants

**Diagnosis:** - High index of suspicion (in acute case as little as 200ml of effusion can result in tamponade)

### Signs & symptoms:

- Tachypnoea, tachycardia, small pulse volume, pulsus paradoxus
- Raised JVP with prominent x descent, Kussmaul's sign
- Absent apex impulse, faint heart sound, hypotension, clear chest

### Investigation:

1. ECG: Low voltage, tachycardia, electrical alternans
2. CXR: enlarged heart silhouette (when >250ml), clear lung fields
3. Echo: RA, RV or LA collapse, distended IVC, tricuspid flow increases & mitral flow decreases during inspiration

### Management:

1. Expand intravascular volume - D5 or NS or plasma, full rate if in shock
2. Pericardiocentesis with echo guidance – apical or subcostal approach, risk of damaging epicardial coronary artery or cardiac perforation
3. Open drainage under LA/GA
  - permit pericardial biopsy  
(Watch out for recurrent tamponade due to catheter blockage or reaccumulation)

*Treating tamponade as heart failure with diuretics, ACEI and vasodilators can be lethal!*

**Additional notes from Clinical Oncology:**

For patients with neoplastic pericardial effusion resulting in cardiac tamponade stabilized by urgent pericardial drainage, please consult oncologist to determine whether patient would benefit from surgical pericardiotomy (pericardial window) or pericardiectomy and to plan the subsequent oncological intervention for underlying disease control.

## ANTIBIOTIC PROPHYLAXIS FOR INFECTIVE ENDOCARDITIS

1. Procedures to dental, oral, respiratory tract or infected skin/skin structure, musculoskeletal tissue in patients at highest risk or adverse outcome in case infective endocarditis developed
  - a) Amoxicillin 2 grams po 1 hr before or
  - b) Ampicillin 2 grams im/iv within 30 mins before or
  - c) # Clindamycin 600 mg or Cephalexin 2 grams or Azithromycin/Clarithromycin 500 mg po 1 hr before or
  - d) # Clindamycin 600 mg im/iv or Cefazolin 1 gram im/iv within 30 mins before procedure.
2. Genitourinary/Gastrointestinal Procedure
  - Antibiotic prophylaxis solely to prevent infective endocarditis is not recommended for GU or GI tract procedures.
  - Antibiotic treatment to eradicate enterococcal infection or colonization is indicated in high risk patients for infective endocarditis undergoing GU or GI procedure.
  - # Allergic to ampicillin/amoxicillin

### High risk category:

- Prosthetic valves
- Previous infective endocarditis
- Cardiac transplant patients with valvulopathy
- Unrepaired cyanotic CHD, including palliative shunts and conduits
- Completely repaired CHD with prosthetic material or device, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure†
- Repaired CHD with residual defects at the site or adjacent to the site of a prosthetic patch or prosthetic device (which inhibit endothelialization)

(Reference: Wilson W et al. Circulation 2007;116(15):1736-54)

## PERIOPERATIVE CARDIOVASCULAR EVALUATION FOR NON-CARDIAC SURGERY

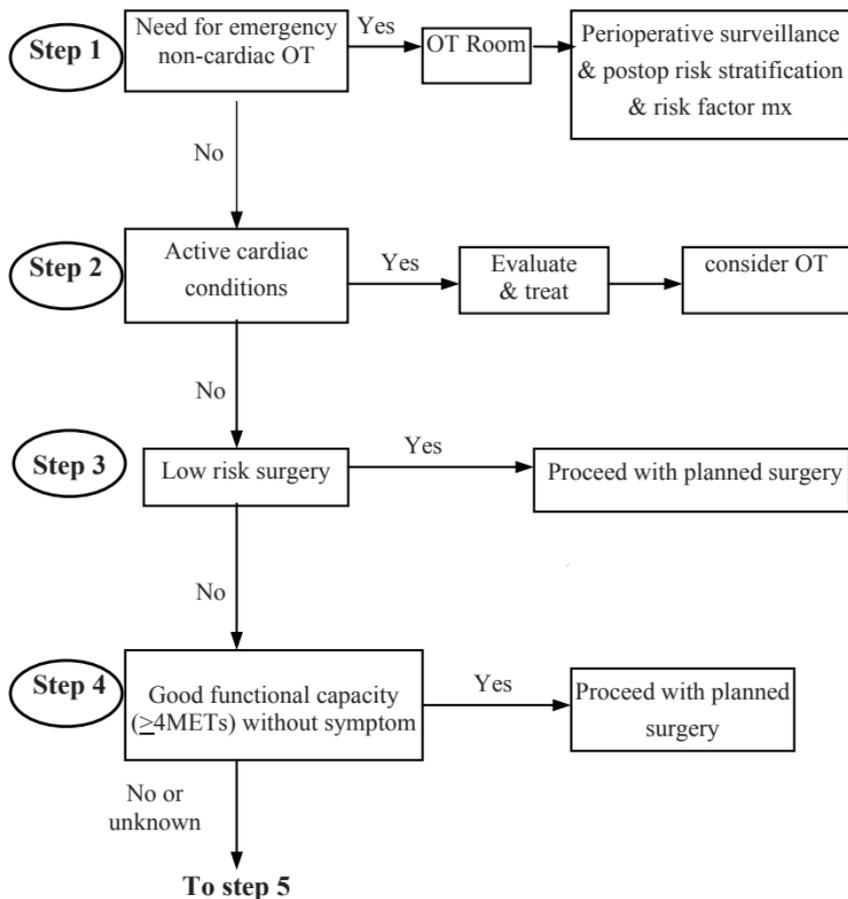
Basic evaluation by hx (assess functional capacity), P/E & review of ECG

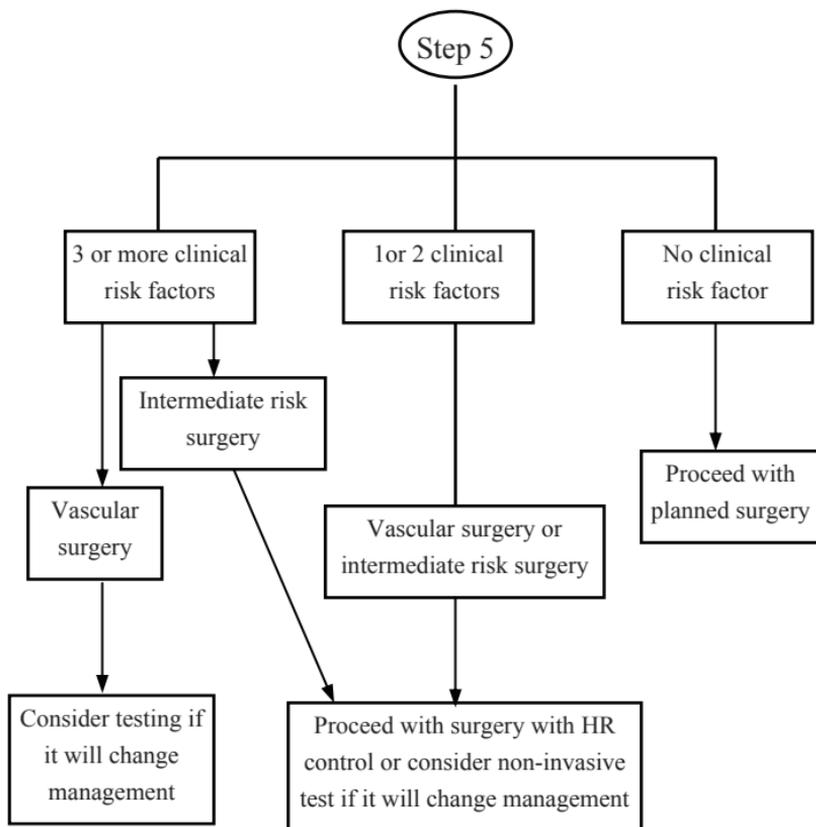
Clinical predictors of increased perioperative CV risk (MI, CHF, death)

- A) Active cardiac conditions mandate intensive Mx (may delay or cancel OT unless emergent)
- Unstable coronary syndrome – recent (<30 days) or AMI with evidence of important ischaemic risk by symptom or non-invasive test, Canadian class III or IV angina
  - Decompensated CHF.
  - Significant arrhythmias – high grade AV block, symptomatic ventricular arrhythmia in presence of underlying heart disease, supraventricular arrhythmia with uncontrolled ventricular rate.
  - Severe valvular disease e.g. severe AS or symptomatic MS.
- B) Clinical risk factors (enhanced risk, need careful assessment of current status)
- History of ischaemic heart disease
  - History of compensated or prior CHF
  - DM
  - Renal impairment
- C) Minor predictors (not proven to independently increase risk)
- Advanced age, abnormal ECG (LVH, LBBB, ST-T abn), rhythm other than sinus
  - Low functional capacity, hx of stroke, uncontrolled systemic HT

### Cardiac risk stratification for noncardiac surgical procedures

- A) high (risk >5%)
- emergent major OT, aortic & other major vascular, peripheral vascular
  - anticipated prolonged surgical procedures with large fluid shifts &/or blood loss.
- B) intermediate (risk 1-5%)
- carotid endarterectomy, head and neck intraperitoneal & intrathoracic
  - orthopaedic, prostatic
- C) low (risk <1%)
- endoscopic procedures, superficial procedure, cataract, breast

Stepwise approach to preoperative assessment



## Disease-specific approach

### 1) Hypertension

- Control of BP preoperatively reduces perioperative ischaemia
- Evaluate severity, chronicity of HT and exclude secondary HT
- Mild to mod. HT with no metabolic or CV abn. – no evidence that it is beneficial to delay surgery
- Anti-HT drug continued during perioperative period
- Avoid withdrawal of beta-blocker
- Severe HT (DBP >110 or SBP >180)  
elective surgery – for better control first  
urgent surgery - use rapid-acting drug to control (esp. beta-blocker)

### 2) Cardiomyopathy & heart failure

- Pre-op assessment of LV function to quantify severity of systolic and diastolic dysfunction (affect peri-op fluid Mx)
- HOCM avoid reduction of blood volume, decrease in systemic vascular resistance or decrease in venous capacitance, avoid catecholamines

### 3) Valvular heart disease

- Antibiotic prophylaxis
- AS - postpone elective noncardiac surgery (mortality risk around 10%) in severe & symptomatic AS. Need AVR or valvuloplasty
- AR - careful volume control and afterload reduction (vasodilators), avoid bradycardia
- MS - mild or mod → ensure control of HR, severe → consider PTMC or surgery before high risk surgery
- MR - afterload reduction & diuretic to stabilize haemodynamics before high risk surgery

### 4) Prosthetic valve

- Minimal invasive procedures – reduce INR to subtherapeutic range (e.g. INR <1.3), resume normal dose immediately following the procedure

- Assess risk & benefit of ↓anticoagulation Vs peri-op heparin (if both risk of bleeding on anticoagulation & risk of thromboembolism off anticoagulation are high)

#### 5) Arrhythmia

- Search for cardiopul. Ds., drug toxicity, metabolic derangement
- High grade AV block – pacing
- Intravent. conduction delays and no hx of advanced heart block or symptoms – rarely progress to complete heart block
- AF - if on warfarin, may discontinue for few days; give FFP if rapid reversal of drug effect is necessary
- Vent. arrhythmia  
Simple or complex PVC or Nonsustained VT – usu require no Rx except myocardial ischaemia or moderate to severe LV dysfunction is present  
Sustained or symptomatic VT – suppressed preoperatively with lignocaine, procainamide or amiodarone.

#### 6) Permanent pacemaker

- Determine underlying rhythm, interrogate devices to determine its threshold, settings and battery status
- If the pacemaker in rate-responsive mode → inactivated
- programmed to AOO, VOO or DOO mode prevents unwanted inhibition of pacing
- electrocautery should be avoided if possible; keep as far as possible from the pacemaker if used

#### 7) ICD or antitachycardia devices

- programmed “OFF” immediately before surgery & “ON” again post-op to prevent unwanted discharge
- for inappropriate therapy from ICD, suspend ICD function by placing a ring magnet on the device (may not work for all ICD devices)

VF/unstable VT – if inappropriate therapy from ICD & external cardioversion is required, paddles preferably >12cm from the device.



# Endocrinology



## DIABETIC KETOACIDOSIS (DKA)

Diagnostic criteria: Plasma glucose > 14 mmol/L, arterial pH < 7.3, plasma bicarbonate < 15 mmol/L, (high anion gap) and moderate ketonuria or ketonemia (or high beta-hydroxybutyrate BAHA.)

	Initial Hour	Subsequent Hours
Ix	Urine & Blood glucose Urine $\pm$ plasma ketones or BAHA  Na, K, P <sub>04</sub> , $\pm$ Mg, Anion gap (AG) Urea, Creatinine, Hb Arterial blood gas (ABG)  If indicated: CXR ECG Blood & urine culture and sensitivity Urine & serum osmolality PT, APTT	Hourly urine and blood glucose  Na, K, urea, AG ( till blood glucose <14 mmol/L  Repeat ABG if indicated (intensive monitoring of electrolytes and acid/base is crucial in the first 24-48 hours)  Repeat urine $\pm$ plasma ketones if indicated
Parameters to be monitored	Hourly BP/pulse, respiratory rate, conscious level, urine output, $\pm$ central venous pressure (CVP) 2-hourly temperature	
Ancillary Measures	Aspirate stomach if patient unconscious or vomiting (protect airway with cuffed endotracheal tube if necessary) Catheterize bladder and set CVP as indicated Give antibiotics if evidence of infection Treat hypotension and circulatory failure	

Rx	Initial Hours	Subsequent Hours
Hydration	1-2 litre 0.9% saline (NS)	1 litre/hour or 2 hours as appropriate When serum Na > 150 mmol/L, use 0.45% NS (modify in patients with impaired renal function). Fluid in first 12 hrs should not exceed 10% BW, watch for fluid overload in elderly. When blood glucose ≤ 14 mmol/L, change to D5
Insulin	Regular human insulin 0.15 U/kg as IV bolus, followed by infusion (preferably via insulin pump)	Regular human insulin iv infusion 0.1 U/kg/hr. Aim at decreasing plasma glucose by 3-4 mmol/L per hour, double insulin dose to achieve this rate of decrease in blood glucose if necessary. When BG ≤ 14 mmol/L, change to D5 and decrease dose of insulin to 0.05-0.1 U/kg/hr or give 5-10 units sc q4h, adjusting dose of insulin to maintain blood glucose between 8-12 mmol/L. ↓ monitoring to q2h-q4h Change to maintenance insulin when normal diet is resumed
K	10 - 20 mmol/hr	Continue 10-20 mmol/hr, change if - K < 4 mmol/L, ↑ to 30 mmol/hr - K < 3 mmol/L, ↑ to 40 mmol/hr - K > 5.5 mmol/L, stop K infusion - K > 5 mmol/L, ↓ to 8 mmol/hr Aim at maintaining serum K between 4-5 mmol/L
NaHCO <sub>3</sub>	If pH between 6.9-7.0, give 50 mmol NaHCO <sub>3</sub> in 1 hr. If pH < 6.9, give 100 mmol NaHCO <sub>3</sub> in 2 hrs. Recheck ABG after infusion, repeat every 2 hrs until pH > 7.0. Monitor serum K when giving NaHCO <sub>3</sub>	

## DIABETIC HYPEROSMOLAR HYPERGLYCEMIC STATES

Diagnostic criteria: blood glucose  $> 33$  mmol/L, arterial pH  $> 7.3$ , serum bicarbonate  $> 15$  mmol/L, effective serum osmolality ( $(2 \times \text{measured Na}) + \text{glucose}$ )  $> 320$  mOsm/kg  $\text{H}_2\text{O}$ , and mild ketonuria or ketonemia, usually in association with change in mental state.

1. Management principles are similar to DKA
2. Fluid replacement is of paramount importance as patient is usually very dehydrated
3. If plasma sodium is high, use hypotonic saline
4. Watch out for heart failure (CVP usually required for elderly)
5. Serum urea is the best prognostic factor
6. Insulin requirement is usually less than that for DKA, watch out for too rapid fall in blood glucose and overshoot hypoglycaemia

## PERIOPERATIVE MANAGEMENT OF DIABETES MELLITUS

### 1. *Pre-operative Preparation*

- a. Screen for DM complications, check standing/lying BP and resting pulse  $\pm$  autonomic function tests
- b. Glucose, HbA1c, electrolytes, RFT, HCO<sub>3</sub>, urinalysis, ECG
- c. Admit 1-2 days before major OT for DM control
- d. Aim at blood sugar of 5-11 mmol/L before operation
- e. Well controlled patients: omit insulin / OHA on day of OT (except chlorpropamide: stop for 3 days prior to OT)
- f. Poorly controlled patients:

- Stabilise with insulin-dextrose drip for emergency OT:

<u>Blood glucose (mmol/L)</u>	<u>Actrapid HM</u>	<u>Fluid</u>
< 20	1-2 U/hr	D5 q4-6h
> 20	4-10 U/hr	NS q2-4h

(Crude guide only, monitor hstix q1h and adjust insulin dose, aim to bring down glucose by 4-5 mmol/L/hr to within 5-10 mmol/L)

- \* May need to add K in insulin-dextrose drip
- \* Watch out for electrolyte disorders
- \* May use sc regular insulin for stabilisation if surgery elective

### 2. *Day of Operation*

- a. Schedule the case early in the morning
- b. Check hstix and blood sugar pre-op, if blood glucose > 11 mmol/L, postpone for a few hrs till better control
- c. *For major Surgery*
  - For patients on insulin or high dose of OHA, start dextrose-insulin-K (DKI) infusion at least 2 hrs pre-operatively:
    - 6-8 units Actrapid HM + 10-20 mmoles K in 500 ml D5, q4-6h (Flush iv line with 40 ml DKI solution before connecting to patient)
    - Monitor hstix q1h and adjust insulin, then q4h for 24 hrs (usual requirement 1-3U Actrapid/hour)

- Monitor K at 2-4 hours and adjust dose as required to maintain serum K within normal range
- Give any other fluid needed as dextrose-free solutions
- Patients with mild DM (diet alone or low dose of OHA)
  - D5 500 ml q4h alone (usually do not require insulin)
  - Monitor hstix and K as above, may need insulin and K

d. *For Minor Surgery*

- May continue usual OHA / diet on day of surgery
- Patients exposed to iodinated radiocontrast dyes, withhold metformin for 48 hours post-op and restart only after documentation of normal serum creatinine)
- For well-controlled patients on insulin:
  - Either:
    - Omit morning short-acting insulin
    - Give 2/3 of usual dose of intermediate-acting insulin am, and the remaining 1/3 when patient can eat
  - Or: (safer)
    - Use DK1 infusion till diet resumed. Then give 1/3 to 1/2 of usual intermediate-acting insulin
- For poorly-controlled patients on insulin:
  - Control first, use insulin or DK1 infusion for urgent OT

3. *Post-operative Care*

- a. ECG (serially for 3 days if patient is at high risk of IHD)
- b. Monitor electrolytes and glucose q6h
- c. Continue DK1 infusion till patient is clinically stable, then resume regular insulin (give first dose of sc insulin 30 minutes before disconnecting iv insulin) / OHA when patient can eat normally

## INSULIN THERAPY FOR DM CONTROL

(For emergency conditions, refer to pages E1-5)

Common insulin regimes for DM control (Ensure dietary compliance before dose adjustments):

1. For insulin-requiring type 2 DM
 

*(May consider combination therapy (Insulin + OHA) for patients with insulin reserve)*

  - a. Fasting Glycaemia alone
    - Give bed-time intermediate-acting insulin, start with 0.1- 0.2 U/kg
  - b. Daytime Glycaemia
    - Start with intermediate-acting insulin 0.2-0.5 U/kg 30 mins before breakfast (AM insulin)
    - Increase AM insulin according to FPG as follows:
      - Give 2 units insulin for every 2 mmol/L FPG > 7.0 mmol/L (change not more than 10 units each time)
      - When AM dose > 40 U, or if pre-dinner hypoglycaemia occurs, reduce AM dose by 20%; giving that 20% as intermediate-acting insulin before dinner (PM dose)
      - Increase PM insulin by 2 units for every 1 mmol/L of FPG above 7.0 mmol/L (change not more than 6 unit each time)
      - If FPG persistently high, check blood sugar at mid-night:
        - If hypoglycaemic, reduce pre-dinner dose by 5-10%
        - If hyperglycaemic, try moving pre-dinner dose to bedtime
      - Give pre-mixed insulin (twice daily) if still post-meal hyperglycemia.
      - Consult endocrinologist for insulin analogues in difficult cases with wide glucose fluctuation.

## 2. For type 1 DM

- Start with twice daily or multiple daily dose regimes
  - Consider use of Pens for convenience and ease of administration
  - Start with 0.5 U/kg/d. Adjust the following day according to hstix (tds and nocte)
- a.** For twice daily regimes:
- Give 2/3 or half of total daily insulin dose pre-breakfast and 1/3 or half pre-dinner in the evening (30 mins before meals) in the form of pre-mixed insulin
  - Advise on “multiple small meals” to avoid late afternoon and nocturnal hypoglycaemia
- b.** For multiple daily dose regimes:
- Give 40-60% total daily dose as intermediate-acting insulin before bed-time to satisfy basal needs. Adjust dose according to FPG
  - Give the remaining 40-60% as regular insulin, divided into 3 roughly equal doses pre-prandially (slightly higher AM dose to cover for Dawn Phenomenon, and slightly higher dose before main meal of the day)
- c.** For difficult cases, consult endocrinologist for considering insulin analogues or continuous subcutaneous insulin delivered via a pump

Sliding scale, if employed at all, must be used judiciously:

1. Hstix must be performed as scheduled
2. Dose adjustment should take into consideration factors that may affect patient’s insulin resistance
3. It should not be used for more than 1-2 days

## HYPOGLYCAEMIA

### 1. Treatment

- a. D50 40 cc iv stat, follow with D10 drip
- b. Glucagon 1 mg or oral glucose (after airway protection) if cannot establish iv line
- c. Monitor blood glucose and h'stix every 1-2 hrs till stable
- d. Duration of observation depends on R/LFT and type of insulin/drug (in cases of overdose)

### 2. Tests for Hypoglycaemia

- a. Prolonged OGTT
  - To document reactive hypoglycaemia, limited use
  - Overnight fast
  - Give 75 g anhydrous glucose po
  - Check plasma glucose and insulin at 60 min intervals for 5 hrs and when symptomatic
- b. Prolonged Fasting Test
  - Hospitalise patient, place near nurse station
  - Fast for maximum of 72 hrs
  - At 72 hrs, vigorous exercise for 20 mins (if still no hypoglycemia)
  - H'stix q4h and when symptomatic
  - Blood sugar, insulin, C-peptide at 0, 24, 48 and 72 hrs and when symptomatic or h'stix  $< 2.2$  mmol/L
  - Terminate test if blood sugar confirmed to be  $< 2.2$  mmol/L
  - Consider to check urine sulphonylureas ( $\pm$  other hypoglycemic agents) level in highly suspected cases.

## THYROID STORM

Note: The following regimen is also applicable to patients with uncontrolled thyrotoxicosis undergoing emergency operation.

1. Close monitoring: often need CVP, Swan-Ganz, cardiac monitor. ICU care if possible
2. Hyperthermia : paracetamol (not salicylate), physical cooling  
Dehydration : iv fluid (2-4 L/d)  
iv Glucose, iv vitamin (esp. thiamine)  
Supportive : O<sub>2</sub>, digoxin / diuretics if CHF/AF ± inotropes  
Treat precipitating factors and/or co-existing illness
3. Propylthiouracil 150-200 mg q4→6h po / via NG tube  
Hydrocortisone 200 mg stat iv then 100 mg q6-8h  
β-blockers (exclude asthma / COAD or frank CHF):  
Propranolol 40-80 mg q4-6h po/NG or Propranolol/Betaloc 1-10 mg iv over 15 min every several hrs  
If β-blockers contraindicated, consider diltiazem 60-120 mg q8h as alternative
4. 1 hour later, use iodide to block hormone release
  - a. 6-8 drops Lugol's solution / SSKI po q6-8h (0.2 g/d)
  - b. NaI continuous iv 0.5-1 g q12h *or*
  - c. Iodate (Oragrafin) po 1-3 g/d
5. Consider LiCO<sub>3</sub> 250 mg q6h to achieve Li level 0.6-1.0 mmol/L if ATD is contraindicated
6. Consider plasmapheresis and charcoal haemoperfusion for desperate cases

## MYXOEDEMA COMA

1. Treatment of precipitating causes
2. Correct fluid and electrolytes, correct hypoglycaemia with D10
3. NS 200 - 300 cc/hr  $\pm$  vasopressors
4. Maintain body temperature
5. T4 200-500  $\mu$ g po stat, then 100-200  $\mu$ g po or  
T3 20-40  $\mu$ g stat, then 20  $\mu$ g q8h po
6. Consider 5–20  $\mu$ g iv T3 twice daily if oral route not possible
7. Hydrocortisone 100 mg q6h iv

## PHAEOCHROMOCYTOMA

1. Phentolamine 0.5-5 mg iv, then 2-20  $\mu$ g/kg/hr infusion or Nitroprusside infusion 0.3-8  $\mu$ g/kg/min
2. Volume repletion
3. Propranolol if tachycardia (only after adequate  $\alpha$ -blockade)
4. Labetalol infusion at 1-2 mg/min (max 200 mg).

## ADDISONIAN CRISIS

1. Investigation:
  - a. RFT, electrolytes, glucose
  - b. Spot cortisol (during stress)  $\pm$  ACTH
  - c. Normal dose (250 $\mu$ g) short synacthen test (not required if already in stress)<sup>#</sup>
  - d. May consider low dose (1  $\mu$ g) short synacthen test if secondary hypocortisolism is suspected<sup>@</sup>
  
2. Treatment
 

Treat on clinical suspicion, do not wait for cortisol results

  - a. Hydrocortisone 100 mg iv stat, then q6h (may consider imi or iv infusion if no improvement)
  - b.  $\pm$  9 $\alpha$ -fludrocortisone 0.05-0.2 mg daily po, titrate to normalise K and BP
  - c. Correct electrolytes
  - d. 4 litres of D5/NS at 500-1000 ml/hr, then 200-300 ml/hr, watch out for fluid overload
  - e. May use dexamethasone 4 mg iv/im q12h (will not interfere with cortisol assays)

### 3. Relative Potencies of different Steroids\*

	<u>Glucocorticoid</u> <u>action</u>	<u>Mineralocorticoid</u> <u>action</u>	<u>Equivalent</u> <u>doses</u>
Cortisone	0.8	0.8	25 mg
Hydrocortisone	1	1	20 mg
Prednisone	4	0.6	5 mg
Prednisolone	4	0.6	5 mg
Methylprednisolone	5	0.5	4 mg
Dexamethasone	25-30	0	0.75 mg
Betamethasone	25-30	0	0.75 mg

\* Different in different tissues

## 4. Steroid cover for surgery / trauma

## - Indications:

- Any patient given suprphysiological doses of
- glucocorticoids (>prednisone 7.5 mg daily) for >2 wks in the past year
- Patients currently on steroids, whatever the dose
- Suspected adrenal or pituitary insufficiency

## a. Major Surgery

- Hydrocortisone 100 mg iv on call to OT room
- Hydrocortisone 50 mg iv in recovery room, then 50 mg iv q6h + K supplement for 24 hrs
- Post-operative course smooth: Decrease Hydrocortisone to 25 mg iv q6h on D2, then taper to maintenance dose over 3-4 days
- Post-operative course complicated by sepsis, hypotension etc: Maintain Hydrocortisone at 100 mg iv q6h till stable
- Ensure adequate fluids and monitor electrolytes

## b. Minor Surgery

- Hydrocortisone 100 mg iv one dose
- Do not interrupt maintenance therapy

## # Normal dose short synacthen test

250µg Synacthen iv/im as bolus

Blood for cortisol at 0, 30, 60 mins

Can perform at any time of the day

Normal : Peak cortisol level > 550 nmol/L

## @Low dose short synacthen test

1 µg Synacthen (mix 250 µg Synacthen into 1 pint NS and withdraw 2 ml) IV as bolus

Blood for cortisol at 0, 30 mins.

Can perform at any time of the day.

Normal: Peak cortisol level > 550 nmol/L

May need to confirm by other tests (insulin tolerance test or glucagon test) if borderline results

## ACUTE POST-OPERATIVE / POST-TRAUMATIC DIABETES INSIPIDUS

1. Remember possibility of a Triphasic pattern:
  - Phase I : Transient DI, duration hrs to days
  - Phase II : Antidiuresis, duration 2-14 days
  - Phase III : Return of DI (may be permanent)
  
2. Mx
  - a. Monitor I/O, BW, serum sodium and urine osmolarity closely (q4h initially, then daily)
  - b. Able to drink, thirst sensation intact and fully conscious: Oral hydration, allow patient to drink as thirst dictates
  - c. Impaired consciousness and thirst sensation:
    - Fluid replacement as D5 or ½ : ½ solution (Calculate volume needed by adding 12.5 ml/kg/d of insensible loss to volume of urine)
    - DDAVP 1-4 µg (0.5-1.0 ml) q12-24h sc/iv  
Allow some polyuria to return before next dose  
Give each successive dose only if urine volume > 200 ml/hr in successive hours
  
3. Stable cases  
Give oral DDAVP 100 - 200 µg bd to tds (tablet) or 60-120 µg bd to tds (lyophilisate) to maintain urine output of 1 – 2 litres/day

## PITUITARY APOPLEXY

1. Definite diagnosis depends on CT / MRI
2. Surgical decompression under steroid cover if
  - signs of increased intracranial pressure
  - change in conscious state
  - evidence of compression on neighbouring structures



# **Gastroenterology & Hepatology**



## ACUTE LIVER FAILURE

### Definition:

- Coagulopathy with INR > 1.5/ PT prolong 4-6 seconds
  - Any degree of mental alteration (encephalopathy)
  - In patient without pre-existing cirrhosis
  - With an illness of <26 week duration
- \*\* Wilson's disease/ vertically acquired HB/ AIH are included only if their recognition < 26 weeks.

### Classification

	Hyperacute	Acute	Subacute
Jaundice to encephalopathy interval	0-7 days	8-28 days	5-26 weeks
Prognosis( survival)	Moderate	Poor	Poor
Cerebral oedema	common	common	Infrequent
PT	Prolonged	Prolonged	Less Prolonged
Bilirubin	Least raised	Raised	Raised

### Evaluate for etiology and severity of ALF

Initial laboratory testing

- CBP/Clotting/RFT/LFT / ABG/ lactate
- Viral hepatitis markers
- Autoimmune markers
- Metabolic markers
- Toxicology screening especially paracetamol level
- Blood ammonia level\*
  - \*High arterial ammonia levels are found predictive of higher mortality and complications.

### Management

1. Patients should be monitored frequently, preferably in ICU
2. Contact with the QMH transplantation centre for appropriate transferral
3. Search for the precise aetiology of acute liver failure to guide further management decisions

### Hepatic encephalopathy

#### Grade I/II

- Consider liver transplantation
- CT brain: to rule out other intracranial cause of change in consciousness
- Avoid stimulation/ sedation
- Lactulose

#### Grade III/IV

- Intubate and mechanical ventilation
- Choice of sedation: propofol (small dose adequate; long T1/2 in patient with hepatic failure and avoid neuromuscular blockade as it may mask clinical evidence of seizure activity)
- Elevate head of patient ~ 30 degree, neck rotation or flexion should be limited
- Immediate control of seizure: minimal doses of benzodiazepam
- Control seizure activity with phenytoin
- Prophylactic anti-convulsant not recommended
- Consider ICP monitoring especially patient listed for liver transplant with high risk of cerebral oedema

### Intracranial hypertension

#### 1. Mannitol

- bolus 0.5-1g/kg
- can repeat once / twice Q4H as needed
- stop if serum osmolality > 320 mosm/L

- risk of volume overload in renal impairment and hypernatraemia
- prophylactic use not recommended
- use in conjunction with RRT in renal failure

## 2. Hyperventilation

- reduce PaCO<sub>2</sub> to 25-30mmHg
- indicated with ICP not controlled with mannitol
- temporarily use
- risk of cerebral hypoxia in secondary to vasoconstriction
- prophylactic use not recommended

## 3. Others: hypertonic saline solution and barbiturate for refractory intracranial hypertension

### **Infection**

- periodic microbial surveillance to detect bacterial and fungal infection
- low threshold to start appropriate wide- spectrum anti-bacterial/ antifungal therapy as usual clinical signs of infection may be absent

### **Coagulopathy and bleeding**

- Spontaneous and clinically significant bleeding occurs rarely despite presence of abnormal PT/INR
- Prophylactic pepcidine or PPI is given to reduced acid-related GIB due to stress
- Variceal bleeding in the setting of ALF should raise suspicion of Budd-Chiari syndrome
- Vitamin K 10mg iv routinely given
- Replacement therapy for thrombocytopenia (<50,000-700,000/mm<sup>3</sup>) and/ or prolonged prothrombin time (INR≥1.5) is recommended only in the setting of hemorrhage or prior to invasive procedures

**Haemodynamic/ Renal failure**

- Fluid replacement for intravascular volume deficits, colloids is preferred
- Aim maintain mean arterial pressure at least 50-60mmHg
- All solutions should contain dextrose to maintain euglycemia
- Systemic vasopressor: epinephrine/norepinephrine/dopamine used when fluid replacement fails to maintain MAP 50-60mmHg
- Adrenal function should be assessed in patient requiring vasopressors
- Pulmonary artery catheterization should be considered in haemodynamically unstable patient to ensure inadequate volume replacement
- CVVH is preferable for acute renal failure requiring dialysis

**Considerations for liver transplantation**

## King's College prognostic criteria

Paracetamol	Non-paracetamol
pH < 7.3 regardless of encephalopathy score	PT > 100 regardless of encephalopathy score
All 3: - PT > 100s / INR 6.5 - Cr > 300umol/ 3.4mg/dL - Stage 3/ HE	3 out of 5 regardless of encephalopathy score - Age < 10 or > 40 - Drug toxicity, indeterminate cause - Bilirubin > 300 umol/L - Jaundice to coma interval > 7 days - PT > 50 / INR 3.5

## HEPATIC ENCEPHALOPATHY

### Child-Pugh Grading of Severity of Chronic Liver Disease

	1	2	3
Encephalopathy	None	I and II	III and IV
Ascites	Absent	Mild	Moderate
Bilirubin (umol/l)	<35	35 – 50	>50
for PBC (umol/l)	<70	70 – 170	>170
Albumin (g/l)	>35	28 – 35	<28
Prothrombin time (sec prolonged)	1 - 3	4 - 6	>6

Grades: A: 5-6 points, B: 7-9 points, C: 10-15 points

### Grading

- I Euphoria, mild confusion, mental slowness, slurred speech, disordered sleep
- II Lethargy, moderate confusion, inappropriate behaviour, drowsiness
- III Marked confusion, incoherent speech, sleeping but arousable
- IV Coma, initially responsive to noxious stimuli, later unresponsive

### Management of hepatic encephalopathy in cirrhotic patients

#### A. Identify and correct precipitating factors

- Watch out for infection, constipation, gastrointestinal bleeding, excess dietary intake of protein, vomiting, large volume paracentesis, vascular occlusion and primary HCC
- Avoid sedatives, alcohol, diuretic, hepatotoxic and nephrotoxic drugs
- Correct electrolyte imbalance ( azotaemia, hyponatraemia, hypokalaemia, metabolic alkalosis/acidosis)

## B. Treatment

- Tracheal intubation should be considered in patient with deep encephalopathy
- Nutrition: In case of deep encephalopathy, oral intake should be withheld 24-48hr and i.v. glucose should be provided until improvement. Enteral nutrition can be started if patients are unable to eat after this period. Protein intake begins at a dose of 0.5g/kg/day, with progressive increase to 1-1.5g/kg/day. Vegetable and dairy sources are preferable to animal protein.
- Oral formulation of branched amino acids may provide better tolerated source protein in patients with chronic encephalopathy and dietary protein intolerance
- Lactulose ( oral / via nasogastric tube) 30-40 ml q8h and titrate until 2-3 soft stools/day
- Antibiotics in suspected sepsis
- Consider liver transplantation in selected cases

## ASCITES

- A. Investigations
  - Diagnostic paracentesis, USG abdomen, alpha-fetoprotein
- B. Conservative Treatment (aim to reduce BW by 0.5 kg/day)
  1. Low salt diet (2g/day)
  2. Fluid restriction if dilutional hyponatremia  $\text{Na} < 120\text{-}125$  mmol/L
  3. Monitor input/output, body weight, urine sodium
  4. Spironolactone starting at 50 mg daily (single morning dose) alone or with lasix 20 mg daily as combination therapy.
  5. Increase the dose stepwise (maintaining the 100mg:40mg ratio) every 5-7days to the maximum spironolactone 400mg/day and lasix 160mg/day if no response if weight loss and natriuresis are inadequate
  6. Amiloride (10-40mg/day) can be substituted for spironolactone in patients with tender gynaecomastia
  7. Once ascites has largely resolved, dose of diuretics should be reduced and discontinued later whatever possible.
  8. All diuretics should be discontinued if there is severe hyponatremia  $< 120$  mmol/L, progressive renal failure, worsening hepatic encephalopathy, or incapacitating muscle cramps
    - Lasix should be stopped if there is severe hypokalemia ( $< 3$  mmol/L)
    - Spironolactone should be stopped if there is severe hyperkalemia ( $> 6$  mmol/L)
- C. Therapeutic paracentesis can be used in refractory ascites
  - Exclude spontaneous bacterial peritonitis before paracentesis
  - Caution in patients with hypotension and raised serum creatinine, monitor vital signs during paracentesis
- D. Consider TIPS
- E. Referral to liver transplant centre

## GENERAL GUIDELINES FOR CONSIDERATION OF ORTHOTOPIC LIVER TRANSPLANTATION (OLT) IN CHRONIC LIVER DISEASE OR HEPATOCELLULAR CARCINOMA

### *Chronic liver disease and hepatocellular carcinoma*

Patients who have an estimated survival of less than 80% chance after 1 year as a result of liver cirrhosis should be referred for consideration of liver transplantation. If any of the following are present, it may be appropriate to refer the patient:

- A. Child-Pugh score 8 or above
- B. Complications of cirrhosis
  - a. Refractory ascites or hydrothorax
  - b. Spontaneous bacterial peritonitis
  - c. Encephalopathy
  - d. Very poor cirrhosis related quality of life
  - e. Early stage of hepato-renal syndrome, hepato-pulmonary syndrome, or malnutrition
  - f. Portal hypertensive bleeding not controlled by endoscopic therapy or transjugular intra-hepatic porto-systemic shunt
- C. For patients with unresectable hepatocellular carcinoma and those with hepatocellular carcinoma *and* underlying cirrhosis
  - a. Solitary tumour of less than 5cm in diameter or those with up to 3 tumours (each of which should be < 3 cm)
  - b. For tumours beyond the above criteria, patients may still be eligible for liver transplantation if
    - i. There is a potential living-related donor  
*and*

- ii. Single tumour not exceeding 6.5cm, or 2-3 lesions none exceeding 4.5cm, with the total tumour diameter less than 8cm

***Acute liver failure/acute on chronic liver failure***

These patients should be referred early to avoid delay in work-up for potential liver transplantation if they have any of the following criteria

- Those with rising INR (>2.5)
- Evidence of early hepatic encephalopathy

***Relative contra-indications to liver transplantation***

- Alcoholic patients with less than 6 months abstinence
- Extra-hepatic malignancy
- Severe/uncontrolled extra-hepatic infection
- Multi-system organ failure
- Significant cardiovascular, cerebrovascular, or pulmonary disease
- Advanced age

## VARICEAL HAEMORRHAGE

- A. Volume resuscitation as in other causes of upper GIB
- maintain mean arterial pressure at 80mmHg
  - avoid overtransfusion, aim for Hb of 8g/dl, haematocrit of 30%
  - correct coagulopathy
- B. NG tube can be inserted for emptying of blood in stomach but no suction should be applied to avoid rupturing varices
- C. Investigations
- CBP, LFT, RFT
  - PT, APTT & platelet
  - Serology for HBV and HCV
  - $\alpha$ FP
  - Abdominal ultrasound
- D. Vasoactive agents, to be given early and maintained for 2 – 5 days.
- Octreotide 50  $\mu$ g iv bolus, then 50  $\mu$ g/h iv infusion
  - Somatostatin 250  $\mu$ g iv bolus, then 250  $\mu$ g/h iv infusion
  - Terlipressin 1 – 2 mg IV bolus Q4 – 6H
  - Vasopressin 0.4 units/min iv infusion  
(Off label use, watch out for cardiovascular complications)
- E. IV thiamine for those with alcohol excess
- F. Anti-encephalopathy regimen
- Correct fluid and electrolyte imbalances
  - Lactulose 10-20 ml q4H-q8H to induce diarrhoea
  - Low protein and low salt diet

## G. Prevention of sepsis

- Short-term prophylactic antibiotic: PO norfloxacin 400mg bd , or PO/IV ciprofloxacin 400-500mg bd, or IV ceftriazone 1g/day or 5 – 7 days

## H. Control of bleeding

- Endoscopy: Endoscopic variceal ligation / sclerotherapy for oesophageal varices  
Tissue glue like N-butyl-cyanoacrylate injection for fundal varices
- Consider balloon tamponade (for <24 hr) if: urgent endoscopy not available

**When vasoactive agent fails to control bleeding, or recurrent bleeding after endoscopy**

- Consider TIPs or surgery.

## UPPER GASTROINTESTINAL BLEEDING

- A. Emergency Management (Consider ICU if severe bleeding)
- Nil by mouth
  - Insert large bore IV cannula
  - Closely monitor BP, Pulse, I/O, CVP if BP < 90 mmHg
  - Blood and fluid replacement as required
  - Cuffed ET tube to prevent aspiration if massive haematemesis, nasogastric tube if massive haematemesis or signs suggestive of GI obstruction or perforation
  - Look out for and treat any medical decompensation secondary to GIB
  - IV H<sub>2</sub>-antagonist and tranexamic acid have NO proven value, IV proton-pump inhibitor treatment prior to endoscopy significantly reduces the portion of patients with stigmata of recent haemorrhage at index endoscopy
  - Arrange endoscopy after initial stabilization
  - After endoscopic treatment of patients with actively bleeding ulcer or ulcer with visible vessel, PPI infusion given for 72 hours reduces the risk of rebleeding
  - PPI Infusion: omeprazole/esomeprazole/pantoprazole 80mg IVI stat followed by 8mg/hr infusion
- B. Indications for Emergency Endoscopy
- Massive haematemesis
  - Haemodynamic shock
- C. Contraindications for Endoscopy
- Suspected intestinal perforation
  - Suspected intestinal obstruction
  - Dysphagia without delineation of level of obstruction
  - Unstable cardiac or pulmonary status
- D. Indications for Emergency Operation
- Arterial bleeding not controlled by endoscopic treatment
  - Transfusion > 8 units
  - Rebleeding after apparently successful endoscopic therapy (in selected cases)

## PEPTIC ULCERS

- A. Anti-*Helicobacter pylori* therapy
- Triple therapy for 1 week  
Proton pump inhibitor bd + Amoxicillin 1gm bd + Clarithromycin 500mg bd or  
Proton pump inhibitor bd + Metronidazole 500mg bd + Clarithromycin 500mg bd
  - Standard dosage of proton pump inhibitors  
Omeprazole / Esomeprazole 20mg  
Rabeprazole 20mg  
Lansoprazole 30 mg  
Pantoprazole 40 mg
- B. Ulcer-healing drugs
- H<sub>2</sub>-antagonists for 8 weeks  
Famotidine 20 mg bd or 40 mg nocte
  - PPI for 4 - 6 weeks  
Omeprazole or esomeprazole 20 mg om  
Rabeprazole 20mg om  
Lansoprazole 30 mg om  
Pantoprazole 40 mg om
  - Sucralfate 1 g qid for 6 - 8 week  
(not recommended for CRF due to its aluminium content)
- C. NSAIDs and Peptic Ulcers
- Prevention: Discontinue NSAID if possible  
Misoprostol 200 µg bd or  
Proton pump inhibitor as prophylaxis
  - Treatment Discontinue NSAID  
Eradicate *H pylori* if it is present  
H<sub>2</sub>-antagonists or PPI
- D. Follow-up Endoscopy
- DU Unnecessary if asymptomatic
  - GU Necessary and repeat biopsy until ulcer heals

## MANAGEMENT OF GASTRO-OESOPHAGEAL REFLUX DISEASE (GERD)

- A. For patients with typical GERD symptoms without complication, an initial trial of empirical acid suppressant is appropriate. A PPI (proton pump inhibitors) test in bd dosage for 2 weeks has a sensitivity of about 70-80% and specificity of 60-70% for GERD with classical and extra-oesophageal/atypical GERD symptoms, in particular atypical chest pain.
- B. Endoscopy is useful to identify suspected Barrett's esophagus and complications of GERD. It should be considered in those who do not respond to PPI test or those with alarming features like dysphagia, anaemia, significant weight loss, repeated vomiting and old age.
- C. For patients with significant reflux oesophagitis (\*LA class B-D or \*\*Savary-Miller grade 2-4), PPIs have been shown to be better than standard dose of H<sub>2</sub> blockers in the healing of oesophagitis and maintenance of remission.
- D. The standard once daily dosage of PPI is : omeprazole 20mg, lansoprazole 30mg, pantoprazole 40mg, rabeprazole 20mg, esomeprazole 40mg. Doubling the dose to bd daily may be necessary in some patients when symptoms or oesophagitis are not well controlled. Maintenance therapy is required to prevent relapse of severe oesophagitis.
- E. For patients without erosions (also known as NERD), treatment success with PPI is variable. When symptoms are well controlled, the dosage of PPI can be reduced. Some patients with clear cut periods of relapses and remissions can be considered for on-demand therapy with PPIs or H<sub>2</sub> blockers for 2-4 weeks.
- F. Anti-reflux surgery is a maintenance option for patient with well-documented GERD

\*Los Angeles classification of reflux esophagitis

- A mucosal break(s) <5mm, no extension between tops of mucosal folds
- B mucosal break >5mm, no extension between tops of mucosal folds
- C mucosal breaks continuous between tops of mucosal folds, but not circumferential
- D mucosal break(s) involving >75% of circumference

\*\*Savary-Miller classification of reflux esophagitis

- Grade I nonconfluent red patches or streaks, may occur singly or may appear in multiple nonconfluent areas
- Grade II confluent mucosal breaks which are not circumferential
- Grade III inflammatory lesions involving the entire circumference
- Grade IVa one or several ulcers which may be associated with circumferential stricturing, oesophageal shortening, or Barrett's metaplasia
- Grade IVb oesophageal stricture but no evidence of erosion or ulceration in the strictured area

## INFLAMMATORY BOWEL DISEASES – (ULCERATIVE COLITIS)

- A. Diagnosis: a combination of history, radiological and endoscopic appearance, histology and -ve stool examination for infectious causes
- CBP, ESR, LFT, RFT, CRP
  - Stool for cultures and *Clostridium difficile* toxin
  - AXR to assess extent of disease (ulcerated colon contains no solid faeces) and to exclude toxic megacolon (transverse colon diameter >5cm)
  - Endoscopy and biopsies
- B. Assessment of disease activities:
- Mild: <4 stools (+/- blood) daily, no systemic disturbance, normal ESR and CRP
  - Moderate: 4 – 6 stools daily with minimal systemic disturbance
  - Severe: >6 stools (usually bloody) daily and evidence of systemic disturbance (fever, tachycardia, anaemia, raised ESR or hypoalbuminaemia)
  - Fulminant: >10 stools daily, continuous bleeding, toxicity, abdominal tenderness and distension, blood transfusion requirement, colonic dilatation on AXR.
- C. Therapy should be guided by disease activity and extend of colitis
- Severe and fulminant disease: Hospitalized
    - Nil per oral
    - Fluid and electrolyte replacement, +/- TPN
    - AXR to monitor colonic dilatation, beware of toxic megacolon
    - Stool for culture, watch out for infection (*C. difficile* and CMV)
    - Medical treatment (see table below)
    - Surgical consultation

**Medical Treatment**

	Induction phase		Maintenance phase	
Mild to Moderate Disease	Topical	<u>Mesalazine</u> Suppository: distal 10cm	500mg bd / 1gm daily	0.5-1gm daily
		Enema: to splenic flexure	1-4 gm daily	1-4 gm daily
		Steroid enema	Prednisolone 20mg daily Budesonide 2g daily	
Systemically ill	Oral	Aminosalicylate Sulphasalazine Mesalazine tab	In divided daily doses 4 – 6 gm 2 – 4.8 gm	In divided daily doses 2 – 4 gm ≥ 2gm
		Mesalazine granules	1.5 – 4 gm	1.5 – 2 gm
		Steroid Prednisolone Budesonide	40-60mg /day 9mg / day	
Systemically ill	Intraven	Azathioprine		1.5 - 2.5mg / kg /day
		Steroid Hydrocortisone	100mg Q6H	
		Cyclosporin	4mg / kg / day	
		Infliximab	5mg/kg at wk 0, 2 and 6	5mg/kg every 8 wks

Limited distal disease: Treatment can be started with topical suppository / enema

Extensive disease: Oral therapy

Combination therapy (oral and topical) is more effective in inducing remission than either modality alone

## 5-ASA available in Hong Kong

	Proprietary name	Formulation	Mechanism	Sites of delivery	Unit strength
Mesalazine	Asacol	Oral tablet	Release at pH $\geq 7$	Terminal ileum to colon	400mg
		Enema		To splenic	4g/100mL
		Suppository		Distal 10cm	500mg
	Pentasa	Oral tablet	Time dependent release	Duodenum to colon	500mg
		Prolonged release granules	Micropellet formulation		1g/sachet 2g/sachet
		Enema		To splenic	1g/100mL
		Suppository		Distal 10cm	1g
	Salofalk	Oral tablet	Release at pH $\geq 6$	Mid jejunum to colon	250mg 500mg
		Granu-Stix sachet	Micropellet formulation		500mg 1 g
		Enema		To splenic	4g/60mL
Suppository			Distal 10cm	250mg 500mg	
Sulphasal	Salazopyrin EN		5-ASA linked to Sulphapyridine by azo bond	Colon	500mg (200mg 5-ASA)

## INFLAMMATORY BOWEL DISEASES – CROHN'S DISEASE

Disease location: terminal ileum, colon, ileocolon, upper GIT

Behaviour: Non-stricturing/structuring, non-penetrating /  
penetrating (fistula +/- abscesses)

### A. Induction of remission

- Mildly active, localized ileo-caecal disease

Sulphasalazine 3 – 6 g /day (most benefit in patients with colonic involvement)

Budesonide 9 mg / day (ileum and right colon involvement)

- Moderate to Severe

Prednisolone 40mg / day up to 1mg/kg/day

Hydrocortisone 100mg q6H

Steroid sparing: Azathioprine

Methotrexate, Infliximab, Adalimumab

Consider surgery for fulminant disease with obstructive complication or those unable to tolerate medical therapy

- Perianal fistulation Crohn's disease

Ciprofloxacin 1000mg / day

Metronidazole 1 – 1.5g / day

Azathioprine, Infliximab, Adalimumab

Consider surgery (Seton placement)

### B. Maintenance of remission

- Budesonide 6mg / day for refractory and severe disease, prolongs the time to relapse
- Azathioprine 2 – 3 mg / kg / day, moderate to severe disease brought into remission with conventional corticosteroids, steroid dependent
- Methotrexate, Infliximab, Adalimumab

## ACUTE PANCREATITIS

High index of suspicion is needed. Suspect acute pancreatitis in any patient with upper abdominal pain (esp. with vomiting), unexplained shock or elevated serum amylase (at least 3 x ULN, excluding other causes of acute abdomen is of paramount importance).

### A. Assessment of severity and prognosis

- Risk factors of severity at admission include older age, obesity (BMI >30), and organ failure
- Clinical Parameters

Variable	Ranson		Glasgow within first 48 hrs	APACHE II admission, then daily
	At 0 hrs	At 48 hrs		
Age (years)	>55		>55	+
WBC count ( $\times 10^9/l$ )	>16		>15	+
Blood glucose (mmol/l)	>11.1		>10	-
AST (U/l)	>250		-	-
LDH (U/l)	>350		>600	-
Serum urea (mmol/l)		$\uparrow >1.8$	>16	creatinine
Serum Ca (mmol/l)		<2	<2	-
Serum Alb (g/l)		-	<32	-
PaO <sub>2</sub> (kPa)		<8	<8	+
Base deficit		>4	-	Arterial pH
Fluid sequestration		>6 L	-	-
Haematocrit (%)		$\downarrow \geq 10\%$	-	+
Serum Na	-	-	-	+
Serum K	-	-	-	+
Temperature	-	-	-	+

Mean arterial BP	-	-	-	+
Heart rate	-	-	-	+
Respiratory rate	-	-	-	+
Glasgow coma scale	-	-	-	(15 - actual score)
Chronic health score	-	-	-	+
Suggested cut off number	11 criteria: <3 criteria indicate mild AP		8 criteria: $\geq 3$ criteria indicate severe AP	14 criteria: $\geq 8$ points* indicate severe AP

\* Points system per variable: from 0 (normal) to +4 (very abnormal). Minimal score: 0, maximum score: 71.

- C-reactive Protein: 150mg/l at 48hrs predicts a severe attack
- Contrast-enhanced CT pancreas: to diagnose severity of AP and to identify complications, especially pancreatic necrosis, full extent of which cannot be appreciated until at least 3 days after symptom onset. Best done on D6-D10 after admission.

Balthazar **CT severity index** = grade of AP (0-4) + percentage of necrosis (0-6). Score of 7-10 associated with morbidity of 92%, mortality 17%.

Grade of Pancreatitis	Points	Percentage of Necrosis	Points
Normal pancreas	0	0%	0
Focal or diffuse enlargement	1	<30%	2
Pancreatic or peripancreatic inflammation	2	30-50%	4
Single peripancreatic fluid collection	3	>50%	6
Multiple fluid collection and/or retroperitoneal air	4		

## B. Watch out for biliary pancreatitis

- ALT > 3 ULN in a non-alcoholic patient would highly suggestive of gallstone etiology
- USG hepatobiliary system for detection of gallstone and dilated bile ducts; pancreas can only be visualized in 50% of cases
- EUS is the most accurate test for diagnosing or ruling out biliary etiology
- Arrange early ERCP and sphincterotomy within 24 to 72 hours after admission, if there is acute cholangitis or evidence of persistent CBD stones

## C. Management (ICU care for severe cases)

- Laboratory Ix for assessment of severity (see above)
- CXR, AXR (erect and supine films for excluding other causes of acute abdomen, serially for monitoring), ECG
- Close monitoring of vital signs, I/O, RFT, Ca, glucose  $\pm$  ABG
- Nil by mouth till nausea and vomiting settle. Nasogastric suction if ileus or protracted vomiting
- Adequate intravenous hydration is crucial (to produce urine output of 0.5ml/kg/hr in the absence of renal failure) and supplemental oxygen
- Correct electrolyte and glucose abnormalities
- Cardiovascular, respiratory and renal support as required
- Analgesics - Pethidine for pain control
- Nutritional support via enteral route is preferred. TPN is to be considered if sufficient calories cannot be delivered through enteral nutrition, as in the case of severe ileus.

Recommended nutrient requirements in acute severe pancreatitis

Energy	25-35 kcal/kg/day
Protein	1.2-1.5 g/kg/day
Carbohydrates	3-6 g/kg/day
Lipids	2 g/kg/day

Fat administration is safe provided hypertriglyceridaemia (>12 mmol/l) is avoided

- Antibiotics
  - Given on demand: biliary sepsis, newly developed sepsis or systemic inflammatory response syndrome, infected pancreatic necrosis, an increase in CRP in combination with other evidence supporting the possibility of infection.
  - Prophylactic antibiotic treatment generally not recommended but may be considered in patients with pancreatic necrosis of >30% involvement by CT. It should be active against enteric organisms (e.g. imipenam) and be given for one to two weeks.
- Look out for complications e.g. pseudocyst or pancreatic sepsis. CT-guided FNA of pancreas for Gram stain and culture if suspected infection of pancreatic necrosis with ongoing fever, leukocytosis and worsening abdominal pain
- Consult surgeon in severe cases or when complication arise



# Haematology



## HAEMATOLOGICAL MALIGNANCIES

### (1) LEUKAEMIA

#### 1. Investigations at diagnosis

##### a. Blood tests

- CBP, PT/APTT, D-dimer, Fibrinogen
- G6PD, HB<sub>s</sub>Ag, antiHBc, antiHBs
- RFT, LFT, Ca/P, Urate, Glucose, LDH, Type&Screen
- HCV Ab, HIV Ab, HBV DNA for HBV carrier
- Serum lysozyme for AML M4/M5/CMML
- Coombs' test and serum protein IEP for CLL
- Tartrate resistant acid phosphatase (TRAP) for HCL

##### b. Bone marrow aspiration and trephine

Contact haematologist for cytogenetic and molecular studies before BM biopsy

#### 2. Initial management

a. Start allopurinol 300 mg daily (↓ dose if RFT is impaired)

b. Ensure adequate hydration

c. Blood product support:

- RBC/blood transfusion if symptoms of anaemia are present
- Platelet transfusion if platelet count  $<10 \times 10^9/L$  or bleeding
- Give FFP if there is evidence of bleeding due to DIC

d. Do sepsis workup if patient has fever

e. Antibiotic therapy:

Give appropriate antibiotic if there is evidence of infection  
PCP prophylaxis for patients with acute lymphoblastic leukaemia:

- i. Septrin tab 2 daily three days per week, or
- ii. Pentamidine inhalation 300mg/dose (or 5mg/kg) once every 4 weeks.

f. Record patient's performance status (PS)

#### 3. Inform haematologist the following medical emergencies

a. Hyperleucocytosis (e.g. WBC  $>100 \times 10^9/L$ ) for chemotherapy

- ± leucopheresis. Avoid blood transfusion till WBC is lowered
- b. APL (acute promyelocytic leukaemia) for early use of all-trans-retinoic acid (ATRA)

#### 4. Subsequent management

- a. Consult haematologist for long-term treatment plan
- b. Arrange Hickman line insertion if indicated
- c. Arrange HLA typing for patient's siblings if BMT is anticipated
- d. CMV negative blood product for potential BMT recipient if patient is CMV seronegative.

## (2) LYMPHOMA

### 1. Investigations at diagnosis

- a. Blood tests
  - CBP, ESR, PT/APTT, G6PD
  - RFT, LFT, Ca/P, LDH, Urate, Glucose, Coombs' test
  - Serum IgG/IgA/IgM levels, serum IEP
  - HB<sub>s</sub>Ag, antiHBc, antiHBs, HBV DNA (optional)
- b. Biopsy
  - Excisional biopsy of lymph node or other tissue (send fresh specimen, no formalin)
  - Send fresh specimen for study (immune markers, EM, DNA)
- c. Bilateral iliac crest aspiration and trephine
- d. Radiology
  - Chest X-Ray and X-ray of relevant regions
  - PET/CT scan or CT scan of thorax, abdomen and pelvis or other sites of involvement
- e. Other investigations
  - Endoscopic and Waldeyer's ring exam for GI lymphoma
  - LP with cytopspin for patients with high risk of CNS lymphoma
    - (high grade lymphoma, nasal/ testicular/ marrow lymphoma)
  - Cardiopulmonary assessment – optional

**2. Initial management**

- Start allopurinol 300 mg daily and ensure adequate hydration
- Record patient's performance status (PS)

**3. Note the following medical emergencies**

- SVC obstruction due to huge mediastinal lymphoma
- Hypercalcaemia
- Tumour lysis syndrome
- Spinal cord compression

**4. Subsequent management**

- Consult haematologist for long-term treatment plan

**(3) MULTIPLE MYELOMA****1. Investigations at diagnosis**

- Blood tests  
CBP, ESR, RFT, LFT, Ca/P, LDH, Urate, Glucose  
Serum Immunoelectrophoresis (IEP) and paraprotein level  
Serum IgG/IgA/IgM level, Serum free light chain level  
 $\beta_2$ M, CRP, HB<sub>s</sub>Ag, antiHBc, antiHBs
- Urinalysis - Bence Jones Protein (BJP) and free light chains
- Radiology – skeletal survey and chest X-Ray
- Bone marrow aspiration and trephine (+/- FISH)

**2. Staging****a. Durie & Salmon staging system (Cancer 36, 842, 1975)**

	I	II	III
Hb(g/dL)	>10	8.5-10	<8.5
Ca <sup>++</sup> (corrected)	<3 mmol/L	<3 mmol/L	>3mmol/L
X-ray lesions	Normal/solitary	Intermediate	Advanced
IgG (g/L)	<50	50-70	>70
IgA (g/L)	<30	30-50	>50
Urine light chain	<4g/24h	4-12g/24h	>12g/24h

A: normal renal function (serum creatinine < 0.12 mmol/L)

B: impaired renal function (serum creatinine > 0.12 mmol/L)

**b. International Staging System (ISS) (JCO 23:3412, 2005)**

Stage	Serum Albumin (g/l)	Serum $\beta$ 2-microglobulin (mg/l)	Median survival ( months )
I	> 3.5	<3.5	62
II	Neither stage I or III		45
III	--	>5.5	29

**c. Symptomatic Vs asymptomatic myeloma**

Symptomatic: presence of end-organ damage: CRAB:

Calcium elevation: (>2.9 mmol/L)

Renal insufficiency: (creatinine >2mg/dl)

Anaemia (Hb <10 or 2g < normal)

Bone disease (lytic or osteopenic)

**3. Initial management**

- Ensure adequate hydration and start allopurinol 300 mg daily  
Correct hypercalcaemia – pamidronate 60 mg iv in 4-6 hrs or Zometa 4 mg iv within 15 minutes
- Renal dialysis  $\pm$  plasmapheresis for patients with renal failure
- Record patient's performance status (PS)
- Consult Radiotherapy or Orthopaedic Team for patients presenting with skeletal complications (pathologic fracture or spinal cord compression)

**4. Subsequent management**

Consult haematologist for long-term treatment plan

**(4) EXTRAVASATION OF CYTOTOXICS (also see page GM28 Oncological Emergency in Gen Int Med section)****1. Prevention**

- Extreme care and never give it in a hurry
- Choose appropriate veins
- Confirm patency of iv site with NS before injection of cytotoxics

- d. Flush with NS on completion of infusion/injection of cytotoxic drugs
- e. Stop when patient complains of discomfort, swelling, redness
- f. Use central line if indicated e.g. Hickman line

## 2. Extravasation suspected

- a. Leave iv needle in place and suck out any residual drug
- b. If there is a bleb, aspirate it with a 25-gauge needle
  - Anthracycline – apply ice pack
  - Vinca alkaloid – apply heat
- c. Potential antidotes
  - Anthracycline- DMSO or hydrocortisone or NaHCO<sub>3</sub> locally
  - Vinca alkaloid- apply hydrocortisone locally
  - Cisplatinium- sodium thiosulphate
- d. Record the event in clinical notes and inform seniors

## (5) INTRATHECAL CHEMOTHERAPY

### 1. Prescription

- a. All intrathecal chemotherapy should be prescribed in a separate prescription form.
- b. Methotrexate, cytarabine and hydrocortisone are the only THREE drugs that can be prescribed for intrathecal chemotherapy administration.
- c. The route of administration “Intrathecal” must be written in full in the prescription.

### 2. Dispensing

- a. All dispensed intrathecal drugs must be labeled with a warning message “ For Intrathecal Use Only”.
- b. All dispensed intrathecal chemotherapy must be dispatched separately in a designated container or in a sealed envelope/bag (marked “Intrathecal drug”).

### 3. Consent

- a. Prior to intrathecal chemotherapy administration, the medical staff who is responsible for the procedure, must obtain an informed written consent from the patient.

#### 4. Administration

- a. Parenteral drug(s) and intrathecal drug must be administered as separate procedures, i.e. separated in time in setting up and initiating the administration.
- b. The staff responsible for the drug administration must verify the 5 “Rights” (Right patient, right time, right drug, right dose and right route) against the prescription. A second trained staff is required to independently verify the patient identification and drug checking process.
- c. Both staff must sign the medication administration (MAR) record.

#### (6) PERFORMANCE STATUS

<b>ECOG</b>	<b>Karnofsky(%)</b>	<b>Definition</b>
0	100	Asymptomatic
1	80-90	Symptomatic, fully ambulatory
2	60-70	Symptomatic, in bed < 50% of day
3	40-50	Symptomatic, in bed > 50% of day
4	20-30	Bedridden

## NON-MALIGNANT HAEMATOLOGICAL EMERGENCIES/CONDITIONS

### (1) ACUTE HAEMOLYTIC DISORDERS

#### 1. Approaches

##### a. Collect evidence of haemolysis

- *evidence of increased Hb break down*  
 ↑ indirect bilirubin, ↓ haptoglobin, ↑ LDH  
 Methaemalbuminaemia\*, Haemoglobinaemia\*,  
 ↑ urinary and faecal urobilinogen, Haemoglobinuria\*  
 Haemosiderinuria\*

##### (\* :evidence of intravascular haemolysis)

- *evidence of compensatory erythroid hyperplasia*  
 Reticulocytosis, erythroid hyperplasia of bone marrow
- *evidence of damage to red cells*  
 Spherocytosis, ↑RBC fragility, Fragmented RBC, Heinz bodies
- *evidence of shortened red cell life span*  
 Chromium<sup>51</sup> labelled red cell study

##### b. Document the cause and nature of haemolysis

- Intracorpuscular/Extracorpuscular defect -Congenital/Acquired
- Intravascular/Extravascular haemolysis - Acute/Chronic

#### 2. Investigations

##### a. Blood tests

CBP, Reticulocyte count, Peripheral smear, Hb pattern  
 RFT, LFT, Bilirubin(direct/indirect), LDH, Haptoglobin  
 Coombs' test, ANF, Viral study, Screening for malaria  
 Cold agglutinins (arrange with laboratory)  
 Sucrose lysis test / PNH screening test(arrange with laboratory)  
 G6PD assay (may be normal during acute haemolysis)

##### b. Urine test

Urobilinogen, Haemoglobin, Haemosiderin

#### 3. Management

- a. Must identify cause of haemolysis, then treat accordingly
- b. Consult haematologist

#### 4. Common agents reported to induce haemolytic anaemia in subjects with G6PD deficiency

##### Unsafe for class I, II, & III variants

Acetanilid  
 Dapsone  
 Furazolidone  
 Methylene blue  
 Nalidixic acid  
 Naphthalene (mothballs, henna)  
 Niridazole  
 Nitrofurantoin  
 Phenazopyridine  
 Phenylhydrazine  
 Primaquine  
 Sulfacetamide  
 Sulfamethoxazole  
 Sulfanilamide  
 Sulfapyridine  
 Thiazosulfone  
 Toluidine blue  
 Trinitrotoluene  
 Chinese Herbs:

plum flower (腊梅花)  
 chuan lianzi (川莲)  
 zhen zhu (珍珠末)  
 jin yin hua (金银花)  
 niu huang (牛黄)

##### Safe for class II & III variants\*

Acetaminophen  
 Aminopyrine  
 Ascorbic acid except very high dose  
 Aspirin  
 Chloramphenicol  
 Chloroquine  
 Colchicine  
 Diphenhydramine  
 Isoniazid  
 L-DOPA  
 Menadione  
 Paraaminobenzoic acid  
 Phenacetin  
 Phenytoin  
 Probenecid  
 Procainamide  
 Pyrimethamine  
 Quinidine  
 Quinine  
 Streptomycin  
 Sulfamethoxypyridazine  
 Sulfisoxazole  
 Trimethoprim  
 Tripeleonnamine  
 Vitamin K

#### 5. Safety for class I variants is usually not known.

Data from Beutler, E, Blood 1994; 84:3613.

Class 1 (severe deficiency with nonspherocytic hemolytic anemia),  
 Class II (severe deficiency with intermittent hemolysis), and  
 Class III (moderate to mild deficiency). Beutler, E, Blood 1994; 84:3613

## (2) IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)

### 1. Definition

Isolated thrombocytopenia due to peripheral destruction with no clinically apparent causes but of presumed autoimmune aetiology

Secondary causes:

- SLE            -MDS            -TTP            -HIV infection
- Gestational thrombocytopenia    -Alloimmune thrombocytopenia
- Lymphoproliferative disorders    -<sup>1</sup>anti-phospholipid syndrome
- Infection (eg. viral, malaria)
- Drugs e.g.heparin induced thrombocytopenia (HIT)

Type 1    HIT – Non-immune phenomenon occurring < 4 days after heparin use. Platelet count is rarely <  $100 \times 10^9/L$ . Recovers in spite of continued heparin use.

Type 2    HIT – Immunoglobulin mediated phenomenon occurring >5days of heparin use. Associated with a  $\geq 50\%$  fall in platelet count ( $< 100 \times 10^9/L$ ) and new sites of thrombosis– Consult haematologist for diagnostic test and management.

### 2. Investigations

- a. CBP and blood film (to ensure no red cell fragments, leukaemia)
- b. Bone marrow examination not mandatory, indicated if
  - i. the diagnosis of ITP is not certain
  - ii. in patients age over 60 years to rule out myelodysplasia
  - iii. prior to splenectomy
  - iv. if response to treatment is poor
- c. Autoimmune profile and APTT
- d. antiHIV serology in patients at risk

### 3. Management

- a. Consult haematologist
- b. Initial treatment: Prednisolone 1 mg/kg/day, or  
Pulse dexamethasone 20- 40mg/day for 4 days

- c. For acute life-threatening bleeding
  - IVIg 0.4 g/kg/day for 5 days or 1.0 g/kg/day for 2 days (80% effective, lasts 2-3 weeks)
  - or Methylprednisolone 1 g iv in 1 hour daily for 3 days
  - or Pulse dexamethasone 40 mg po daily for 4 days
  - or Intravenous anti-Rh0 (D)
- d. Avoid aspirin and other antiplatelet agents and im injection
- e. Platelet transfusion only for life-threatening bleeding

#### 4. Management of ITP in Pregnant Women

- a. Consult haematologist
- b. During pregnancy
  - Platelet count  $> 50 \times 10^9/L$  and no bleeding – no treatment
  - Platelet count  $< 50 \times 10^9/L$  - use steroid or IVIg
  - Be cautious with use of steroid in first trimester
- c. At delivery

- Mode of delivery according to obstetrical indication.

Maternal platelet count  $> 50 \times 10^9/L$  is sufficient to prevent complications due to vaginal delivery or cesarean section.

- Avoid epidural or spinal anaesthesia if platelet count  $< 80 \times 10^9/L$ .
- Check infant's platelet count at delivery

### (3) THROMBOCYTOPENIC THROMBOTIC PURPURA (TTP)

#### 1. Diagnosis

- a. A pentad of symptoms – anaemia, thrombocytopenia, fever, renal impairment, neurologic symptoms and signs
- b. Redefined as a syndrome of *Coombs'-negative haemolytic anaemia* and *thrombocytopenia* in the absence of other possible causes of these manifestations
- c. Important to examine blood film for micro-angiopathic features

#### 2. Investigations

CBP, Peripheral smear (for features of micro-angiopathic haemolytic anaemia), retic, RFT, LFT, LDH, Haptoglobin,



## **(6) PROPHYLAXIS OF VENOUS THROMBOSIS IN PREGNANCY**

### **1. Pre-delivery and delivery**

- a. Consult haematologist for dosage of LMWH and monitoring
- b. Monitoring of plasma anti-Xa activity may be required
- c. If need epidural/spinal anesthesia, withhold LMWH 12-24h before the procedure.

### **2. Post-delivery**

- a. Same dose of LMWH is continued until INR on warfarin is 2.0 to 3.0
- b. Warfarin is continued for 6-8 weeks

## SPECIAL DRUG FORMULARY AND BLOOD PRODUCTS

### (1) ANTI-EMETIC THERAPY

1. **5-HT<sub>3</sub> antagonists** (for patients on cytotoxic chemotherapy)
  - a. Zofran (ondansetron) 8 mg iv Q8H/Q12H *or* 8 mg po tds
  - b. Kytril (granisetron) 3-6 mg iv once daily
  - c. Navoban (tropisetron) 5 mg iv/po once daily
2. **Maxolon** 10 mg iv Q6H prn
3. **Emend ( Aprepitant )**  
use in combination with corticosteroid or other 5-HT<sub>3</sub> antagonist : 125mg po on day 1, 80mg po daily on day 2-3

### (2) HAEMOPOIETIC GROWTH FACTORS

Granulocyte Colony Stimulating Factor (G-CSF)

#### 1. Indications

- Mobilization of haemopoietic stem cells for transplantation
- Shortening of neutropenia after chemotherapy given when absolute neutrophil  $<1 \times 10^9/L$
- Drug-induced agranulocytosis
- Other conditions of severe neutropenia associated with infection e.g. cyclical neutropenia

#### 2. Dosage (usage endorsed by haematologist)

G-CSF: 5mcg/kg/day sc/iv (1 vial contains-300mcg)

### (3) IMMUNOGLOBULIN THERAPY

#### 1. Indications

- a. As replacement  
Primary immunodeficiencies with significant past infections  
Secondary Ab deficiencies: CLL, multiple myeloma, post BMT patients with chronic GvHD and significant past infections
- b. As an immunomodulator (haematology)  
Proven benefit-ITP with life threatening bleeding or pregnancy

Probable benefit – autoimmune haemolytic anaemia  
post infectious thrombocytopenia

Possible benefit – coagulopathy with factor VIII inhibitor

## 2. Dosage

- Replacement – 0.2 g/kg Q3weeks
- Immunomodulator e.g. ITP – 0.4 g/kg/day for 5 days or 1g/kg/day for 2 days

## 3. Contraindications

- Previous history of allergy to IVIg
- IgA deficiency

## (4) ANTITHYMOCYTE GLOBULIN (ATG)

### 1. Indication – Severe Aplastic Anaemia (SAA)

Criteria of SAA

- Hb <10g/dL, Reticulocytes <1 x 10<sup>9</sup>/L  
Neutrophils <0.4 x 10<sup>9</sup>/L, Platelets <20 x 10<sup>9</sup>/L
- Bone marrow cellularity < 20%

### 2. Premedication (1 hour before ATG)

- Paracetamol 1gm and chlorpheniramine (piriton) 4mg po
- Methylprednisolone 2-3 mg/kg in 100ml normal saline iv in 1 hour

**3. Test dose:** 10mg ATG in 100ml normal saline iv in 1 hour  
*Physician in attendance, anaphylaxis 1 in 50*

**4. Daily dose:** ATG 40mg/kg iv in 4 hours for 4 days

## (5) rFVIIa (NOVOSEVEN)

Dosage:

90-120ug/kg/dose

may be repeated every 2-4 hours

Indications: (Please refer to latest HA drug formulary)

- haemophilic patients with inhibitor activity and active bleeding
- factor VII deficiency
- patients with acquired inhibitors and active bleeding

## (6) REPLACEMENT FOR HEREDITARY COAGULATION DISORDERS

### 1. General information for therapy in hereditary coagulation disorders

<i>factors</i>	<i>half life</i>	<i>replacement material</i>
VIII*	10 hrs	VIII conc <sup>1</sup> cryoprecipitate <sup>2</sup> FFP <sup>3</sup> DDAVP <sup>4</sup>
IX*	25 hrs	FFP IX conc <sup>5</sup>
VWF	-	cryoprecipitate FFP DDAVP intermediate purity VIII conc
fibrinogen	90 hrs	cryoprecipitate FFP
V	15 hrs	FFP
VII	5 hrs	FFP
X	40 hrs	FFP
XI	45 hrs	FFP

<sup>1</sup> 1 unit/kg BW of infused Factor VIII raises plasma level by 2%

<sup>2</sup> 1 unit of cryoprecipitate contains about 60-100 U of Factor VIII

<sup>3</sup> 1 unit FFP contains about 140-175 units of Factor VIII

<sup>4</sup> DDAVP is useful for mild haemophilia A if a 3x increase in Factor VIII suffices. 0.3 µg/kg in 50 ml normal saline iv in 20 minutes causes a peak in Factor VIII level at 30 minutes. Intranasal DDAVP may be used. As DDAVP stimulates fibrinolysis, EACA 4g Q4H or tranexamic acid 500 mg Q8H is used concomitantly for dental procedures. Prolonged use of DDAVP causes tachyphylaxis

<sup>5</sup> 1 unit/kg BW of infused Factor IX raises plasma level by 1%

\* for Factor VIII and Factor IX deficiencies, use FFP only when specific factor concentrate is not available

**2. Recommended dosage of human AHG for Haemophilia A**

<i>Type of procedure/injury</i>	<i>Post infusion level required</i>	<i>Replacement for 50 kg man</i>
Uncomplicated spontaneous haemarthrosis or haematoma	10%	1 T stat dose
Haemarthrosis or haematoma after injury	20%	2 T once daily for 2 days
Haematoma in dangerous sites	40%	4T stat, then 2T Q12H for 3 doses
Dental extraction		
- deciduous teeth	15%	1.5T QD for 2 days
- single extraction	15%	1.5T QD for 5 days
- 2-9 extraction	30%	3T QD for 5 days
- major extraction (10 or impacted wisdom teeth)	40%	4T stat, then 2T Q12H for 5 days
Major surgery	100%	3T Q8H for $\geq 7$ days

1 T = 2 AHG = 3 FFP = 6 cryoprecipitate

**3. Recommended dosage of cryoprecipitate in vWD**

<i>Type of Bleeding</i>	<i>Desired Level</i>	<i>Initial Dose (unit/10 kg)</i>		<i>Maintenance Dose</i>
		<i>Mild vWD</i>	<i>Severe vWD</i>	
<b>Spontaneous Haemorrhages</b>				
Epistaxis, skin injury	20	0.5	1	as needed
Menorrhagia	30	1	1.5	as needed
GI bleeding	50	1	2	as needed
Head Injury	60	1.5	2.5	7 days
Intracranial haemorrhage	60	1.5	3	7 days
<b>Surgical Procedures</b>				
Dental surgery	40	0.5	1	1/2 dose x 7d
Appendicectomy	50	1.5	2	1/2 dose x 7d
Tonsillectomy	60	2	3	1/2 dose x 8d
Hysterectomy	60	2	3	1/2 dose x 8d
Cholecystectomy	60	2	3	1/2 dose x 8d
Coronary Bypass	80	3	4	1/2 dose x 8d
Delivery	50	1.5	2	1/2 dose x 8d

**4. Recommended dosage of factor IX for Christmas disease**

<i>Type of bleeding or intervention</i>	<i>Post infusion level required</i>	<i>Initial dose (u/kg)</i>	<i>Maintenance dose (u/kg)</i>
Haemarthrosis			
- mild	20	20	20 if needed
- major	40	40	20 Q12H for 7 days
Muscle bleeding	40	40	20 Q12H for 7 days
Epistaxis	20	20	10 Q12H if needed
Dental extraction	20	20	EACA for 10 days
GI bleeding	40	40	20 Q12H for 7 days
Life-threatening condition	60	30	Q12H for 10-14 days

## TRANSFUSION

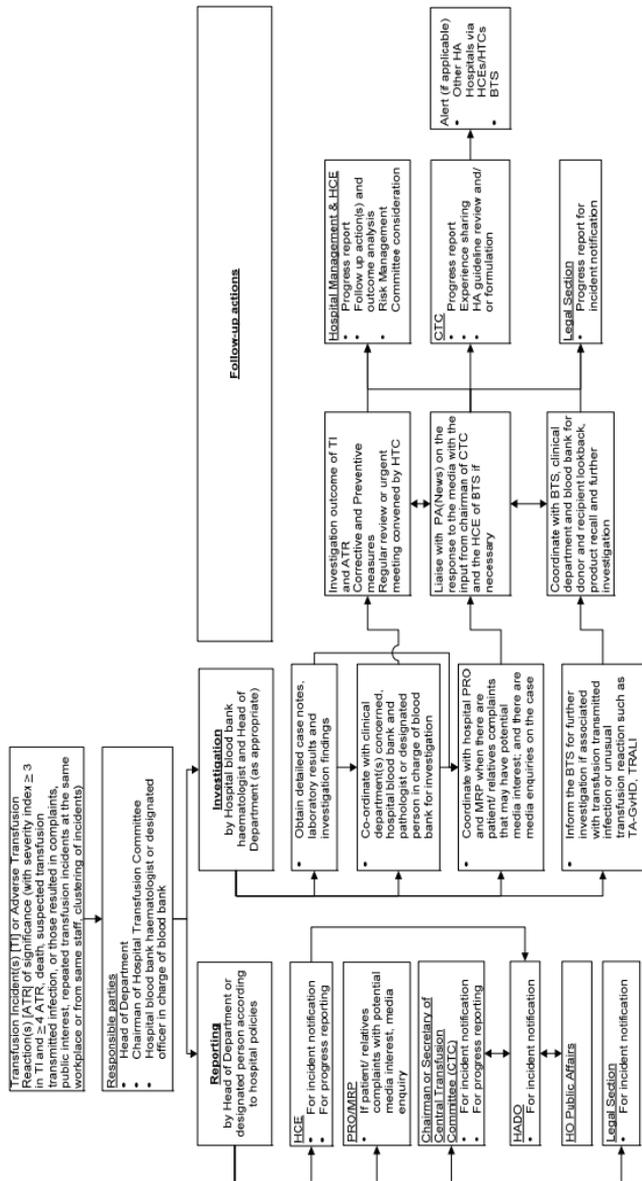
Please refer to latest version of HAHO Transfusion Guidelines at  
HA web Page (version 1.6, effective date: 4 Oct 2010)

<i>Acute Transfusion Reaction (Estimated risk)</i>	<i>Cause</i>	<i>Signs &amp; Symptoms</i>	<i>Management</i>
Allergic reaction (1:100 to 1:300)	Sensitivity to plasma protein or donor antibody	<ol style="list-style-type: none"> <li>Flushing</li> <li>Itching, rash</li> <li>Urticaria, hives</li> <li>Shortness of breath, wheezing</li> <li>Laryngeal oedema</li> <li>Anaphylaxis</li> </ol>	<ol style="list-style-type: none"> <li>Stop transfusion immediately and keep vein open</li> <li>Give Antihistamine as directed</li> <li>Observe for anaphylaxis</li> <li>If hives are the only sign, the transfusion may sometimes continue at a slower rate</li> <li>For anaphylaxis, adrenaline injection may be required.</li> </ol>
Febrile, non-haemolytic transfusion reaction (FNHTR) (1:100 with non-leukoreduced blood components)	Immunological reactions between recipient HLA or granulocyte specific antibodies with donor leukocytes or reaction to the pyrogenic cytokines released from donor leukocytes during storage	<ol style="list-style-type: none"> <li>Flushing</li> <li>Fever</li> <li>Tachycardia</li> <li>sometimes rigors</li> </ol> <p>Symptoms usually occur about 30 min to 2 hr after starting a red cell transfusion. Even earlier after a platelet transfusion</p>	<ol style="list-style-type: none"> <li>Stop transfusion immediately, keep vein open and inform clinician for assessment</li> <li>Clerical check for compatibility between recipient and blood unit(s) given</li> <li>Antipyretic e.g. paracetamol can be given</li> <li>For mild febrile reaction and rapidly resolving symptoms, transfusion may be resumed slowly.</li> <li>For severe febrile reaction (e.g. rise in temperature &gt; 1.5 °C), the same unit should not be restarted.</li> <li><b><u>Haemolytic transfusion reaction and septic reaction should always be suspected and investigated and managed accordingly.</u></b></li> </ol>
Septic reaction (Red cell 1 : 500,000 Platelet 1 : 10,000)	Transfusion of bacterial contaminated blood or blood components	<ol style="list-style-type: none"> <li>Rapid onset of chills and rigors</li> <li>High fever usually &gt; 2 °C</li> <li>Nausea, vomiting, diarrhoea</li> <li>Hypotension</li> <li>DIC</li> <li>Intravascular haemolysis</li> <li>Renal failure</li> </ol>	<ol style="list-style-type: none"> <li>Stop transfusion immediately, keep vein open and inform clinician for assessment</li> <li>Monitor patient closely for septicæmic shock</li> <li>Clerical check for compatibility between recipient and blood unit(s) given and exclude haemolytic transfusion reaction accordingly</li> <li>Obtain patient's blood for septic workup and send blood bags and administration set for culture</li> <li>Treat septicæmia with intravenous broad spectrum antibiotics with adequate anti-pseudomonas coverage</li> <li>Report through hospital blood bank to HKRCBTS for further investigation</li> </ol>

<b>Acute Transfusion Reaction (Estimated risk)</b>	<b>Cause</b>	<b>Signs &amp; Symptoms</b>	<b>Management</b>
Circulatory overload (1 : 10,000)	Blood component(s) was administered at a rate or volume more than the recipient circulatory system can accommodate.	<ol style="list-style-type: none"> <li>Rise in jugular venous pressure with distended neck veins</li> <li>Dyspnoea</li> <li>Cough</li> <li>Crackles in bases of lung</li> </ol>	<ol style="list-style-type: none"> <li>Withhold transfusion immediately and exclude other causes</li> <li>Support treatment e.g. place patient upright with feet in dependent position; give diuretics, oxygen supplement, etc.</li> <li>May require intubation if severe dyspnoea</li> </ol>
Haemolytic transfusion reaction (1 in 250,000 – 1,000,000)	Infusion of incompatible blood components	<ol style="list-style-type: none"> <li>fever, chills and rigors or both</li> <li>pain at the infusion site or localized to the loins, abdomen, chest or head</li> <li>hypotension, tachycardia or both</li> <li>agitation, distress and confusion; particularly in the elderly</li> <li>nausea or vomiting</li> <li>dyspnoea</li> <li>flushing</li> <li>haemoglobinuria</li> </ol>	<ol style="list-style-type: none"> <li>Stop transfusion immediately and spigot off the unit. (<b>save the blood units and blood giving set for investigation</b>)</li> <li>Use a new giving set and keep vein open with normal saline</li> <li>Inform clinician for urgent assessment</li> <li>Clerical check for compatibility between recipient and blood unit(s) given</li> <li>Inform blood bank to return blood units for investigations and collect additional blood samples</li> <li>Treat shock if present</li> <li>Collect urine samples</li> <li>Maintain BP with IV colloid solutions. Give diuretics as prescribed to maintain adequate urine output</li> <li>Insert indwelling catheter to monitor hourly urine output. Patient may require dialysis if renal failure occurs</li> </ol>
Transfusion related acute lung injury (TRALI) (1 in 50,000 – 200,000 reported in the literature)	? due to the presence of antibodies (anti-granulocyte-specific, anti-HLA class I, anti-HLA class II, anti-IgA, other ?) from donors to cause immune reaction in the recipient resulting in the clinical manifestation in the lung.	<ol style="list-style-type: none"> <li>Acute respiratory distress occurring within 6 hour of starting a transfusion</li> <li>Severe bilateral pulmonary edema</li> <li>Severe hypoxia</li> <li>Fever</li> <li>Chest X ray shows peri-hilar and nodular shadowing in the mid and lower zone</li> </ol>	<ol style="list-style-type: none"> <li>Withhold transfusion immediately and exclude other causes of shortness of breath e.g. circulatory overload</li> <li>Prompt and full respiratory support</li> <li>If properly treated, reversible and recovered without sequelae (pulmonary edema can clear usually within 72 hr)</li> <li>Report through hospital blood bank to HKRCBTS for further investigation</li> </ol>

Blood/ blood component	Dosage	Indications
Fresh whole blood ( $\leq$ 5 days from donation)	1 - 2 units	Exchange transfusion or massive blood loss in neonates
Whole blood/ Red cells	<p>Dosage depends on clinical situations</p> <p>One standard unit (derived from 450 ml whole blood donation) should raise Hb level by up to 1.2 g/dL in a 70 kg adult.</p> <p>One small unit (derived from 350 ml whole blood donation) should raise Hb level by about 0.85 g/dL in a 70 kg adult.</p> <p>For children, 4 ml/kg should raise Hb level by 1 g/dL</p>	<p>There is no single haemoglobin value that must be taken as the transfusion trigger. However, a trend towards cautious blood transfusion trigger has been observed but patients' condition may affect clinical decision. The initiation of transfusion is a clinical decision by the attending clinician. In general, the following principles are considered:</p> <ol style="list-style-type: none"> <li>1. Haemoglobin concentration <math>&lt;7</math>g/dL and assessment on the rate of ongoing red cell loss.</li> <li>2. For haemoglobin concentration between 7 and 10 g/dL, transfusion strategy is less clear but general view is that transfusion is often not justified purely based on haemoglobin concentration.</li> <li>3. A higher haemoglobin concentration may be required in patients who may tolerate anaemia poorly, e.g. patients over the age of 65 years and patients with cardiovascular or respiratory disease.</li> </ol>
Platelet concentrates (either prophylactic or therapeutic)	<p>4 random donor units (each derived from 350 ml or 450 ml whole blood donation) for adults up to 70 kg;</p> <p>each unit should raise platelet count by <math>7-10 \times 10^9/L</math></p> <p>5 units/<math>M^2</math> for paediatric patients</p> <p>1 unit of apheresis platelet concentrate is equivalent to one standard adult dose (for adults up to 70 kg)</p>	<ol style="list-style-type: none"> <li>1. Platelet <math>&lt;10 \times 10^9/L</math> in stable patients (usually NOT indicated in ITP, SLE, TTP and HUS).</li> <li>2. Platelet <math>&lt;20 \times 10^9/L</math> in patients with fever or sepsis.</li> <li>3. Platelet <math>&lt;50 \times 10^9/L</math> with diffuse microvascular/mucosal bleeding, major bleeding or before invasive procedures.</li> <li>4. Platelet <math>&lt;100 \times 10^9/L</math> with retinal or CNS bleeding/ surgery, or with active bleeding in postcardiopulmonary bypass.</li> <li>5. Platelet <math>&lt;50 \times 10^9/L</math> in stable premature neonates or platelet <math>&lt;100 \times 10^9/L</math> in sick premature neonates</li> <li>6. Suspected platelet dysfunction with active bleeding or before invasive procedures.</li> <li>7. Suspected platelet deficiency with severe active bleeding or following massive transfusion.</li> </ol>

Blood/ blood component	Dosage	Indications
Buffy coat/ granulocytes (must be irradiated) (Require special arrangement with the HKRCBTS)	10 units/day for $\geq 4$ days or until fever subsides	1. Neutropenia ( $<0.5 \times 10^9/L$ ) with documented infection unresponsive to broad spectrum antibiotics including antifungal agents for at least 48 hours.
Fresh frozen plasma	Typical dosage: 2 - 4 units for adults 12 - 15 ml/kg for paediatric patients ** always reassess for clinical and laboratory responses	1. Thrombotic thrombocytopenic purpura (TTP). 2. When clotting factors deficiency is suspected or anticipated with active bleeding during operation or following massive transfusion, and PT/APTT is not readily available 3. Immediate reversal of warfarin overdose (bleeding or impending surgery). 4. PT/APTT $>1.5x$ control values with active bleeding or before invasive procedure in the following situations: <ul style="list-style-type: none"> <li>▪ Single or multiple clotting factor deficiency (other than haemophilia A/B).</li> <li>▪ Disseminated intravascular coagulopathy (DIC).</li> <li>▪ Hepatic failure.</li> <li>▪ Massive transfusion.</li> </ul>
Methylene Blue treated FFP	Supply for pediatric patients only.	As for fresh frozen plasma, with lower residual infectious risk
Cryoprecipitate	Depends on the target factor levels in particular diseases and clinical situations, ranging from 6 - 30 units/dose; 10 units per dose for adults up to 70 kg	1. von Willebrand disease (if DDAVP or factor concentrate is inappropriate). 2. Documented fibrinogen deficiency ( $<100$ mg/dL) or dysfunction. 3. Documented factor XIII deficiency.
Leukodepleted (filtered) red cells	Same as other red cell preparations	1. All thalassaemia patients on regular transfusion regimens; 2. Haematological diseases; 3. Documented severe febrile non-haemolytic transfusion reaction ( $\geq 2$ episodes); 4. Paediatric oncology patients.
Irradiated cellular blood components	Same as non-irradiated counterparts	For prevention of transfusion-related graft versus host disease in circumstances such as: <ol style="list-style-type: none"> <li>1. Foetuses requiring intrauterine transfusion.</li> <li>2. Patients with severe congenital cellular immunodeficiency.</li> <li>3. Stem cell transplantation patients.</li> <li>4. Patients receiving transfusion from close relatives.</li> </ol>
Rh(D) negative red cells	Same as Rh(D) positive red cells	1. Haemolytic disease of newborn due to anti-D. 2. Rh(D) negative individuals with anti-D. 3. Rh(D) negative females prior to menopause. 4. Emergency resuscitation of Caucasian females in reproductive age with unknown Rh(D) status. 5. Other Rh(D) negative individuals (lower priority; availability depending on stock).



Flowchart 5 shows framework of action(s) to be taken following transfusion incident and adverse transfusion reactions of significance.

HA Transfusion Guideline 1.6

Effective date: 4 Oct 2010

# Nephrology



## **RENAL TRANSPLANT– DONOR RECRUITMENT**

### Protocol for preparation and management of potential organ donor:

#### Identification of potential organ donor:

- a. definite diagnosis, irreversible CNS damage;
- b. brain death is imminent;
- c. put on mechanical ventilation;
- d. GCS 3-5 / 15, both pupils fixed to light

#### Exclusion criteria:

- Age  $\geq$  71 (for kidney donors);
- Uncontrolled fulminant infection;
- Risk of transmission of disease caused by prions, including Creutzfeldt-Jakob disease, rapid progressive dementia or degenerative neurological disease;
- History of IV drug abuse;
- HIV +ve cases or has risk factors for HIV infection;
- Presence or previous history of malignant disease (except primary basal cell carcinoma, carcinoma in-situ of uterine cervix and some primary tumor of CNS)

#### Maintenance of organ perfusion of potential donor:

##### Aim:

Maintain SBP 100 - 140mmHg, AR 60-120 bpm

Maintain Mean BP  $>$  80mmHg

Maintain CVP of 8-12cm H<sub>2</sub>O

Maintain hourly urine output  $\sim$ 100ml

Maintain intake and output balance and cover insensible loss

Maintain  $\text{SaO}_2 \geq 95\%$

Maintain body temperature  $> 36^\circ\text{C}$

- a. Monitor BP, P, CVP, urine output,  $\text{SaO}_2$ , ventilator status q1h, body temperature q2h
- b. Monitor electrolytes, RLFT,  $\text{Ca}/\text{PO}_4$  q6-8h, H'stix q2-4h
- c. Set two good IV lines, preferably one central line
- d. Monitor BP:
  - If persistently hypertensive (MBP  $> 120\text{mmHg}$ ), start labetalol 5mg IV over 1 min and repeat at 5 min intervals if necessary
  - If persistently hypotensive (SBP  $\leq 100\text{mmHg}$ )
    - : Start fluid replacement by infusing crystalloid or colloid
    - : Add dopamine 2.5 – 10  $\mu\text{g}/\text{kg}/\text{min}$  if BP persistently low despite adequate fluid replacement
    - : Add adrenaline 0.1 – 10  $\mu\text{g}/\text{kg}/\text{min}$ 
      - If BP persistently low: start hydrocortisone 100mg stat & 100 mg q8h
- e. Monitor urine output: If massive urine output ( $> 200\text{ml}/\text{hour}$ )
  - : Control hyperglycaemia (H'stix  $> 12\text{mmol}/\text{L}$  persistently) by Actrapid HM hourly infusion at 2 – 6 units
  - : Control diabetes insipidus (serum Na  $\geq 150\text{mmol}/\text{L}$ ) by dDAVP 2-6 $\mu\text{g}$  IV q6-8h
  - : Control hypothermia (body temperature  $\leq 35^\circ\text{C}$ ) by apply patient warming system
  - If oliguric (hourly urine  $< 30\text{ml}$ )
    - : check Foley patency
    - : oliguria with low or normal CVP, start fluid replacement
    - : oliguria with high CVP, start lasix 20 – 250mg IVI
- f. Add prophylactic antibiotics after blood culture if fever  $> 38^\circ\text{C}$ .

Routine arrangement:

- a. Inform transplant coordinator via hospital operator at any time
- b. Interview family for grave prognosis, do not discuss organ donation with family until patient is confirmed brain death
- c. Once the patient meets brain death criteria, arrange qualified personnel to perform brain stem death test

## ELECTROLYTE DISORDERS

### Hypokalaemia

- Hints - Check drug history, most likely attributed to diuretic therapy;
- Usually associated with metabolic alkalosis;
  - Start intravenous therapy if serum K < 2.5 mM;
  - Consider magnesium depletion if hypoK is resistant to treatment;
  - Don't give potassium replacement therapy in dextrose solution.
- Ix: - serum RFT, total CO<sub>2</sub> content, chloride, magnesium;
- simultaneous blood and urine x TTKG (trans-tubular potassium gradient)
  - check baseline ECG (esp. those patients on digoxin therapy)

Mx: If serum K > 2.5 mM & ECG changes are absent:

KCl 20-30 mmol/hour in saline infusion (up to 60-80 mmol/L) as continuous IV infusion; may combine with oral KCl 30-40 mmoles (3-4 gm syr KCl) Q4H; maximum total treatment dose: 100 – 200 mmoles per day (~ 3 mmoles/kg/day).

If serum K < 2.5 mM &/or ECG changes present:

Consult ICU / cardiac monitor;

KCl 30-40 mmol/hour in saline infusion (concentration up to 80 mmol/L); may combine with oral KCl 30-40 mmoles (3-4 gm syr KCl) Q4H; maximum total treatment dose: 100 – 200 mmoles per day (~ 3 mmoles/kg/day).

Hypokalaemia associated with metabolic acidosis

Give potassium citrate solution (1 mmole/mL) 15-30 mL QID in juice after meals; start K replacement before bicarbonate therapy in separate IV line if indicated.

Dosage form:

Syrup KCl ( 1 gram = 13.5 mmoles K );  
 Slow K ( 8 mmoles K / 600 mg tablet );  
 Potassium citrate ( 1 mL = 1 mmole K );  
 Phosphate-sandoz ( 3 mmoles K, 16 mmoles phosphate / tablet ).

Pre-mixed K-containing solution for maintenance IV infusion for HA Hospitals

0.9% NS with 10 mmoles K / 500 mL ( K conc: 20 mM)  
 0.9% NS with 20 mmoles K / 500 mL ( K conc: 40 mM)  
 5% D5 with 10 mmoles K / 500 mL ( K conc: 20 mM)  
 5% D5 with 20 mmoles K / 500 mL ( K conc: 40 mM)  
 Lactated Ringer's with 2 mmoles K /500 mL (K conc: 4 mM)

**Hyperkalaemia**

Hints: Exclude pseudohyperK e.g. haemolysis, esp. in those with relatively normal renal function;  
 discontinue K supplement, NSAID, ACEI, K-sparing diuretic.

Ix: Repeat RFT CO<sub>2</sub> chloride, ECG

Rx: For urgent cases ( serum K > 6 mM &/or ECG changes of hyperK )

1. 10% Calcium gluconate 10 mL IV over 2-3 minutes

with cardiac monitoring; repeat if no effect in 5 minutes (onset: 1-3 min; duration: 30-60 min ). If digoxin toxicity is suspected, omit calcium gluconate infusion.

2. Dextrose-insulin infusion: give 250 mL D10 or 50 mL D50 with 8-10 units Actrapid HM over 30 minutes; repeat every 4-6 hrs if necessary (onset: 30 minutes; duration: 4-6 hrs ).
3. Sodium bicarbonate 8.4% 100-150 mL over 30-60 min; to be given after calcium infusion in separate IV line; watch out for fluid overload (onset: 5-10 minutes; duration: 2 hrs).
4. Resonium C / A: 15-50 g orally Q 4-6 hrs or as retention enema; may be given in 100-200 mL 10% mannitol as laxative; one gm resonium will bind 1 mmole of K. (onset: 1-2 hrs; duration: 4-6 hrs).
5. Salbutamol 10-20 mg in 3 mL NS by nebulizer (onset: 15-30 minutes; duration: 2-3 hrs).
6. Diuretics: furosemide 40-80 mg IV bolus.
7. Emergency haemodialysis or peritoneal dialysis.

For chronic cases:

1. Low K diet (< 2 g/ day).
2. Diuretics: furosemide / thiazide
3. Correct acidosis with sodium bicarbonate 300-900 mg tds (~10-30 mmoles/day).
4. Fludrocortisone 0.1-0.2 mg daily (for Type IV RTA).

## Hypercalcaemia

Hints: calculated corrected serum calcium level based on serum albumin concentration

Corrected calcium =  $0.02 * (40 \text{ g/L} - \text{patient's albumin (g/L)}) + \text{serum Ca}$ ; commonly associated with dehydration.

Ix: check ionized calcium,  $\text{PO}_4$ , RFT, ECG

Rx:

1. Off calcium / vitamin D supplement if any.
2. Volume repletion with NS at 100-500 mL/hr infusion ( guided by CVP / urine output ); start furosemide after rehydration 20-40 mg IV Q 2-12 H; aim at a urine output of ~ 200 mL/Hr; close monitoring of Na K Ca Mg level.
3. Pamidronate 30-90 mg in 250-500 mL NS infused over 4-6 hrs; maximum effect is not seen for several days; repeat another dose after a minimum of 7 days if necessary.
4. Salmon calcitonin 4 IU/kg IMI / SC Q 12 H; Ca level begins to fall within 2-3 hrs; tachyphylaxis occurred within 2-3 days.
5. Mithramycin: 25  $\mu\text{g/kg}$  IV in 500 mL D5 over 3-6 hrs infusion; Ca begins to decrease in 12 hrs; peak action at 48 hrs; repeat dose at 3-7 days interval if necessary (usually reserve for malignancy-related hypercalcaemia ).
6. Hydrocortisone 5 mg/kg IV Q 8 H then prednisolone 40-100 mg QD ( onset: 3-5 days; useful in haematological malignancy, vitamin D intoxication, some CA breast).
7. Sandoz-phosphate 2-8 tablets per day; avoid if severe hypercalcaemia or hyperphosphataemia.
8. Haemodialysis with zero or low Ca dialysate.

## Hypocalcaemia

Hints: usually due to chronic renal failure;

Ix: check ionized Ca level, PO<sub>4</sub>, ALP, Mg, RFT, amylase, CK, ECG.

Rx: Symptomatic hypocalcaemia: 10% Calcium gluconate 20 mL IV over 10-15 minutes then 30 mL 10% Ca gluconate in 500 mL NS/D5 Q 4-6 H /pint; monitor Ca level.

Chronic cases: ( add Vit D if no response after 2-4 gm elemental Calcium )

1. Ca supplement: Caltrate=600 mg elemental Ca / tablet  
Oscal=250 mg elemental Ca / tablet  
Titalac=168 mg elemental Ca / tablet  
Ca gluconate=27mg elemental Ca / tablet
2. Vit D: Calcitriol/1- $\alpha$ -hydroxycholecalciferol: 0.25-2ug daily

## Hypomagnesaemia

Hints: may be associated with hypoK, hypoCa, arrhythmia.

Ix: check RFT, K, Ca, ECG.

Fractional excretion (FE) of Mg

$$= 100 \times (U_{Mg} \times P_{Cr}) / (0.7 \times P_{Mg} \times U_{Cr})$$

( if HypoMg, FE > 2.5% indicates renal loss of Mg).

Rx: Emergency:

4 mL 50% MgSO<sub>4</sub> ( 8 mmoles ) solution IV in 20 mL NS/D5 infused over 15 minutes then 10 mL 50% MgSO<sub>4</sub> ( 20 mmoles ) in 500 mL NS/D5 over 6 hrs.

Less urgent cases:

4 mL 50% MgSO<sub>4</sub> ( 8 mmoles ) solution 500 mL NS/D5 Q 8 H/pint for 1 day ( up to 50% of the infused Mg will be excreted in urine; slow and sustained correction of hypoMg is preferred)

Chronic cases:

Normal average daily intake of Mg ~ 15 mmoles ( ~ 1/3 is absorbed )

1. Mg supplement : Mylanta / Gelusil : 3.5 mmoles/tablet
2. Amiloride: 5 – 10 mg daily PO ( decrease urinary loss of Mg )

## Hypermagnesaemia

Hints: Uncommon in the absence of Mg administration or renal failure;

Mild cases ( < 1.5 mM ) usually require no treatment.

Rx: Take off Mg supplement if any;  
Saline diuresis: NS 300 – 500 mL / hr infusion;

## K - 10

10% Calcium gluconate 10 – 20 mL in 100 mL NS over 15 minutes;

Furosemide 20 – 40 mg Q2-4 Hr ( aim at urine output ~ 200 mL/hr );

Haemodialysis if necessary.

**Hyperphosphataemia**

Hints: Usually attributed to chronic renal failure;  
 Usually resolved in 6-12 hrs if RFT normal;  
 Aim at a serum phosphate level of ~ 1.4 mM for uraemic patients.

Ix: RFT Ca PO<sub>4</sub> CO<sub>2</sub> ALP

Rx: 1. Low phosphate diet (< 1 gm / 30 mmoles per day ).

2. Start phosphate-binder:

If serum phosphate < 2 mM:

Caltrate tab 1-2 tds with meal

Titralac tab 1-2 tds with meal

Ca acetate tab 1-2 tds with meal

If serum phosphate > 2 mM:

Alusorb tab 1-3 tds with meal

Alutab tab 1-3 tds with meal

3. Arrange dialysis if necessary.

**Hypophosphataemia**

Hints: usually required no treatment if serum PO<sub>4</sub> > 0.5 mM;  
 Replacement rate < 2 mg (0.067 mmoles)/kg per 6 hrs,  
 otherwise may be associated with metastatic calcification.

Ix: check RFT serum Ca / PO<sub>4</sub> ALP;

Fractional excretion (FE) of phosphate

$$FE = 100 \times (U_p \times P_{Cr}) / (U_{Cr} \times P_p)$$

(In the presence of hypoPO<sub>4</sub>, FE >5% indicates urinary loss)

Rx: IF serum PO<sub>4</sub> < 0.5 mM with symptoms:

6 mL potassium di-phosphate solution in 500 mL D5 Q 12 H infusion

## K - 12

(Potassium di-phosphate solution : 14.5 mmoles  $\text{PO}_4$  + 25 mmoles K per 10 mL solution)

### Chronic therapy:

Sandoz-phosphate tab 1 QID PO (16 mmoles  $\text{PO}_4$ ; 20 mmoles Na; 3 mmoles K / per tablet)

## Hyponatraemia

Ix: RFT, serum / urine osmolarity, spot urine x Na.

### 1. Isovolaemia:

(urine Na > 20 mM: SIADH, hypothyroid, Addison's disease;  
urine Na < 10 mM: water intoxication )

Rx: restrict water intake < 1000 mL per day;

High salt diet (> 8 gm/day) ± sodium supplement:

Syr NaCl 2 gm tds (100 mmoles);

demeclocycline 600-1200 mg daily;

For symptomatic hypoNa: 100 mL 5.85% NaCl (1 mmole/mL) over 4-6 hrs + furosemide 40 mg IV; repeat if necessary until serum Na > 120 mM or patient is asymptomatic (rapid collection > 0.5 mM / Hr elevation in serum Na may lead to central pontine myelinosis ).

### 2. Hypovolaemia:

(urine Na < 10 mM: fluid loss, hypotension, dehydration; urine Na > 20 mM: diuretics, adrenal insufficiency, salt wasting)

NS 500 mL/hr till BP normal, then replace Na deficit with NS;

Sodium deficit = BW (kg) x 0.6 x (desired [Na] – measured [Na]); replace first 50% of deficit over 4-6 hrs and the other 50% over next 18-20 hrs till serum Na level reaches 120 mM or increase by 10-12 mM over 24 hrs.

### 3. Hypervolaemia:

( urine Na < 10 mM: CHF, cirrhosis; urine Na > 20 mM: acute / CRF )

Rx: restrict water intake < 1000 mL per day;

Furosemide 40-80 mg IV / 20 – 500 mg PO daily.

**Hypernatraemia**

Ix: serum / urine x osmolality.

Rx: Hypervolaemia:

(Primary Hyperaldosteronism, Cushing's syndrome, acute salt overload)

Start D5 infusion to correct water deficit;

Add furosemide 40-80 mg IV or PO Q12-24 H

Isovolaemia or Hypovolaemia:

(Diabetes insipidus, large insensible water loss, renal / GI loss )

- If volume is depleted, give NS 500 mL/hr infusion till no orthostatic hypotension, then replace water:  
Serum Na < 160 mM: give water PO  
Serum Na > 160 mM: replace fluid with D5 or half half saline;
- body water deficit (L) =  $\{0.6 \times \text{BW}(\text{kg}) \times (\text{measured } [\text{Na}] - 140)\} / 140$ ;  
replace half of the body water deficit over first 24 hrs, then remaining deficit over next 1-2 days ( correct Na at a rate < 0.5 – 1 mM/hr; rapid correction may lead to cerebral edema );
- For acute DI: give DDAVP 4-8  $\mu\text{g}$  Q 3-4 H prn;
- For chronic central DI: DDAVP 10-40 $\mu\text{g}$  daily intranasally (in one to two divided dose)
- For chronic nephrogenic DI: thiazide diuretic, e.g. hydrochlorothiazide 25 mg daily, indapamide 2.5 mg daily, amiloride 5 mg daily

## SYSTEMATIC APPROACH TO THE ANALYSIS OF ACID-BASE DISORDERS

1. Hx and PE for causes of acid-base disturbance.
2. Identify the primary acid-base disturbance.
3. Assess adaptive response to primary acid-base disorder.

	<i>I<sup>o</sup> response</i>	<i>Adaptive response</i>
<b>Metabolic</b>		
Acidosis	↓HCO <sub>3</sub>	↓pCO <sub>2</sub> : 1.6 kPa per 10 mM ↓in HCO <sub>3</sub> pCO <sub>2</sub> =(1.5 x HCO <sub>3</sub> ) +8 ±2 mmHg
Alkalosis	↑HCO <sub>3</sub>	↑pCO <sub>2</sub> : 0.9 kPa per 10 mM ↑in HCO <sub>3</sub>
<b>Respiratory</b>		
Acidosis	↑pCO <sub>2</sub>	<i>acute</i> : 0.77 mM ↑HCO <sub>3</sub> per 1 kPa ↑pCO <sub>2</sub> <i>chronic</i> : 2.7 mM ↑HCO <sub>3</sub> per 1 kPa ↑pCO <sub>2</sub>
Alkalosis	↓pCO <sub>2</sub>	<i>acute</i> : 1.5 mM ↓HCO <sub>3</sub> per 1 kPa ↓pCO <sub>2</sub> <i>chronic</i> : 3 mM ↓HCO <sub>3</sub> per 1 kPa ↓pCO <sub>2</sub>

Suspect mixed metabolic / respiratory acid-base disorder if compensation is not appropriate (common in clinical practice!).

4. Calculate serum anion gap (Na - Cl - HCO<sub>3</sub>; normal 10 ± 4)

High AG metabolic acidosis:

- Treat underlying disorder, consider HCO<sub>3</sub> therapy if serum HCO<sub>3</sub> < 10.

Normal AG metabolic acidosis:

- Use IV NaHCO<sub>3</sub> (1 mL = 1 mmoles of HCO<sub>3</sub>) if serum HCO<sub>3</sub> < 10 (To be given in large vein over 1-2 hrs, watch out for fluid / salt overload).
- IV NaHCO<sub>3</sub> required = (15 - measured HCO<sub>3</sub>) x BW (kg) x 0.5  
(Correct to HCO<sub>3</sub> > 15 mM is usually sufficient)

5. For patients with acidosis:

Compare  $\Delta$ AG with  $\Delta$ serum  $\text{HCO}_3^-$  (abnormal if discrepancy  $> 5$ ):

$\Delta$ AG  $>$   $\Delta$  serum  $\text{HCO}_3^-$ : mixed metabolic acidosis / alkalosis

$\Delta$ AG  $<$   $\Delta$  serum  $\text{HCO}_3^-$ : mixed normal AG /  $\uparrow$ AG metabolic acidosis

6. Measure urine electrolytes / pH:

a) For patients with metabolic alkalosis

urine Cl  $<$  15 mM – Cl responsive metabolic alkalosis, e.g. vomiting

urine Cl  $>$  15 mM – Cl resistant metabolic alkalosis, e.g. mineralocorticoid excess, during diuretic therapy.

b) For suspected renal tubular acidosis

urine anion gap :  $\text{Na} + \text{K} - \text{Cl}$  (normal: negative)

urine osmolar gap:  $[\text{urine osmolality} - 2(\text{Na} + \text{K}) - \text{urea}] / 2$   
(normal:  $>30$ )

abnormal value indicates low ammonium excretion, e.g. distal RTA

*\*false positive conditions:* - present of an unusual anion in urine, e.g. ketone; excessive bicarbonaturia, urine pH  $>$  6.5

Causes for high anion gap metabolic acidosis (MULEPAK)

M = methanol, U = uraemia, L = lactic acidosis,

E = ethylene glycol P = paraldehyde, A = aspirin, K = ketosis

Causes for normal anion gap metabolic acidosis (USED CAR)

U = ureteroenterostomy, S = saline infusion, E = endocrinology

e.g.: Addison, D = diarrhoea, C = carbonic anhydrase inhibitor,

A = ammonium chloride R = renal tubular acidosis

**Therapeutic Options in patient with metabolic acidosis:**

Hints: In order to avoid being misled by acute hyperventilation or hypoventilation, plasma  $[\text{HCO}_3^-]$  is, in general, a better guide to the need of  $\text{NaHCO}_3$  therapy than systemic pH.

1. Correction of metabolic acidosis with  $\text{HCO}_3^-$ 

- Oral  $\text{NaHCO}_3$ : 300 mg ( 3.6 mmoles ) per tablet
- $\text{NaHCO}_3$  required (mmoles) = (desired – measured  $\text{HCO}_3^-$ ) x BW(kg) x 0.5
- Give over 1 – 2 hours as 8.4%  $\text{NaHCO}_3$  IVI ( 1 mL = 1 mmole  $\text{HCO}_3^-$  )
- Overcorrection may increase  $\text{CO}_2$  production, which can aggravate respiratory acidosis in a poorly ventilated patient. Watch out for hypercapnia which may cause paradoxical increase in acidaemia after  $\text{NaHCO}_3$  therapy
- Can worsen or precipitate hypokalaemia.

2. Hyperventilation:

If the patient with severe metabolic / respiratory acidosis is in pulmonary oedema, one should consider ventilating the patient to lower  $\text{P}_{\text{CO}_2}$  appropriately to treat acidaemia. Acidaemia responds much faster to lowering the  $\text{P}_{\text{CO}_2}$  than to IV  $\text{NaHCO}_3$  therapy.

3. Dialysis:

- Especially in those patients with volume overload;
- Use  $\text{HCO}_3^-$  bath for haemodialysis.

**Therapeutic options in patients with metabolic alkalosis:**

Hints: Metabolic alkalosis is a disorder caused by mechanisms whereby  $[\text{HCO}_3^-]$  is elevated; and a renal basis, e.g. hypovolaemia, to maintain an elevated  $[\text{HCO}_3^-]$  level. Both processes must be corrected if possible for an optimal response to therapy.

**Chloride-responsive metabolic alkalosis ( urine chloride  $< 15$  mM ):**

- give NS  $\pm$  KCl to correct ECF volume;
- give  $\text{H}_2$  antagonist if alkalosis due to NG suction;
- acetazolamide 250 mg QID PO / IV ( may promote K loss ).

**Chloride-resistant metabolic alkalosis ( urine chloride  $> 15$  mM ):**

- Block mineralocorticoid effect with spironolactone 100 – 400 mg daily PO.

## PERI-OPERATIVE MANAGEMENT IN URAEMIC PATIENTS

1. Assess fluid status, BP control.
2. Check Na, K, urea, Creatinine, Ca/PO<sub>4</sub>, CBP, arterial blood gases, CXR, ECG.
3. Consult renal team for need of peri-operative dialytic support.  
 HD: preferably 1 day before operation (pre-dilution / tight heparin).  
 PD: continue CAPD. Cap off Tenckhoff catheter and drained out PDF for abdominal operation.  
 Transplant recipient: continue usual dose of immunosuppressive agents
4. Steroid cover for those patients on oral steroid.
5. Treatment of bleeding tendency: **(arrange dialysis if available)**

	<u>Dosage</u>	<u>Onset time</u>	<u>Remark</u>
A) Blood Transfusion	-----		<i>Hb &gt; 8 g/dL, Hct &gt; 0.26. fluid overload.</i>
B) dDAVP	0.3 µg/kg SC (Octostim: 15 µg/ml) or 40 µg intranasally BD	1 hour	for 2 days then off.
C) Cryoppt	10 bags	1 hour	Major bleeding
D) FFP	5 units	1 hour	Major bleeding
E) Premarin	0.6 mg/kg IV daily x 5/7	> 6 hour	For major surgery or long lasting effect.

## RENAL FAILURE

Hints: *Exclude pre-renal failure:* Orthostatic hypotension, congestive heart failure, cirrhosis

*Exclude post-renal failure:* PR exam, feel for bladder, bedside USG

Ix: CBP, RLFT, CO<sub>2</sub>, Cl, Ca, PO<sub>4</sub>, amylase, urate, arterial blood gases, CXR, ECG;

24 hr urine x Na K P Cr Cr Clearance;

MSU x RM C/ST, urine x dysmorphic RBC;

Autoimmune markers : ANF, DsDNA, C3/4, ANCA, anti-GBM, etc ;

HBsAg/Ab, anti-HCV (urgent HBsAg if hemodialysis is anticipated);

Urgent USG kidneys, KUB.

### Treatment of suspected acute renal failure:

1. Fluid intake = 500 mL + urine output;  
Fluid challenge: NS 500-1000 mL over 1-2 hrs for hypovolaemia;  
Add furosemide 10 mg/hr IV infusion for fluid overload;  
metolazone 5-10 mg daily PO;  
Dopamine 2.5 µg/kg/min to improve renal blood flow.
2. Correct electrolyte disturbances: hyperkalemia, metabolic acidosis.
3. Low salt diet (< 100 mmoles per day), low K (<20 mmoles/day), low phosphorus diet (<800 mg day), low protein diet (40 gm HBV).
4. Strict I/O chart, daily BW (< 1 kg increase in BW per day)
5. Emergency indications for dialysis: uncontrolled hyperkalemia (>6 mM); uncontrolled metabolic acidosis (HCO<sub>3</sub> <10 mM); uncontrolled pulmonary edema.

6. Less urgent indications for dialysis: uraemic pericarditis, uraemic encephalopathy, intractable uraemic symptoms.
7. Inform on-call renal physician for acute HD support if indicated.
8. Avoid nephrotoxic drugs if possible, e.g. NSAID, aminoglycoside, etc.

### **Treatment of chronic renal failure:**

1. Consult nephrologist for assessment of feasibility of long-term renal replacement therapy.
2. No blood taking / BP measurement from AV fistula arm.
3. Monitor AV fistula daily / exit site dressing daily for CAPD patients.
4. Strict I/O chart, daily BW ( < 1 kg increase in BW per day ).
5. Diet ( ± consult dietitian ):
  - Calorie     30-35 kcal/kg/day ( 500-700 kcal from PD already for CAPD patients );
  - Protein:    0.6-0.75 gm/kg/day for CRF patients  
               1.2-1.3 gm/kg/day for CAPD patients  
               1-1.2 gm/kg/day for HD patients.
  - Na: < 100 mmoles per day for CRF / HD patients (except salt-loser )  
       No restriction for euvolaemic CAPD patients.
  - K: < 1 mmole/kg/day.
  - PO<sub>4</sub>: <800 mg/day.
  - Vitamin:    Ascorbic acid 100 mg/day (optional)  
               Folic acid 5 mg/day (optional)  
               Rocaltrol / Alfacalcidol: 0.25-2 µg /day ( For renal osteodystrophy).
6. Control hypertension (<140/90 mmHg): long-acting calcium channel blocker, beta-blocker, ACEI (monitor RFT, K ).

7. Correct metabolic acidosis, hyperK, hypocalcaemia.
8. Symptomatic anaemia: transfusion ( preferably during dialysis using pack cell); give Lasix 20-80 mg IV before transfusion; sustanon 250 mg IMI Q 3-4 week; consider EPO therapy for refractory anaemia.

## EMERGENCIES IN RENAL TRANSPLANT PATIENTS

### Fever:

Both infection and acute graft rejection can present as fever;

a. Infection:

- Consider opportunistic infection if < 6 months post-transplant;
- Usual pattern of infection if > 6 months post-transplant;
- Search for infection: Hx, PE, culture from wound, urine, IV lines, sputum, blood, viral culture & serology, CMV pp-65 Ag, CXR;
- Check CBP D/C, RLFT, CsA / Tacrolimus trough level, 24 hr urine x P & Cr;
- Avoid macrolide antibiotics / fluconazole (may increase CsA / Tacrolimus level)

b. Acute graft rejection:

- Acute increase in serum creatinine > 20% after excluding other causes;
- May present as oliguria, graft tenderness, fever, ankle edema, hypertension;
- Check CBP, RLFT, CsA / tacrolimus trough level, 24 hr urine x P & Cr, MSU;
- Arrange urgent USG kidney + Doppler study;
- Consider renal biopsy

### Oligouria / Anuria:

- DDX: acute graft rejection  
acute CsA, tacrolimus toxicity  
obstructive uropathy  
urinary leakage  
acute tubular necrosis  
acute vascular ( arterial or venous ) thrombosis.
- Treatment according to the cause

## K - 24

- Check CBP, RLFT, CsA / tacrolimus trough level, MSU RM C/ST, 24 hr urine x P Cr
- Monitor I/O chart, hourly urine output
- Urgent USG graft kidney + Doppler study
- Arrange standby MAG-3 / DTPA scan
- Renal biopsy.

**DRUG DOSAGE ADJUSTMENT IN RENAL FAILURE**

(D: reduce dose (in %), same interval as in normal; I: same dose as normal, increase interval between 2 dose (in hrs))

Name	Adjustment for Renal Failure				Supplement for Dialysis	
	GFR (ml/min)				HD	PD
	D/I	>50	10-50	<10 or ESRF		
Adriamycin	D	100	100	75	?	?
Allopurinol	D	100	75	50	?	?
	I	8	8-12	12-24		
Amiloride	D	100	50	avoid	?	?
Atenolol	D	100	50	25	+	-
	I	24	48	96		
Azathioprine	D	100	100	75	+	-
Captopril	D	100	75	50	-	-
Carbamazepine	D	100	100	75	-	-
Chlorpropamide	I	24	avoid	avoid	-	-
Cimetidine	D	100	50	25	-	-
Colchicine	D	100	100	50	-	-
Cyclophosphamide	D	100	100	50-75	+	-
	I	24	24	36		
Digoxin	D	100	25-75	10-25	-	-
Disopyramide	I	none	12-24	24-40	+	-
Gemfibrozil	D	100	50	25	?	?
Hydralazine	I	8	8	8-16	-	-
Insulin	D	100	75	50	?	?
Methyldopa	I	6	8-12	12-24	+	-
Nadolol	D	100	50	25	+	-
Neostigmine	D	100	50	25	-	-
Penicillamine	D	100	avoid	avoid	?	?
Probenecid	D	100	avoid	avoid	?	?

Procainamide	I	4	6-12	8-24	+	-
Spironolactone	D	100	50	avoid	?	?
	I	6-12	12-24	avoid		
Sulindac	D	100	100	50	?	?

### Common Drugs not requiring dosage adjustment in Renal Failure

Barbiturates	Benzodiazepines	Bromocriptine	Cefoperazone
Ceftriaxone	Cholestyramine	Cloxacillin	Diltiazem
Erythromycin	Furosemide	Heparin	Ketoconazole
Levodopa	Lignocaine	Minoxidil	Nifedipine
Nitrates	Prazosin	Propylthiouracil	Quinidine
Na valproate	Steroids	Streptokinase	Theophylline
Tolbutamide	Verapamil	Warfarin	

### **Drug interaction with calcineurin inhibitor (tacrolimus, cyclosporine)**

#### Increase drug level:

Imidazole:	ketoconazole, fluconazole
Macrolide:	erythromycin, clarithromycin
Calcium channel blocker:	verapamil, diltiazam
Antidepressant:	fluoxetine (Prozac)
Grapefruit juice	

#### Decrease drug level:

Anti-TB drug:	isoniazid, rifampicin, ethambutol
Anti-convulsant:	phenytoin
Lipid-lowering agent:	cholestyramine

Sulfamethoxazole

Ethanol

#### Additive nephrotoxicity:

Aminoglycoside

Amphotericin B  
Sulphonamide / Trimethoprim  
Colchicine  
NSAID

Others:

Hyperkalaemia with ACEI, K-sparing diuretics, NSAID  
Myopathy / rhabdomyolysis with HMG-CoA reductase inhibitor

Estimation of Creatinine Clearance

$$\text{Cr Cl (ml/min)} = [(140 - \text{Age}) \times \text{BW (kg)}] / [0.82 \times \text{Cr } (\mu\text{M})]$$

\*\* value x 0.85 for women

## **PROTOCOL FOR TREATMENT OF CAPD** **PERITONITIS**

(BASED ON RECOMMENDATION OF ISPD, 2010)

### **1. Treatment of peritonitis in CAPD patients**

When patient have signs and symptoms of peritonitis S/S:

- Turbid fluid
  - Abdominal pain
  - Fever
- a. Ask patient to come back immediately to dialysis unit for collection of PDF
  - b. Send PDF :
    - White cell count with differential, gram smear
    - Culture
  - c. Rapid flushing of 3 bags of PDF with heparin 500 units per litre for symptomatic relief
  - d. Adequate analgesia
  - e. Increase to 4 exchanges per day to improve ultrafiltration
  - f. Heparin: 500-1000 units/ L until signs and symptoms subsided or until fibrin clots no longer visible
  - g. Preliminary antibiotics regime:
    - Empiric antibiotics must cover both gram-positive and gram-negative organisms.
    - Gram-positive organisms may be covered by vancomycin or a cephalosporin, and gram-negative organisms by a third/forth-generation cephalosporin (ceftazidime, cefepime), aminoglycoside or carbapenam

**Suggested protocol****A. CAPD (intermittent dosing method)**

- Daily urine output > 100 ml per day or deafness or recent history of aminoglycoside in recent 3 months:

## ❖ Protocol 1

Loading dose:

Cefazolin 1 gram and Cefepime 1gram loading IP, allow to dwell for at least 6 hours

Maintenance dose:

Cefazolin 1 gram + Cefepime 1gram into last bag QD (at least 6 hours dwell) x 13 days

- Daily urine output < 100 ml per day and no recent history of or contraindication to aminoglycosides:

Cefazolin 1 gram and Gentamicin 80 mg IP as loading dose, then Cefazolin 1 gram and Gentamicin 40 mg IP into last bag x 13 days.

- Substitute vancomycin (1gram iv or IP every 5-7 days) for cefazolin if MRSE or MRSA suspected; **no routine use of Vancomycin to avoid emergence of VRE**
- Change antibiotics regime once culture and sensitivity result available
- For St. aureus or pseudomonas peritonitis, antibiotics should be given x **21 days**; otherwise **14 days** of antibiotics are adequate
- For refractory, recurrent or relapsing peritonitis, add Nystatin oral suspension to prevent Candida peritonitis

**B. CCPD (intermittent dosing method)**

- Can convert to CAPD temporarily
- Intermittent dosing not recommended for severe cases
- Mild to moderate case: Cefazolin with Cefepime 1 gram

into long daytime dwell

- h. If patient has evidence of septicemia, admit patient and give **parenteral** antibiotics
- Cefazolin 500 mg i.v.i. Q12Hr + Cefepime 1 Gm i.v.i. Q24H (if daily urine > 100 ml per day)
  - Cefazolin 500 mg i.v.i. Q12Hr + Gentamicin 100 mg Q48Hr (if anuria and no recent aminoglycosides in 3 months)
- i. Change antibiotics later according to culture and sensitivity result and give adequate duration of antibiotics (14 – 21 days)
- j. Repeat PDF x WCC and gram smear, culture on D4, reassess the S/S
- k. Consider removal of Tenckhoff catheter if peritonitis fails to respond to appropriate antibiotic within 5 days
- l. Change transfer set after completion of antibiotics if patient recovered

## 2. Treatment of fungal peritonitis

- Arrange removal of Tenckhoff catheter
- Arrange insertion of triple-lumen central venous catheter for amphotericin B infusion and haemodialysis
- Continue CAPD until on call to OT, drain out the PDF before going to OT
- Amphotericin B:  
Test dose – 1 mg in 100 ml D5 over 1 hr  
then 10 mg / 200 ml D5 over 6 hr on D1, 20 mg / 200 ml D5 over 6 hr from D2-21  
alternative: Fluconazole: 200 mg loading and then 100 mg QD  
p.o. x 3 weeks

## 3. Antibiotic prophylaxis for procedure:

- For dental procedure, a single oral dose of amoxicillin (2 g) 2 hours before extensive dental procedures
- For patients undergoing colonoscopy with polypectomy – Ampicillin (1 g) plus a single dose of an aminoglycoside (1.5 mg/kg, max 80 mg), with or without metronidazole, given IV just prior to the procedure
- The abdomen should be emptied of fluid prior to all procedures involving the abdomen or pelvis (such as colonoscopy, renal transplantation, and endometrial biopsy)

## **PROTOCOL FOR TREATMENT OF CAPD EXIT SITE INFECTIONS**

(BASED ON RECOMMENDATION OF ISPD, 2010)

### **Exit site infection:**

1. Purulent discharge from exit site

### **Treatment:**

1. Equivocal exit site infection
  - Hibitane dressing TDS
  - Local treatment: 0.1% Gentamycin cream, 2% mupirocin cream or otosporin ear drops to exit wound TDS
  
2. Exit site infection
  - Take exit site swab for microscopy and culture
  - Empirical treatment depends on clinical appearance of the exit site
  - Oral penicillinase-resistant penicillin (Cloxacillin 500 mg qid) or a first generation cephalosporin (Cephalexin 500 mg bd to tds) x 14 days if gram positive organism was suspected
  - Oral fluoroquinolones e.g. Ciprofloxacin 250 mg BD p.o. x 14 days if gram negative organism was suspected (avoids medication contains multi-valent cations including Sevelamer, Ca or Fe supplements, Mg-Al containing antacids, sucralfate, milk; a minimal spacing of 2 hours from ciprofloxacin if cannot discontinue). Treatment for 3 weeks is probably necessary for exit site infection caused by *P. aeruginosa*.
  - Change antibiotics regime according to culture and

- sensitivity result once available
- For slowly resolving or severe *S. aureus* exit site infection, add Rifampicin 450 mg daily
  - For Gram-ve organisms, if no improvement, parental antibiotics may be needed
  - If ESI + peritonitis: arrange early removal of Tenckhoff catheter
  - Consult nephrologist for assessment if ESI is persistent before further courses of antibiotics
  
  - Refractory ESI:
    - For double-cuffed Tenckhoff catheter, consider shaving of external cuff if external cuff is eroded and extruded
  - Recurrent ESI:
    - Counsel on personal hygiene, review exit site care, avoid excessive traction on TC
    - Take nasal swab x R/M, c/st. If repeatedly grow *S. aureus*, give mupirocin cream LA TDS x 1 wk to eradicate nasal carriage



# Neurology



## COMA

*Coma is a medical emergency characterized by the total absence of arousal and of awareness. It can be due to primary cerebral disorders, or secondary cerebral manifestations of systemic toxic, metabolic, or endocrine derangements. Essential management includes prompt stabilization of vital physiologic functions, aetiological diagnosis, and directed therapy.*

- 1. Correct any compromised airway, breathing or circulation (ABC):** intubate if GCS  $\leq$  8, maintain SaO<sub>2</sub> > 90% and MAP > 70mmHg.
- 2. Establish aetiology by adequate history, P/E and Ix**
  - a) All patients must have blood sugar checked
  - b) P/E – T<sup>o</sup>, pulse oximetry, BP/P, alcohol smell, evidence of trauma, and a detailed neurological examination including level of consciousness (Glasgow Coma Scale), cranial nerve examination, motor examination, and respiratory pattern. Additional clues by examining head and neck (e.g., meningism), optic fundi (e.g., subhyaloid hemorrhage in SAH), and skin (e.g., purpuric lesions in meningococcal meningitis). Structural causes indicated by lateralizing deficits and brainstem dysfunction. The neck should be immobilized until cervical spine instability is ruled out.
  - c) Ix – blood sugar with h'stix, RFT, LFT, ABG, blood and urine toxicology, SXR, XR cervical spine, CXR, ECG
  - d) Other Ix (in selected patients) – CT brain, lumbar puncture and CSF examination, EEG, thyroid function tests, cortisol, serum osmolality, ammonia level, MRI.
- 3. Initiate specific therapy where appropriate**
  - a) Thiamine 200 mg iv for alcoholic or malnourished patient
  - b) D<sub>50</sub> 40 ml iv for hypoglycaemia, after iv thiamine.

- c) Naloxone (Narcan) 0.4 mg to 2 mg iv stat, then every 2 mins prn up to 10 mg for suspected narcotic overdose
- d) Flumazenil (Anexate) 0.2 mg followed by 0.3 mg at 1 min , then 0.5 mg every 1 min to a total of 3 mg for suspected benzodiazepine overdose
- e) Antidote or specific therapy (if available) for other drug overdose
- f) Hyperventilation, mannitol 0.5 – 1.0 g/kg if clinical evidence of increased ICP / herniation
- g) Definitive treatment for the cause of coma

#### 4. Supportive

- a) Close monitoring of vital signs and neurological status
- b) Proper positioning and turning to avoid aspiration, pressure nerve palsy, contracture, pressure sore
- c) Bladder catheterization
- d) Adequate hydration, oxygenation and nutrition
- e) Chest and limb physiotherapy
- f) Hypromellose eyedrops and secure eyelids if no spontaneous blinking

## ACUTE CONFUSIONAL STATE (DELIRIUM)

*An acute transient organic mental syndrome characterized by a global disorder of cognition and attention, abnormally increased or reduced psychomotor activity and disturbed sleep-wake cycle. Consciousness can be fluctuating and may be depressed, lethargic or excited. It is a non-specific manifestation of a wide variety of acute conditions, especially in elderly.*

There are 3 variants: hyperactive, hypoactive and mixed. It is the hyperactive form with autonomic arousal that is more distinctive but the hypoactive form with inactivity, and on occasions falls and incontinence, is more common.

The diagnosis of delirium is primarily clinical and is based on careful bedside observation. In the elderly, delirium is a common manifestation of acute illness and a detail drug history is essential.

### 1. Choice of Ix according to the clinical presentation

- a) CBP, ESR, urea, electrolytes, Ca, R/LFT, thyroid function tests, blood glucose, ABG, urine analysis and culture, blood culture, ECG, CXR, EEG, blood/urine drug screen
- b) in selected cases: CRP, troponin, Serum B<sub>12</sub>, folate level, syphilis serology, lumbar puncture, toxicology, urinary porphyrins, HIV antibodies, autoantibodies, serum Mg, CT brain

### 2. Management

- a) Definitive treatment directed against the cause of delirium
- b) Review medications and withdraw the precipitating drugs
- c) Supportive and symptomatic treatment
- d) Fluid and electrolytes balance, adequate nutrition and vitamins
- e) Reassuring supportive nursing care in well illuminated, quiet place

- f) Only use drugs if patient is at risk of causing harm to themselves or others
- g) Low dose haloperidol 1-3 mg daily in divided dose if sedation necessary
- h) Benzodiazepines are drug of choice in case of withdrawal from alcohol/sedatives

## ACUTE STROKE

*It is essential to identify site, subtype, cause and risk factors of stroke.*

- 1. Admit to designated acute stroke unit.**
- 2. Initial assessment:** vital signs including airway, respiration, haemodynamics, conscious level & neurological impairment.
- 3. Ix :** Urgent non-contrast CT brain, CBP, R/LFT, PT, aPTT, blood glucose, lipid, CXR, ECG.
- 4. Special Ix (in selected cases):** Magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), computer tomography angiography (CTA), Echocardiography, Duplex study of carotid arteries, Transcranial Doppler (TCD), cerebral angiography, hyper-coagulopathy assessment and autoimmune screening.
- 5. Supportive management:**
  - a) Regular monitoring of neurological and vital signs
  - b) Swallowing assessment before feeding, positioning  $\pm$  splinting to avoid aspiration, contractures, pressure nerve palsy, shoulder subluxation, pressure sores, etc
  - c) Ensure good hydration, nutrition and oxygenation
  - d) Meticulous control of blood sugar & pyrexia
  - e) Cautious and gradual lowering of elevated blood pressure
    - In ischaemic stroke, lowering of blood pressure is considered:
      - ◆ in case of hypertensive emergencies (eg: hypertensive encephalopathy, aortic dissection, acute renal failure, acute pulmonary edema or acute myocardial infarction)
      - ◆ when the systolic blood pressure  $>220$  mmHg, or the diastolic blood pressure is  $>120$  mmHg, according to repeated measurements 20 minutes apart.
      - ◆ when thrombolytic therapy is considered/given
    - In hemorrhagic stroke, lowering of blood pressure is considered:

- ◆ if systolic blood pressure >200 mmHg or the mean blood pressure is >150mmHg
  - ◆ if systolic blood pressure >180 mmHg or the mean blood pressure is >130mmHg when there is no clinical evidence of elevated ICP
  - ◆ recent studies suggested that acute lowering of systolic BP to 140mmHg is probably safe
- f) Seizure should be treated promptly but prophylactic anticonvulsant is not indicated for ischaemic or haemorrhagic stroke.
- g) Early allied health therapists' referral and assessment.

## 6. Specific therapy:

### Ischaemic Stroke

- a) **Aspirin** 75mg to 325 mg stat dose within 24 to 48 hours of onset of acute ischaemic stroke. It should be withheld for the first 24 hrs if thrombolytic therapy was given.
- b) **Thrombolytic therapy:** in hospitals with stroke thrombolysis program implemented, inform the thrombolysis team immediately for urgent evaluation if a potential candidate is identified. (see protocol for individual hospital for details)

#### *Usual indication:*

- ◆ Ischaemic stroke onset within 3 to 4.5 hr
- ◆ Good premorbid function

#### *Usual contraindication for intravenous thrombolysis:*

- ◆ Presence of extensive early infarct changes in CT
- ◆ Active internal bleeding
- ◆ Use of warfarin with INR > 1.5
- ◆ Prior intracranial haemorrhage
- ◆ Any intracranial surgery, serious head injury or previous ischaemic stroke within 3 months
- ◆ Known AVM or aneurysm
- ◆ Clinical presentation suggestive of SAH
- ◆ Pregnancy

c) **Immediate anticoagulation** may be considered for acute ischaemic stroke in:

- Arterial dissection
- Documented cardiac source of embolism
- Cerebral venous thrombosis

***Contraindications and precautions***

*e.g. BP > 180/110 mmHg, large infarct.*

The use of anti-coagulation in acute stroke due to large artery thrombosis is controversial.

d) **Decompressive Hemicraniectomy:** urgently consult neurosurgeon to consider decompressive surgery in patient with malignant MCA syndrome (massive middle cerebral artery territory infarct with eye deviation, dense hemiplegia and progressive drowsiness +/- unequal pupil size. Serial CT will show significant infarct with swelling and midline shift).

**Intracerebral Haemorrhage**

a) **Urgent reversal of warfarin effect:** for patients with elevated INR due to warfarin:

- ◆ Give vitamin K<sub>1</sub> 5 to 10mg iv
- ◆ Give prothrombin complex concentrate (PCC) 25 to 50 IU/kg +/- FFP (PCC have shorter preparation/infusion time and much less fluid volume. It is reasonable to consider as an alternative to FFP since PCC can reverse warfarin effect much faster than FFP. Fluid overload is not a concern for PCC).
- ◆ Give FFP as soon as possible if PCC is not available

b) **Neurosurgical consultation:**

- ◆ Cerebellar haematoma or large cerebellar infarct with significant mass effect
- ◆ Large cerebral haematoma (> 30ml) with mass effect
- ◆ Impending or established hydrocephalus
- ◆ Subarachnoid haemorrhage

**7. Rehabilitation:**

All acute stroke patients should be assessed for rehabilitation potential and admission to organized rehabilitation programmes

**8. Secondary prevention:**

- a) Risk factor modification for all types of stroke
- b) Oral anticoagulation in cardioembolic stroke (including non-valvular AF) and anti-phospholipid antibody syndrome
- c) Aspirin 80-300mg daily for ischaemic stroke if anti-coagulation not indicated. Aspirin + controlled release dipyridamole or clopidogrel are other options for first line anti-platelet agents. Dual anti-platelet agents may be considered in very high risk patient on individual basis, preferably for a short course.
- d) Carotid Endarterectomy (CEA) or carotid stenting is indicated for symptomatic extracranial carotid stenosis of 70-99%, depending on the availability of expertise and their own track record of peri-interventional complication. Intervention for symptomatic stenosis of 50-69% can only be considered in centre with very low complication rate (less than 3%). Carotid stenting will be preferable in case of: (i) difficult surgical access, (ii) medical co-morbidities with high risk of surgery eg: IHD, (iii) radiation induced arteriopathy, (iv) re-stenosis after CEA. (Please refer to individual hospital logistic for referral of those patients for carotid intervention to different involved specialties)

## SUBARACHNOID HAEMORRHAGE

### Investigations

1. CT brain as soon as possible
2. Lumbar puncture if CT is negative, to look for bloody CSF and send CSF for xanthochromia. Xanthochromia is expected if LP is performed > 12 hr after presumed SAH onset. If LP is performed within 6 hr from headache onset, absence of xanthochromia is not reliable to rule out SAH.
3. In patient with high clinical suspicion of CT negative SAH, if LP result is inconclusive, it is reasonable to proceed to urgent CT angiogram of brain.
4. Urgent cerebral angiogram if early surgery is considered. If DSA cannot be arranged urgently, CT angiogram of brain should be arranged. Most of the aneurysm with size > 5mm can be detected by CTA.

### Management

1. Correct any compromised airway, breathing and circulation
2. Confirm diagnosis (CT  $\pm$  LP) and consult neurosurgeons
3. Assess severity (Hunt and Hess<sup>1</sup>) and neurological status
4. Early surgery/endovascular coiling should be considered in patients with grade 1, 2 and 3 SAH after aneurysm demonstrated by DSA/CTA.
5. Begin nimodipine 60 mg po q4h, or 1 mg/hr iv infusion in grade 1, 2 and 3 patients (use of nimodipine should be individualized in grade 4 and 5 patients) with BP check
6. Monitor BP closely and control high BP very carefully (exact level of target BP is controversial, but avoid treating reactive HT due to raised ICP). BP should be monitored and controlled to balance the risk of hypertension-related rebleeding, and maintenance of cerebral perfusion pressure.
7. Antifibrinolytic agent (transamine): recent evidence suggests that early treatment with a short course of antifibrinolytic agents (to reduce rebleeding) combined with early aneurysm treatment followed by discontinuation of the antifibrinolytic agent (to reduce its side effect of aggravating ischaemic

complication) may be reasonable.

8. Monitor GCS, brainstem reflexes, neurological deficits
9. Correct for any abnormalities in T<sup>o</sup>, fluid balance, electrolytes, osmolality, blood glucose, SaO<sub>2</sub> and cardiac rhythm. Dehydration should be avoided, which might aggravate the severity of vasospasm if developed subsequently
10. Anticonvulsant if seizures occur
11. Analgesics, sedatives, acid suppressants and stool softener prn
12. Prophylactic anti-convulsant may be considered (benefit controversial)

**<sup>1</sup>Hunt & Hess Grading:**

- Grade 1 Asymptomatic/slight headache
- 2 Mod/severe headache and nuchal rigidity but no focal or lateralizing neurologic signs except cranial nerve palsies
  - 3 Drowsiness, confusion and mild focal deficit
  - 4 Stupor, hemiparesis, early decerebrate rigidity and vegetative disturbances
  - 5 Deep coma and decerebrate rigidity

## TONIC-CLONIC STATUS EPILEPTICUS

### Operational definition:

1. *Two or more epileptic seizures without full recovery of consciousness between attacks*
2. *Continuous seizure lasting more than 5 minutes.*

### Management

1. Establish ABC, administer oxygen
2. Ensure good oxygenation and IV access
3. Check glucose and h'stix, electrolytes (include Ca  $\pm$  Mg), ABG, urea, anticonvulsant level
4. Give D50 50 ml iv and/or 200 mg thiamine iv where appropriate. Treat acidosis if severe
5. Suppress clinical seizures rapidly with iv lorazepam 2 – 4mg over 2 minute, up to 8mg. Alternative: iv diazepam 5 – 10 mg over 1-2 minutes, up to 20 mg.
6. Give simultaneously long acting anti-epileptic drug: Phenytoin – iv loading dose 15mg/kg (elderly) to 20mg/kg (adult), at rate of 50mg per minute. Lower infusion rate for elderly or underlying cardiac disease. Undiluted or diluted in normal saline (phenytoin precipitates with dextrose). Monitor ECG and BP for cardiorespiratory depression, hypotension and arrhythmias. Maintenance dose 5mg/kg/day (usually 100mg Q8H iv).
7. If above agents unsuccessful, ICU admission advisable for ventilatory assistance and second line agents eg. Thiopentone, midazolam or propofol, iv valproate /levetiracetam with EEG monitoring.
8. Monitor BP/P,RR, ECG and document further seizures. Continue intensive treatment for 12-24 hrs after last clinical or EEG seizure.
9. Search for and treat any acute symptomatic cause e.g. acute stroke (infarct or haemorrhage), head injury, CNS infection, electrolyte/metabolic disturbances, alcoholism, drug

intoxication. If there is a history of epilepsy, look for abrupt anticonvulsant withdrawal. Identify and treat any complications.

10. If a patient fails to gradually recover after the convulsive movements stop, EEG monitoring may be needed to ensure cessation of electrical seizure activity.

# GUILLAIN-BARRÉ SYNDROME

## Clinical Presentation

1. Subacute progressive polyneuropathy
2. Bilateral and flaccid weakness of the limbs
3. Generalized areflexia or hyporeflexia
4. Monophasic illness pattern; clinical plateau by about 4 weeks
5. Miller Fisher syndrome: bilateral ophthalmoparesis, ataxia, areflexia
6. Look for preceding infection e.g. *Campylobacter jejuni*, *Mycoplasma pneumoniae*; recent vaccination

## Diagnosis

1. Should NOT have new-onset upper motor neuron signs or sensory level.
2. Consider paralysis due to other acute neuropathies e.g. toxic neuropathy (alcohol, heavy metals, insecticides, solvents, drugs like cytotoxic agents), vasculitis, lymphomatous infiltration, porphyria, critical illness polyneuropathy; or neuromuscular junction disorders e.g. MG crisis, botulism
3. Arrange nerve conduction study (may be normal in 1<sup>st</sup> week)
4. Perform lumbar puncture: look for cytoalbuminologic dissociation  
(Raised CSF protein (may be normal in 1<sup>st</sup> week, ~80% abnormal in 2<sup>nd</sup> week, peak in 3-4 weeks) and CSF total white cell count < 50 cells/uL)
5. Nerve biopsy: if presentation atypical or other causes are suspected e.g. vasculitis.
6. Anti-GQ1b antibody is closely associated with Miller-Fisher Syndrome.

## Management

1. Supportive care remains the cornerstone of treatment e.g. adequate nutrition and hydration, physiotherapy, appropriate splinting, clear secretions.
2. Monitor neurological status and FVC regularly.
3. Consider assisted ventilation if FVC < 15-20 ml/kg, NIPPV is in general NOT appropriate
4. Cardiac monitoring (life-threatening autonomic dysfunction accounts for significant mortality)
5. In severe cases, give intravenous immunoglobulin 0.4g/kg/day for 5 days; alternatively start plasma exchange, totally 50ml/kg/session of plasma for 5 - 6 exchanges over 7-14 days.
6. Steroid treatment has no benefit.

## MYASTHENIC CRISIS

*Crisis: severe generalized weakness and need for respiratory support. \*Tensilon test - diagnostic test in untreated disease; not reliable in differentiating myasthenic and cholinergic crisis and not without risk, hence not recommended.*

### Management

1. Watch out for respiratory failure in any patient with progressive weakness and bulbar symptoms
2. Closely monitor FVC, SaO<sub>2</sub> ± ABG
3. General supportive measures and ICU care
4. Intubate and initiate mechanical ventilation if FVC < 15-20 ml/kg, hypercarbia, hypoxia or patient exhausted
5. Stop anticholinesterase if patient is intubated
6. Give IVIG 0.4 g/kg/day for 5 days. An alternative is plasma exchange 50 ml/kg daily or on alternate days until adequate response achieved (usually after 5 - 6 exchanges)
7. Resume anticholinesterase at a smaller dose 48-72 hours after stabilization and titrate according to response
8. Start prednisolone 1 mg/kg/day; beware that early steroid-induced deterioration may occur
10. Identify and treat any precipitating conditions (e.g. underlying infection)
11. Be cautious with the use of any drug that might worsen MG. e.g. aminoglycosides, quinine, quinidine, procainamide, β-blockers, muscle relaxants, penicillamine, magnesium.

## ACUTE SPINAL CORD SYNDROME

(Also refer to page GM24 and GM38)

*It is of paramount importance to make an early diagnosis of acute spinal cord compression, to provide the patient with the best chance for neurological recovery. "Sensory level" can be falsely localizing and imaging of spinal cord rostral to clinical sensory level is advisable.*

### Investigations to delineate level and nature of spinal cord lesion

1. XR spine
2. MRI spine of relevant level if immediately available; otherwise myelogram and CT myelogram
3. Send CSF obtained during myelogram for microscopy, culture, biochemistry, Ig and cytology
4.  $\pm$  Spinal angiogram, Vitamin B12 and folate

### Management

1. Correct any compromised airway, breathing and circulation
2. Immobilize relevant level of spine in case of traumatic spinal cord injury or spine instability.
3. Initiate appropriate treatment for specific spinal cord lesions:
  - neurosurgical / orthopaedic consultation for structural lesions
  - antimicrobial therapy for abscess or other infections
  - methylprednisolone 1 gm intravenously over one hour daily for 3 days, may be useful in non-infectious inflammatory myelitis
4. Institute general supportive care:
  - proper positioning & splinting
  - adequate hydration and nutrition
  - bladder catheterization
  - regular monitoring of vital signs
5. Close monitoring of respiratory function (FVC, respiratory rate) in case of high cord lesions
6. If HR drops to  $<45$ /min, give Atropine 0.3 – 0.6mg
7. Consider prophylaxis against DVT

## DELIRIUM TREMENS

*Manifests as tremulousness, hallucinations, agitation, confusion, disorientation and autonomic overactivity including fever, tachycardia and profuse perspiration. Consciousness may fluctuate.*

*Usually occurs 24-48 hours after complete cessation of drinking in alcohol-dependent individuals, rarely may occur in a patient still drinking a diminished amount or following withdrawal of other sedative drugs*

- Diagnosis based on clinical features and exclusion of other causes of delirium

### Management

1. General supportive care
2. Monitor BP/P, I/O, T<sup>o</sup>, cardiac rhythm
3. Correct fluid and electrolyte disturbance. Watch out especially for hypomagnesaemia, hypokalaemia and hypoglycaemia
4. Start benzodiazepine: chlordiazepoxide 10 mg – 20 mg TDS oral or lorazepam 2 mg TDS (if liver impairment) . Adjust dose according to severity. Reduce dose in elderly. Taper dosage gradually over 5-7 days.  
Avoid chlorpromazine because of its epileptogenicity.
5. Give thiamine 200 mg iv before iv dextrose
6. Ensure adequate nutrition and vitamins
7. Search out for and treat any concurrent illnesses
8. Reassuring nursing care in well-illuminated, quiet place.

Reference: McKeon et al. Alcohol Withdrawal Syndrome. J Neurol Neurosurg Psychiatry 2008 Aug;79(8):854-62.

## WERNICKE'S ENCEPHALOPATHY

*Clinical syndrome of acute or subacute onset of neurological signs in alcoholics or severely malnourished patients, including ophthalmoplegia, ataxia and delirium with anterograde amnesia. Presentation can be partial.*

### Investigations

- Urea and electrolytes, R/LFT, serum magnesium, ammonia
- Blood glucose, H<sup>+</sup>stix
- ABG
- Serum and RBC thiamine or transketolase activities before initiating therapy if available, but this should not delay treatment.

### Management

1. General supportive care
2. Monitor BP/P, I/O, T<sup>o</sup>, cardiac rhythm
3. Monitor neurological signs closely, esp. ophthalmoplegia (should respond within hours to thiamine Rx)
4. Correct fluid and electrolyte disturbance. Watch out especially for hypomagnesaemia, hypokalaemia and hypoglycaemia
5. 200 mg thiamine in 100 ml of normal saline, given by infusion over a period of 30 min, three times per day for 2–3 days, may need higher doses. (*Oral thiamine is inadequate.*)
6. Give parenteral B complex in initial treatment
7. Balanced high calorie diet, vitamins and adequate hydration
8. Watch out for and treat any concurrent illness

Reference: R Galvin et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. *European Journal of Neurology* 2010;17:1408-1418.

## PERI-OPERATIVE MANAGEMENT IN PATIENTS WITH NEUROLOGICAL DISEASES

*High risk of peri-operative pulmonary complications:  
Parkinsonism, myasthenia gravis, other neuro-muscular disorders affecting respiratory muscles and any neurological deficits compromising respiratory effort.*

### **Peri-operative management:**

1. Comprehensive pulmonary assessment before operation
2. Optimal control of neurological conditions
3. Vigorous peri-operative chest physiotherapy
4. Regular monitoring of FVC, respiratory rate, SaO<sub>2</sub>, ABG
5. Continue anti-epileptic, anti-cholinesterase and anti-parkinsonism drugs as close to normal schedule as possible.

Resume as soon as possible after operation.

*Alternative preparation or drugs:*

Anti-cholinesterase: Neostigmine 0.5 mg im/iv q4-6h

Anti-epileptic: phenytoin / sodium valproate/ levetiracetam available in iv form

Transdermal patch of Rotigotine and parenteral apomorphine is available if anti-parkinsonism drugs cannot be resumed quickly.

- 6a Bridging therapy is recommended for patient with high risk of thromboembolic event after anti-coagulant is stopped
- 6b Discontinue anti-platelet agents 1 week before elective surgery, but aspirin may be continued in the following procedures: (i) endoscopies with biopsies and polypectomies, (ii) ophthalmologic procedures, (iii) peripheral vascular procedure, (iv) neuraxial anesthesia. Warfarin can be continued for most dental procedures if INR is kept at a lower range before the

procedure and close monitoring in the day ward after the procedure is available.

7. Avoid aminoglycosides, quinolones, morphine, quinidine,  $\beta$ -blockers, procainamide, penicillamine for myasthenia gravis

### **Risk of Peri-operative stroke**

1. Increase in hypertension
2. Asymptomatic carotid bruit not an independent risk factor
3. Symptomatic carotid stenosis should be repaired before non-emergency operation. Symptomatic large vessel stenosis in the posterior circulation need to have aggressive intraoperative maintenance of blood pressure to avoid prolonged hypotension
4. Decreased by avoiding hypotension, hypovolemia, polycythaemia and anaemia
5. Postpone elective procedures for at least 6 weeks after an ischaemic stroke to allow healing at the infarct site; smaller stroke or lacunae may require shorter waiting period

# Respiratory Medicine



## MECHANICAL VENTILATION

### 1. Indications

- Respiratory failure not adequately corrected by other means
- Marked increased work of breathing as evidenced by significant tachypnoea (>40 bpm), retractions, and other physical signs of respiratory distress
- Failure to protect the airway - usually from declining mental status (e.g. GCS<8)
- Cardiac and/or respiratory arrest
- Clinical instability e.g. severe hypotension (due to sepsis, shock, congestive heart failure etc)
- Surgical conditions: postoperative care, trauma or neurosurgical causes
- Remarks: neither physiologic parameters nor ABG criteria can be absolute indications. Clinical assessment is the most important determinant of the need for mechanical ventilation

### 2. Suggested initial ventilator settings

<i>Disease condition</i>	<i>Acute Resp distress syndrome (ARDS)</i>	<i>Acute pulmonary oedema</i>	<i>*Obstructive lung disease (COPD/ Asthma)</i>	<i>Restrictive lung disease</i>
Tidal volume (ml/kg predicted BW)	6	8 – 10	6 – 8	12 – 14
Frequency (breath/min)	Permissive hypercapnia (keep pH just > 7.25 as “lung protective strategy”)	Assisted control/ SIMV/ pressure support (PS) mode to achieve patient comfort	10 – 14 Ensure long enough expiratory time to avoid air-trapping	To achieve desired pH and ABG
Positive end-expiratory pressure/ PEEP (cmH <sub>2</sub> O)	May need > 10 (open lung approach)	High (5 – 10) initially, can be rapidly tailed down	0 – 3 max	3 – 5

\*Peak pressure usually targeted at <35 cmH<sub>2</sub>O, but <30 cm H<sub>2</sub>O for COPD and need to monitor for intrinsic PEEP (auto-PEEP)

**3 Monitoring during mechanical ventilation**

- a. General: vital signs, bowel motion, conscious level, psychological status
- b. P/E: Signs of upper airway obstruction (excessive inspiratory efforts, inspiratory in-sucking of lower rib cage), ETT (patency, positioning), chest wall movement (especially asymmetry), pressure sores, signs of DVT, hydration & nutritional status
- c. Important parameters:
  - i. Cuff pressure: 16-20 (<24) cm H<sub>2</sub>O
  - ii. Ventilatory status:
    - Volume-controlled mode or SIMV (VC + PS): avoid excessive airway pressure
    - Pressure-controlled mode or SIMV (PC + PS): monitor tidal volume which varies with airflow obstruction or lung compliance
    - Pressure support mode: avoid excessive/inadequate tidal volume and long/short inspiratory time
    - Pause or plateau pressure (PP): Barotrauma risk ↑ if PP ≥ 35 cm H<sub>2</sub>O
    - Auto-PEEP

#### 4 Patient-ventilator asynchrony

Do not simply sedate a patient who is asynchronous with the ventilator, look for possible underlying cause(s).

Checklist for trouble-shooting:

<i>Problems</i>	<i>Examples</i>
a. Airway-related	Inappropriate size/position (Normal 4-6 cm above carina) of ET tube, leaky cuff/excessive cuff pressure, blocked /kinked tube, dislodgement
b. Ventilator-related	Inadequate humidification, obstruction/ leak in circuit, ventilator malfunction
c. Inappropriate ventilator settings	Inappropriate TV/IFR (or I:E) /sensitivity settings, inadequate FiO <sub>2</sub> and/or ventilation with persistent hypoxaemia or hypercapnia
d. Underlying disease	Stiff lungs, low cardiac output, poor cerebral perfusion, septic state
e. Complications of mechanical ventilation	Atelectasis, ventilator-associated pneumonia, pneumothorax, endobronchial intubation
f. Others	Fear, anxiety, pain, secretions in airway, hunger, inability to open bowels/to move, pressure sore

## OXYGEN THERAPY

### Common oxygen delivery methods

#### Standard dual-prong nasal cannula

- $FiO_2$  0.23 to 0.40 if  $O_2$  flow rate set at 1 to 6 L/min
- Actual  $FiO_2$  non-specific, affected by the  $O_2$  flow setting, oropharyngeal geometry, tidal volume, respiratory rate, pattern, and is roughly  $20\% + (4 \times \text{oxygen litre flow per minute})$
- Most comfortable and cost-effective

#### Venturi mask

- Accurate  $FiO_2$  adjustable from 0.24 to 0.50 if  $O_2$  flow rate set at 3 – 15 L/min ( $O_2$  required to drive can be read off from the Venturi device)
- Maintains a constant (pre-set)  $FiO_2$

#### Simple face mask with no reservoir bag

- $FiO_2$  up to 0.50 if  $O_2$  flow rate set at 6 to 10 L/min
- Actual  $FiO_2$  non-specific, depends on patient's inspiratory flow
- $O_2$  flow rate set below  $<5L/min$  may cause  $CO_2$  rebreathing

#### Rebreathing mask with reservoir bag

- $FiO_2$  0.70 if  $O_2$  flow rate set at 6 to 10L/min
- $O_2$  flow must be  $\geq 6$  L/min to keep reservoir bag inflated throughout inspiration & expiration
- No one way valve between reservoir bag and mask

#### Non-rebreathing mask with reservoir bag

- $FiO_2$  0.60 – 1.00 if  $O_2$  flow rate set at 10 – 15 L/min
- Equipped with one-way valves to prevent exhalation into reservoir bag and inhalation through mask exhalation ports (but usually only one of the two valves on the mask exhalation ports is installed for safety reason)

**Other common oxygen delivery methods**

1. T-piece to endotracheal or tracheostomy tube: O<sub>2</sub> delivered through the shorter end, open window by one-third if PCO<sub>2</sub> is high
2. Thermovent to endotracheal or tracheostomy tube: watch out for sputum blockage
3. Tracheostomy mask: consider to use humidification in non-infectious situation (e.g. heated humidifier)

The goal of O<sub>2</sub> therapy is to *deliver the minimum concentration required for adequate tissue oxygenation with the least risk of toxicity*. Prescriptions should be precise and adequately monitored (e.g. by SpO<sub>2</sub> or ABG), and techniques of administration should be compatible with safe and effective therapy which is associated with the greatest patient comfort and acceptance at the least cost.

**Indications for long-term O<sub>2</sub> therapy in COPD**

Start only when clinically stable for 3-4 weeks and after optimization of other therapy

Continuous oxygen:

1. Resting PaO<sub>2</sub> ≤7.3 kPa (55 mm Hg) or SaO<sub>2</sub> ≤88%: to maintain PaO<sub>2</sub> ≥8 kPa (60 mm Hg or SaO<sub>2</sub> ≥90%)
2. Resting PaO<sub>2</sub> 7.4 to 7.9 kPa (56 to 59 mm Hg) or SaO<sub>2</sub> ≥89% in the presence of any of the following:
  - Dependent edema suggestive of congestive heart failure
  - P pulmonale on ECG (P wave >3mm in standard leads II, III, or aVF)
  - Erythrocythaemia (haematocrit >56%)

Noncontinuous oxygen:

Oxygen flow rate and number of hours per day must be specified

1. During exercise: PaO<sub>2</sub> ≤7.3 kPa (55 mmHg) or oxygen saturation ≤88% with a low level of exertion
2. During sleep: PaO<sub>2</sub> ≤7.3 kPa (55 mmHg) or oxygen saturation ≤88% with associated complications, such as pulmonary hypertension, daytime somnolence, and cardiac arrhythmias.

## MASSIVE HAEMOPTYSIS

Definition: Arbitrary, expectorated blood ranging from >100-200ml/day. Important management considerations include rate of bleeding and underlying lung function. Increased volume of bleeding confers a much higher risk of death due to asphyxia than to haemodynamic derangement. *Airway protection is most important in massive haemoptysis, close observation and treatment in ICU/HDU is desirable*

### Management objectives

Prevent asphyxia, localize bleeding site, stop bleeding, determine cause of bleeding and treat underlying cause

### Management

1. Close monitoring of vital sign, i.e. BP/P, RR, SaO<sub>2</sub>
2. O<sub>2</sub> supplement
3. Establish IV access
4. Take blood for CBP, clotting, ABG and X-match
5. Sputum for C/ST, AFB & cytology
6. Avoid sedation and cough suppressant
7. Antibiotic if infection is suspected, e.g. bronchiectasis, TB
8. Lie lateral on side of bleeding if lateralized
9. **If depressed conscious state with risk of asphyxia, intubate for suction and ventilation** (single lumen ET if urgent airway access is required; double lumen ET placement by anaesthetist is better for isolation of bleeding side)
10. Early bronchoscopy to localize bleeding, diagnose endobronchial lesion and for therapy

### Persistent life-threatening haemoptysis

- Consult radiologist for bronchial arteriogram ± bronchial artery embolization if expertise available
- Consult surgeon for emergency lung resection if bleeding is localized and adequate pulmonary reserve

# SPONTANEOUS PNEUMOTHORAX

(Ref. ACCP Delphi Consensus Statement 2001)

Suspect tension pneumothorax if associated hypotension

## Definition

**Size:** determined by lung apex-to-thoracic cupola distance in upright CXR.

*Small* < 3cm & *large* ≥ 3cm

**Clinical stability:** *Stable* if RR < 24/min, HR > 60/min or HR < 120/min, SaO<sub>2</sub> (RA) > 90% and complete sentence(s) between breaths. If not, *unstable*

## Management

O<sub>2</sub> and analgesic prn

### Primary spontaneous pneumothorax (no underlying lung abnormalities)

1. Clinically stable with small pneumothorax  
Conservative: monitor symptom and CXR
2. Clinically stable with large pneumothorax  
Small bore catheter (≤ 14F) or 16-22F chest drain\*
3. Clinically unstable with large pneumothorax  
16-22F chest drain\*. 24-28F if bronchopleural fistula or mechanical ventilation anticipated

Persistent air leak > 4 days, surgical referral for thoracoscopy#

### Secondary spontaneous pneumothorax (underlying lung disease)

Should be hospitalized even if clinically stable

1. Clinically stable with small pneumothorax  
Conservative or chest drain\* depending on symptom and course of pneumothorax
2. Clinically stable with large pneumothorax  
16-22F chest drain\*
3. Clinically unstable with large pneumothorax  
24-28F chest drain\*

Persistent air leak > 5 days, surgical referral for thoracoscopy#

\*attached to water-seal device. Suction should be applied if lung fails to reexpand

#chemical pleurodesis can be considered if surgery contraindicated or patient refuses operation or poor prognosis from patient's underlying disease.

## Adult Acute Asthma (Ref: GINA Guidelines 2009)

### Features of moderate severe asthma

Talks in phrases, RR>25/min, pulse>110/min, SaO<sub>2</sub> (on air) ~91-95%, PEF~60-80% predicted or personal best

### Features of acute severe asthma

Cannot complete sentence in one breath, RR>30/min, pulse>120/min, SaO<sub>2</sub> (on air) ≤90%, PEF<60% predicted or personal best

### Life threatening features (*dangerous even if only one feature present*)

PEF<33% predicted/best, silent chest, cyanosis, feeble respiratory effort, bradycardia, hypotension, exhaustion, confusion, coma, low pH, normal/high PaCO<sub>2</sub> (5-6kPa), severe hypoxia (PaO<sub>2</sub><8kPa or SaO<sub>2</sub>≤90% with O<sub>2</sub>), and/or paradoxical thoraco-abdominal movement

#### 1. Monitoring

Vital signs, pulse oximetry, PFR, ABG, electrolytes, CXR

#### 2. Management

*Moderate episode (life threatening features absent)*

- Give 35-50% O<sub>2</sub>, maintain SaO<sub>2</sub>>90%
- Salbutamol 5mg or Terbutaline 10mg nebulised with O<sub>2</sub>  
OR inhaled Salbutamol/Terbutaline 6 puffs
- Prednisolone 30-60mg po OR Hydrocortisone 200mg iv  
OR Methylprednisolone 40mg iv

*Severe episode (life threatening features present)*

- Consider ICU care, standby equipment for intubation
- Same as treatment for moderate episode *plus*
- Nebulised preservative-free ipratropium 0.25-0.5%  
(1ml/20 drops) OR inhaled ipratropium 3-4 puffs

- IV Salbutamol/Terbutaline (250µg over 10min) or Aminophylline (250mg over 20min). *Do not give bolus aminophylline for patients taking oral theophylline*
  - May consider magnesium sulphate 1.2-2g iv over 2 minutes for very severe cases
- A. If satisfactory response
- Continue O<sub>2</sub> to keep SaO<sub>2</sub> >90%
  - Prednisolone 30-60mg/d, or Hydrocortisone 100mg iv q6h
  - Continue inhaled (MDI or nebulised) β<sub>2</sub> agonist q4h
- B. If unsatisfactory response
- Nebulised β<sub>2</sub> agonist OR inhaled β<sub>2</sub> agonist 6-10 puffs up to q15min
  - Nebulised ipratropium 0.25-0.5mg OR inhaled ipratropium 6puffs q4h
  - Aminophylline iv infusion 0.5-0.9mg/kg/h
  - Consider IV salbutamol 5µg/min (3-20µg/min) /terbutaline (1.5-5µg/min). Adjust rate according to response. Monitor closely and watch out for cardiac arrhythmia and other side effects
- C. Consider ICU admission if
- Life threatening features present
  - Deterioration in PEF
  - Worsening or persistent hypoxia or hypercapnia
  - Respiratory failure requiring IPPV
  - Respiratory or cardiorespiratory arrest
- D. After improvement
- Stabilize in ward
  - Discharge home when symptoms have cleared, PEF >75% predicted or previous best AND PEF variability <25%
  - Actions recommended on discharge include identifying & avoiding trigger factor(s) that precipitated attack,

Prednisolone tablets (30mg daily) tapering over 1-3 weeks as reserve, proper follow up arrangements & long term treatment plan esp. inhalational steroids, AND reviewing technique on use of inhaler and peak flow meter

- E. Therapies NOT recommended during acute attacks
- Sedatives (avoid strictly)
  - Cough suppressant (avoid as far as possible)
  - Mucolytic drug (may worsen cough)
  - Chest physiotherapy (may increase patient discomfort)
  - Antibiotics (unless has concomitant bacterial infection)
  - Hydration with large volumes of fluid

Note

- Medication from MDI inhaler is preferably given via a spacer
- Nebulized bronchodilator is preferably given in areas with negative pressure installed.

## Long Term Management of Asthma (Ref: GINA Guidelines 2009)

### NOTE

- a. The goal of asthma care is to achieve and maintain control of the clinical manifestations; and control of expected future risks such as exacerbations, accelerated decline of lung function and side effects of treatment.
- b. Each patient is assigned to one of five “treatment steps” depending on their current *level of asthma control* and treatment should be adjusted in a *continuous cycle* driven by changes in patients’ asthma control status
- c. In treatment-naïve patients with persistent asthma, treatment should be started at *Step 2*, or *Step 3* if very symptomatic.
- d. Reliever medication (rapid-onset bronchodilator) should be provided for quick relief of symptoms at each treatment step.
- e. Patients should avoid or control triggers at all times.
- f. All therapy at every step must include patient education.

<b>Level of Asthma Control</b>			
<b>Character-istic</b>	<b>Controlled (All of the following)</b>	<b>Partly Controlled (Anyone present in any week)</b>	<b>Uncontrolled</b>
<b>Daytime symptoms</b>	None ( $\leq 2x/\text{week}$ )	$> 2x/\text{week}$	$\geq 3$ features of partly controlled asthma present in any week
<b>Limitations of activities</b>	None	Any	
<b>Nocturnal symptoms/awakening</b>	None	Any	

<b>Need for reliever/ rescue treatment</b>	None ( $\leq 2x/\text{week}$ )	$> 2x/\text{week}$	
<b>Lung function (PEF or FEV<sub>1</sub>)</b>	Normal	$< 80\%$ predicted/ personal best (if known)	
<b>B. Assessment of Future Risk</b> (exacerbation/ instability/ rapid decline in lung function, treatment side effect):			
<i>Increased risk if anyone of the following features present:</i> Poor clinical control, frequent exacerbations in past year*, ever admitted to critical care for asthma, low FEV <sub>1</sub> , exposure to cigarette smoke, high dose maintenance requirement			

\*Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate

## TREATMENT (preferred treatments are bolded)

### STEP 1: As-needed reliever medication

- For untreated patients with occasional daytime symptoms
- Short-acting bronchodilator as reliever: **Inhaled  $\beta_2$ -agonist** prn (but  $\leq 2$ times/week). Inhaled anticholinergic, short-acting po  $\beta_2$ -agonist or theophylline may be used as alternatives
- Inhaled  $\beta_2$ -agonist**, leukotriene modifier or cromoglycate before exercise or allergen exposure.
- Long-term preventive treatment not required.

### STEP 2: Reliever medication plus a single controller

- Reliever: **Inhaled  $\beta_2$ -agonist** prn (but  $\leq 2$ times/week).
- Daily controller medication: Either **inhaled corticosteroids** (200–500 $\mu\text{g}$ )\* or leukotriene modifier, cromoglycate or nedocromil or theophylline SR.

**STEP 3: Reliever medication plus one or two controllers**

- a. Reliever: **Inhaled  $\beta_2$ -agonist** prn (but  $\leq 2$  times/week).
- b. (i) Daily **inhaled corticosteroids** ( $\geq 500\mu\text{g}$ )\* PLUS either **long-acting inhaled  $\beta_2$ -agonist<sup>#</sup>** or theophylline SR or leukotriene modifier, OR  
(ii) Daily inhaled corticosteroids of medium or high dose ( $800\text{--}2000\mu\text{g}$ )\*
- c. Consider leukotriene modifier for aspirin sensitivity or exercise-induced asthma.
- d. Referred to specialist for advice and management

**STEP 4: Reliever medication plus two or more controllers**

- a. Short-acting bronchodilator: **Inhaled  $\beta_2$ -agonist** prn.
- b. Daily **inhaled corticosteroids** ( $800\text{--}2000\mu\text{g}$  or more)\* **AND long-acting inhaled  $\beta_2$ -agonist** and/or **theophylline SR** and/or long-acting PO  $\beta_2$ -agonist and/or leukotriene modifier

**STEP 5: Reliever medication plus additional controller options**

- a. As in Step 4 plus **oral glucocorticosteroid** (at lowest possible dose) and/or addition of anti-IgE treatment

Steroid doses are for beclomethasone dipropionate.

<sup>#</sup> Adding long-acting inhaled  $\beta_2$ -agonist may offer more effective symptom control than increasing the steroid dosages.

**Step-down**

Review treatment every 3–6 months. If control has been sustained for  $>3$  months, consider a gradual stepwise reduction.

**Step-up**

If control is not achieved, consider stepping up AFTER reviewing patient's medication technique, compliance and environmental control (avoidance of allergens/trigger factors).

## Chronic Obstructive Pulmonary Disease

### Treatment of stable COPD

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines 2009:

Stage 1 = mild ( $FEV_1/FVC < 70\%$ ,  $FEV_1 > 80\%$ ,  
with/without symptoms)

- Avoidance of risk factor(s): most importantly smoking cessation
- Influenza vaccination
- short-acting bronchodilator when needed

Stage 2 = moderate ( $FEV_1/FVC < 70\%$ ,  $50\% \leq FEV_1 < 80\%$ , with or without symptoms)

- as for stage 1, add
- regular treatment with one or more long-acting bronchodilators, and rehabilitation

Stage 3 = severe ( $FEV_1/FVC < 70\%$ ,  $30\% \leq FEV_1 < 50\%$ , with or without symptoms)

- as for stage 2, add
- inhaled glucocorticoids if repeated exacerbations

Stage 4 = very severe ( $FEV_1/FVC < 70\%$ ,  $FEV_1 < 30\%$  or  $FEV_1 < 50\%$  predicted + chronic respiratory failure)

- as for stage 3, add
- long term oxygen if chronic respiratory failure, and
- consider surgical treatment (bullectomy, lung volume reduction surgery, lung transplantation)

Other points to note:

1. Steroid trial not predictive of response to inhaled steroid
2. Long-term oxygen therapy (generally in stage 4 COPD)
  - Start only when clinically stable for 3-4 weeks after optimization of other therapy, in COPD patients who have:

- A. Continuous oxygen therapy (for  $\geq 15$  hours/day):
- Resting PaO<sub>2</sub>  $\leq 7.3$  kPa (55 mm Hg) or SaO<sub>2</sub>  $\leq 88\%$ : to maintain PaO<sub>2</sub>  $\geq 8$  kPa (60 mm Hg or SaO<sub>2</sub>  $\geq 90\%$ ); or
  - Resting PaO<sub>2</sub> 7.4 to 7.9 kPa (56 to 59 mm Hg) or SaO<sub>2</sub>  $\geq 89\%$  in the presence of any of the following:
    - i Dependent edema suggestive of congestive heart failure
    - ii P pulmonale on ECG (P wave  $> 3$  mm in standard leads II, III, or aVF)
    - iii Erythrocythaemia (haematocrit  $> 56\%$ )
- B. Non-continuous oxygen: Oxygen flow rate and number of hours per day must be specified.
- During exercise: PaO<sub>2</sub>  $\leq 7.3$  kPa (55 mmHg) or oxygen saturation  $\leq 88\%$  with a low level of exertion
  - During sleep: PaO<sub>2</sub>  $\leq 7.3$  kPa (55 mmHg) or oxygen saturation  $\leq 88\%$  with associated complications, such as pulmonary hypertension, daytime somnolence, and cardiac arrhythmias”

### Treatment of acute exacerbation

1. Controlled low dose oxygen administration (start with 24% Venturi mask or 1-2L/min by nasal prongs). Check ABGs within 30-60 mins of starting oxygen, modify flow rate according to PaO<sub>2</sub> and pH
2. Inhaled (using spacer device)  $\beta_2$  agonist and ipratropium bromide alone or in combination
3. If no response, consider iv aminophylline (second line therapy)
4. Corticosteroids (hydrocortisone 100 mg iv Q6-8 hours or Prednisolone 30-40 mg orally per day). Steroid should be discontinued after the acute episode (e.g. 7-10 days)
5. Prescribe an antibiotic if exacerbation is severe and requires invasive or non-invasive ventilation and/or two or more of the following are present (one being increased sputum purulence):
  - Increased breathlessness;

- Increased sputum volume;
  - Development of purulent sputum
6. Indications for NIV:
- Moderate to severe dyspnoea with use of accessory muscles and paradoxical abdominal motion
  - Moderate to severe acidosis ( $\text{pH} \leq 7.35$ ) and/or hypercapnia ( $\text{PaCO}_2 > 6.0 \text{ kPa}$ ,  $45 \text{ mmHg}$ )
  - Respiratory frequency  $> 25$  breaths per minute
  - Check ABG 1-2 hours after initiation of NIV. Do not delay intubation and IPPV if improvement is absent
7. IPPV is likely to be appropriate in all other patients when
- There is a clearly reversible basis for the current deterioration
  - It is the first episode of respiratory failure
  - There is an acceptable quality of life
  - The patient has not previously had a full medical assessment
  - There are few if any co-morbidities
  - NIV fails

### **Indications for intensive monitoring and treatment e.g. ICU**

1. Severe dyspnoea with inadequate response to initial emergency therapy
2. Confusion, lethargy, or respiratory muscle fatigue (as evidenced by paradoxical diaphragmatic movement)
3. Persistent or worsening hypoxemia despite supplemental oxygen, or severe/worsening respiratory acidosis ( $\text{pH} < 7.30$ )
4. Assisted ventilation is required, whether by means of mechanical ventilation or NIPPV

## PLEURAL EFFUSION

### *Diagnosis*

1. Diagnostic tapping + pleural biopsy if exudative
2. Ultrasound or CT guided pleural tapping if fluid appeared loculated or concomitant lung collapse +/- mediastinal shift is evident
3. Thoracoscopic biopsy is indicated if aetiology of pleural effusion remains undiagnosed after multiple thoracocentesis and pleural biopsies
4. Bilateral pleural effusion is rarely due to underlying lung disease but can occur in TB and malignancy. Systemic causes should always be sought e.g. heart failure, SLE, pancreatitis, hypoalbuminemia
5. Bronchoscopy is useful if endobronchial / mass lesion in parenchymal is suspected
6. CT thorax to assess pleural space anatomy, screen parenchymal lesion, therapeutic result after drainage in complicated cases

### *Suspect empyema/ complicated parapneumonic effusion if any of followings*

1. Frank pus on diagnostic tapping
2. Loculation on CXR or pleural thickening with contrast enhancement on CT thorax
3. Positive gram-stain +/- positive culture of pleural fluid
4. Pleural fluid biochemistry: pH <7.2, LDH >1000 IU/l or glucose <2.2mmol/L

**Consult pulmonologist to consider intrapleural fibrinolytic in selected cases**

***Indication for chest drain insertion***

1. Empyema or complicated parapneumonic effusion
2. Symptomatic malignant pleural effusion (see below)
3. Hemothorax (surgical consultation is usually indicated)

***Management of persistent/ recurrent malignant pleural effusion***

1. Supportive care
2. Consult respiratory physician for difficult cases
3. Tube drainage and chemical pleurodesis
  - Agent: Talc up to 5g in 100ml NS
  - Must be performed under adequate analgesia +/- sedation
  - Clamp drain for 1 hour post sclerosant application, then release clamp
  - Chest tube kept unclamped thereafter for drainage until daily output <150ml /day and CXR shows the lung to be re-expanded with most of the effusion drained
4. Surgical pleurodesis (can be considered in patients with good performance status)
5. Long term ambulatory indwelling pleural catheter drainage (including patients with trapped lung)

## OBSTRUCTIVE SLEEP APNOEA

Suspect OSA if

- (1) Snoring at night, **PLUS**
- (2) Excessive daytime sleepiness (EDS)
  - Mild*: activity with little attention needed e.g. public transport
  - Moderate*: activity with some attention e.g. conference
  - Severe*: activity with much concentration e.g. phone call, conversation; **OR**
- (3) Any two out of the followings:
  - (i) Intermittent nocturnal arousal, (ii) Nocturnal choking,
  - (iii) Unrefreshed sleep at waking, (iv) Daytime fatigue,
  - (v) Impaired daytime concentration

Indications for diagnostic sleep study

1. Suspect OSA
2. Unexplained pulmonary hypertension
3. Recurrent cardiovascular events e.g. CVA, angina, CHF; or poorly controlled hypertension despite adequate medical therapy and optimization of risk factors

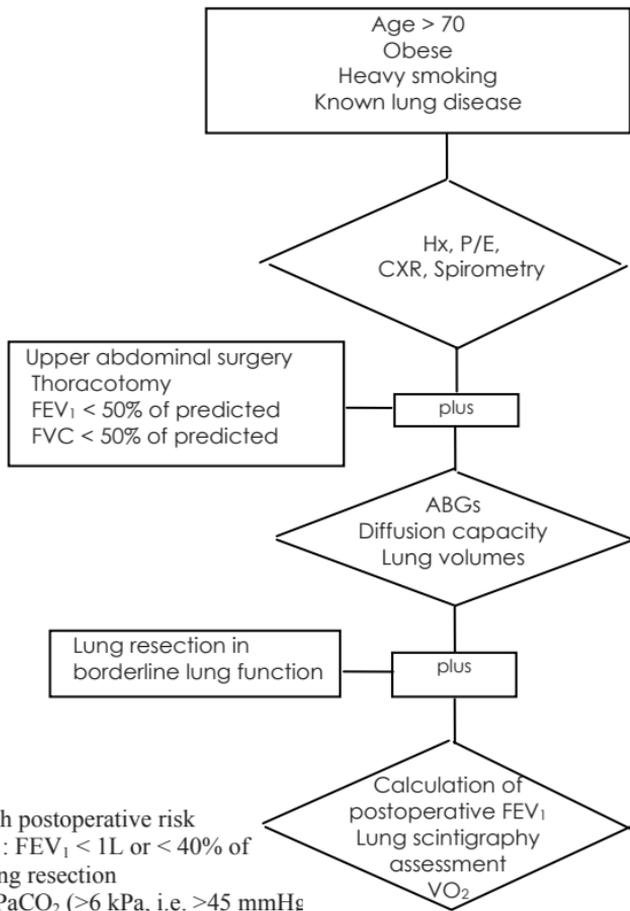
Severity of OSA based on apnoea-hypopnoea index (AHI)

Mild: 5-15/hr	Moderate: 15-30/hr	Severe: > 30/hr
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Indications for urgent arrangement of nasal CPAP

1. Pickwickian syndrome with daytime alveolar hypoventilation, pulmonary hypertension or cor pulmonale
2. Nocturnal malignant arrhythmia related to the OSA
3. Nocturnal angina related to the OSA
4. Severe EDS that may impose risk to the patient and/ or others e.g. professional driver especially with history of road traffic accident

## PREOPERATIVE EVALUATION OF PULMONARY FUNCTION



Results indicating high postoperative risk

1. Thoracic surgery : FEV<sub>1</sub> < 1L or < 40% of predicted after lung resection
2. ABG - Elevated PaCO<sub>2</sub> (>6 kPa, i.e. >45 mmHg)
3. FEV<sub>1</sub>, FVC or MVV <50% of predicted
4. Evidence of pulmonary hypertension
5. Preoperative cardiopulmonary exercise testing:  
VO<sub>2max</sub> <15 ml/kg/min

Consult respiratory physician in high risk cases

## NON-INVASIVE VENTILATION (NIV)

### More evidence of efficacy in:

1. COPD with respiratory acidosis pH 7.25-7.35
2. Hypercapnic respiratory failure secondary to chest wall deformity or neuromuscular disease
3. Cardiogenic pulmonary edema
4. Weaning from tracheal intubation
5. Acute respiratory failure in immunosuppressed states
6. Post-operative hypoxaemia (except in upper GI surgery)

### Less efficacious or even harmful in:

1. Acute severe asthma
2. Acute lung injury (ALI) or Acute respiratory distress syndrome (ARDS)
3. Pneumonia, esp if copious secretions
4. Treatment of established post-extubation respiratory failure

**Contraindications:** respiratory arrest, medical instability, inability to protect airway, excessive secretions, uncooperative or agitated status, unfitting mask, and recent upper airway or gastrointestinal surgery

### Practical aspects

1. Machine: sophisticated ICU ventilator (independent insp/exp limbs, higher max flow); or smaller-sized ventilator dedicated for NIV delivery (single limb only, with expiratory port which can be just a hole or a dedicated device, e.g. Whisper-Swivel valve); or a hybrid type of ventilator with functionality in between the above two types
2. Interface: nasal mask, face mask, total face mask, helmet, nasal pillows (In acute respiratory failure, start with a mask.)
3. Mode of delivery : Singel level (CPAP) or Bi-level (IPAP + EPAP)

**Factors associated with success:** less sick (lower APACHE II score), higher pH, lower respiratory rate (RR), lower PaCO<sub>2</sub>, subjective improvement within one hour of start

**Factors associated with failure:** edentulous, pneumonia, excess secretions, mouth leaks, poor coordination, ARDS, PaO<sub>2</sub>/FiO<sub>2</sub> ≤146, sicker patient (Simplified Acute Physiology Score (SAPS II) ≥35).

### Common setting

1. Spontaneous/ timed (ST) mode or Spontaneous (S) mode
2. CPAP/EPAP: Pulmonary oedema: 6 to 10 cmH<sub>2</sub>O; COPD: 4 to 5 cmH<sub>2</sub>O
3. IPAP: For COPD, start at 12-15 cmH<sub>2</sub>O, titrate up to 20 cmH<sub>2</sub>O. Aim at tidal volume (Vt) ≥ 7ml/kg BW and RR ≤ 25/min;
4. Backup RR: 0 to 12; with I:E ratio: 1:2 to 1:3

### Points to note

1. Watch out for gastric distension
2. Monitor ABG: Within 1<sup>st</sup> 1-2 hours after start to determine success,
3. Consider invasive mechanical ventilation if there is no objective signs of improvement after 1 hour of use
4. Consider repeat ABG at 4-6 hours if first set ABG show little improvement. If still no response, consider intubation
5. Apply NIV for 4-6 hours, then remove mask for short periods every few hours for meals, sputum clearance or bronchodilator inhalation
6. Stringent infection control measures should be taken during NIV for patients with suspected respiratory infections (refer to your hospital guidelines).

# **Rheumatology & Immunology**



## APPROACH TO INFLAMMATORY ARTHRITIS

### Assessment

- Arthralgia – pain in a joint without demonstrable synovitis
- Inflammatory Arthritis (Synovitis) – joint swelling, warmth, pain and tenderness
- Polyarthralgia/polyarthritis – 5 or more joints.
- Chronic polyarthralgia/polyarthritis – more than 6 weeks.

### Major causes of polyarthralgia/polyarthritis

- Bacterial arthritis (staphylococcal, streptococcal, gonococcal, meningococcal)
- Bacterial endocarditis
- Viral arthritis
- Reactive arthritis
- Crystal-induced arthritis: gout, pseudogout
- Rheumatoid arthritis
- Seronegative arthritis: ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease
- Connective tissue diseases: SLE, systemic vasculitis, systemic sclerosis, Still's disease
- Others: sarcoidosis, palindromic rheumatism, malignancy, hyperlipoproteinemias, Lyme disease, rheumatic fever

### Major causes of monoarthritis

- Septic arthritis
- Crystal-induced arthritis: gout, pseudogout
- Haemarthrosis / trauma / overuse
- Tuberculous arthritis
- Osteoarthritis
- Spondyloarthropathies: ankylosing spondylitis, psoriatic arthritis
- Monoarthritic onset rheumatoid arthritis
- Reactive arthritis

- Other uncommon causes: avascular necrosis, synovial metastasis

### Relevant investigations

- CBP, ESR, CRP
- Renal function, liver function, calcium, phosphate, urate, urinalysis
- ANA, RF (if SLE or RA is suspected)
- X-ray of the affected joints, MRI if indicated
- Joint aspiration
- Synovial biopsy (in undetermined cases)

### Joint fluid analysis

Send fluid for:

- gram stain and bacterial culture
- white cell count
- crystal microscopy

### Joint fluid white cell count:

Classification	Clarity	WBC/ml	% of neutrophils
Normal	Transparent	< 200	< 25
Non-inflammatory	Transparent	< 2000	< 25
Inflammatory	Translucent	2,000-100,000	25 – 75
Septic	Opaque	50,000-300,000	> 90

### Crystal microscopy:

- Urate crystals are slender and needle-shaped and have strong negative birefringence under polarized light
- Calcium pyrophosphate crystals are pleomorphic or rhomboid-shaped, and have weakly positive birefringence under polarized light

## GOUTY ARTHRITIS

### Clinical features

- Acute gout (monoarticular, polyarticular)
- Chronic tophaceous gout
- Uric acid calculi
- Gouty nephropathy

### Diagnosis

#### Definite gout

Intracellular negative birefringent urate crystal seen on joint fluid microscopy

#### Presumed gout

Classical history of episodic acute arthritis rapidly resolved with NSAID (or colchicine) + history of hyperuricaemia

### Management

#### Acute Gouty arthritis

##### 1. NSAID/COX II inhibitors

High dose, tapering over 5 days, reduce dose in renal impairment:

- a) indomethacin 50mg tds -> 25mg tds -> 25mg bd
- b) naprosyn 500mg stat -> 250mg tid -> 250mg bd
- c) ibuprofen 800mg stat -> 400mg qid -> 200mg tid

##### 2. Colchicine

0.5mg tds x 1-2 days (stop if nausea/diarrhoea, + simple analgesic)

Reduce frequency in renal impairment

Q hourly – Q2 hourly x 10 doses regime is **not** recommended.

##### 3. Corticosteroid

- a) Intra-articular kenacort injection after exclusion of septic arthritis
- b) Prednisolone 20-40mg daily x 1 week,  
(for patients with NSAID/ colchicine contraindication or renal failure)

### Urate lowering therapy

Low purine diet is advisable but only small changes in serum uric acid can be attained. Urate lowering therapy is indicated in patients with hyperuricaemia and more than 2 attacks of acute gout in one year, tophaceous gout or urate renal calculi.

#### 1. Xanthine oxidase inhibitor

**Allopurinol** 300mg po daily (usual dose)

Reduce dose in renal impairment

5% skin side effects

Start allopurinol only when acute gout has subsided

+ colchicine 0.5mg daily or bid, for 3-6 months, to prevent acute gout attacks

Target to reduce serum uric acid < 0.36 mmol/L

#### 2. Uricosuric drugs

**Probenecid** 250mg bd to 1gm tds

(Contraindications: moderate renal impairment, urate renal stone, tophaceous gout, high 24 hour urine uric acid excretion)

**Benzbromarone** is licensed in Hong Kong but not under HA formulary

**Sulfinpyrazone** is not licensed in Hong Kong

#### 3. Novel treatment

a. **Febuxostat** – a new nonpurine selective xanthine oxidase inhibitor

b. **Uricase**: recombinant urate-oxidase enzyme, Rasburicase, for paediatric pre-chemotherapy

## SEPTIC ARTHRITIS

1. A hot, swollen and tender joint should be regarded as septic arthritis until proven otherwise, even in the absence of fever, leucocytosis, elevated ESR or CRP. Septic arthritis can present as monoarthritis (80-90%), oligoarthritis or polyarthritis. Delay in diagnosis and treatment can result in irreversible joint destruction.
2. Prompt aspiration of the joint is warranted. Synovial fluid should be sent for:
  - Differential cell counts: Usually  $>50,000$  WBC/ml and often  $>100,000$ /ml, predominantly neutrophils.
  - Gram stain
  - Culture and sensitivity
  - Polarising microscopy for crystals (septic arthritis may co-exist with crystal arthropathies)
3. Other investigations: CBC with differentials, RFT, LFT, blood culture, X-ray of the joint. Swabs of pharynx, urethra, cervix and anorectum if gonococcal infection suspected.
4. Start empirical IV antibiotics immediately according to suspected organisms and gram stain. Modify according to culture and sensitivity results. Opinion from microbiologists is helpful.
5. Repeat aspiration of the joint to dryness.
6. Consult orthopaedic surgeon for drainage especially for infected prosthetic joint. Open drainage is usually necessary for hip infection.
7. Start physiotherapy early.
8. NSAIDs for pain relief
9. IV antibiotics for at least 2 weeks or until signs improved for non-gonococcal arthritis, then orally for an additional 2-4 weeks.

Suggested choice of antibiotics:

Synovial fluid gram stain	Organism	IV Antibiotics
Gram +ve cocci (clusters)	Staph. Aureus MSSA	Cloxacillin 1-2g q6hr or Cefazolin 1-2 g q8hr
Gram +ve cocci (chains)	Streptococcus	Penicillin 2 MU q4hr or Cefazolin 1-2g q8hr
Gram -ve Bacilli	Enterobacteriaceae	Ceftriaxone 2 g q24hr or Cefotaxime 1g q8hr
	Pseudomonas	Cefepime 2g q12hr or Piperacillin 3g q6hr or Imipenem 500 mg q6hr Plus gentamicin
Gram -ve diplococci	Neisseria gonorrhoeae**	Ceftriaxone 2g q24hr or Cefotaxime 1g q8hr or Ciprofloxacin 400mg q12hr
Empirical initial therapy	1. No risk factors for atypical organisms	Cloxacillin or Cefazolin or Ceftriazone
	2. High risk for gram-ve sepsis (elderly, frail, recurrent UTI, recent abdominal surgery, immunocompromised)	Cloxacillin plus Ceftriaxone or Cefotaxime
	3. Gonorrhoea suspected	Ceftriazone or cefotaxime or ciprofloxacin
	4. MRSA suspected:	Vancomycin 1g q12hr plus Ceftriaxone or Cefotaxime

\*\*Treat possible concurrent Chlamydia trachomatis infection with doxycycline (100 mg BD for 7 days) in patients with gonococcal infection.

## RHEUMATOID ARTHRITIS

### 1. Diagnosis:

#### 1987 ACR criteria for the classification of established RA

##### At least 4 of the following features

- Morning stiffness >1 hour
- Arthritis and soft tissue swelling of  $\geq 3$  joint areas
- Arthritis of hand joints
- Symmetric arthritis
- Subcutaneous nodules in specific places
- Rheumatoid factor at a level above 95<sup>th</sup> percentile
- Radiographic changes suggestive of joint erosion

Clinical symptoms must be present for **at least 6 weeks**

#### 2010 ACR/EULAR classification criteria for RA

##### 6/10 points – classified as having definite RA

- Joint involvement
  - 1 large joint (0)
  - 2-10 large joints (1)
  - 1-3 small joints (with or without large joints) (2)
  - 4-10 small joints (with and without large joints) (3)
  - >10 joints (at least 1 small joint) (5)
- Serology (at least 1 laboratory result)
  - Negative RF and negative anti-CCP (0)
  - Low positive RF or low positive anti-CCP (2)
  - High positive RF or high positive anti-CCP (3)
- Acute phase reactants (at least 1 laboratory result)
  - Normal CRP and normal ESR (0)
  - Abnormal CRP or ESR (1)
- Duration of symptoms
  - < 6 weeks (0)
  - $\geq 6$  weeks (1)

### 2. Investigations

- ESR and C-reactive protein (CRP)
- RF (sensitivity ~70%)
- Anti-citrullinated cyclic peptide antibody (anti-CCP) – highly specific for RA, helpful in undetermined situations
- Plain X-ray of the hands and feet for erosion
- MRI or USG may be useful for detecting early bony erosion

### 3. Clinical assessment

Includes: subjective & objective evidence of active synovitis; efficacy, tolerability & need for adjustment of present Rx; associated comorbidities (cardiovascular / osteoporosis) & extra-articular problems

Useful parameters:

- degree of joint pain
- duration of morning stiffness
- number of tender and swollen joints
- functional status
- patient's and physician's global assessment
- ESR or CRP (if persistently raised without obvious synovitis – beware of infection)
- radiographic progression

### 4. Management overview:

Goal: control synovitis/prevent joint damage/preserve function (multidisciplinary team care)

- (a) Patient education / counseling
- (b) Medications (plain analgesic / NSAID / DMARDs / biological DMARD / judicious use of steroid)
- (c) Non-pharmacological: P/T, O/T, podiatrist, dietitian, etc.
- (d) Surgery
- (e) Management of associated comorbidities & their risk factors

### 5. **EARLY aggressive use of DMARDs is indicated for patients with poor prognostic factors**

- High disease activity at onset ( $\geq 18$  joints)
- High baseline joint damage (erosive disease)
- Persistently high CRP level
- Positive IgM rheumatoid factor or anti-CCP (esp. high titer)
- Positive family history of RA
- Nodular disease
- Extra-articular manifestations

### 6. **Special considerations in the use of conventional DMARDs**

- All are slow-acting and take time to act. Therefore DO NOT delay starting DMARDs
- Usually start with one drug, but combination DMARDs should be considered early in patient with severe disease
- DON'T be slow in building up target doses of DMARDs
- Switching to or adding another DMARD promptly if synovitis uncontrolled
- Counsel patients on the effects and side effects and their slow action

### 7. **Conventional synthetic DMARDs:**

Methotrexate, Sulphasalazine, Leflunomide,  
 Hydroxychloroquine, Low dose prednisolone ( $<10\text{mg/day}$ ),  
 Azathioprine, Cyclosporin A, Intramuscular Gold

### 8. **Biological DMARDs**

- Should be prescribed by rheumatologist & with reference to relevant local & international guidelines
- Examples: Adalimumab, Etanercept, Infliximab, Golimumab, Rituximab, Abatacept, Tocilizumab
- Safety Net available for infliximab, etanercept, adalimumab

and rituximab; check HAHO intranet site for details under Samaritan fund

## Response criteria

### 1. ACR response criteria

ACR20/50/70 responses

≥ 20%/50%/70% improvement in

- (a) Swollen joint count
- (b) Tender joint count
- (c) Improvement in at least 3 of the following 5 measures
  - Patient's global assessment of disease activity
  - Physician's global assessment of disease activity
  - Patient's assessment of pain
  - Acute-phase reactant (ESR, CRP)
  - Disability scores (HAQ)

### 2. EULAR response criteria

#### Disease activity score (DAS)

DAS44 and DAS28 (more convenient in daily clinical practice)

$$\text{DAS28} = 0.56 \cdot \sqrt{(t28)} + 0.28 \cdot (\text{sw28}) + 0.70 \cdot \text{Ln}(\text{ESR}) + 0.014 \cdot \text{GH}$$

- Number of tender joints among 28 joints (t28)
- Number of swollen joints among 28 joints (sw28)
- Erythrocyte sedimentation rate (ESR, mm/hour)
- General health status (GH) using a 100-mm visual analog scale (VAS)

**High disease activity >5.1, low disease activity ≤ 3.2, remission <2.6**

Present score	Decrease in DAS28		
	>1.2	0.6-1.2	<0.6
<3.2	Good response	Moderate response	No response
3.2-5.1	Moderate response	Moderate response	No response
>5.1	Moderate response	No response	No response

## ANKYLOSING SPONDYLITIS

1. **Modified New York criteria for definite AS (1984)**
  - a. Radiological criterion
    - Sacroiliitis,  $\geq$  grade II bilateral or grade III to IV unilaterally
  - b. Clinical criteria (at least 1 out of 3 )
    - i. Low back pain & stiffness for > 3 months that improve with exercise but not relieved by rest
    - ii. Limitation of motion of lumbar spine in both sagittal & frontal planes
    - iii. Limitation of chest expansion relative to normal correlated for age & sex
2. **ASAS criteria for axial spondyloarthritis (SpA) (2009):**
  1. **Imaging evidence of sacroiliitis (XR, MRI or CT) plus one SpA features \***
  2. **HLA-B27 positivity plus 2 other SpA features \***
    - \* SpA features
      - inflammatory back pain age of onset <40
      - arthritis
      - enthesitis
      - psoriasis
      - uveitis
      - dactylitis
      - Crohn's/colitis
      - Good response to NSAIDs
      - Family history for SpA
      - Elevated C-reactive protein (CRP)
      - HLA-B27
3. **Other extra-skeletal features** – apical fibrosis, aortic insufficiency
4. **Measurements**

- a. Modified Schober test
- b. Occiput to wall distance, tragus to wall distance
- c. Chest expansion
- d. Lateral lumbar flexion
- e. Cervical spine rotation
- f. Intermalleolar distance

#### 4. Investigations

- a. XR sacroiliac joints and spine
- b. MRI / CT SI joints in doubtful cases
- c. HLA-B27 (if imaging inconclusive)

#### 5. Disease assessment

- a. BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), active disease defined as  $\geq 4$  (0-10)
- b. BASFI (Bath Ankylosing Spondylitis Functional Index)
- c. BAS-G (Patient's / Physician's Global score)
- d. BASMI (Bath Ankylosing Spondylitis Metrology Index )
- e. Acute phase reactants (ESR/CRP), can be normal in patients with predominant axial involvement.

#### 6. Treatment

- a. Education, exercise & physiotherapy
- b. NSAIDs for pain and stiffness at optimal tolerated dose
- c. Addition of gastroprotective agents or use selective COX-2 inhibitor in patients with high GI risks (elderly, history of peptic ulcer, comorbidity)
- d. Analgesics such as paracetamol and opioids for patients in whom conventional NSAIDs or COX-2 inhibitor are insufficient, contraindicated or intolerated
- e. Sulphasalazine for patients with peripheral arthritis

- f. Anti-TNF therapy for patients with persistent high disease activity despite adequate trial of the above treatment including 2-3 NSAIDs (at least 2 months for each unless contraindicated). Refer rheumatologist for assessment of disease activity and indications for anti-TNF therapy

7. **ASAS 50 Response criteria:** ↓ BASDAI by 50%

## PSORIATIC ARTHRITIS

### Diagnostic criteria

1. Moll & Wright criteria 1973
  - ♦ inflammatory arthritis (peripheral arthritis and/or sacroiliitis or spondylitis)
  - ♦ the presence of psoriasis
  - ♦ the absence of rheumatoid factor
  
2. The Classification of Psoriatic Arthritis criteria (CASPAR)

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Inflammatory articular disease (joint, spine or enthesal)  
[mandatory]

---

With 3 or more points from the following:

1. Current psoriasis (scores 2 points)
  2. Personal history of psoriasis (if current psoriasis not present)
  3. Family history of psoriasis (if personal history of psoriasis or current psoriasis not present)
  4. Psoriatic nail dystrophy
  5. A negative test for rheumatoid factor
  6. Current dactylitis
  7. History of dactylitis (if current dactylitis not present)
  8. Radiological evidence of juxta-articular new bone formation
- 

### Clinical features

- ♦ 30% psoriasis population has arthritis
- ♦ 60% psoriasis precedes arthritis, 20% arthritis precedes psoriasis, 20% concurrent

### Features distinguishing PsA from RA

- ♦ Presence of psoriasis
  - (Hidden lesions common, e.g. scalp, hairline, behind the ear and inside ear canal, guttate lesions on back, under the breasts, around umbilicus, around the perineum or even natal cleft)
- ♦ Nail dystrophy
  - Onycholysis, pitting, ridging, etc
- ♦ Distal phalangeal joint involvement
- ♦ Spondylitis or sacroiliitis
- ♦ Enthesitis (inflammation of junction of tendon and bone)
- ♦ Dactylitis

### Treatment

#### Early DMARD treatment

- ♦ Active arthritis (> 3 tender/ swollen joints, dactylitis counted as one active joint)
 

Eg. Methotrexate, sulphasalazine, leflumomide, cyclosporin A

Anti-TNF $\alpha$  therapy (to be used by specialist)
- ♦ For skin psoriasis
  - (a) Topical steroid (potency)
    - Fluocinolone < betamethasone < clobetasol (to be used by specialist)
    - Lotion < cream < ointment < occlusive dressing
    - Common e.g.: 0.1% betamethasone cream, Diprosalic (betamethasone + salicylate)
  - (b) Topical Tar products, e.g. shampoo, bathing soap
  - (c) Vit D analogues: e.g. Dovonex (calcipotriol) (to be used by specialist)
  - (d) UVA or UVB (to be used by specialist)
  - (e) Anti-TNF $\alpha$  therapy and other biologics (to be used by specialist)

## SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

**American College of Rheumatology (ACR) criteria for the classification of SLE (Tan et al. 1982, revised 1997, Hochberg et al.)**

1. Malar rash
  2. Discoid rash
  3. Photosensitivity
  4. Oral ulcers
  5. Arthritis
  6. Serositis (pericarditis, peritonitis, pleuritis)
  7. Renal disease (proteinuria  $> 0.5\text{g/day}$ , or +++ by dipstick, or cellular casts)
  8. Neurological (seizure, or psychosis)
  9. Hematological (hemolytic anemia, or leucopenia  $< 4 \times 10^9/\text{L}$ , lymphopenia  $< 1.5 \times 10^9/\text{L}$ , on two or more occasions, or thrombocytopenia  $< 100 \times 10^9/\text{L}$ )
  10. Immunological (anti-dsDNA, or anti-Sm, or false +ve VDRL for more than 6 months, or the presence of the antiphospholipid antibodies)
  11. Positive anti-nuclear antibody (ANA)
- $\geq 4$  criteria, serially or simultaneously = classified as SLE (specificity = 96%)**

### Anti-ENA antibodies

- Anti-Ro: associated with photosensitivity and an increased risk of congenital heart block (~2% incidence). Pre-pregnancy counseling and ultraviolet light protection should be advised.
- Anti-ENA antibodies seldom sero-convert and repeating tests is not necessary.

### Anti-phospholipid antibodies

- Lupus anticoagulant (LAC) and anti-cardiolipin (aCL) antibody (IgG) are available in most HA hospitals.
- They are strongly associated with cerebro-vascular accidents in Chinese SLE patients. Other associations: thrombocytopenia, livedo reticularis, valvular heart lesions, recurrent miscarriages and venous thrombosis.
- Twice positive tests 12 week apart are necessary for the Dx of antiphospholipid syndrome. Only strongly positive aCL is clinically relevant.
- Because of the association with recurrent abortions and miscarriages, these antibodies have to be checked before pregnancy.
- Anti- $\beta$ 2-GPI antibody is more specific than aCL for thrombosis. Because of its limited sensitivity, anti- $\beta$ 2-GPI should only be considered in patients in whom antiphospholipid syndrome is suspected but yet aCL and LAC is negative.

### Monitoring of disease activity

- Clinical assessment (signs and symptoms of disease flares)
- Serology: C3 and C4 level, anti-dsDNA titer

### Points to note

- The ANA titer only correlates with disease activity very roughly and is not reliable for disease monitoring. Thus, **there is no need to repeat ANA every visit.**
- C-reactive protein (CRP) is usually not elevated in patients with active SLE. An elevated CRP in SLE may indicate persistent synovitis / arthritis, serositis or infection. Infection has always to be considered before augmentation of immunosuppressive therapy.

### Disease activity scoring system

The ACR SELENA-SLEDAI is one of the most widely used disease activity index. Items can be used as a check-list for disease flares

Seizure (8)	New skin rash (2)
Psychosis (8)	Alopecia (2)
Organic brain syndrome (8)	Fever (1)
Lupus headache (8)	Leukopenia ( $< 3 \times 10^9/L$ ) (1)
Cranial nerve disorder (8)	Thrombocytopenia (1)
Cerebrovascular accident (8)	Increase in anti-dsDNA titre (2)
Retinal hemorrhage / infarct / optic neuritis (8)	Decrease in C3 (2)
Vasculitis (8)	Proteinuria (4)
Arthritis ( $> 2$ joints) (4)	Urine cast (4)
Myositis (4)	Red blood cell cast in urine (4)
Oral ulcer (2)	Sterile pyuria (4)
Pleuritis (2)	
Pericarditis (2)	

**\* Only new features or manifestations are scored**

### Treatment of SLE

**General:** Patient education and counseling, sun-screening, screening and treatment of cardiovascular risk factors and osteoporosis

### Mild SLE manifestations

- NSAIDs (arthritis, serositis, fever)
- Hydroxychloroquine (arthritis, skin lupus)
- Methotrexate, Leflunomide (persistent and refractory arthritis)
- Topical steroid (skin lupus)
- Small to moderate doses of prednisolone (fever, systemic upset, mild cytopenias, more severe serositis and skin lupus)
- Azathioprine (hematological, mild renal disease, steroid

sparing)

### Severe SLE manifestations

Glomerulonephritis, neuropsychiatric lupus, severe cytopenias, thrombotic thrombocytopenic purpura, pulmonary hemorrhage, myocarditis, pneumonitis, pulmonary hypertension

- Moderate to high doses of prednisolone
- Intravenous pulse methylprednisolone
- Azathioprine
- Cyclophosphamide (intravenous pulse or oral)
- Mycophenolate mofetil (MMF)
- Cyclosporin A and Tacrolimus
- Plasma exchange
- Intravenous immunoglobulin
- Rituximab
- Vasodilatation (bosentan, inhaled iloprost, sildenafil)
- Anticoagulation

### Lupus nephritis (ISN/RPS Classification 2003)

**Class I:** Minimal mesangial lupus nephritis

**Class II:** Mesangial proliferative lupus nephritis

**Class III:** Focal proliferative lupus nephritis

**Class IVG:** Diffuse global proliferative lupus nephritis

**Class IVS:** Diffuse segmental proliferative lupus nephritis

**Class V:** Membranous lupus nephritis

**Class VI:** Advanced sclerotic lupus nephritis

MMF is increasingly used as first line treatment for proliferative lupus nephritis because of lower frequency of adverse effects. Cyclophosphamide remains the conventional treatment for those with rapidly progressive crescentic glomerulonephritis and those with impaired renal function

**Neuropsychiatric lupus**

19 Neuropsychiatric syndromes according to the 1999 ACR classification

**Central nervous system**

Aseptic meningitis

Cerebrovascular disease

Demyelinating syndrome

Headache

Movement disorder

Myelopathy

Seizure disorder

Acute confusional state

Anxiety disorder

Cognitive dysfunction

Mood disorders

Psychosis

**Peripheral nervous system**

Guillain-Barre syndrome

Autonomic neuropathy

Mononeuropathy

(single/multiplex)

Myasthenia gravis

Cranial neuropathy

Plexopathy

Polyneuropathy

**Diagnosis**

- Till now, no specific confirmatory serological & imaging tests
- A diagnosis by exclusion (to rule out CNS infections, metabolic encephalopathy, effects of drugs / toxins including corticosteroids, electrolyte disturbances, rarely brain tumor)
- Lupus activity in other systems increases likelihood of active neuropsychiatric lupus but CNS infection may coexist with active neuropsychiatric lupus
- CT brain, MRI brain / spinal cord for anatomical diagnosis
- Lumbar puncture to rule out CNS infection
- EEG
- Antiphospholipid antibodies
- Anti-ribosomal P antibody (private laboratory) is associated with lupus psychosis but its usefulness is limited by the low

sensitivity

### **Treatment**

- Symptomatic: anti-convulsants, anti-psychotics, anti-depressants, sedatives
- Secondary prophylaxis for atherosclerotic vascular disorders: aspirin / warfarin
- Immunosuppressive or immunomodulating treatment (eg. high dose corticosteroids, pulse methylprednisolone, cyclophosphamide, IVIG, rituximab): severe psychosis, acute confusional state, myelopathy, myasthenia gravis, neuropathies, demyelinating syndrome.

### **Novel / investigational therapies for SLE**

- Sirolimus, Belimumab, Ocrelizumab, Epratuzumab, Abatacept, Anti-type I interferons
- Immunoablative cyclophosphamide  $\pm$  stem cell rescue
- Mesenchymal stem cell therapy

## RHEUMATOLOGICAL EMERGENCIES

### CERVICAL SUBLUXATION

- Suspect in RA patients with long standing and severe disease
- Commonly presents with neck pain radiating towards the occiput, clumsiness, abnormal gait, spastic quadriparesis, sensory and sphincter disturbances. May cause cord compression and death.
- 4 forms in descending order of frequency: anterior, posterior, lateral, vertical

#### **Investigations:**

- Plain AP and lateral XR of cervical spine with flexion and extension views
- Anterior subluxation: distance between the posterior aspect of the anterior arch of the atlas and the anterior aspect of the odontoid process (Atlanto-dens interval, ADI)  $\geq 4\text{mm}$
- Dynamic (flexion-extension) MRI (if surgery indicated)

#### **Management:**

##### Medical

- High-impact exercises and spinal manipulation are contraindicated
- Soft collars may serve as reminder for patients and physicians but provide little structural support
- Stiff cervical collars may provide marginal benefit but compliance is a problem
- Neuropathic pain relief

##### Surgical

- Urgent referral to orthopaedic surgeons or neurosurgeons if signs of cord compression
- Patients with severe subluxation but without signs of cord compression are at risk for severe injury and perhaps death due to a variety of insults including falls, whiplash injuries, and intubation. Surgical decision should be individualized.
- Surgical options: craniocervical decompression, cervical or occipito-cervical fusion (alone or in combination)

**GIANT CELL ARTERITIS (GCA)**

**Presentation:** At least 3 of the following 5 criteria

1. Age  $\geq 50$  years
  2. Localized headache of new onset
  3. Tenderness or decreased pulse of the temporal artery
  4. ESR  $> 50$  mm/hr
  5. Biopsy revealing a necrotizing arteritis with a predominance of mononuclear cells or a granulomatous process with multinucleated giant cells.
- Polymyalgia Rheumatica (PMR) is characterized by aching and morning stiffness in the shoulder and hip girdles, occurring in 40-50% of GCA patients.
  - Other presentations: jaw or arm claudication, weight loss, PUO
  - Complications: Ischaemic optic retinopathy (visual loss 15-20%). Blindness is abrupt and painless, may be preceded by amaurosis fugax.
  - Aneurysms, dissections, stenotic lesions of the aorta and its major branches

**Investigations**

- Elevated ESR, often  $>100$ mm/hr (5% of GCA has ESR  $< 40$ mm/hr)
- Temporal artery biopsy of the affected side.

**Treatment**

- High dose prednisolone (1mg/kg/day)
- For visual symptoms or signs (eg, amaurosis fugax, partial or complete visual loss), start empirical steroid before temporal artery biopsy result
- Acute visual changes - consider IV pulse methylprednisolone (250-1000mg) daily for 3 days

**SEPTIC ARTHRITIS** (see page R5-6)

## NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

- Do not use > 1 NSAID at a time
- Use the lowest possible dosage and frequency sufficient for pain relief
- Efficacy is similar among various NSAIDs. Cheaper ones such as naproxen, ibuprofen and indomethacin are equally effective.
- If one NSAID is not working despite 2-3 week of treatment at full dosage, shifting to another NSAID may be considered.
- Coexisting hypertension, fluid retention and/or renal impairment – consider sulindac

### Adverse Effects

- GI: dyspepsia, peptic ulcer, GI bleeding and perforation
- Renal: renal impairment
- CVS: fluid retention, worsening of hypertension, increased cardiovascular events
- Liver: raised transaminases
- CNS: headache, dizziness and cognitive impairment, especially use of indomethacin in elderly
- Skin: may range from mild rash to Steven Johnson's Syndrome
- Resp: may precipitate or exacerbate bronchospasm in aspirin sensitive individuals

### Risk factors for gastrointestinal toxicity:

- a. Chronically disabled
- b. Age > 60 years
- c. Previous history of proven peptic disease
- d. Co-administration of high dose prednisolone or anticoagulation
- e. Higher dosage of NSAIDs
- f. Extent of inflammatory disease for which NSAIDs is prescribed

### COX-2 inhibitors (COXIB)

Efficacy: similar to non-selective conventional NSAIDs

Advantages:

- Reduce gastrointestinal toxicity.
- Less effect on platelet function, hence less bleeding risk.
- Less risk of precipitating bronchospasm

Adverse effects:

- Increase risk of cardiovascular events (AMI, stroke). Risk  $\propto$  dosage. May worsen BP control and heart failure
- Nephrotoxicity, hepatotoxicity, cardiotoxicity similar to conventional NSAIDs
- Celecoxib should be avoided in patients with sulphonamide allergy

### **Current recommendations for patients receiving NSAIDs**

1. Prescribe lower-risk agents. Weigh the GI vs the CV risk in individual patient.
  - If estimated risk of life-threatening GI bleeding  $>$  risk of CV events, consider use of NSAIDs with gastroprotection or the COXIBs.
  - If risk of CV events  $>$  the risk of GI bleeding, COXIBs should be avoided.
2. Limit duration, frequency and dosage.
3. Patients with known H pylori infection should undergo eradication before NSAID therapy.
4. For patients at higher risk for GI complications, consider assessing for and treating H pylori if present and co-therapy with gastroprotective agents.
5. Gastroprotection.
  - Misoprostol
  - Proton pump inhibitors (PPIs)
  - COXIB alone is beneficial in reducing GI risks, but with the possible trade-off of increasing CV risk.
  - COXIB with concurrent PPI therapy may be considered in ultra-high risk patients eg. recurrent ulcer bleeding.

# Infections



## COMMUNITY-ACQUIRED PNEUMONIA (Ref: IMPACT 3<sup>rd</sup> Editon 2005)

1. **Outpatient pneumonia**
  - **PO**  $\beta$ -lactam/ $\beta$ -lactamase inhibitor (e.g. Augmentin/Unasyn)  $\pm$  Macrolide, OR
  - **PO** Amoxicillin + a newer macrolide, OR
  - Fluoroquinolone for those with DRSP risk(s) or Penicillin intolerance
2. **Hospitalised patients with mild to moderate infection** (these patients have risk factors requiring hospitalisation)
  - **IV/PO** Augmentin/Unasyn  $\pm$  Macrolide, OR
  - Cefotaxime or ceftriaxone  $\pm$  Macrolide
  - With modifying factors such as bronchiectasis:
    - Ticarcilline-tazobactam/Piperacillin-tazobactam/Cefepime + macrolide, OR
    - Fluoroquinolone + an aminoglycoside
3. **Severe hospitalised community-acquired pneumonia**  
(Either 1 out 3 major **OR** 2 out of 6 minor)  
Major criteria: a) ARF, b) Septic shock, c) Require MV  
Minor criteria: a) RR>30/min, b) PaO<sub>2</sub>/FiO<sub>2</sub><250, c) SBP<90 or DBP<60mmHg, d) Urea>7mmol/L, e) Mental confusion, f) Multilobar involvement
  - **IV** Piperacillin-tazobactam/Cefotaxime/Ceftriaxone + macrolide, OR
  - Cefepime + a macrolide

# DRSP risk (age>70, antibiotics within the last 3/12, immunosuppressive therapy, coexisting illness, recent hospitalisation, institutionalisation)

\* *Modify antibiotics according to C/ST when available*

\**In general, therapy should not be changed within the 1st 72 hrs unless there is marked clinical deterioration.*

	Organisms	Antibiotics
CAP, not hospitalized	<ul style="list-style-type: none"> <li>• <i>S. pneumoniae</i></li> <li>• <i>H. influenzae</i></li> <li>• <i>M pneumoniae</i></li> <li>• <i>C. pneumoniae</i></li> </ul>	<ul style="list-style-type: none"> <li>• PO Amoxicillin-clavulanate ± a newer macrolide or</li> <li>• Amoxicillin + a newer macrolide</li> </ul>
CAP, hospitalized in general ward	As above	<ul style="list-style-type: none"> <li>• IV/PO Amoxicillin-clavulanate,</li> <li>• Ceftriazone or Cefotaxime ± a newer macrolide</li> </ul>
Serious CAP, requiring ICU care	As above + Enterobacteriaceae	<ul style="list-style-type: none"> <li>• IV Piperacillin-tazobactam,</li> <li>• Cefepime,</li> <li>• Ceftriazone or Cefotaxime + a newer macrolide</li> </ul>

### Remarks

1. In HK, macrolide/azalide or tetracycline should not be used alone for empiric treatment of CAP as 50-70% pen-S and pen-R *S. pneumoniae* isolates are multiply resistant to these agents
2. For *S. pneumoniae* causing pneumonia (but not otitis media and meningitis), the following revised categorization was suggested:  $\leq 1 \mu\text{g/ml}$ , sensitive;  $2 \mu\text{g/ml}$ , intermediate;  $\geq 4 \mu\text{g/ml}$ , resistant. Penicillin or ampicillin or amoxicillin are generally viewed as the beta-lactam drugs of choice for treatment infections with Pen-S and Pen-I strains of *S. pneumoniae*.
3. Augmentin 375mg tds + amoxil 250mg tds may be an acceptable alternative to high dose Augmentin 1gm bd as they were demonstrated to be bioequivalent.
4. Use of fluoroquinolone in CAP may lead to: (1) delay in diagnosis of tuberculosis; (2) increased fluoroquinolone resistance among *M. tuberculosis*. Thus, fluoroquinolone is not recommended as first line therapy in Hong Kong for CAP.

5. Indications for use of fluoroquinolones in CAP
  - Failed first line regimen
  - Allergic to alternative agents
  - Documented infection due to pneumococci with high level penicillin resistance ( $MIC \geq 4\mu\text{g/mL}$ ).
6. Drugs with activity against both *P. aeruginosa* and DRSP include cefepime, piperacillin, piperacillin-tazobactam, imipenem and meropenem.
7. With pseudomonas risk (e.g. bronchiectasis), give piperacillin-tazobactam or cefepime + a macrolide; or fluoroquinolone + aminoglycoside.

## HOSPITAL ACQUIRED PNEUMONIA (HAP)

Pneumonia occurring  $\geq 48$  hr after admission and excluding any infection that is incubating at the time of admission

### 2 empiric Rx categories :

1. **Patients with early-onset pneumonia ( $\leq 4$  days admission) with no risk factors for multidrug-resistant (MDR) pathogens and any disease severity**
  - 3rd generation cephalosporin OR
  - $\beta$ -lactam/ $\beta$ -lactamase inhibitor
  - (Amoxicillin-clavulanate/ Ampicillin-sulbactam)
2. **Patients with late-onset pneumonia ( $>4$  days admission) OR risk factors for MDR pathogens and all disease severity**
  - Antipseudomonal  $\beta$ -lactam/ $\beta$ -lactam inhibitor OR
  - Antipseudomonal cephalosporin OR
  - Antipseudomonal carbapenem
  - $\pm$  aminoglycoside OR fluoroquinolone
  - $\pm$  Linezolid OR Vancomycin after careful assessment of indication

**Risk factors for MDR pathogens (*Pseudomonas aeruginosa*, *ESBL-producing Enterobacteriaceae*, *Acinetobacter* species and *MRSA*)**

- Antimicrobial therapy in preceding 90 days
- High frequency of antibiotic resistance in the community or in the hospital unit
- Hospitalization for  $\geq 2$  days in the preceding 90 days
- Residence in a nursing home or extended care facility
- Chronic dialysis within 30 days
- Home wound care
- Family member with multi-resistant pathogen
- Immunosuppressive disease and/or therapy

**Empiric antibiotic may need modification/de-escalation once the results of blood or respiratory tract cultures become available**

	<b>Organisms</b>	<b>Antibiotics</b>
Onset <4 days after admission with no previous antibiotics	<ul style="list-style-type: none"> <li>• <i>S. pneumoniae</i>,</li> <li>• <i>H influenzae</i></li> <li>• <i>M. Catarrhalis</i></li> <li>• <i>S. aureus</i></li> </ul>	<ul style="list-style-type: none"> <li>• IV/PO Amoxicillin-clavulanate or</li> <li>• Cefuroxime if penicillin allergy (non-type I hypersensitivity)</li> </ul>
Onset $\leq 4$ days after admission + had received antibiotic recently, OR onset $\geq 5$ days after admission OR mechanical ventilation	<ul style="list-style-type: none"> <li>• MRSA;</li> <li>• <i>P aeruginosa</i>,</li> <li>• <i>Acinetobacter</i>,</li> <li>• <i>Klebsiella</i> spp.,</li> <li>• <i>Enterobacter</i> spp.</li> </ul>	<ul style="list-style-type: none"> <li>• IV cefoperazone-sulbactam,</li> <li>• Cefepime,</li> <li>• Ticarcillin-clavulanate or</li> <li>• piperacillin-tazobactam <math>\pm</math> an aminoglycoside <math>\pm</math> Vancomycin after careful assessment of indications</li> </ul>

# PULMONARY TUBERCULOSIS

## Recommendations

\*Directly observed treatment (DOT) should be given as far as possible.

- Uncomplicated new cases – 6 months in total
  - 2 HRZ + (E or S)<sub>7</sub>/ 4 HR<sub>7</sub> (When Rx started in hospital or when 3x/week regimen not tolerated)
  - 2 HRZ + (E or S)<sub>7</sub>/ 4 HR<sub>3</sub>
  - 2 HRZ + (E or S)<sub>3</sub>/ 4HR<sub>3</sub> (Government Chest Clinic regimen)
- Retreatment cases – 9 months in total.
  - 3 (or 4) HRZES<sub>7</sub>/ 6 (or 5) HR ± E<sub>7</sub>

### Notations

Figures in front of drug combinations = duration in months.

Subscript '3' = thrice weekly & '7' = daily.

The slash "/" is used to separate different phases of Rx.

### Drugs and dosages

	Daily		3x/week	
	BW	Dose	BW	Dose
H = Isoniazid	--	300 mg <sup>a</sup>	--	10-15 mg/kg
R = Rifampicin	<50 kg ≥50 kg	450 mg 600 mg	--	600 mg
Z = Pyrazinamide	<50 kg ≥50 kg	1-1.5 g 1.5-2 g	<50 kg ≥50 kg	2 g 2.5 g
E = Ethambutol <sup>b</sup>	--	15 mg/kg	--	30 mg/kg
S = Streptomycin	<50 kg ≥50 kg	500-750 mg <sup>c</sup> 750 mg	<50 kg ≥50 kg	500-750 mg 750-1000 mg

- Some elderly and/or malnourished can only tolerate 200 mg.
  - Vitamin B6 10 mg/d for malnutrition, alcoholism, pregnancy.
  - May cause peripheral neuropathy, encephalopathy and convulsions especially in renal impairment.
  - Drug interaction with phenytoin & carbamazepine.
- Assess baseline visual symptoms & acuity before starting Rx with close monitoring during therapy & consult ophthalmologist prn
- Lower dose for > 60 years old.

Reference: Chemotherapy of TB in HK – updated in 2006.

[www.info.gov.hk/tb\\_chest](http://www.info.gov.hk/tb_chest)

## CNS INFECTIONS

*Consider CNS infections in the presence of sepsis and one or more of the followings: meningism, seizures, headache, impaired consciousness, photophobia, confusion, signs of increased intracranial pressure ( $\uparrow$  ICP), focal neurological deficits, presence of parameningeal focus of sepsis. Signs and symptoms may be subtle or absent in elderly or immunocompromised host.*

1. CSF examination is crucial in the diagnosis of meningitis
2. Watch out for signs of  $\uparrow$ ICP and do urgent CT brain before LP. If LP is contraindicated, likely to be delayed or fails, empirical antibiotics can be started after taking blood cultures
3. CSF analysis: cell count, protein, glucose (simultaneous blood sugar), gram stain, culture, AFB (smear and C/ST), cryptococcus (India ink smear, Ag and culture), viral studies Do not wait for C/ST results before starting Rx
4. Other Ix: CBP, RFT, LFT, CXR, EEG, XR skull, sinuses and mastoid
5. Look for any predisposing factors: sinusitis, endocarditis, otitis media, skull fracture, immunocompromised state, etc

### Typical CSF findings in meningitis

	Normal	Viral	Bacterial	TB / Cryptococcal
Appearance	clear	clear	turbid	turbid/viscous
Mononuclear cells (/mm <sup>3</sup> )	<5	10-100	<50	100-300
PMN (/mm <sup>3</sup> )	nil	nil	200-3000	0-200
Protein (g/l)	0.2-0.4	0.4-0.8	0.5-2.0	0.5-3.0
CSF/blood glucose	>1/2	>1/2	<1/2	<1/2

**Initial empirical anti-microbial regimes**

Bacterial meningitis	Ceftriaxone 2 g q12h OR Cefotaxime 1.5-2 g iv q4h iv + Vancomycin <sup>S</sup> 500 -1000 mg q6-12h + Ampicillin 2g iv q4h (if risk of listeriosis anticipated <sup>@</sup> )
Brain abscess	Ceftriaxone 2 g q12h OR Cefotaxime 1.5-2 g iv q4h iv + Metronidazole 500 mg iv q8h
TB meningitis	INAH 300-600 mg daily Rifampicin 450-600 mg daily Pyrazinamide 1.5-2 g daily Ethambutol 15 mg/kg/d daily (25 mg/kg/d for first 2/12) Pyridoxine 100 mg daily ± Streptomycin 0.75 g im daily
Cryptococcal meningitis	Amphotericin B 0.7 – 1 mg/kg iv infusion over 4-6 hrs + 5-Flucytosine 25 mg/kg q6h po for 2 weeks, then fluconazole at least 400mg/d for a minimum of 8 weeks (immunocompetent patients)
Viral encephalitis	Acyclovir 10 mg/kg iv q8h (or 500mg iv q8h)

§ Aim at trough concentration 15-20µg/ml

@ Immunocompromized, pregnancy and elderly

- Dexamethasone 4 mg q6h in complicated TB meningitis or brain abscess with significant cerebral oedema.
- Dexamethasone (0.15 mg/kg q6h for 2-4 days with the first dose administered 10-20 min before, or at least concomitant with, the first dose of antimicrobial therapy) in adults with suspected or proven pneumococcal meningitis
- Prophylactic anti-convulsant may be considered in cerebral abscess and subdural empyema
- Duration of Rx for brain abscess 6-8 weeks
- Duration of Rx for meningitis: ≥ 7days for *H. influenzae*, 10-14 days for *S. pneumoniae*, 14-21 days for *L. monocytogenes* and *S. agalactiae*, and 21 days for Gram negative bacilli. DO NOT change to oral therapy.
- Consider prophylaxis for contacts in cases of meningococcal meningitis: ciprofloxacin 500mg stat, ceftriazone 250mg IM stat

## URINARY TRACT INFECTION

Diagnosis	Organisms (a)	Antibiotics
Cystitis	<i>E. coli</i> ; <i>S. saprophyticus</i> ; Gp B streptococcus; <i>Proteus</i> spp; <i>klebsiella</i> spp.	<ul style="list-style-type: none"> <li>• PO Nitrofurantoin(b, c)</li> <li>• Amoxicillin-clavulanate(c)</li> <li>• TMP-SMX(d)</li> </ul>
Acute pyelonephritis	<i>E. coli</i> ; other enterobacteriaceae; <i>enterococcus</i>	<ul style="list-style-type: none"> <li>• IV Amoxicillin-clavulanate</li> <li>• 3rd cephalosporins (e) ± Aminoglycoside (f)</li> <li>• IV/PO Fluoroquinolone (d, f)</li> </ul>

### Remarks

- a. *Escherichia coli* is the most causative pathogen. ESBL strain is not uncommonly seen in Enterobacteriaceae. Empiric Carbapenem may be considered after careful clinical assessment and indication.
- b. Nitrofurantoin is well tolerated, and demonstrates a consistently low level of resistance among *E. coli*, gram-positive cocci (including *Enterococcus* and *S. saprophyticus*), but inactive against most *Proteus*, and *Klebsiella* strains. Nitrofurantoin should not be used to treat pyelonephritis since it does not achieve reliable tissue levels.
- c. Give 5-7 day course of amoxicillin-clavulanate or Nitrofurantoin as 3-day course may not be as effective as ciprofloxacin and TMP-SMX.
- d. There is the increasing problem of resistance to TMP-SMX and fluoroquinolone.
- e. For example ceftriaxone and cefotaxime. A 14-day regimen is generally recommended for upper UTI.
- f. Aminoglycosides and fluoroquinolones achieve higher tissue levels, relative to serum levels, than do beta lactams

# ENTERIC INFECTIONS

*Acute infective diarrhoea may be due to viruses e.g. Norovirus, bacteria and their toxin, and sometimes protozoa. Most are self-limiting.*

## Clinical presentation

### 1. *Secretory diarrhoea (Non-inflammatory enteritis)*

- Commonly caused by salmonellosis
- Norovirus: pronounced vomiting
- Cholera classically presents as acute painless profuse rice water diarrhoea without blood or mucus

### 2. *Invasive diarrhoea (Inflammatory enteritis)*

- Presents as dysenteric syndrome i.e. transient diarrhoea followed by abdominal colic, tenesmus, fever, blood and mucus in stool
- Commonly caused by shigellosis (bacillary dysentery), non-cholera vibrios (*Vibrio parahaemolyticus* and *Plesiomonas shigelloides*) and occasionally *Entamoeba histolytica* (amoebic dysentery).

### 3. *Typhoid and paratyphoid fever (enteric fever)*

- Caused by *Salmonella typhi* (typhoid fever) and *Salmonella paratyphi* (paratyphoid fever)
- Suspect in patient of high fever with relative bradycardia, ↓platelet, N to ↓WCC, no localized focus of infection.

### 4. *Enteric infections associated with systemic complications*

- *E coli* O157:H7 — haemolytic-uraemic syndrome
- *Campylobacter* enteritis — Guillain-Barré syndrome
- Non-polio enteroviruses — Hand-foot-mouth disease, myocarditis, encephalitis, etc.

### 5. **Enteric infections are often more severe in immuno-compromised patients**, e.g. elderly, diabetes mellitus, cirrhosis, anatomical or functional hyposplenism, concurrent immunosuppressant therapy

*Management for enteric fever*

1. Dx of enteric fever confirmed by culture from blood & stool, occasionally bone marrow aspirate. Widal serology unreliable.
2. Antibiotics treatment:
  - **Levofloxacin** 500mg - 750mg daily iv/po OR **ciprofloxacin** 500mg - 750mg bd po x 7 days.
  - **Alternative:** Ceftriaxone 1-2g iv q24h x 10 – 14 days \_
  - **Strains with nalidixic acid resistance (a surrogate marker predicting clinical failure with fluoroquinolone therapy):**  
Azithromycin 500mg qd x 7 days or Ceftriaxone 1-2g iv q24h x 10 – 14 days \_

*Management for other bacterial enteric infections*

1. Adequate fluid and electrolyte supplement
2. Routine antibiotic not recommended for mild to moderate gastroenteritis
3. Consider fluoroquinolone e.g. **levofloxacin** 500mg daily po OR ciprofloxacin 500mg BD po for 3 - 5 days for severe gastroenteritis (> 6 unformed stools/day, fever > 38.5°C, tenesmus, faecal blood or WBC +ve)

NOTE: If *Campylobacter* enteritis is suspected and antimicrobial is indicated on clinical grounds, a **macrolide** (e.g. clarithromycin or azithromycin) is preferred because of increasing report of fluoroquinolone resistance.

**Reference**

1. HA fact sheet on typhoid and paratyphoid fever (Nov 2003)
2. HA factsheet on cholera (Oct 2005)
3. HA fact sheet on Management of E coli O157: H7 (Oct 2005)
4. HA infection control guideline on *Clostridium difficile* infection (Aug 2010)

# ACUTE CHOLANGITIS

## 1. Investigations

- a) CBP, LFT, RFT
- b) PT, APTT, Glucose
- c) Blood culture
- d) Abdominal USG

## 2. Management

- a) Active resuscitation and monitor vital signs
- b) IV antibiotics for mild to moderate cases:
  - Amoxicillin-clavulanate ( $\pm$  Aminoglycoside)
  - Cefuroxime + metronidazole ( $\pm$  Aminoglycoside)
  - If penicillin allergy, Levofloxacin + metronidazole
  - IV antibiotic can be switched to oral formulary for completion of therapy if clinically stable.
- c) IV antibiotics for severe cases: Consider Tazocin, carbapenems, 3<sup>rd</sup> generation cephalosporin or levofloxacin + metronidazole.
- d) Duration of Rx: limited to 4-7d unless difficult to achieve biliary decompression.
- e) Early decompression of biliary obstruction

## 3. Preparation for ERCP

1. Indications for emergency ERCP
  - Increasing pain and guarding in epigastrium or RUQ
  - Hypotension despite resuscitation
  - High fever ( $> 39^{\circ}\text{C}$ )
  - Mental confusion, which is a predictor of poor outcome
2. Correct coagulopathy
3. Fast patient

## 4. Care for patients who have nasobiliary or percutaneous (PTBD) drainage of obstructed biliary tract

- a) Check input/output chart (including NB drain) daily
- b) Check hydration status, RFT,  $\text{HCO}_3$  and correct fluid and electrolyte derangement as necessary

## SPONTANEOUS BACTERIAL PERITONITIS

*High index of suspicion is necessary*

1. Cirrhotic patients may have an insidious onset of fever and lack of peritoneal signs, perform diagnostic paracentesis, send ascitic fluid for:
  - Cell count (EDTA bottle to haematology laboratory, request differential WBC)
  - Low protein level is consistent with spontaneous bacterial peritonitis
  - Fluid for bacterial culture in blood culture broth
  - Cytology
2. Diagnostic criteria:
  - ascitic fluid WCC  $> 500/\text{mm}^3$  or neutrophil  $> 250/\text{mm}^3$
3. Perform blood culture
4. Common organisms: *E.coli*, *Klebsiella* sp, Pneumococcus, *Enterococci*.
5. Empirical treatment:
  - IVI Ceftriaxone 2gm q24h OR IVI Cefotaxime 2 gm q8h (q4h if life-threatening)
  - May consider reassessment by repeating paracentesis 48 hours later.
  - Usual duration of treatment : 5-10 days
6. Watch out for hepatic encephalopathy.

## NECROTIZING FASCIITIS

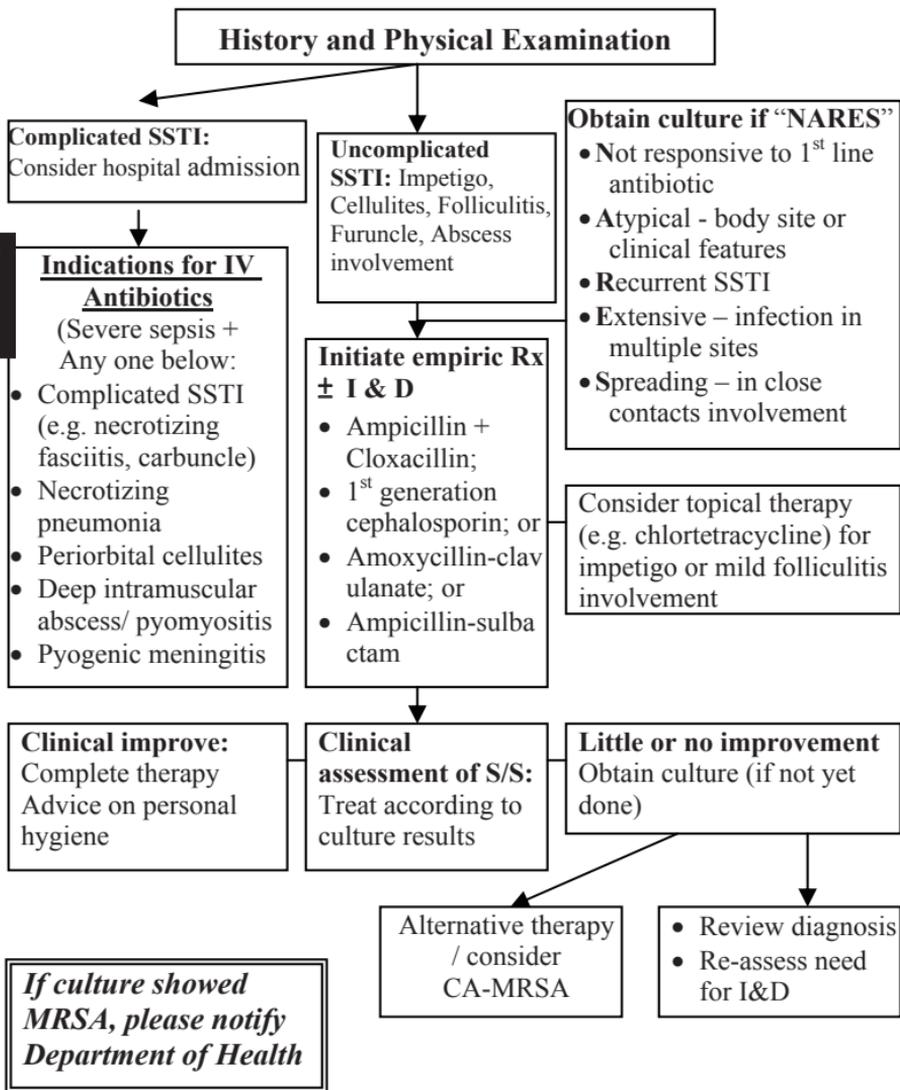
Necrotizing Fasciitis is a deep seated infection of the subcutaneous tissue that results in progressive destruction of fascia and fat, but may spare the skin. Early Recognition is important because there may be a remarkably rapid progression from an inapparent process to one associated with extensive destruction of tissue, systemic toxicity, loss of limb or death.

### Diagnosis and Management:

1. Difficult to distinguish from cellulitis in early stages.
2. Excruciating pain and presence of systemic toxicity out of proportion to the local findings.
3. Skin breakdown with bullae and frank cutaneous gangrene can be seen.
4. Risk factors assessment and urgent Gram stain may guide choice of antibiotics.
5. Immediate surgical intervention and antibiotic therapy are the mainstay of treatment.

Risk Factors	Organisms	Antibiotics
Following exposure to freshwater, seawater or seafood	<ul style="list-style-type: none"> <li>• <i>Aeromonas</i> spp.</li> <li>• <i>Vibrio vulnificus</i></li> </ul>	<ul style="list-style-type: none"> <li>• IV Levofloxacin 500-750mg daily</li> </ul> <p><b>Plus</b></p> <ul style="list-style-type: none"> <li>• IV Amoxicillin-clavulanate 1.2gm Q8H</li> </ul>
Following intraabdominal, gynecological or perineal surgery	<ul style="list-style-type: none"> <li>• Polymicrobial</li> <li>• Enterobacteriaceae</li> <li>• <i>Streptococci</i></li> <li>• Anaerobes</li> </ul>	<ul style="list-style-type: none"> <li>• IV penicillin G 4MU Q4H</li> </ul> <p><b>Plus</b></p> <ul style="list-style-type: none"> <li>• IV clindamycin 600mg Q8H</li> <li>• ± IVIG (1-2g/kg for 1 dose) for streptococcal toxic shock syndrome</li> </ul>
Following cuts, abrasion, recent chickenpox, IVDU, healthy adults	<ul style="list-style-type: none"> <li>• Group A <i>Streptococcus</i></li> </ul>	<ul style="list-style-type: none"> <li>• IV penicillin G 4MU Q4H</li> </ul> <p><b>Plus</b></p> <ul style="list-style-type: none"> <li>• IV clindamycin 600mg Q8H</li> <li>• ± IVIG (1-2g/kg for 1 dose) for streptococcal toxic shock syndrome</li> </ul>

## GUIDELINE FOR CLINICAL MANAGEMENT OF SKIN & SOFT TISSUE INFECTION AND CLINICAL SYNDROMES COMPATIBLE WITH STAPHYLOCOCCAL INFECTION



## SEPTIC SHOCK

### Terminology:

**Systemic inflammatory response syndrome (SIRS):** manifests by 2 or more of the following conditions:

- Temperature  $> 38^{\circ}\text{C}$  or  $< 36^{\circ}\text{C}$
- Heart rate  $> 90$  bpm
- Respiratory rate  $> 20$  bpm or  $\text{PaCO}_2 < 4.3\text{kPa}$
- WBC  $> 12,000/\mu\text{L}$ ,  $< 4000/\mu\text{L}$ , or 10% immature (band) forms

**Sepsis:** SIRS due to a documented infection. With sepsis, at least 1 of the following manifestations of inadequate organ function/perfusion also must be included:

- Alteration in mental state
- Hypoxemia
- Elevated plasma lactate level
- Oliguria (urine output  $< 30$  mL or  $0.5$  mL/kg for at least 1 h)

**Septic shock:** A subset of severe sepsis with hypotension despite adequate fluid resuscitation, along with the presence of perfusion abnormalities.

### Principles of management

- Early recognition: high index of suspicion and perform sepsis work-up whenever appropriate
- Early and adequate antibiotic therapy: choice based on the suspected primary site of infection and risk factor(s) for drug resistant pathogens
- Source control: e.g. removal of indwelling devices, drainage of abscess
- Early hemodynamic resuscitation and continued support: targeted MAP  $\geq 60$  mmHg. Fluid resuscitation initially. Start vasopressor (e.g. dopamine, noradrenaline) if patient does not respond to fluid resuscitation (e.g.  $\geq 4\text{L}$  of crystalloid) or evidence of fluid overload is present
- Proper ventilator management with low tidal volume in patients with ARDS
- Strategies with less clear value:
  - Corticosteroids (refractory vasopressor-dependent shock)
  - Drotrecogin alpha (Severely ill if APACHE II  $> 25$ )
  - Tight glycaemic control

## ANTIMICROBIAL THERAPY FOR NEUTROPENIC PATIENTS

*(Neutrophil  $\leq 0.5 \times 10^9/L$  or  $\leq 1 \times 10^9/L$  with a predictable decline to  $\leq 0.5 \times 10^9/L$  in 24 - 48h)*

### 1. Preventive measures:

- Reverse isolation and aseptic nursing care
- Weekly CXR and surveillance cultures from Hickman catheter, urine, sputum, throat, nasal and rectal swabs for bacteria and fungus
- Bactericidal mouthwash (Chlorhexidine)
- Antimicrobial prophylaxis may be considered – Fluconazole 200 mg daily po  $\pm$  Levofloxacin 500 mg daily

### 2. Empirical therapy for neutropenic fever (stepwise approach):

- Pyrexia  $> 38.3^{\circ}C$  or  $> 38^{\circ}C$  for more than 1 hour, after appropriate cultures taken, commence broad spectrum antibiotics with anti-pseudomonas activity
  - e.g. Cefotaxime 1-2 g q8h IV
  - Imipenem 500 mg q6h IVI
  - Meropenem 500mg q6-8h to 1 g q8h IVI
  - Tazocin 4.5 g q6-8h IVI
  - Cefepime 2 g q12h or 1g q8h IVI
  - Sulperazon 1-2g q8-12h IV
- In ill cases, add Aminoglycoside (e.g. IVI Amikacin 15mg/kg over 1h q24h, 750mg q24h or 375mg q12h)
- Add vancomycin 500 mg q6h or 1gm Q12H if culture +ve or highly suggestive of MRSA/skin/catheter infection
- If no response after 5 days and culture –ve, add Amphotericin B 0.5 – 1.0 mg/kg/day

*Reference: 2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer.*

Additional notes from Clinical Oncology:

Neutropenia can be resulted from either the disease or treatment  
e.g. chemotherapy

Prompt initiation of broad-spectrum antibiotics after immediate sepsis workup is important as patients with febrile neutropenia can rapidly deteriorate.

## MALARIA

### Management of Acute Attack

1. Anti-malarial chemotherapy should be administered as soon as the diagnosis is made
2. Monitor blood for parasites and repeat testing is needed if the diagnosis is strongly suspected
3. Maintain fluid and electrolytes balance; avoid overhydration
4. Renal failure regime for blackwater fever; treat hypoglycaemia and/or shock if present
5. Pulmonary oedema may develop, treated by prop up, oxygen, loop diuretic, venodilator; if hypoxic may need positive pressure ventilation
6. Avoid sedatives and corticosteroids
7. Watch for relapse (usually within 2 months) and signs of peritoneal irritation (splenic rupture)

### Anti-malarial Chemotherapy

#### A. *Uncomplicated P. vivax, P. malariae and P. ovale*

*Chloroquine* 600 mg base po stat

and 300 mg base 6 hours later

then 300 mg base daily for 2 more days

**plus** *Primaquine* 15 mg base (0.25 mg/kg) po daily taken with food for 14 days in *P. vivax* and *P. ovale* infection to eradicate hypnozoites in the liver.

NOTE 1 Chloroquine-resistant *P. vivax* reported from Oceania, Indonesia and South America, Rx similar to that of *P. falciparum* malaria is required.

NOTE 2 Primaquine-resistant *P. vivax* reported in South-east Asia and Western Pacific. An increased of the dose to 22.5 – 30 mg daily (or 0.5 mg/kg) is effective

NOTE 3 Primaquine is contraindicated in pregnancy. In G6PD deficiency, primaquine is safe in dosage of 0.75mg/kg once a week for 8 weeks. Monitor Hb level.

**B. Uncomplicated *P. falciparum* malaria**

1. **Definition:** symptomatic malaria without signs of severity or evidence of vital organ dysfunction
2. **Treatment:**
  - a. *Artesunate* 200 mg (4 mg/kg) po daily for 3 days  
**plus** *Mefloquine* 1000 mg base po on day 2, then 500 mg po on day 3
  - b. *Quinine* 600 mg salt (10 mg/kg) po 8 hourly for 7 days  
**plus** *Doxycycline* 100 mg po bid for 7 days

**C. Severe *P. falciparum* malaria**

1. **Definition:** presence of **one or more** of the following clinical or laboratory features, after excluding other obvious cause of their symptoms:
  - a. **Clinical:** Prostration, Impaired consciousness, Respiratory distress (acidotic breathing), Multiple convulsions, Circulatory collapse, Pulmonary oedema (radiological), Abnormal bleeding, Jaundice, Haemoglobinuria
  - b. **Laboratory:** Severe anaemia, Hypoglycaemia, Acidosis, Renal impairment, Hyperlactataemia, Hyperparasitaemia (>5%)
2. **Treatment:**
  - a. *Artesunate* 2.4 mg/kg i.v. or i.m. given on admission (time = 0), then at 12 h and 24 h, then once a day until oral medication could be taken, treat for a total of 7 days  
**plus** *Doxycycline* 100 mg po bid for 7 days once oral medication could be taken **or** *Mefloquine* as in above section B2a
  - b. *Quinine dihydrochloride* 20 mg/kg loading dose in 5% dextrose infused over 4 hours, maintenance dose 10 mg/kg infused over 2 – 4 hours every 8 hours. Change to oral dose when feasible to complete a 7-day course  
**plus** *Doxycycline* as in above section C2a

Note 1 Consider *Primaquine* 45 mg single dose to eradicate gametocytes in blood at the end of treatment of falciparum malaria

Note 2 Do not use loading dose if patient has received quinine, quinidine, or mefloquine in preceding 24 hours.

## CHICKENPOX / HERPES ZOSTER

### Diagnosis

1. Virus detected by DIF, PCR or culture from clinical specimens
2. Paired serology in acute and convalescent phases

### Management

1. Keep patients from school / work for at least 5 days after onset of eruption or until vesicles become dry
2. Airborne and contact precautions for chickenpox/ disseminated zoster when in hospital
3. Give acyclovir 10 – 12 mg/kg q8h IV infusion for 7 days for severe zoster or chickenpox in elderly or immuno-compromised patients
4. Therapy for neuralgia usually required for zoster
5. Watch for development of severe secondary skin infection (Staphylococcus/Streptococcus) and consider antibiotics (e.g. oral cloxacillin) if necessary.
6. For herpes zoster with ophthalmic involvement, urgent eye consultation is recommended.
7. Varicella-zoster immunoglobulin (VZIG) within 96 hours of exposure may prevent / modify disease in susceptible contacts prone to severe varicella. e.g. in pregnancy or immunocompromised hosts.

### Reference:

HA factsheet on chickenpox. 7 March 2008.

## HIV / AIDS

### Diagnosis of HIV infection and AIDS:

1. HIV infection: HIV antibody test by screening (ELISA) and confirmatory (usually Western Blot) tests
2. AIDS: Laboratory evidence of HIV infection plus clinical evidence of indicator disease for AIDS
3. Obtain informed consent before performing HIV Ab test
4. Counselling is crucial because of major psychological and social implications of a positive result, the need for confidentiality and the importance of effecting behavioral modification irrespective of HIV status
5. Referral for counselling and medical consultation available from QEH Special Medical Service (2958 5855) & CHP Kowloon Bay Integrated Treatment Centre (2116 2888)
6. Voluntary reporting of HIV infection and AIDS to Department of Health (DH2293 form) is encouraged for epidemiological purpose.

### Clinical management of HIV/AIDS

1. Baseline assessment:
  - CD4/CD8 count
  - HIV RNA level
  - Serological evidence of HBV and HCV coinfection
  - Syphilis serology
  - CXR for evidence of tuberculosis
2. For patients with respiratory symptoms:
  - CXR, ABG
  - Sputum for C/ST, AFB, pneumocystis
  - Empirical Rx for pneumocystis if hypoxaemia present
  - Bronchoscopy for non-responsive cases
3. For patients with GI symptoms:
  - Stool for microscopy and C/ST
  - Stool for cryptosporidia /isospora / microsporidia
  - Stool for AFB smear and culture

- OGD for dysphagia, colonoscopy for chronic diarrhoea, USG for deranged LFT
- 4. For patients with neurological symptoms:
  - CT / MRI brain, CSF examination
  - Toxoplasma serology, cryptococcal Ag
  - Nerve conduction studies for neuropathy
- 5. For patients with haematological problems:
  - Marrow biopsy for histology, AFB smear and culture
- 6. For patients with PUO:
  - Blood culture for fungus and mycobacteria
  - Marrow aspirate for histology, AFB and fungal culture
  - Blood for CMV pp 65 antigen, cryptococcal Ag and penicillium serology/ galactomannan
  - CXR, CT abdomen

### Antiretroviral therapy

<b><i>Nucleoside/Nucleotide reverse transcriptase inhibitors (NRTIs):</i></b>	
Zidovudine (Retrovir, AZT, ZDV)	250 – 300 mg bd
Didanosine (Videx, ddi)	250 – 400 mg daily
Lamivudine (Epivir, 3TC)	150 mg bd
Stavudine (Zerit, d4T)	30 – 40 mg bd
Abacavir (Ziagen, ABC)	300 mg bd (check HLA B*5701 before initiation)
Tenofovir (Viread, TDF)	300 mg daily
<b><i>Non-nucleoside reverse transcriptase inhibitors (NNRTIs)</i></b>	
Nevirapine (Viramune, NVP)	200 mg daily for 2 weeks, then 200 mg bd (*avoid in female with CD4 > 250 and male with CD4 > 400)
Efavirenz (Stocrin, EFV)	600 mg nocte (*avoid in women of child-bearing age)
Etravirine (Intelence, ETR)	200 mg bd
<b><i>Protease inhibitors (PIs)</i></b>	
Indinavir (Crixivan, IDV)	800 mg (with RTV 100 mg) bd
Saquinavir (Invirase, SQV)	1000 mg (with RTV 100 mg) bd
Lopinavir /Ritonavir	2 tab bd

(Kaletra, LPV/RTV)	(400/100 mg)
Atazanavir (Reyataz, ATV)	300 mg (with RTV 100 mg) daily or 400 mg daily
Darunavir (Prezista, DRV)	600 mg (with RTV 100 mg) bd 800 mg (with RTV 100 mg) daily (for treatment naïve patients)
Tipranavir (Aptivus, TPV)	500 mg (with RTV 200 mg) bd
Ritonavir (Norvir, RTV)	Used in low-dose (100 mg) for boosting level of other PIs
<b><i>Integrase inhibitor</i></b>	
Raltegravir (Isentress, RAL)	400 mg bd
<b><i>Entry inhibitor (CCR5 antagonist)</i></b>	
Maraviric (Celsentri, MVC)	300 mg bd (dose adjustment needed for drug interaction)
<b><i>Fusion inhibitor</i></b>	
Enfuvirtide (Fuzeon, ENF, T20)	90 mg SC q12h
<b><i>Combination formulations</i></b>	
Combivir	AZT + 3TC
Kivexa	ABC + 3TC
Truvada	TDF + emtricitabine (FTC)
Atripla	TDF + FTC + EFV

1. Patients should be prescribed combination anti-retroviral therapy (cART) consisting of three active drugs. The first-line regimen usually consists of 2 NRTIs + 1 PI (usually boosted with RTV) or 2NRTIs + 1 NNRTI. The other classes of drugs are generally reserved for patients with HIV drug resistance.
2. cART should be initiated for the following clinical settings:
  - AIDS or symptomatic HIV disease
  - CD4 count <350/ul
  - Pregnancy
3. Treatment may be considered for asymptomatic patients with CD4 count between 350 - 500/ul in the following clinical settings:
  - Rapidly declining CD4 count (> 100 per year) or high HIV viral load (>100,000 copies/ml)
  - HBV coinfection when treatment of HBV is indicated

- HIV-associated nephropathy
- 4. Important to assess and reinforce drug adherence to prevent emergence of viral resistance
- 5. CD4 count and HIV RNA level should be monitored regularly and genotypic resistance assay should be arranged for patients with non-suppressed viral load
- 6. Precautions with drug interaction when patient is receiving PI or NNRTI: amiodarone, flecainide, quinidine, simvastatin, astemizole, terfenadine, cisapride, midazolam, ergotamine, rifampicin.

### Opportunistic Infection Prophylaxis

#### 1. *Pneumocystis jiroveci* pneumonia (PCP)

- Indications:
- a. after an episode of PCP
  - b. when CD4 count falls below 200/u/l

First line: Septrin 960 mg thrice weekly to daily

Second line: Aerosolised pentamidine 300 mg every 4 weeks (\*should be conducted in facilities with adequate ventilation to prevent transmission of TB)

Dapsone 100 mg daily

#### 2. Mycobacterium avium complex (MAC)

- Indication: CD4 <50/u/l
- Azithromycin 1000 mg once weekly OR clarithromycin 500 mg BD

### Treatment of Opportunistic Infections

#### 1. *Pneumocystis jiroveci* pneumonia

- a) Consider in patients with fever, dry cough and dyspnoea
- b) May have normal CXR during early stage
- c) Diagnosis by sputum induction with hypertonic saline / BAL/ transbronchial lung biopsy, hypoxaemia on ABG
- d) Oxygen supplement
- e) Septrin at TMP 15 mg/kg/d po/IV (3-4 tab qid) for 3 weeks
- f) If acutely ill or PaO<sub>2</sub> <8: add Prednisone 40 mg bd for 5 days, then 40 mg qd for 5days, then 20 mg qd for 11 days

## g) Alternative regimen:

- Clindamycin 600 mg IV q8h + Primaquine 30 mg daily po for 3 weeks
- Pentamidine isethionate 4 mg/kg/d IV for 3 weeks

- |                         |   |
|-------------------------|---|
| 2. Tuberculosis         | Combination therapy (DOTS): isoniazid, rifampicin, pyrazinamide and ethambutol; levofloxacin and streptomycin for patients with adverse reaction to first-line drugs  |
| 3. MAC                  | Combination therapy with 3 - 4 drugs:<br>Ciprofloxacin 750mg bd/ levofloxacin 500mg/day<br>Clarithromycin 500mg bd/azithromycin 500mg/day<br>Ethambutol 15 mg/kg/day<br>Rifabutin 300 mg daily<br>Amikacin 10 - 15 mg/kg/day IV |
| 4. Cryptosporidiosis    | Nitazoxanide 500 mg bd po x 2 weeks   |
| 5. Isosporiasis         | Septtrin 960 mg qid for 10 days, then BD for 3 weeks  |
| 6. Cryptococcosis       | Amphotericin B 0.7 mg/kg/d IV (Max 1.5 mg/kg/d) ± flucytosine 25 mg/kg q6h for 2 weeks, then fluconazole 400 mg/d po for total of at least 10 weeks   |
| 7. Toxoplasmosis        | Pyrimethamine 200 mg po x 1 then 50-75 mg/d + clindamycin 600 mg qid + folinic acid 10-20 mg daily for 6 weeks<br>Maintenance: Pyrimethamine 25-50 mg/d + clindamycin 300-450 mg qid + folinic acid 10-20 mg daily              |
| 8. CMV retinitis        | Ganciclovir 5 mg/kg IV q12h, foscarnet 60 mg/kg IV q8h or valganciclovir 900 mg po bd for 3 wks<br>Maintenance: Valganciclovir 900 mg daily po  |
| 9. Candida oesophagitis | Fluconazole 100 mg/day (higher dose up to 400 mg/day for refractory cases) or   |

Itraconazole solution 200 mg daily for 2 – 3 weeks

10. Penicilliosis      Induction: amphotericin B 0.6 mg/kg/day IV for 2 weeks  
                                 Maintenance: itraconazole 200 mg bd
11. Microsporidiosis      Albendazole 400 mg bd for 3 weeks

## RICKETTSIAL INFECTION

Rickettsiae are obligate intracellular bacteria. They are maintained in nature through cycle involving reservoir mammals and arthropod vectors except louse borne typhus. Humans are incidental hosts via arthropod vector. In Hong Kong, majority of the reported cases contracted the diseases locally and mostly related to outdoor activities. Vasculitis of small vessels is basic underlying pathology. The severity of disease can range from mild to multi-organ failure and even fatal outcome. Patients usually present with triad (i.e. fever, skin rash/eschar and headache).

### Diagnosis

1. Weil-Felix test: non-sensitive and non-specific
2. Indirect immunofluorescence assay (sent to PHLC):
  - Spotted fever group
  - Typhus group
  - Scrub typhus

### Management

1. All beta-lactams and aminoglycosides are not effective.
2. Doxycycline is the most effective drug
3. The usual adult oral dose of doxycycline is 100mg twice daily for 7-14 days.
4. Azithromycin is an option for those who are contraindicated for tetracycline such as pregnant women and children.
5. Notify to CHP

## INFLUENZA

*An acute viral disease of the respiratory tract caused by the influenza A ( $H_3N_2$ ,  $H_1N_1$ ,  $H_5N_1$  etc.), B and C viruses, with fever, headache, myalgia, prostration, coryza, sore throat and cough.*

### Diagnosis

1. Nasopharyngeal aspirates/ tracheal aspirates/ bronchoalveolar lavage specimens for direct antigen detection (immunofluorescence or EIA), AND viral culture; PCR in selected cases (consult clinical microbiologist).
2. Acute and convalescent sera for specific Ab rise

### Complications

Primary viral pneumonia, secondary bacterial pneumonia, myocarditis, myositis, rhabdomyolysis, Guillain-Barré syndrome, transverse myelitis, Reye's syndrome (associated with use of aspirin in children)

### Management

1. Droplet precautions
2. Treatment
  - *Effective against influenza A and B*
    - Oseltamivir 75 mg bd po x 5 days
    - Zanamivir 10 mg bd inhaler puff x 5 days

*N.B.*

- *Beneficial effects of treatment are most apparent if started early (i.e. within 48 hrs of symptom onset). However, in severe, hospitalized cases, therapy should still be considered beyond the 48-hr window period.*
- *In complicated cases (e.g. viral pneumonia), increased dose of oseltamivir (150 – 300mg bd for  $\geq 5$  days) may be considered.*
- *Seasonal influenza A/H1N1 virus exhibits a high level of oseltamivir*

*resistance (except for the influenza A/ H1N1 (2009) virus, which caused pandemic in 2009 – 2010.)*

- *Intravenous preparations of zanamivir and peramivir may be considered as salvage therapy for critical cases.*

### **Special points on Avian Influenza (H5/7/9)**

1. A statutory notifiable disease
2. Influenza A/H5N1 virus is a highly pathogenic form of avian influenza that caused outbreak in various countries.
3. Pay attention to epidemiological link (**T**Travel/ **O**ccupation/ **C**ontact/ **C**lustering) in evaluation of patients with fever +/- URTI.

### **Reference**

1. HA fact sheet on antiviral therapy against influenza (Jan 2009)
2. HA guideline on Management Approach of Influenza-like Illness (ILI) & Community-acquired Pneumonia (CAP) Suspected of Avian Influenza (Jan 2009)
3. HA fact Sheet on H5N1 Avian Influenza (Jan 2009)

## INFECTION CONTROL

### Hand Hygiene (HH)

Good hand hygiene practices is utmost important to prevent healthcare associated infections.

“Five moments” for HH (WHO recommendations):

1. Before patient contact
2. Before aseptic task
3. After body fluid exposure risk
4. After patient contact
5. After contact with patient surroundings

### Precautions to prevent transmission of infectious agents

#### **2 tiers of precautions:**

#### **1. Standard precautions (SP)**

Applied to all patients in all healthcare setting, regardless of suspected or confirmed presence of an infectious status. HCWs should apply SP when contact with

- blood;
- all body fluids, secretions, and excretions except sweat, regardless of whether or not they contain visible blood;
- nonintact skin; and
- mucous membranes.

#### **2. Transmission-based precautions**

Applied to patients who are known or suspected to be infected or colonized with infectious agents, including epidemiologically important pathogens which require additional control measures to effectively prevent transmission. These composed of droplet, contact and airborne precautions.

<b>Precautions</b>	<b>Prevent transmission of infectious agents</b>
Contact	spread by direct/ indirect contact with patients or patient's environment e.g. Norovirus, RSV, <i>C. difficile</i> , MRSA

Droplet	spread through close respiratory or mucous membrane contact with respiratory secretions e.g. Influenza, <i>N. meningitides</i> , <i>B. pertussis</i>
Airborne	that remain infectious over long distance when suspended in air e.g. Measles, Chickenpox, <i>M. tuberculosis</i>

### 3. Syndromic and empiric applications of transmission-based precautions

Diagnosis of many infections require laboratory confirmation. Appropriate Transmission-based precautions should be implemented when test results are pending based on the clinical presentation and likely pathogens. Examples:

Clinical syndrome	Potential pathogens	Empiric precautions
Acute diarrhoea with likely infectious cause in an incontinent/diapered patient	Enteric pathogens	Contact
Abscess/draining wound that cannot be covered	MSSA, MRSA, Group A Streptococcus	Contact
Vesicular rash	Varicellar-zoster, variola	Airborne + Contact
Petechial/ecchymotic with fever ; meningitis	<i>N.meningitides</i>	Droplet (for 24 hrs.of antimicrobial therapy); mask and face protection for intubatiion
Maculopapular rash with cough, coryza and fever	Measles	airborne
Cough/ fever/ pulmonary infiltrate and other clinical features suggestive of TB	<i>M. tuberculosis</i>	airborne

## NEEDLESTICK INJURY OR MUCOSAL CONTACT TO HIV, HBV AND HCV

Prevention of transmission of HIV, HBV and HCV in healthcare setting is based on the principle of **Standard Precautions**.

1. Avoid recapping needles
2. Dispose of sharps immediately after use
3. Plan for safe handling and disposal before beginning any procedures using sharps
4. Use safety devices, if available

### Measures that involve exposure to blood, body fluids, and tissues:

Procedures	Handhygiene	Gloves	Gown / plastic apron	Mask	Eye Protection
1. Suctioning	+	+	*	*	*
2. Insertion of airways	+	+	*	*	*
3. Artificial Airway care	+	+	*	*	*
4. CPR	+	+	*	*	*
5. Assisting with					
- intubation	+	+	*	+	+
- bronchoscopy	+	+	+	+	+
- tracheotomy	+	+	+	+	+
6. ABG punctures	+	+	*	*	*
7. Cleansing surfaces or equipment	+	+	*	*	*
8. Blood taking	+	+	*	*	*

+ *Routinely*

\**if soiling or spluttering likely*

## Management of needle-stick injuries or mucosal contact with blood and body fluids

1. **First Aid** (of utmost importance for lowering the risk of infection)
  - Express blood gently and wash immediately and thoroughly with soap and water.
  - In case of mucosal contact such as spillage into the eyes, wash immediately and liberally with running water
  - wound should be disinfected and dressed
  - Attend A & E
2. **Reporting:** Injured staff should report to his unit head or physician i/c and Infection Control Team.
3. **Counselling**
4. **Management of occupational exposure to HIV:**
  - Risk of HIV transmission is about 0.3% after needlestick injury and 0.1% after mucosal exposure.
  - Source patient should be assessed for risk of HIV infection. Counselling and HIV testing with consent should be offered where appropriate.
  - The injured staff should be encouraged to undergo HIV testing at 0, 3 and 6 months; additional test at 12 months for those who have taken PEP; or have become infected with HCV after exposure to source co-infected with HIV and HCV to detect delayed HIV conversion.
  - Post-exposure prophylaxis with a 28-day course of HAART (zidovudine, lamivudine and a protease inhibitor e.g. Kaletra) should be initiated as soon as possible, **preferably within 2 hours after the exposure.**
  - PEP can be initiated at any A&E department followed by referral to the **Therapeutic Prevention Clinic**, CHP (<http://www.info.gov.hk/aids/english/itc/tpclinic.htm>; Tel:2116 2929) or Special Medical Service, QEH (Tel:2958 5855) for counselling, follow up and HIV testing.

### 5. Post-exposure prophylaxis against hepatitis B infection

- Save blood for HBV status of source and injured staff, if status unknown.
- If source person can't be traced, may treat as if he is HBsAg +ve
- No treatment is required if injured staff is anti-HBs is +ve
- HBIG and HB Vaccine can be offered to injured staff if anti-HBs is negative (depends on HBsAg status of source and vaccination history of injured staff)

Source HBsAg status	POST-EXPOSURE PROPHYLAXIS				
	Previously Vaccinated			Unvaccinated	
	Known Responders	Known Non-responders	Unknown Response	HBV markers -ve <sup>φ</sup>	HBV markers +ve <sup>ψ</sup>
HBsAg +ve	Nil	HBIG within 24 hrs, rept after 1/12	Depends on anti-HBs status of exposed	HBIG + HB Vac	Nil
HBsAg -ve	Nil	Nil	Nil	HB Vac	Nil
HBsAg unknown	Nil	Depends on source HBsAg status	Depends on anti-HBs status of exposed person	HBIG + HB Vac or HBVac, depending on source HBsAg status	Nil

φ means HBsAg -ve AND anti-HBs -ve

ψ means HBsAg +ve OR anti-HBs +ve

- Where indicated, one dose of HBIG (0.06 ml/kg) should be given within 24 h of exposure, and preferably within 7 days
- If HBIG has been given, the first dose of vaccine can be delayed for up to 1 week after exposure.
- HBIG and HB vac can be given together but at a different sites

- Injured staff can be referred to the Viral Hepatitis Preventive Service of DH (Tel: 21129911) for vaccination.

## **6. Post-exposure management against Hepatitis C infection**

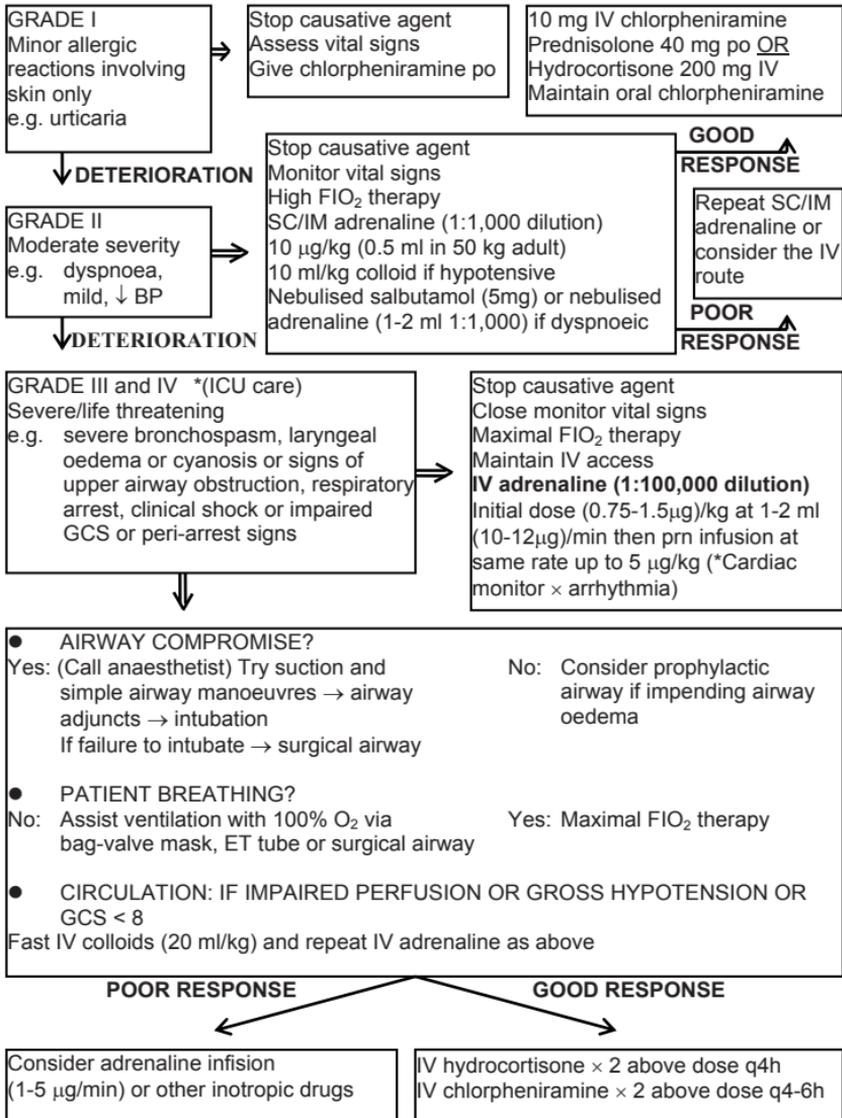
- There is no universally accepted effective therapy for preventing HCV infection after accidental occupational exposure. Early identification of acute HCV infection and treatment with Interferon plus ribavirin may prevent chronic HCV.
- Check anti-HCV of source patient.
- Check anti-HCV and aminotransferase (ALT) of exposed person soon after exposure and again at 6 months. Repeat at 12 month if source is HIV-HCV co-infected.
- If source is HCV infected /IV drug addict /unknown HCV status, Check ALT of injured at 1<sup>st</sup> and 3<sup>rd</sup> month after exposure, test HCV-RNA if ALT elevated. Refer the injured to specialist if HCV-RNA positive.



# **General Internal Medicine**



## ACUTE ANAPHYLAXIS



\* Label patient allergic to that agent thereafter

## **ACUTE POISONING**

(All dosages quoted are for adult)

Call HKPIC – 27722211 or 26351111 for any enquiry on poisoning patient management issues

### **General management of acute poisoning**

#### **(1) General measures**

- Maintain ABC with precaution of secondary contamination
- Close monitor vital signs + neurological status
- Watch out and treat concomitant injuries; eg. head injury
- Obtain history of offending poison, dose, timing of ingestion
- Ix : Blood gas, CBP, L/RFT, glucose, H'stix,  
Urine, blood & gastric contents for toxicology  
Specific drug level: panadol ,ethanol, salicylate, as indicated  
ECG (assess for HR, QRS, QTc, arrhythmia)
- Correct fluid, electrolyte disturbance and treat arrhythmia
- Psychi consultation, suicidal precautions as appropriate

#### **(2) Consider GI decontamination**

##### **Activated Charcoal (AC)**

- If present within first 1-2 hr. Dose : 1g / kg PO
- Not for small molecules (Fe, Li, alcohol), caustic, hydrocarbon

##### **Gastric lavage (GL)**

- For potentially life-threatening toxin ingestion
- Preferably within first hour post ingestion
- Intubation needed for confused, comatose patient
- 36-40F oro-gastric tube, 200-250ml NS followed by aspiration for total 4-6L or until return fluid is clear

##### **Multiple dose activated charcoal (MDAC)**

- 1g/kg PO, follow by 0.5g/kg q2-4hr.
- Consider for Theophylline, Phenobarbital, Phenytoin, Digoxin, Carbamazepine and GI concretion forming drug; aspirin and sustained release (SR) preparation

**Whole bowel irrigation (WBI)**

- SR preparation, body packers, drugs not adsorbed to AC
- PEG 1-2 L/hr till clear rectal effluent (orally or via a NG tube)

**(3) Consider use of specific Antidotes****(4) Enhanced Elimination as needed****Urinary Alkalinization**

- Useful in Aspirin, Phenobarbital, Chlorpropamide, Formate
- 1-2 mEq/kg NaHCO<sub>3</sub> IV bolus, then 50mEq NaHCO<sub>3</sub>(8.4%) in 500ml D5 Q4-6hr IV infusion
- Works by ion trapping, must get urine pH>7.5 to be effective
- Monitoring serum pH, avoid >7.55, avoid hypokalaemia

**Hemodialysis / Hemoperfusion**

	Hemodialysis	Hemoperfusion
Strong Indication	Methanol / Ethylene Glycol Lithium, Aspirin	Theophylline
Rarer Indication	Ethanol / Isopropanol	Carbamazepine, Phenytoin Phenobarbital

**Treatment of specific drug poisoning****Benzodiazepine overdose**

- Supportive measure is the mainstay of treatment
- Flumazenil – start with 0.2 mg IV over 30 sec, larger dose can be given, but if no response after 2-3mg, think for other diagnosis
- C/I : patient with undifferentiated coma. epilepsy,  
benzodiazepine dependence, co-ingestion of seizure prone poisons; eg.TCA

**Opioid overdose**

- Supportive measure is the mainstay of treatment

- Naxolone –0.4 mg – 2 mg as an IV bolus & repeated as needed. For chronic user, start with low dose of 0.1 mg
- Naxolone infusion if repeated dose of naxolone needed  
(2/3 of initial effective naloxone bolus on an hourly basis:  
ie. 4X initial effective dose + 500ml NS, Q 6 hour)

### Amphetamine / Cocaine overdose

- Agitation, Hyperthermia - Rapid cooling, IV benzodiazepine
- HT- Phentolamine 1-5mg IV & repeat every 10 minutes or Nitroglycerin 0.25-0.5ug/kg/min
- Cocaine (Na channel blocking effect) – NaHCO<sub>3</sub> 1-2mEq/kg IV bolus till QRS <100ms or pH >7.55

### Paracetamol overdose

- Acute toxic dose: >150mg/kg.
- Check paracetamol level at 4 hour, LRFT
- AC if within 1<sup>st</sup> hour, NAC if toxic level above Tx line
- NAC has full protection if given within 8 hr post-ingestion, useful even on late administration

	NAC dose	In D5	Rate
Loading	150mg/kg	200ml	in 1hr
then	50mg/kg	500ml D5	in 4 hr
then	100mg/kg	1000ml D5	in 16 hr

- With evidence of liver injury, check prognostic markers:  
PT, APTT, L/RFT, blood gas, lactate, PO<sub>4</sub>, αFP

### Salicylate overdose

- >150mg/kg acetylsalicylate (aspirin) – potentially toxic
- Pure methyl salicylate (oil of wintergreen): 10ml → 14g salicylate
- Ix: R/LFT, blood gas, serial salicylate level, glucose, urine ketone
- Consider GL, AC, MDAC, WBI (depend on amount / formulation)
- Hydration, urine alkalinization if ASA >40mg/dL (>2.9mmol/L)

- HD if end organ failure or ASA  $>100\text{mg/dL}$  ( $>7.3\text{mmol/L}$ )

### **Anti-cholinergic poisoning**

- Physostigmine – 0.5-1mg slow IV, repeated up to 2 mg  
C/I : TCA, widen QRS, CV disease, asthma, gangrene

### **Beta-blocker overdose / Calcium channel blocker overdose**

- GI decontamination, haemodynamic and cardiac monitoring

- Treatment options for hypotension and bradycardia :

- Atropine – 0.6mg IVI (up to 3mg) and iv fluid
- Glucagon; 2-5mg IVI over 1 min (up to 10mg) follow by 2-5mg/hr in D5 (for  $\beta$  blocker poisoning)
- $\text{CaCl}_2$  1g or Ca gluconate 3g slow IV, repeat Q10min  
(For CCB poisoning, 2-3 doses can be safely given without check Ca level)
- High Dose Insulin / Dextrose – Start with 0.5U/kg/hr, titrate up 1U/kg/hr (Start early for the Tx take time to be effective)
- Inotropes : Adrenaline - 0.02  $\mu\text{g/kg/min}$  and titrate up  
Noradrenaline - 0.1  $\mu\text{g/kg/min}$  and titrate up  
Dobutamine - 2.5  $\mu\text{g/kg/min}$  and titrate up  
Isoproterenol - 0.1  $\mu\text{g/kg/min}$  and titrate up  
(Dopamine not suggested due to its indirect effect)
- $\text{NaHCO}_3$  1-2 mEq/ kg IV bolus for propranolol poisoning if QRS  $> 100\text{ms}$ , repeat as indicated.

(Co-administration of calcium and glucagon is useful in refractory or mixed cases)

### **Digoxin overdose**

- Ix : RFT, digoxin level, ECG

- GI decontamination : consider GL, AC, MDAC

- Bradydysrhythmias – atropine

- Tachydysrhythmia – Tx hypoK, hypoMg, lignocaine, amiodarone

- Cardioversion – may precipitate refractory VT, VF, start with low dose: 10-25J, pre-Tx with lignocaine or amiodarone

- Digoxin Immune Fab fragments indications :

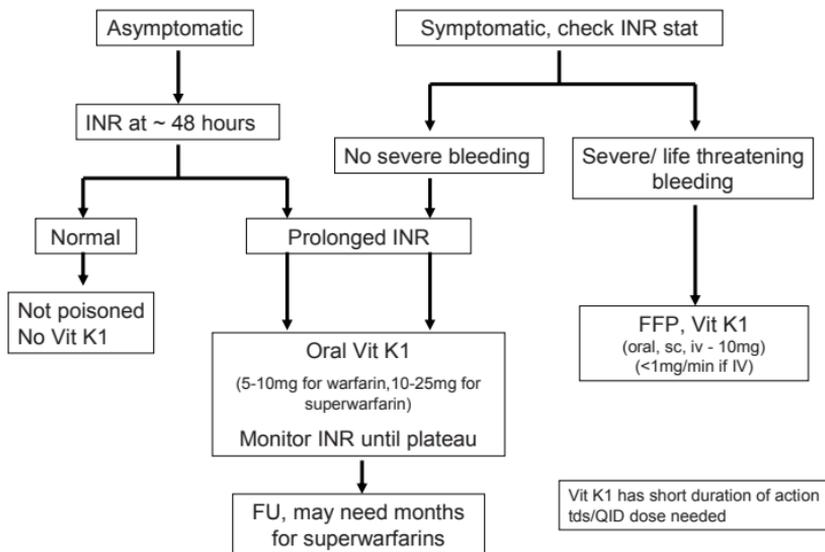
- Brady or Vent arrhythmia not responsive to atropine
- Serum  $\text{K}^+$   $> 5\text{mEq/dL}$  in acute DO

- Digoxin level: 10-15ng/mL (13-19.5nmol/L) in an acute DO
- Digoxin ingestion of > 10 mg

Situation	Dose of digitalis antidote® *
Known amount	No. of vial = Amount ingested in mg
Known level	No of vial = (Digoxin level (ng/mL)) x (wt in kg) / 200
Empiric dose	Acute overdose – 5 vials
(Unknown dose or digoxin level)	Chronic overdose – 2 vials

(Need to multiply by 2 if using Digibind® and DigiFab®)

## Warfarin or superwarfarin rodenticide overdose



## Mx guideline for warfarin patient with over anti-coagulation

INR	Bleeding	Recommendation/Action
< 5	No	Reduce dose or omit next few doses
> 5 but < 9	No	If no risk factors for bleeding, omit next few doses; if risk factors for bleeding, administer 1.0–2.5 mg oral vitamin K
> 9	No	3.0–5.0 mg oral vitamin K
> 20	Yes (serious)	10 mg IV vitamin K and FFP or PCC
Any	Yes (life-threatening)	10 mg IV vitamin K and PCC

### *1998 and 2001 ACCP Recommendations for Reversing Excessive Warfarin-Associated anti-coagulation*

## Theophylline poisoning

- Ix : Theophylline level, electrolytes, ECG
- ABC monitoring and supportive measures.
- GI decontamination : GL / MDAC
- Patient died from tachyarrhythmia, hypotension and seizure

- Hypotension – IV fluid,  $\alpha$ -agonist (Phenylephrine, Norepinephrine)
- Tachyarrhythmia – diltiazem or  $\beta$ -blockers (esmolol, propranolol)
- HP indication: Ileus / IO prevents use of MDAC  
Theophylline level >80mg/L (acute) or 60mg/L (chronic)  
Elderly with level > 40mg/L with severe symptoms

## **Psychiatric Drugs**

### **Antipsychotics poisoning**

- Supportive care, ECG, GI decontamination as indicated
- Hypotension – IV fluid, inotropes ( $\alpha$ -adrenergic agonists)
- Cardiotoxicity, widen QRS – treat like TCAs
- Dystonia – diphenhydramine or cogentin
- Look out for neuroleptic malignant syndrome

### **Tricyclic antidepressant overdose**

- Ix : Blood gas, ECG[ sinus tachycardia, widen QRS; > 100msec, terminal 40ms right axis deviation (R in aVr)]
- Ensure ABC with intensive monitoring
- Consider GL and AC 1g/kg if < 1-2 hr post ingestion, MDAC
- Aggressive supportive care & early serum alkalization
- Physostigmine & Flumazenil are contraindicated
- Serum alkalization by NaHCO<sub>3</sub>

Indications	QRS > 100ms	Vent arrhythmia	Hypotension
Dose	1-2 mEq per kg IV bolus May need repeated bolus or infusion to meet endpoints		
End points	QRS <100ms or pH 7.5-7.55	Reversal of arrhythmia or pH 7.5-7.55	Correction of BP or pH 7.5-7.55
Contra- indications	pH > 7.55 [Consider hypertonic saline] Intolerable to Na/fluid load [Consider hyperventilation]		

**SSRI (selective serotonin reuptake inhibitors) and others**

- Supportive care, ECG, GI decontamination as indicated
- Treatment for serotonin syndrome (SS) if present  
Remove offending drugs, Benzodiazepine, hydration, cooling, cyproheptadine ( 8-12mg, then 2mg Q2hr, up to 32mg in 1<sup>st</sup> 24 hr), neuromuscular blockage.
- Citalopram – observe for > 24 hr, cardiac monitoring [for prolonged QT, Tdp (especially with dose >400mg) ]
- Venlafaxine – seizure; esp with dose >1.5g , prolonged QRS

**Lithium poisoning**

- Ix : RFT, serial Lithium level (Q4hr), AXR
- GI decontamination : GL, WBI
- Volume replacement and correction of hyponatraemia
- Haemodialysis if ↑ level esp. >4mEq/L, sig DO +/- neuro-toxicity

**Valproic acid poisoning**

- Ix : LFT, valproic acid level, ammonia
- ABC monitoring and supportive measures.
- GI decontamination : AC , GL / MDAC / WBI
- L-Carnitine for VPA induced ↑ ammonemia, encephalopathy ,hepatotoxicity.
- IV Naloxone (0.4mg-2mg) for CNS and respiratory depression
- Haemodialysis / Haemoperfusion : rarely considered

**Carbamazepine poisoning**

- Ix: Tegretal level, ECG (widen QRS)
- ABC monitoring and supportive measures.
- GI decontamination : AC / MDAC
- NaHCO<sub>3</sub> for widen QRS>100ms (theoretically beneficial)
- Hemoperfusion

**Non-Pharmaceutical****Organophosphate poisoning**

- Decontamination and staff protection, supportive care
- Ix : plasma cholinesterase, ABG

- Atropine - Initial dose of 0.6-1.2 mg IV, repeat and double the dose every 5 min until lungs clear (huge dose has been used)
- Pralidoxime - 1-2 g to 100ml NS IV over 30 min, follow by infusion at 4-8 mg/kg/hr, can be titrated up to 20 mg/kg/hr.

### **Carbamate poisoning**

- Similar to organophosphate poisoning
- Atropine - 0.6-1.2 mg IV, repeat and double the dose Q5min until lungs clear.
- Pralidoxime – not usually recommended

### **Paraquat poisoning**

- More than 10ml 20% paraquat ingestion is potentially fatal
- GI decontamination : GL in early presentation, AC
- Largely supportive treatment, use lowest FiO2 as possible
- Contact HKPIC for option of anti-inflammation therapy in severe paraquat poisoning.

### **Household products**

- Disinfectants and multi-purpose cleaners ( Dettol®, Salvon®, Swipe® , Green water, Household hypochlorite bleach, etc )
- No antidote, mainstay of treatment is supportive
- GI decontamination is potential harmful
- Mainly irritant effect, upper endoscopy is not routinely indicated
- Can be caustic if large quantity & high concentration are ingested

### **Methanol / Ethylene glycol [EG] poisoning**

Ix: Blood : CBP, LRFT, ethanol level, anion gap, osmolar gap, methanol or ethylene glycol level

Urine for Ca oxalate and fluorescence [in EG poisoning]

#### **Management:**

- Consider NG suction, IV NaHCO3 to correct acidosis
- IV Absolute alcohol (16g/20ml), diluted to 10% solution

Loading: 0.8g/kg in 30min

Maintenance: start at 0.1g/kg/hr, titrate upwards prn

OR

- PO brandy or whisky (~50%)
- 1ml/kg loading → 0.5ml/kg q2hr, titrate upwards  
[aim at ethanol level-100mg/dL]

- HD indication :

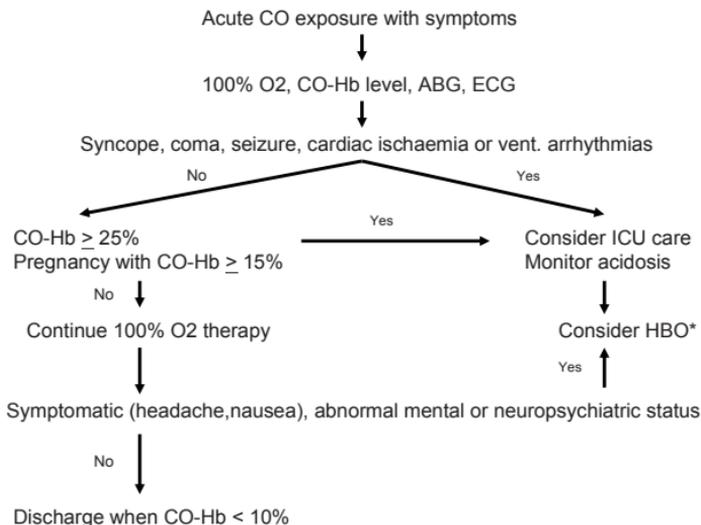
- Methanol or ethylene glycol level >250mg/L
- High osmolar gap without other cause
- Acid/base abnormality, End-organ toxicity
- IV folinic acid 1mg/kg q4-6hr (for methanol poisoning)
- Thiamine 100mg and pyridoxine 50mg q4-6hr (for Ethylene glycol)
- Fomepizole is available as Level III antidote.  
[Contact HKPIC for its indication and mobilization if needed]

### **Cyanide poisoning**

- ABC monitoring and supportive measures.
- Surface decontamination and staff protection
- Treat seizure and correct metabolic acidosis
- GI decontamination : consider AC +/- GL if within 1 hr
- Ix : RFT, ABG, lactate, AV O<sub>2</sub> gradient (PaO<sub>2</sub> – PvO<sub>2</sub>),  
CO-Hb, met-Hb, Cyanide level
- Early use of antidotes : Sodium nitrite and thiosulphate
  1. Sodium nitrite - 10ml of 3% (300mg) IV over 5 min  
(Adverse effect : hypotension, methaemoglobinemia)
  2. Sodium thiosulphate - 50ml of 25% (12.5g) IV  
(Thiosulphate can be repeated if there is no response in 30 min)
- Other antidote (available in many HA hospitals)  
Hydroxocobalamin: 5g IV in 15-30 min (can be repeated at 2-4 hr)

### **Carbon monoxide poisoning**

- Pulse oximeter not detect CO-Hb; can be misleading
- Hyperbaric oxygen treatment\* (HBO)
  - Usefulness remains controversial
  - Potential risk for patient and medical staffs (during transfer / in the chamber)
  - No definite evidence to support routine use
  - Referral is a case to case individual decision by the in-charge physician

Suggested guideline for CO poisoningPulmonary irritant inhalation

- Highly water soluble gas  
Sulfur dioxide, Ammonia, HCl, Chloramine  
Cause upper airway, eye and nose irritation, rapid onset
- Intermediate water solubility: Chlorine  
Delayed irritation, potential prolonged exposure, acute lung injury)
- Low water solubility : Phosgene, Nitrogen dioxide  
Non-irritating, affect lower airway, lack of noticeable effects → prolonged exposure and acute lung injury

Clinical effects ranging from:

*Stridor, bronchospasm → lung injury, bronchiolitis obliterans*  
*High water solubility irritant → Low water solubility irritant*

Monitoring / Ix

- Vital sign / SaO2 / PFR / FEV1/ FVC / voice quality
- ABG, ECG, CXR, Lung function test, fiberoptic bronchoscopy

Treatment

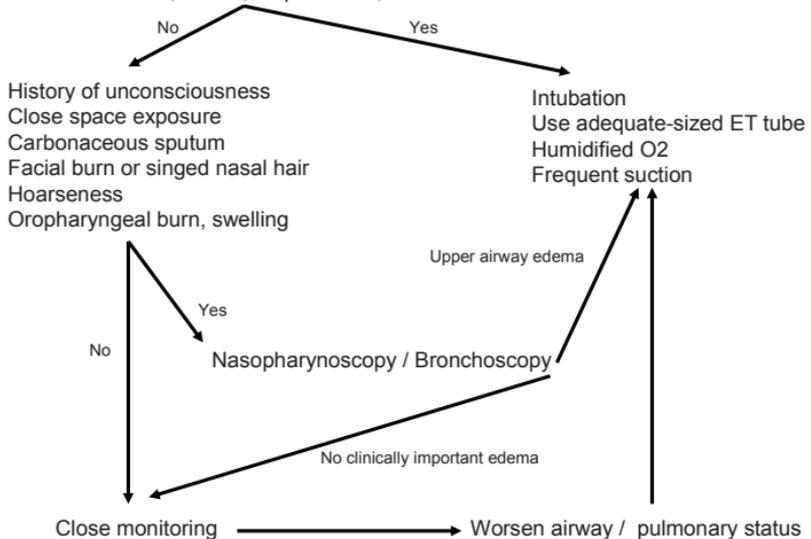
- Remove from exposure, ABC monitoring, O<sub>2</sub> and supportive care
- Nebulized  $\beta$ -agonists for bronchospasm
- No role for steroids, other than for bronchospasm
- Nebulized bicarbonate for Cl<sub>2</sub>, HCl or other acidic gas  
[ 2ml NaHCO<sub>3</sub> 8.4% + 2ml water/saline ]

### Observation

- SO<sub>2</sub>, NH<sub>3</sub>, NH<sub>2</sub>Cl, HCl exposure have no delayed toxicity.  
(Improving patients will continue to do well; only need to be observed for the duration of their symptoms)
- Cl<sub>2</sub>, COCl<sub>2</sub>, NO<sub>2</sub>; Low and intermediate water solubility agents  
(Potential for acute lung injury with delayed onset of symptom. Observe all patients with any symptoms for at least 24 hour. Aware of risk of bronchiolitis obliterans)

### Smoke inhalation management flow-chart

Unconsciousness, stridor, resp distress, PaO<sub>2</sub><8kPa



**Snake Bite**

<b>Local venomous Snake found in the countryside in HK</b>		<b>Toxicity</b>
<b>Viper 蝮蛇</b>		
Bamboo Snake 青竹蛇		Local pain swelling +/- bruising, Systemic coagulopathy, DIC Hypotension
Chinese Habu 烙鐵頭		
Mountain Pit Viper 山烙鐵頭		
<b>Elapidae 眼鏡蛇</b>		
Banded Krait 金腳帶		Paralysis , minimal local reaction
Many Banded Krait 銀腳帶		
Chinese Cobra 飯鐘頭		Early local necrosis (severe pain and swelling) Rhabdomyolysis, Paralysis
King Cobra 過山鳥		
Coral snake 珊瑚蛇		Neurotoxicity with paralysis
<b>Colubridae 游蛇</b>		
Red-necked Keel Back snake 紅脖游蛇		Prolonged bite required for effective envenomation to cause DIC
<b>Hydrophiidae 海蛇</b>		
Mangrove Water snake 黑斑水蛇		Neurotoxic, myotoxic with rhabdomyolysis
Chinese Water snake 中國水蛇		
Plumbeous Water snake 鉛色水蛇		

<b>Imported Snakes (Usually highly venomous)</b>		<b>Toxicity</b>
<b>Vipers</b>		
Hundred pacer 百步蛇		Local pain swelling and bruising, Bleeding wounds, coagulopathy
Malaysian Pit viper 馬來亞腹蛇		
Agistrodon halys 蝮蛇		
Russel's Viper 鎖鍊蛇		Local pain swelling, bruising, coagulopathy, Pulmonary edema, Rhabdomyolysis, ARF
Rattle Snakes 響尾蛇		Local tissue damage, coagulopathy, neurotoxic

**Investigation**

- CBP, APTT, PT (esp. whole blood clotting time), RFT, CPK
  - Urine for myoglobin and hemoglobinuria
  - ECG, Bed side spirometry for FVC if available, serial PFR, CXR
- Investigations should be repeated in the following situations
- Progression of local or systemic symptoms.

- Abn result from initial test until normal or other cause identified
- After anti-venom administration
  
- Snake identification is useful (Photographing at safe distance)  
[head, tail, dorsal, ventral feature important for identification]  
(Consult HKPIC for urgent contact with biologist for snake identification and advice on anti-venom use)

### Treatment

- Supportive care, analgesic, Tetanus prophylaxis
- Q1/2 hour assessment for local / systemic S/S for first few hours
- Antivenoms should be considered for
  - Local progression, necrosis, compartment syndrome.
  - Systemic toxicities, i.e. coagulopathies, weakness, rhabdomyolysis, hypotension etc.
  - First S/S of neurotoxicity after krait bite

### Snake anti-venom available in HA

Antivenoms	Starting Dose	Snake covered
Agistrodon halys (China)	6000U	Bamboo snake 青竹蛇 Chinese Habu 烙鐵頭 Mountain Pit Viper 山烙鐵頭
Bungarus multicinctus (China)	10000U	Many Banded Krait 銀腳帶 King Cobra 過山鳥
Bungarus fasciatus (China)	5000U	Banded Krait 金腳帶
Naja Naja (China)	2000U	Chinese Cobra 飯鐘頭
Agistrdon actus (China)	8000U	Hundred Pacer 百步蛇
Australian Tiger Snake	3000U	?? Sea snake
Russel's Viper (Thailand)	0.6mg	Russell's viper 鎖鍊蛇

### Available Thai Red-Cross anti-venin

- Green-pit viper (Bamboo snake)
- Cobra, King-cobra
- Banded-krait which may be more species specific

*[May be considered for having different species specificity from that of China, please consult HKPIC for further information]*

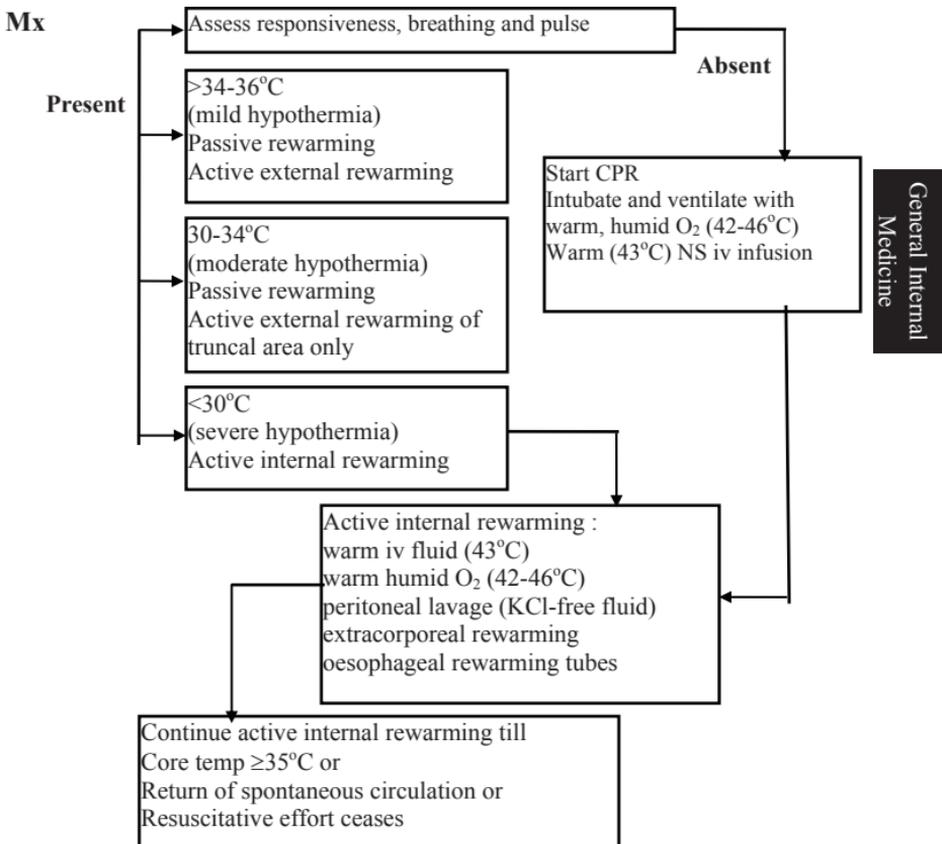
Precautions and pre-treatment in anti-venom administration

- Resuscitation equipment stand-by
- Pre-treatment with anti-histamine and hydrocortisone is advised
- 1st dose to 500 ml NS, give at 100ml/hr.
- If no allergy after 5-10min., fasten rate, dose finish in 30 min.
- May need further doses if clinically indicated
- No evidence to support routine prophylactic antibiotic use
- Debridement and surgery for compartment syndrome as indicated

## ACCIDENTAL HYPOTHERMIA

(Use low temp thermometer for core temp)

**Ix** - CBP, RFT, blood glucose, h'stix, ABG, amylase, cardiac enzymes, coagulation profile, TSH, blood culture (esp in elderly), CXR, ECG, toxicology screen and SXR in comatose patient



\* Give prophylactic broad-spectrum antibiotics (esp in elderly)

\*\* Cannot be certified dead before core temp  $\geq 36^{\circ}\text{C}$

## HEAT STROKE / EXHAUSTION

*HEAT STROKE is caused by over-heating of the body core when sweating is limited.*

*HEAT EXHAUSTION is caused by sustained heat stress that causes water and salt depletion (may be complicated by heat stroke in advanced stage).*

	Heat Stroke	Heat Exhaustion
Risk factors	drugs or diseases causing limited sweating esp. in elderly, infants	
Skin	hot and dry	warm and wet
Core body temp.	40-41°C	38-39°C
Acid-base disorder	respiratory alkalosis lactic acidosis	
Renal failure	common	pre-renal failure

### Management

1. Check CBP, RFT, ABG, coagulation profile, urine myoglobin
2. Monitor vital signs (esp urine output) and core temp
3. Cooling of body by removing all clothing, tepid water sponging, fanning (Immersion in ice water is dangerous)
4. Oral fluid and salt replacement in heat exhaustion (25 g NaCl in 5 litres of water)
5. Correction of electrolyte disturbances and hypovolaemia
6. Lactic acidosis not responding to volume expansion should be treated with bicarbonate
7. Convulsion should be treated with anticonvulsive therapy
8. Look out and support multiorgan failure in heat stroke

## NEAR DROWNING

*The most important consequence of near-drowning is asphyxia which leads to hypoxaemia, hypercapnia and metabolic acidosis*

1. Monitor and maintain ABC. Clear airway and CPR if necessary
2. Ix: ABG, RFT, ECG, CXR, SXR and X ray cervical spine, cardiac monitoring and body temperature monitoring
3. Beware of head and cervical spine injury and hypothermia
4. Correct hypoxia and metabolic acidosis. Give O<sub>2</sub> therapy (PEEP may be necessary for severe hypoxia). Treat bronchospasm with  $\beta_2$ -agonist. Bronchoscopy may be necessary if persistent atelectasis or localized wheezing
5. Treat seizure with anticonvulsant
6. Consider antibiotics for pneumonia
7. Rule out drug effects e.g. alcohol, hypnotics, narcotics

## ELECTRICAL INJURY

*Electrical injuries cause cardiopulmonary arrest, burn, acute renal failure due to hypovolaemia or myoglobinaemia, injuries to nervous system, damages to vessels causing thrombosis or haemorrhage*

*Alternate current (AC) is more dangerous than direct current (DC)  
Current with frequency of 50-60 cycles/sec is more dangerous*

- Ix : ECG, ABG, RFT, CPK, LDH, urine myoglobin
- Monitor: Vital signs, cardiac rhythm, neurological status, urine output and colour
- CPR if necessary
- Antiarrhythmic drugs depend on nature of arrhythmia
- IV fluid replacement
- Treat burn and compartment syndrome as appropriate

## RHABDOMYOLYSIS

### Dx:

Red or brown urine +ve for blood but no RBC under microscopy

Urine +ve for myoglobin

Pigmented granular casts in the urine

↑↑ CPK

Others: hyperkalaemia, hypocalcaemia, hyperphosphataemia, hyperuricaemia, DIC, ARF

### Mx:

Aim : correction of hypovolaemia, enhance clearance of heme proteins, mitigate the adverse consequences of heme proteins on the proximal tubular epithelium

- NS infusion 1-1.5 L/hr
- Monitor urine output & haemodynamic parameters
- Continue IV infusion with 500ml NS alternating with D5 1 L/hr after satisfactory BP and urine output achieved
- Keep urine output at 300ml/hr until myoglobinuria ceased
- Add  $\text{NaHCO}_3$  50meq/L to each 2nd or 3rd bottle of D5 to keep urinary pH > 6.5
- Add 20% mannitol at a rate of 1-2g/kg BW over 4 hr with plasma osmolar gap kept below 55 mosm/kg
- Withhold mannitol and  $\text{HCO}_3$  if marked diuresis not achieved
- May try furosemide & renal dose dopamine for anuric patients
- Extracorporeal elimination of heme protein is controversial
- Look out and treat significant compartment syndrome

### **NB**

- Regimen is less effective if began after the first 6 hrs when renal failure may already be established
- Elderly patient may require slower volume replacement
- Look out for hypercalcaemia in recovering phase of ARF's

## SUPERIOR VENA CAVA SYNDROME

**Causes:** 80% due to malignancy

\*Iatrogenic cause subclavian line, pacemaker wire

**P/E:** Dilated superficial veins over anterior chest wall

Engorged jugular veins  $\pm$  facial and arm veins

Oedema of face, neck, and upper extremities with cyanosis

**DDx:** Pericardial effusion with tamponade

**Ix:** CXR, CT, bronchoscopy

**Tx:** Look out for upper airway obstruction (stridor) - may be life-threatening

*Corticosteroids* (iv dexamethasone 4mg q6h) - transiently decrease oedema and inflammatory reactions associated with tumor necrosis and irradiation

*Radiotherapy* - primary therapy for most cases of malignant SVC syndrome (consult oncology dept promptly)

*Systemic chemotherapy* - for small cell lung carcinoma or non-Hodgkin's lymphoma

*Central venous catheter* - removal under anticoagulation  $\pm$  regional fibrinolytic therapy

## CLINICAL ONCOLOGY

### MALIGNANCY-RELATED SUPERIOR VENA CAVA SYNDROME

Malignancy accounts for 80% of SVC syndrome

Non-small cell lung carcinoma (50%)

Small cell lung carcinoma (25%)

Non-Hodgkin lymphoma (10%)

Others e.g. germ cell neoplasms, breast carcinoma, thymoma etc

Treatment is tailored to the specific neoplasm, therefore tissue diagnosis is essential prior to empirical treatment, which could jeopardize histological evaluation, e.g. corticosteroid in lymphoma.

#### **Ix**

**For immediately life-threatening situations** e.g. upper airway obstruction due to tumor compression or severe laryngeal edema, impaired conscious state due to cerebral edema

Stabilize airway, breathing, circulation

Urgent Oncology consultation for immediate treatment

Urgent endovascular stenting can provide the most rapid relief without affecting subsequent tissue diagnosis. Total SVC occlusion and SVC thrombus are not absolute contraindications for stenting. Post stenting short-term anti-thrombotic therapy recommended e.g. dual antiplatelets for 3months.

#### **For stable /stabilized patients**

Clinical examination and investigations targeted to establish tissue diagnosis by minimally invasive methods.

Sputum cytology, serum AFP,  $\beta$  HCG levels, LN biopsy, pleural fluid cytology/pleural biopsy, bone marrow biopsy, endoscopic biopsy, image-guided biopsy. For suspected lymphoma, excisional biopsy of enlarged lymph node is essential.

Watch out for coexisting pericardial effusion/cardiac tamponade.

## **Tx**

### **Empirical**

Prop up for head elevation

Oxygen supplement

Dexamethasone 4mg q6h iv

### **Disease-specific (Consult Oncology)**

Chemotherapy

Radiotherapy.

Targeted therapy

### **Presence of SVC thrombus**

Long term anticoagulation, if not contraindicated, for at least 3 to 6 months AND until the cancer resolved – LMWH is preferred over warfarin in malignancy-related thrombosis for lower rate of recurrent thromboembolism. Both have similar bleeding risks.

## NEOPLASTIC SPINAL CORD/CAUDA EQUINA COMPRESSION

(Also refer to page N16 and GM38.)

Etiologies

Prostate cancer (20%)

Breast cancer (20%)

Lung cancer (20%)

Others : non-Hodgkin lymphoma, plasma cell myeloma/plasmacytoma, renal cell carcinoma etc

Prompt diagnosis and immediate treatment important in maximizing neurological outcome

### **Ix**

Diagnosis confirmed with MRI of entire thecal sac since multiple level involvement present in 33% of patients (CT myelography if contraindicated for MRI)

For patients without known malignancy, actively search for potential primary. Tissue diagnosis is essential for subsequent management.

### **Tx**

#### **General**

dexamethasone 4mg q6h iv

adequate pain control

bowel care

bladder catheterization for retention of urine

compression stockings

#### **Specific (Consult Oncology)**

RT for most metastatic cancers

Chemotherapy for chemosensitive tumours

Hormonal therapy for selected cases

Surgery for suspected malignancy without tissue diagnosis and no alternative site for biopsy, presence of spinal instability or radiotherapy/chemotherapy-resistant tumours.

## HYPERCALCEMIA OF MALIGNANCY

(Please also refer to subsection Palliative Medicine on page GM37.)

Etiologies (in decreasing order of frequency)

Humoral hypercalcemia of malignancy (PTHrP) e.g. squamous cell/renal cell/transitional cell carcinomas, breast/ovarian cancers etc

Osteolysis from bone metastases

Calcitriol-secreting lymphoma

Ectopic PTH secretion

\*\*Initial approach to and control of hypercalcemia covered in Electrolyte Disturbances section

Oncology specific aspects:

Ensure adequate pain control

Workup for the cause of hypercalcemia e.g. previously undiagnosed malignancy, new development of bone metastasis, recurrence of cancer etc

Consult Oncology for disease control of the underlying cancer

Systemic corticosteroid can be helpful for calcitriol-secreting lymphoma in some circumstances, but to be avoided if the specific tissue diagnosis has not been made yet, please discuss with oncologist first.

## TUMOUR LYSIS SYNDROME

TLS can occur after cytotoxic therapy or spontaneously in high-grade malignancy or high tumor burden, most commonly lymphoblastic leukemia/high-grade lymphomas especially Burkitt's.

### Ix/monitoring

Fluid input/output, ECG/cardiac monitoring, serum potassium, calcium, phosphate, urate, creatinine, LDH, G6PD level

### Diagnosis

Laboratory TLS – **At least 2** of the following abnormal serum biochemistries occurring within 3 days before/7 days after beginning chemotherapy despite adequate prophylaxis :

- potassium  $\geq 6$ mmol/L or 25% increase from baseline
- urate  $\geq 0.5$ mmol/L or 25% increase from baseline
- phosphate  $\geq 1.45$ mmol/L or 25% increase from baseline
- calcium  $\leq 1.75$ mmol/L or 25% decrease from baseline

Clinical TLS – laboratory TLS **AND any** of the following :

- increased serum creatinine to  $\geq 1.5$  times ULN
- seizure
- cardiac arrhythmia
- sudden death

### Prophylaxis

Adequate hydration 3-4L/day, aim for urine output  $\sim 150$ ml/hr, +/- diuretics

Hypouricemic agents : allopurinol adjusted for renal function, (or rasburicase if the patient is of high risk of TLS, please note rasburicase is contraindicated in patients with G6PD deficiency)

### Tx

Correct electrolytes disturbances (see Electrolyte Disturbances section)

Maintain I/O balance

Monitor and treat arrhythmias

For persistent hyperkalemia, hyperphosphatemia, hyperuricemia, hypocalcemia or oliguria, Nephrology consultation with a consideration of dialysis support.

## EXTRAVASATION OF CHEMOTHERAPEUTIC AGENTS

(Also see page H4-5 in Haematology Section.)

The escape of an irritant (causing tissue inflammation) or vesicant (causing tissue necrosis) drug into the extravascular space.

Commonly used vesicants :

Anthracyclines e.g. doxorubicin, epirubicin, daunorubicin, idarubicin

Vinca alkaloids e.g. vinblastine, vincristine, vinorelbine

**Prevention of extravasation** is the best strategy against extravasation injury

Proper infusion technique is of paramount importance

Consider the use of central venous catheter for vesicant infusion

For peripheral infusion of chemotherapy, use a newly set IV line in a large peripheral vein with close monitoring of any evidence of extravasation.

### When extravasation is suspected

Stop the infusion immediately

Leave the catheter in place

Aspirate fluid from the extravasation area

DO NOT flush the line or apply local pressure.

Administer antidote if applicable before removal of catheter.

Access the extravasation kit for specific antidote

Anthracyclines : topical DMSO 50%, consider IV dexrazoxane if available

Taxanes : topical + SC hyaluronidase

Mechlorethamine, dacarbazine, cisplatin : SC sodium thiosulphate

Mitomycin : topical + SC DMSO 50%

Elevate the extremity with extravasation.

Apply heat locally for vinca alkaloids and epipodophyllotoxins (e.g. etoposide); apply cold locally for other agents.

Take clinical photos of the extravasation injury.  
Document the extravasation process and measures taken.  
Monitor the healing process, full-thickness skin or surrounding tissue necrosis may necessitate surgical intervention.

## Palliative Medicine

### ANOREXIA

Anorexia can be due to multiple causes, leading to early satiety or loss of desire to eat; may or may not be associated with cachexia.

#### **Causes:**

1. Concomitant symptoms: pain, depression, constipation, dyspnoea, dysphagia, nausea, vomiting, anxiety
2. Oral problems: dry mouth, candidiasis, ulcers, ill fitting denture, change in taste
3. Delayed gastric emptying: hepatomegaly, autonomic neuropathy
4. Medications: opioids, antibiotics
5. Odour: foul smelling discharge, fungating mass, incontinence

#### **Management:**

1. Treatment of reversible causes
2. Maintain good oral hygiene
3. Provide frequent small meals or food on demand, allow patient to eat what they wish, keep company during eating
4. Acknowledge concerns on prognosis, body image, social impact

#### **Appetite stimulating agents:**

1. Corticosteroids: e.g. dexamethasone 4 mg daily
  - rapid onset, but effect tails off after 4 weeks
  - increase food intake, but no weight gain
  - may reduce nausea and improve sense of well being
  - discontinue after 1 week if no benefit; if effective, keep minimal effective dose; tail off if effect wears off
2. Progestogen: e.g. megestrol acetate 160 mg daily to Qid
  - Improve appetite and weight gain
  - Less rapid onset but action lasts longer than corticosteroid
  - S/E: nausea, fluid retention, thromboembolism
3. Prokinetics e.g. metoclopramide 5-10mg tid

- For early satiety, delayed gastric emptying, gastroparesis

### Practical points:

1. Appetite stimulating agents does not reverse cachexia.
2. To give steroid, look out for DM, TB before starting; give OM or before noon to avoid disrupting diurnal rhythm; monitor mouth condition for oral candidiasis.

## NAUSEA & VOMITING

### Causes:

1. GI related: GIO, constipation, gastroenteritis, gastric irritation, GERD, autonomic neuropathy
2. Metabolic: hypercalcaemia, uraemia, liver failure
3. Drugs: opioids, anticholinergics, SSRI
4. Cancer treatment: chemotherapy, radiotherapy
5. CNS: increase ICP, brainstem disease, motion sickness

### Management:

1. Elucidate and remove cause of nausea and vomiting if possible (e.g. constipation, hypercalcaemia).
2. Pay attention to environment, odour, food presentation.
3. Antiemetics (If oral absorption is in doubt, use other routes)
  - Prokinetic: e.g. metoclopramide 5-10mg tid, domperidone 10mg tid.
  - Central anti-dopaminergic drugs e.g. haloperidol 1-5 mg bid (e.g. uraemia, opioid-induced).
  - Dexamethasone 16 mg OM initially for brain tumour while pending tumour targeted treatment; 8 mg OM initially for reducing compression on gut by tumour masses.
  - 5HT<sub>3</sub> antagonists e.g. granisetron.

### Practical points:

1. Do NOT use metoclopramide in complete GIO.
2. Avoid metoclopramide in renal failure.

## CANCER PAIN MANAGEMENT

### Basic General Principles:

1. By the Mouth: oral route the preferred route.
2. By the Clock: regular analgesics.
3. By the Ladder (WHO Analgesic Ladder)  $\pm$  adjuvants.
  - Ladder 1: non-opioids e.g. paracetamol, NSAID.
  - Ladder 2: weak opioids e.g. codeine, dihydrocodeine, tramadol.
  - Ladder 3: strong opioids e.g. morphine, methadone, fentanyl.
  - Adjuvants: antispasmodics, antidepressants, anticonvulsants.

### Practical points:

1. Pethidine **NOT** recommended because of adverse S/E profile.
2. FDA recommended withdrawal of propoxyphene in 2010.
3. Potency of Tramadol is between weak and strong opioids; similar S/E profile; watch out for drug-drug interaction e.g. SSRI, TCA, warfarin.
4. Fentanyl patch is **NOT** for opioid naïve patients, acute pain or initial titration. Consult specialists.
5. In ESRD, paracetamol is the first line drug. Weak opioids, morphine, NSAID, COX II should be **AVOIDED**. Methadone and fentanyl as suitable strong opioids, consult specialist.
6. COX II is no different from NSAID in renal toxicity.

### GUIDELINES ON USE OF MORPHINE FOR CHRONIC CANCER PAIN CONTROL

1. Morphine is the strong opioid of choice for moderate to severe cancer pain.
2. Morphine has no standard upper dose range. The optimal dose is the dose providing adequate pain relief with minimal or tolerable S/E.
3. Oral route is preferred unless not feasible e.g. GIO, dysphagia
4. Use immediate release morphine i.e. syrup morphine for titration.

5. Start with syrup morphine 5mg Q4H regularly, not PRN. Some prefer to double the dose at bedtime to avoid waking the patient up at 4 am.
6. Consider a lower starting dose of 2.5mg for patients susceptible to S/E e.g. old age, COPD, frailty, sleep apnoea.
7. Dose increment: e.g. 5mg→10mg→15mg→20mg→30mg etc.
8. For breakthrough pain, prescribe the SAME dose as the one for regular use in between the regular intervals, given up to hourly. Review within 24 hours and adjust the regime according to breakthrough requirement.
9. AVOID morphine in renal failure as active metabolites are excreted by renal route.
10. Side effect of opioids and their management:

GI	Nausea, vomiting, constipation
ANS	Dry mouth, urinary retention, postural hypotension
CNS	Sleepiness, cognitive impairment, delirium, hallucination, respiratory depression, myoclonus, seizure, hyperalgesia
Skin	Itchiness, sweating

- a. Good explanation is important.
- b. Ensure adequate hydration or rehydrate patient.
- c. Give laxatives CONCURRENTLY if not contraindicated, preferably a combination of stimulant and stool softener e.g. Senna 15mg Nocte and lactulose 10ml tid.
- d. Nausea may occur initially. May prescribe antiemetic PRN e.g. metoclopramide 5-10mg tid, haloperidol 1-5mg daily.
- e. May consider methylphenidate 5 – 20mg daily for sleepiness
- f. Consider reduce dose of morphine if pain is well controlled; abrupt discontinuation may precipitate withdrawal symptom.
- g. Consider adjuvant analgesics.
- h. Consult specialist to switch to another strong opioid.

### **Dose conversion of oral morphine to parenteral route**

1. Parenteral route has NO special advantage over oral route.
2. SC route is the preferred alternate route, or IV if access available. No indication for IMI generally.

3. Dose conversion
  - **Oral** daily dose of morphine  $\div 2$  = daily dose of morphine **SC**
  - **Oral** daily dose of morphine  $\div 3$  = daily dose of morphine **IV**
  - E.g. Morphine 60mg **PO** = 30mg **SC** = 20mg **IV**

### Practical points on parenteral drugs:

Generally, parenteral drugs for symptom control can be given by:

1. Syringe driver (10ml syringe or specified syringe) OR
2. Infusion pump by adding drugs to 500ml parenteral fluid to be given SC (NS only for SC) or IV.

### Practical points on laxatives:

1. Metamucil requires good fluid intake and has high K content; NOT for frail patients with reduced water intake.
2. Mg Trisilicate has high Mg content; NOT for ESRD.
3. Fleet enema contains high phosphorus content; NOT for ESRD.

## DYSPNOEA

Causes:

Dyspnoea is usually multifactorial in advanced cancer.

1. Cardiopulmonary: lung masses, pleural effusion, chest infection, major airway obstruction, SVCO, lymphangitis carcinomatosa, haemoptysis, pneumothorax, pericardial effusion, pulmonary embolism.
2. Systemic: anaemia, cachexia, muscle weakness, gross hepatomegaly or tense ascites, metabolic acidosis
3. Non-malignant: co-existing COPD, heart failure, arrhythmia.

Management:

1. Identify and treat as many reversible causes as possible e.g. pleural, pericardial or abdominal tapping, chest drain insertion, antibiotics, blood transfusion, bronchodilators, diuretics, tranexamic acid 250-500mg tid for haemoptysis.
2. Oxygen for hypoxic patients, nasal prong better tolerated than face mask.
3. Dexamethasone 4-8 mg daily for lymphangitis carcinomatosa; 16mg daily for SVCO, major airway obstruction

4. Opioid: for opioid naïve patients, start with morphine 1-2 mg Q4H PO or SC and titrate up; monitor mental state, RR, SaO<sub>2</sub>.
5. Anxiolytic: indicated for patient with strong anxiety or panic.
6. Non-drug measures: prop up, face fan / good air circulation.

### Practical points:

1. CXR is useful in elucidating most underlying causes.
2. SaO<sub>2</sub> / lung function parameters do NOT correlate with intensity of dyspnoea.
3. Look out for trapped lung in chest tapping, stop if patient coughing or develop chest pain; document in patient's record to guide decision on chest tapping in subsequent admission.
4. USS guidance is helpful in chest tapping especially in the presence of loculations.
5. Before abdominal tapping, watch out for coagulopathy; for patients with suspected haemoperitoneum, consider the risk of removing the tamponade effect on a ruptured tumour with release of intra-abdominal pressure upon tapping.

## DELIRIUM

Delirium has acute onset and fluctuating course; due to disease or treatment; characterized by disturbed consciousness and cognitive impairment; can be hyperactive, hypoactive, and mixed pattern. Prompt relief is essential to reduce the patient and carer distress.

Underlying causes:

1. Dehydration, faecal impaction, urinary retention, uncontrolled pain.
2. Drugs: opioid, anticholinergic, steroid, sedative, antidepressant.
3. Metabolic: liver or renal failure, hypercalcaemia, infection, hypoxia, CO<sub>2</sub> retention, disturbed Na and blood glucose.
4. CNS: brain tumour, stroke, infection.

Management:

1. Explain to patient and family to relieve anxiety, patient can often recall distressing episode.
2. Reduce noise of environment and provide adequate lighting.

3. Treat specific causes; perform PR exam and feel for the bladder.
4. Review drugs and S/E, if opioid toxicity is likely, reduce dose by one-third and rehydrate as appropriate.
5. CT scan brain if CNS causes suspected.
6. Haloperidol 1-5 mg PO/SC stat  $\pm$  SC infusion 5-30 mg q24h via syringe driver.

### **MALIGNANT INTESTINAL OBSTRUCTION**

1. Assess if surgery is feasible, more likely for patient with single level obstruction with good performance status.
2. For inoperable cases, symptoms can often be managed without need for Ryle's tube insertion. Obstruction may be reversible.
3. Stop stimulant laxatives and prokinetic agents if complete GIO.
4. Laxatives for co-existing constipation in incomplete GIO.
5. Pharmacological treatment: can start with SC infusion of following drugs via syringe driver. Titrate upwards if needed.
  - a. Morphine 15mg SC Q24H for analgesia.
  - b. Haloperidol 3mg SC Q24H for nausea and vomiting.
  - c. Buscopan 40mg SC Q24H to reduce colic and secretions.
  - d. May also add dexamethasone 8mg SC or IV Q24H.
  - e. In refractory GIO with high output, try octreotide 0.1-0.3mg tid SC; consider venting gastrostomy or stenting.
  - f. Do NOT combine metoclopramide with anticholinergic.
- g. Ryle's tube: assess patient's preference. Some patient prefers vomiting one or twice a day to RT insertion.

## PALLIATIVE CARE EMERGENCIES

### MASSIVE HAEMORRHAGE

Anticipation:

Important for care planning; identify potential lesions e.g. H&N tumour eroding carotid artery; repeated episodes of haemoptysis; invasion into internal structures e.g. aorta; tumour rupture e.g. HCC

Management:

1. Apply direct pressure with adrenaline (1 in 1000) soaked dressing to any external bleeding point.
2. Use green surgical towels to reduce the frightening visual impact of the bright red blood.
3. Sedate with midazolam 5-10 mg SC or diazepam 5-10 mg per rectal stat to relieve panic and fear.
4. Address emotional impact on family and staff.

### MALIGNANT HYPERCALCAEMIA

Cross reference in Clinical Oncology on page GM25.

**Presentation:** delirium, malaise, thirst, constipation

**Common primary:** myeloma, breast, lung, kidney, thyroid

**Management:**

1. Monitor Ca, P, RFT, urine output
2. Rehydration with NS 2-3 litres/day
3. Bisphosphonate infusion:
  - Review drugs that may aggravate bisphosphonate renal toxicity
  - Pamidronate infusion depends on the corrected Ca level
    - 2.6-3.0 mmol/L -pamidronate 30mg in 500ml NS over 2-4hrs
    - 3.0-3.5 mmol/L -pamidronate 60mg in 500ml NS over 2-4hrs
    - >3.5 mmol/L -pamidronate 90mg in 500ml NS over 2-4hrs
  - Adjust dose in renal impairment.
  - If GFR<20ml/min, consider risk and benefit, toxicity less with slower infusion.

4. Haloperidol 1-5mg daily for delirium.
5. Maintain IV hydration till patient can maintain oral hydration.

### **Practical points:**

1. Check calcium level at day 5 to assess effectiveness of pamidronate. Do **NOT** repeat pamidronate until day 7 after infusion to avoid hypocalcaemia.
2. Patient may look exceptionally ill with hypercalcaemia, on the other hand, pamidronate may not be appropriate at EOL, if in doubt, consult.
3. Effect of pamidronate lasts for 4 weeks, plan accordingly.

## **SPINAL CORD COMPRESSION**

(Also refer to page GM24 and GM38)

**Common primary:** breast, lung, kidney, thyroid, myeloma, lymphoma

### **Presentation:**

1. Back pain aggravated by coughing or lying down; neuropathic pain radiating from back to thigh or around the trunk; motor weakness or impaired sensation; sphincter disturbance is a late sign with poor prognosis in functional outcome
2. Perform a **FULL** neurological examination in ANY cancer patient with the slightest suspicion
3. Can be the first presentation of cancer
4. Site of pain may not correlate with level of compression

### **Investigation:**

1. Plain X ray may not show bone lesion till bone loss is considerable.
2. Urgent MRI of the whole spine.
3. Start dexamethasone 16mg daily PO or IV
4. Urgent referral for RT; tail down steroid after RT
5. Consult O&T for surgical intervention which may be appropriate in selected cases

**Practical points:**

1. Functional status at the time of treatment is the most important factor in determining the prognosis and outcome; early diagnosis important
2. CNS examination can be normal to begin with; keep monitoring

**LAST DAYS OF LIFE**

1. Patients approaching end-of-life (EOL) have one or all of the following: unable to take drugs orally, only able to take sips of water, profound weakness, semi-comatose or comatose.
2. Diagnosing EOL by clinicians is important in triggering the care process and communication with patients and families.
3. Inappropriate interventions, investigations and medications should be withheld to focus on comfort measures.
4. **Anticipatory prescription** facilitates timely symptom control e.g. pain, delirium, dyspnoea, death rattle, myoclonus.

**Pain:** Morphine 2.5-5mg SC prn hrly or fentanyl 12.5 microgram SC hrly if not on regular opioid; step up the regular dose of opioid if already on opioid and change to SC route.

**Nausea / vomiting:** Haloperidol 0.5-1 mg SC prn hourly.

**Agitation / anxiety:** Midazolam 2.5mg SC prn hourly.

**Myoclonus:** Midazolam 2.5mg SC prn hourly.

## DEATH RATTLE

1. Due to excessive respiratory secretions, the noise of which can be distressing for relatives; explain that patient is not choking.
2. Avoid excessive fluid.
3. Gentle suction.
4. Hyoscine butylbromide (Buscopan®) 20-60 mg q24h SC.

## TERMINAL DYSPNOEA

1. Oxygen for patients with hypoxia.
2. For intermittent dyspnoea: morphine 1.5-2.5mg SC stat or fentanyl 12.5microgram SC stat for ESRD.
3. For persistent or refractory dyspnoea requiring continuous infusion of opioid and midazolam, consult specialist. Patient and family should be informed about the purpose, possible impairment in communication, and this is not euthanasia. Start with morphine 5mg SC Q24H  $\pm$  1mg SC prn. For ESRD, start with fentanyl 50-100 microgram SC Q24H.

### Practical points:

1. Do NOT use morphine for sedation
2. Poor circulation may not give accurate SaO<sub>2</sub>; upward titration of oxygen with plateau of dyspnoea relief or oxygen saturation is not indicated. High oxygen flow may cause more discomfort to patient.

## BRAIN DEATH

(Based on HA Guidelines on Diagnosis of Brain Death, 4 October 2010, ref: HA752/10/1/3)

Use updated Brain Death Certification Form HA0090/MR.

- For patients who are 5 yrs of age or older

Concept: Brain death equates with death both medically and legally.

### 1. Pre-conditions and exclusions for considering diagnosis of brain death

*\* All the following should coexist*

a) Diagnosis of severe irremediable brain injury which is consistent with progression to brain death (the clinical diagnosis is usually confirmed by neuro-imaging). The diagnosis of a disorder which can lead to brainstem death should have been fully established.

b) Apnoeic patient on a ventilator

- Muscle relaxants and other drugs should have been excluded as a cause of such findings

c) Exclusion of potentially reversible causes of coma

- Depressant drugs or poisons; peripheral nerve stimulator to confirm intact neuromuscular conduction.
- Primary hypothermia: core temp  $>35^{\circ}\text{C}$  before diagnostic tests of brain stem death are carried out
- Metabolic and endocrine disturbances (e.g. severe electrolyte or endocrine disturbances)
- Arterial hypotension as the cause for the coma should be excluded.

### 2. Tests for confirming brain death

*\* All brainstem reflexes must be absent.*

*\*The testing of all the following is considered sufficient*

a) Both pupils - fixed in diameter and non-reactive to light

b) Absence of bilateral corneal reflexes

- c) Absence of vestibulo-ocular reflexes - no eye movement occurs during or after the slow injection of at least 20 ml ice-cold water into at least one external auditory meatus, or preferably into each external auditory meatus in turn. Clear access to the tympanic membrane should be established by direct inspection. This test may be contraindicated on one or other side by local trauma
  - d) No motor responses within the trigeminal nerve distribution can be elicited by adequate pain stimulation of any somatic area
  - e) Absence of gag reflex
  - f) Absence of cough reflex
  - g) Testing for apnoea: should be done last. No respiratory movements occur when the patient is disconnected from the mechanical ventilator for long enough to ensure that the PaCO<sub>2</sub> rises above the threshold for stimulating respiration (ie PaCO<sub>2</sub> > 8.0 kPa and arterial pH < 7.30). ABG must be available for this test to be performed. The patient should be disconnected from mechanical ventilator when PaCO<sub>2</sub> is close to normal. Hypoxaemia during disconnection should be prevented by preoxygenation and administration of oxygen during the test, e.g. by delivering O<sub>2</sub> through a catheter into the trachea
- \* Period of observation and repetition of tests: 2 full separate examinations should be performed. The first examination should be performed after all pre-conditions met, and after at least 4 hrs of observation of coma (Glasgow Coma Scale of 3) with absent brain-stem function. The second examination can be performed any time after the first examination, so that total period of observation is at least 4 hours. The minimum period of observation need to be totally 24 hours after cardiorespiratory arrest.
- \* Medical practitioners:
- One of the doctors must be a specialist recognised by the appropriate College as having demonstrated skill and knowledge

in the certification of death following irreversible cessation of brainstem function (usually an Intensivist, Critical Care Physician, Neurologist or Neurosurgeon).

- The other doctor should preferably be of the same qualification but should be at least 6 years after registration and possess the skill and knowledge in the certification of death following irreversible cessation of brainstem function
- The person authorizing removal of tissues and the person removing tissues MUST NOT be responsible for determining brainstem death.

\* Confirmatory IX

If the preconditions for clinical diagnosis and confirmation of brainstem death cannot be satisfied, objective demonstration of absence of intracranial blood flow is required (after the 4 hour period of observation of coma and of absent brainstem responses, where these can be tested).

- \* Time of death - the time when certification of brain death has been completed (ie following the second confirmatory examination) or if a confirmatory investigation is used, then the time of death should be after the confirmatory investigation.
- \* Clinical observations compatible with diagnosis of brain death
  - movements of limbs in response to a stimulus outside the distribution of cranial nerves
  - sweating, blushing, tachycardia
  - normal BP without pharmacologic support
  - absence of diabetes insipidus
  - deep tendon reflexes
  - extensor plantar reflex
- \* Features NOT COMPATIBLE with brainstem death:
  - decerebrate or decorticate posturing.
  - seizure.



# Procedures

For all procedures,  
**INFORMED CONSENT**  
Must be obtained except  
in an emergency life-saving  
situation

**Correct side-marking before procedure  
is essential when indicated**



## ENDOTRACHEAL INTUBATION

### Indications

1. Respiratory / ventilation failure, including CPR
2. To protect airway against aspiration
3. To manage excessive airway secretions

### Equipment

1. Bag-valve device
2. IV access
3. Cardiac monitor & pulse oximeter
4. Oropharyngeal / nasopharyngeal airways
5. Direct laryngoscope with functioning light bulb and blade of appropriate size (start with size 3, usually size 3-5 for adults)
6. Endotracheal tube (Male 8-8.5 mm, female 7-8.5 mm internal diameter) with low pressure cuff
  - with syringe for cuff inflation, check cuff for leakage (Inflate with 10 ml syringe, then deflate completely)
  - If stylet used, lubricate and insert into ETT. Its tip must be recessed > 1 cm from distal end of tube
7. End-tidal CO<sub>2</sub> monitor if available
8. Yankauer sucker
9. Bougie if indicated
10. A spare endotracheal tube with size 0.5 – 1mm smaller

### Note

1. Consult anaesthetists in expectedly difficult case
2. In patients with suspected unstable cervical spine, leave intubation to expert hands if possible, otherwise, do in-line stabilization during intubation
3. Do not attempt intubation for >15 sec at a time. Achieve adequate oxygenation before the next attempt

### Procedure

1. Position patient supine

2. Place patient in sniffing position (neck flexed and head extended), Open airway by head tilt-chin lift / jaw thrust
3. Remove dentures and other foreign bodies
4. Fit a face mask tightly on patient's nose and mouth and ventilate using a bag-valve device connected to oxygen
5. Pre-oxygenate for 5 minutes
6. Apply cricoid pressure (Sellick's manoeuvre) to prevent aspiration of gastric contents due to gastric insufflation
7. Perform Rapid Sequence Induction (RSI)
  - Give a short acting sedative (e.g. midazolam or propofol)
  - followed immediately by a paralytic agent such as suxamethonium or rocuronium
8. Insert direct laryngoscope: Push tongue to the left, expose larynx by pulling jaw towards ceiling
9. Gently slide ETT in between cords and immediately remove stylet. Advance ETT till marking at incisor is 22-24 cm for males, 20-22 cm for females
10. For more difficult case, consult anesthetist / senior. In selected case, may consider the use of bougie for assistance: insert as a guidewire, then thread ETT through afterwards
11. Inflate cuff (4-6 mls air to achieve cuff pressure 20 - 24 cm H<sub>2</sub>O)
12. Connect ETT to bag-valve device
13. Confirm ETT position by observing lung expansion, auscultation (bilateral chest and epigastrium), or by end-tidal CO<sub>2</sub> device
14. Off cricoid pressure AFTER endotracheal intubation is confirmed

\*\* In case of failed intubation, maintain mask ventilation and summon help

### **After-care**

Urgent CXR to check ETT position (ETT tip  $4 \pm 2$ cm from carina, exclude pneumothorax/pneumomediastinum)

## SETTING CVP LINE

### Indications

1. Haemodynamic monitor
2. Administration of TPN, vasopressors

### Contraindications

1. Bleeding tendency
2. Ipsilateral carotid artery aneurysm

### Internal Jugular Vein (IJV) Puncture

- Aseptic technique, use Gauge 14 or 16 angiocatheter
- Preferably US-guided
- IJV runs behind the sternocleidomastoid (SCM) close to the lateral border of the carotid artery
- Place patient in a 20° head-down position with the head turned to the opposite side
- Right side preferred to avoid injury to the thoracic duct
- (1) **Anterior approach:** Insert angiocath 0.5cm – 1cm lateral to carotid pulse at midpoint of the sternal head of SCM.
- (2) **Central approach:** Insert angiocath at apex of triangle formed by two muscle bellies of SCM and clavicle.
- Advance angiocath towards ipsilateral nipple with the syringe at 30-45° above the skin. Maintain gentle aspiration till a gush of blood (dark red) is aspirated
- Gently withdraw stylet of angiocath while pushing angiocath into position, connect infusion set to angiocatheter
- If the artery is punctured (bright red blood), withdraw everything and apply firm pressure for at least 5 minutes
- *(Never advance beyond clavicle. Pneumothorax can kill)*
- **Always make sure that the catheter is in vascular space**  
*(Check siphoning: Venous blood backflows upon lowering infusion set below the patient & blood level should oscillate with respiration)*
- **Read the first CVP reading yourself**
- Always take a CXR afterwards to exclude pneumothorax
- Maintain catheter patency with infusion of fluid

## DEFIBRILLATION

*The speed with which defibrillation performed is the major determinant of the resuscitation success. Rapid diagnosis of VF and pulseless VT followed by immediate defibrillation is important.*

1. CPR before defibrillator available.
2. Attach and turn on defibrillator when available.
3. Check rhythm and identify shockable rhythm (VF and pulseless VT).
4. Apply appropriate conductive material to hand-held paddles or use defibrillator electrode pads. Do not rub the 2 paddles together.
5. Select energy level  
 Monophasic defibrillator – 360J  
 Biphasic defibrillator – device specific; if waveform type unknown, use 200J  
 (150J to 200J for biphasic truncated exponential waveform or 120J for rectilinear biphasic waveform).
6. Press charge button on machine or paddle.
7. Apply firm pressure with one paddle at cardiac apex, the other over base of heart (if paddles are used)\*
8. Warn everybody to stay clear of the patient.
9. Deliver the shock by pressing both discharge buttons simultaneously.
10. Resume CPR immediately after the shock and give 5 cycles of CPR (one cycle of CPR: 30 compressions then 2 breaths). Then check rhythm.

\* For patient with permanent pacemaker, anterior-posterior orientation is preferred or with paddles > 10cm from pacemaker. Interrogate pacemaker after defibrillation to ensure normal functions.

## TEMPORARY PACING

1. Equipment: Venous puncture set, temporary pacing wire and pacemaker, cardiac monitor, defibrillator/transcutaneous pacing standby.
2. Select venous access (femoral, internal jugular or subclavian).
3. Give local anaesthesia and perform venipuncture under aseptic technique.
4. Manipulate pacing wire to RV apex  $\pm$  fluoroscopic guidance.
5. Connect pacing wire to temporary pacemaker.
6. Test pacing threshold with a pacing rate above the patient's own rate. Accept site if threshold  $<1$  volt. Set output at  $>3x$  threshold or 3V whichever is higher.
7. Test for sensing threshold with pacing rate less than patient's own rate if clinically feasible. Set sensitivity to  $1/2$  of sensing threshold (i.e. more sensitive than the sensing threshold).
8. Set desirable pacing rate, eg. 70-80/min.
9. Secure pacing wire at insertion site and cover with dressing.
10. Record the rhythm.

### Aftercare

- Full lead ECG and portable CXR.
- Continue cardiac monitoring.
- Check pacing threshold daily and adjust output accordingly.
- Watch out for complications (infection, bleeding, haematoma, pneumothorax, thrombophlebitis, etc).

### Transcutaneous Pacing (TCP)

- As interim measure before transvenous pacing.
- Anterior TCP patch at cardiac apex and posterior patch over left infrascapular region. Turn the pacer ON  $\pm$  consider analgesia.
- Set the rate to  $\sim 60$ /min (adjusted to clinical condition). Set the current output 2mA above the level with consistent mechanical capture (safety margin). (Do not assess carotid pulse to confirm mechanical capture as muscular jerking may mimic carotid pulse.)

## LUMBAR PUNCTURE

### Indications

1. To check intracranial pressure (ICP) and obtain cerebrospinal fluid (CSF) for diagnosing a wide variety of neurological and neurosurgical conditions
2. To drain CSF
3. To give intrathecal injection

### Precautions

Always examine the patient for evidence of raised intracranial pressure and focal cerebral lesion before performing LP (papilloedema, false localising signs)

1. LP may be performed in some exceptional circumstances if such evidence is present. Always consult the Neurology Team (Medicine) or Neurosurgery Department before making a decision under such circumstances.
2. In case of doubt, a CT scan of the brain should be performed first to exclude contraindications of LP. Perform blood culture and start antibiotic for bacterial meningitis if such diagnosis is suspected and CT brain cannot be done shortly.
3. Do not perform LP if there is uncorrectable bleeding tendency or local infection in the area of needle insertion.

### Procedures

1. Lie patient in left lateral position with back and knees flexed (may try sitting position if failure after 2-3 attempts)
2. Aseptic technique
3. Infiltrate skin with local anaesthetic
4. Advance LP needle between spinous processes of L3/4 or L4/5. Use fine-bore (# 23) needle if raised ICP suspected
5. At about 4-5 cm, a 'give' sensation indicates that the needle has pierced through ligamentum flavum
6. Remove stylet to allow CSF fluid to come out
7. Note the appearance of the CSF and measure CSF pressure

8. Lie patient flat for 4-6 hours after LP (24 hours if ICP increased)
9. Depending on provisional clinical diagnosis, send CSF fluid for:
  - Biochemistry (use fluoride bottle for CSF glucose, check simultaneous blood glucose)
  - Microscopy and cell count, cytology
  - Gram stain and culture, CIE for bacterial antigen (patient already on antibiotics)
  - AFB smear and culture  $\pm$  PCR, VDRL / FTA
  - Indian Ink preparation, fungal culture and cryptococcal antigen
  - Viral isolation and antibody titre  $\pm$  PCR
  - IgG / albumin ratio and oligoclonal bands (with serum)

## BLEEDING TIME

Normal ranges: 2.3 to 9.5 minutes

Preferably to be done by a designated person e.g. a haematologist or a pathologist

1. Ensure the platelet count is normal
2. Use the Simplate II Bleeding Time Device
3. Inform patient of the possibility of a faint scar after the test. Keloid formation, though rare, can occur in some patients
4. Place a sphygmomanometer cuff around patient's arm above the elbow
5. Clean the volar surface of the forearm with alcohol swab and choose an area of skin devoid of visible superficial veins
6. Remove the device from the blister pack and twist off the white tear-away tab on the side of the device. Do not push the trigger or touch the blade slot
7. Inflate the sphygmomanometer cuff to 40 mmHg. Ensure maintenance of pressure during test procedure
8. Place the device firmly on the forearm. The incision must be made either parallel or perpendicular to the fold of the elbow
9. Depress the trigger and start the timer simultaneously.
10. Remove the device approximately one second after triggering
11. Blot off the blood exuding from the linear cut gently and completely with a filter paper or equivalent at 30s intervals
12. Stop the timer when blood no longer stains the filter paper
13. Remove cuff, clean forearm, apply covering bandage. Advise patient to keep bandage in situ for 24 hrs
14. Record the bleeding time

## BONE MARROW ASPIRATION & TREPHINE BIOPSY

### **Bone Marrow (BM) Aspiration & Trephine Biopsy**

1. Obtain informed consent
2. Use either a reusable BM Biopsy needle supplied by CSSD or a disposable one e.g. Jamshidi or 'J' style BM Biopsy needle
3. Site: Posterior superior iliac crest (patient in lateral recumbent position)
4. Clean the skin overlying the posterosuperior iliac crest with aseptic technique
5. Infiltrate overlying skin and periosteum with anesthetic agent
6. Incise skin with a scalpel (2-3 mm incision)

### **BM Aspiration**

1. Hold needle at right angle to iliac crest
2. Advance needle with firm pressure in a clockwise-anticlockwise motion till a decrease in resistance is felt
3. Remove the stylet
4. Apply gentle suction with a 20 ml syringe, reinsert the stylet
5. Make marrow smear on clean slides before the specimen clots, and send marrow clot in a EDTA specimen bottle for section
6. Put additional material in appropriate media for special tests e.g. cytogenetic study, microbiological culture

### **BM Trephine Biopsy**

1. Following the BM aspiration, with the stylet locked in the needle, push out the needle to the periosteal surface, and advance needle with firm pressure in a clockwise-anticlockwise motion in a slightly different angle (not the same track as that of BM aspiration) till a decrease in resistance is felt
2. Push, rotate and advance the needle till the needle reaches the trabecular bone
3. Remove the stylet, advance further for 1-1.5 cm using a circular rotating motion of the needle along its long axis to include a core of marrow within the needle
4. Withdraw needle by 2-3 mm, then with less pressure advance 2-

3 mm in a different direction to break specimen

5. Withdraw needle by rotation with quick full twists
6. Push the specimen from needle by inserting the stylet at the tip and put the specimen in a formalin bottle

N.B. For patients with hematological malignancies or myelodysplastic syndrome, arrange with laboratory haematologist beforehand for cytogenetic, cytochemistry and immunophenotyping studies (if available)

## CARE OF HICKMAN CATHETER

### Hickman Catheter Irrigation & Heparin Lock

1. Wash hands thoroughly with anti-microbial soap and water.
2. Put on non-sterile Latex Gloves.
3. Draw 5 ml of Heparin-Saline (50unit / 5 ml) into a 10ml syringe and 10 ml 0.9% Normal Saline in another 10 ml syringe, and eliminate air from the syringes.
4. Swab end one-inch of catheter and the junction (catheter with Heparin cap or with IV tubing) with Alcohol wipe vigorously with friction for at least 3 times. Allow the antiseptic to air dry.
5. Ensure that the catheter clamp is closed.
6. Disconnect the Heparin block or IV tubing and swab the hub vigorously with friction for at least 3 times with Alcohol wipe. Allow the antiseptic to air dry.
7. Perform each catheter irrigation and catheter cap:
  - Weekly Heparin-Saline flushing
    - Connect an empty 10 ml syringe.
    - Release clamp, and aspirate 5 ml of blood (3 times the catheter volume) to clear the catheter.
    - Reclamp catheter. Remove and discard the blood syringe
    - Inject 10ml 0.9% Normal Saline, then 5ml Heparin Saline
    - Swab the hub with Alcohol wipe and insert a new catheter cap

### Clearing of Blocked Hickman Catheter

#### Stage I – If infusion rate is slow:

1. Wash hand thoroughly with soap and water.
2. Put on non-sterile Latex Gloves.
3. Prepare 10ml 0.9% Normal Saline in a 10ml syringe.
4. Wipe end one-inch of catheter and the junction (catheter with Heparin block or with IV tubing) with Alcohol wipe

vigorously with friction for at least 3 times. Allow the antiseptic to air dry.

5. Ensure catheter clamp is closed.
6. Disconnect the Heparin block or IV tubing. Swab the hub vigorously with friction for at least 3 times with Alcohol wipe. Allow the antiseptic to air dry.
7. Verify catheter occlusion by attaching an empty syringe to catheter and attempt to aspirate. If all clots in the catheter can be aspirated successfully, follow with catheter irrigation and Heparin block or resume IV infusion.
8. If catheter is still occluded, attempt clearing by using a gentle alternating irrigation and aspiration (push and pull) with a 20 ml syringe half filled with 0.9% Normal Saline. If this fails, try with Heparinised-Saline.

N.B. 1. Do not force fluid as catheter damage may result.

2. If necessary, obtain an X-ray image of catheter to check it is in-situ

**Stage II – If the first procedure has failed or the catheter has been blocked for over 2 hours:**

Repeat procedure in stage I but with 3 ml pure Heparin (1000 units/ml) by Doctor.

**Stage III – If stage I & II have failed:**

A fibrinolytic agent e.g. Urokinase can be used. Please contact haematologist or haematology nurse

## RENAL BIOPSY

### **Relative contraindications:**

1. Active infection e.g. acute pyelonephritis
2. Very small kidneys (<8 cm)
3. Single kidney
4. Uncontrolled hypertension
5. Bleeding tendency

### **Preparation:**

1. Check CBP, platelets, PT, aPTT, bleeding time
2. Type and screen/X-match 1 pint packed cells
3. Trace film / report of USG or IVP
4. USG for localization

### **Biopsy:**

(Preferably done in early morning on a weekday)

1. *Platelet count should be  $>100 \times 10^9 /L$ , PT, aPTT normal*
2. Check baseline BP/P
3. Fresh biopsy specimen put into plain bottle with NS and send for histology, immunofluorescence  $\pm$  electron microscopy

### **Post-Biopsy Care:**

1. Encourage fluid intake
2. Complete bed rest for 24 hours
3. BP/P monitoring at least hourly for 4 hrs (every 15 mins for one hour), then q4h if stable
4. Save all urine samples for inspection and for RBC
5. Appropriate oral analgesics
6. Inform if gross haematuria, falling BP (SBP<100 mmHg), increasing pulse rate (>100/min), oozing of blood or severe pain at biopsy site

## INTERMITTENT PERITONEAL DIALYSIS

### I. Tenckhoff catheter in-situ

1. Use automatic peritoneal dialysis machine
  - Regular Rx once to twice a week
  - Heparinisation (optional):     during IPD   100 - 500 units/L  
  Post-dialysis up to 5,000 units
- IP
- 2.

Duration of				Medication (per litre fluid)
PD	PD programme	Dialysis	Drain	
1 <sup>st</sup> 20-80 L	1L/cycle	30 mins	20 mins	Heparin 100-500 units (optional)
Subsequently	2L/cycle	30 mins	20 mins	Optional

### II. Acute PD catheter insertion for patients without a Tenckhoff Catheter

1. Empty bladder
2. Prime abdomen with 2 litres 1.5% PD Fluid via a #16 angiocatheter at 2 cm below umbilicus
3. Ensure smooth flow. Watch out for extraperitoneal infusion in obese patients
4. Give local anaesthesia
5. Aseptic technique
6. Insert catheter for acute PD at 2-3 cm below umbilicus in midline, with catheter tip towards rectovesical pouch

7. Bed cage to protect catheter after insertion
8. IPD order: Total duration 40 hours
  - 2 litres 1.5%\* PD fluid per shift
  - Add heparin 100-500 units/litre
  - Add 4 mEq KCl /litre if serum K < 4 mmol/l
  - Inflow + indwelling 40 mins; outflow 20 mins
  - (\* may adjust % of PD fluid as required e.g. use 4.25% PD fluid if fluid overload)
  - (\*Use 1 litre exchanges if in respiratory distress)
9. Monitor inflow/outflow, if poor, reposition patient / give laxatives/ adjust or replace catheter
10. Add soluble insulin (4-6 units/bag for 2L of 2.5% PD fluid) for diabetics. Monitor h'stix q4-6 hours, aim at sugar ~10 mmol/l

### **Relative contraindications to peritoneal dialysis:**

1. Severe bleeding tendency
2. Multiple lower abdominal scar, recent abdominal surgery
3. Suspicion of abdominal pathology
4. Respiratory failure
5. Pleuroperitoneal leak
6. Aortoiliac graft
7. Burns or other hypercatabolic state or life threatening hyperkalemia (not efficient enough)

### **Preparation for Tenckhoff Catheter Insertion**

1. Give laxatives the night before T.C. insertion
2. Transfuse if Hb <8 g/dl, or Hct <0.26
3. Give dDAVP to correct bleeding tendency
4. Antibiotics prophylaxis (optional) :
  - Regime 1 :*
  - Ampicillin 500 mg iv + cloxacillin 500 mg iv before insertion, then Ampicillin 500 mg and Cloxacillin 500 mg qid
  - Regime 2 :*
  - Vancomycin 1 g in 100 ml NS, infuse over 1 hr
5. Empty urinary bladder before Catheter insertion

## PERCUTANEOUS LIVER BIOPSY

### Contraindications

1. PT > 3 secs prolonged; platelet count <  $60 \times 10^9/L$ ; bleeding time > 10 mins; haematocrit < 25%
2. Gross ascites
3. Patient unable to hold breath
4. Extrahepatic biliary obstruction, cholangitis
5. Vascular tumour, hydatid cyst, subphrenic abscess
6. Amyloidosis
7. Morbid obesity

### Procedure

(Biopsy preferably done on a weekday in the morning)

1. Discontinue anti-platelet agents for several to 10 days and warfarin for 5 days before procedure. Withhold heparin 10-24 hours.
2. Check CBP, platelet, INR, APTT +/- bleeding time in patients with renal impairment or chronic liver disease
3. X-match 2 pints whole blood for reserve and consider antibiotic prophylaxis in selected cases
4. Check BP/P before procedure
5. Instruct patient on how to hold breath in deep expiration for as long as he can
6. Palpate the abdomen and percuss for liver dullness in the mid-axillary line
7. Ultrasound guidance with marking of the optimal biopsy site performed immediately preceding biopsy, by the individual performing the biopsy, is preferred
8. Choose rib space with maximum liver dullness (may ascertain puncture site with USG)
9. Aseptic technique, anaesthetise skin, make a small incision

10. Use the Hepafix needle or spring loaded cutting needle. Follow instructions in the package.  
**Make sure that the patient is holding his breath in deep expiration before introducing the biopsy needle into liver.**  
**Avoid lower border of ribs.**
11. Send specimen for histology in formalin or formalin-saline
12. One pass is usually enough

### Post-biopsy Care

1. BP/P every 15mins for 1 hr, then every 30mins for 1 hr then hourly for 4 hrs, then q4h if stable
2. Watch out for fall in BP, tachycardia, abdominal pain, right shoulder and pleuritic chest pain
3. Complete bed rest for 8 hrs; patient may sit up after 4 hrs.
4. Simple analgesics prn
5. Diet: full liquid for 6 hrs, then resume regular diet
6. Avoid lifting weights greater than 5 kg in the first 24 hours.
7. Anti-platelet agents may be restarted 48-72 hours after biopsy
8. Warfarin may be restarted the day following biopsy

## ABDOMINAL PARACENTESIS

1. Routine prophylactic use of fresh frozen plasma or platelets before paracentesis is not recommended because bleeding complications are infrequent.  
\* However, abdominal paracentesis should be avoided in patient with disseminated intravascular coagulation and hyperfibrinolysis
2. Site: left lower quadrant preferred - 2 finger breaths (3cm) cephalad and 2 finger breaths medial to the anterior superior iliac spine. Right lower quadrant is suboptimal in the setting of dilated caecum or an appendectomy but it is preferred in case of gross splenomegaly.
3. Aseptic technique
4. May infiltrate with 1% lignocaine
5. Insert needle (#19 or 21) and aspirate fluid or use commercial paracentesis set
6. Send for microscopy and C/ST (use blood culture bottle), white cell count (total and PMN), biochemistry (albumin and protein) for initial screening
7. Albumin infusion may not be necessary for a single paracentesis of less than 4-5L. On the other hand, for large volume paracentesis, consider albumin infusion of 8g/ litre after every 5L ascitic fluid removed

## PLEURAL ASPIRATION

1. Review latest CXR to confirm diagnosis, location and extent of effusion. (Pitfall: Be careful NOT to mistake bulla as pneumothorax or collapsed lung as effusion). Correct side marking is essential before procedure.
2. Patient position: A) 45° Semi-supine with hand behind head. Or B) Sitting up leaning over a table with padding
3. Use ultrasound guidance if available
4. Best aspiration site guided by percussion. Aseptic technique. Puncture lateral chest wall, preferably at safety triangle, along mid- or posterior axillary line immediately above a rib. (The “triangle of safety” is bordered anteriorly by the lateral edge of pectoralis major, laterally by the lateral edge of latissimus dorsi, inferiorly by the line of the fifth intercostal space and superiorly by the base of the axilla)
5. Anaesthetise all layers of thoracic wall down to pleura
6. Connect a fine-bore needle (21G)/angiocath to syringe for simple diagnostic tap. 3-way tap may be used if repeated aspiration is expected.
7. Avoid large bore needle.
8. Throughout procedure, avoid air entry into pleural space. (If 3-way tap is used, ensure proper sealing of all joints of the tap)
9. Withdraw 20-50 ml pleural fluid and send for LDH, protein, cell count & D/C, cytology (yield improves if larger volume sent), gram stain & C/ST, AFB smear & culture. Check fluid pH & Sugar (contained in fluoride tube) if infected fluid/empyema is suspected. Check concomitant serum protein and LDH
10. For therapeutic tap, connect 3-way tap (+/- connect to bed side bag) and aspirate slowly and repeatedly. Do not push any aspirated content back into pleural cavity. DO NOT withdraw more than 1-1.5 L of pleural fluid per procedure to avoid re-expansion pulmonary oedema.
11. Take CXR and closely monitor patient to detect complications

### Complications

1. Commonest: Pneumothorax(2-15%), Procedure failure, Bleeding(haemothorax, haemoptysis), Pain, Visceral damage(liver and spleen)
2. Others: Re-expansion pulmonary oedema from too rapid removal of fluid, pleural infection/empyema, vagal shock, air embolism, seeding of mesothelioma (avoid biopsy if this is suspected)

## PLEURAL BIOPSY

### Contraindications:

1. Uncooperative patient
2. Significant coagulopathy

### Procedure: Correct side marking is essential before procedure.

1. Ensure there is pleural fluid before attempting biopsy. Assemble and check the Abrams needle before biopsy. A syringe may be connected to the end hole of Abrams needle.
2. Preparation as for *Steps 1 to 4 of Pleural Aspiration*  
(NB: If fluid cannot be aspirated with a needle at the time of anesthesia, do not attempt pleural biopsy)
3. After skin incision (should be made right above a rib), advance a CLOSED Abrams needle (with inner-most stylet *in situ*) through soft tissue and parietal pleura using a slightly rotary movement
4. Once the needle is in the pleural cavity, rotate the inner tube counter-clockwise to open biopsy notch (spherical knob of inner tube will click into position in the upper recess of the groove of the outer tube)  
(Aspiration of fluid by the connected syringe confirm pleural placement of the Abrams needle)
5. Apply lateral pressure on the notch against the chest wall anteriorly, posteriorly or downwards (but NOT upwards to avoid injuring the intercostal vessels and nerve) with a forefinger, at the same time slowly withdraw the needle till resistance is felt when the pleura is caught in the biopsy notch
6. Hold the needle firmly in this position and sharply twist the grip of inner tube clockwise to take the specimen
7. Repeat Steps 4 to 6 above in the remaining two directions, totally take at least 3 specimens if possible
8. Firmly apply a dressing to the wound and quickly remove the needle when the patient is exhaling
9. While an assistant presses on wound, remove stylet of needle, open inner tube and flush specimen(s) out with NS
10. If tapping is necessary, aspirate as for *Steps 5-8 of Pleural Aspiration*
11. Take CXR to detect complication(s)

**Complications:** As for *Pleural Aspiration*

## CHEST DRAIN INSERTION

**Correct side marking is essential before procedure.**

1. Preparation as for *Pleural Aspiration*. (Preferred patient position in BTS guideline: Semi-supine on the bed, slightly rotated, with arm on the side of the lesion behind his/her head to expose axillary area.)
2. Always check the number of rib space from sternal angle. Re-confirm insertion site by percussion, incise skin right above the rib at anterior or mid-axillary line in 5th or 6th intercostal space. (Alternate site: 2nd intercostal space, mid-clavicular line, is uncommonly used nowadays)
3. USG guidance is strongly recommended if available
4. Insertion site should be within the “safe triangle.” (A space bordered by anterior border of latissimus dorsi, lateral border of pectoralis major and a horizontal line superior to nipple or 5<sup>th</sup> intercostal space.)
5. Anaesthetise all layers of thoracic wall including pleura. (*Do not proceed if needle for anaesthesia cannot aspirate free gas/ fluid*).
6. Proceed with blunt dissection of intercostal muscle with artery forceps down to parietal pleura.
7. Preferred insertion method: Double-clamp outer end of Argyle drain (24 Fr to drain air/fluid, 28 Fr to drain blood/pus). Apply artery forceps in parallel with tip of drain. Breach pleura with finger. Insert drain tip, release forceps & use them to direct drain into place.
8. Alternate method: Insert Argyle drain with inner trocar. Withdraw trocar by 1 cm into drain immediately after puncturing pleura. Match every 1 cm advancement of drain with 1-2 cm trocar withdrawal. Double-clamp chest drain when trocar tip appears outside chest wall
9. Direct drain apically to drain air and basally to drain fluid
10. Attach chest drain to 2 cm underwater seal. Ensure fluid level swings with respiration and coughing.
11. Apply a skin suture over the wound and make a knot, leaving appropriate length on both sides. Form a 2 cm “sling” by tying another square knot 2 cm from previous knot. Tie the “sling” to the drain; make several knots using remaining threads to prevent slipping.
12. Apply dressing.
13. Take CXR to confirm tube position and detect complication(s)

**Complications:** As for *Pleural Aspiration*



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