# YLLSoM Seniors Teaching Initiative M3 Programmes AY14/15

## Case-Based Sessions

**Introduction**

**Summary of Cases**

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<td>24</td>
<td>13 year-old girl with bruises and pallor</td>
<td>111</td>
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</table>
INTRODUCTION

Each session will last around 3 – 4 hours and will cover 3 – 5 cases. Each case will revolve around a clinical stem and there will be various questions to tackle per case which will be used as a guide for discussion and development of clinical reasoning.

You are encouraged to read around the approach to those presenting symptoms and attempt the cases (which will be sent out at least 2 – 3 days prior to sessions) before coming! However, if you have no time to read, the cases can still serve as a revision.

Objectives

- Link basic science to clinical disciplines (physiology, anatomy, pathology to medicine, surgery, etc)
- To integrate the different clinical disciplines (e.g. General Surgery, Orthopaedic)
- To compare and contrast diseases - their presentation and management (even though they may the same presenting complaint)
- History / Physical Examination
  - Usage of schemata (algorithm) in History-Taking and Physical Examination
  - Learn to perform a focused physical examination (Hypothesis-driven)
- Basic understanding of probability concepts

Overall Schedule and Logistics for M3

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<th>Date</th>
<th>Time</th>
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<th>Venue</th>
<th>Facilitator</th>
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<td>07/3/15</td>
<td>9 am – 1 pm</td>
<td>M3 cases session 1</td>
<td>MD1: Level 9, Tutorial Room 1, 2, 4*</td>
<td>Nicholas (92326757)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Kennedy (91387657)</td>
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<td>Liang Sai (92384350)</td>
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<td>14/3/15</td>
<td>9 am – 1 pm</td>
<td>M3 cases session 2</td>
<td>MD6: 02-01G, 02-02A, 02-02B</td>
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<td>Joel Soon (96184907)</td>
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<td>Daniel Lim (97307915)</td>
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<td>21/3/15</td>
<td>9 am – 1 pm</td>
<td>M3 cases session 3</td>
<td>MD1: Level 9, Tutorial Room 1, 2, 4*</td>
<td>Eugene (98639207)</td>
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<td>Nigel (97351438)</td>
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<td>28/3/15</td>
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<td>M3 cases session 4</td>
<td>MD1: Level 9,</td>
<td>Eugene (98639207)</td>
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<tr>
<td>Date</td>
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<tr>
<td>25/4/15 Sat</td>
<td>9 am – 1 pm</td>
<td>M3 cases session 5</td>
<td>Nigel (97351438) Wilnard (91904805)</td>
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<td></td>
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<td></td>
<td>MD6: 01-02, 02-02A, 02-02B</td>
<td>Wilnard (91904805) Gilbert (96375331)</td>
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<td>Daniel Lim (97307915)</td>
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*The door to the Tutorial Rooms in MD 1 are locked in the weekends and require card access which only the Year 4s have. Please call the M4 facilitators so that they can open the door for you.

**Notes:**

- All of you will be split evenly between the 3 facilitators.
- Content can be adjusted based on your feedback and requests. We are happy to do additional sessions based on your needs. Please email us.
- Sessions will provide a basic & structured introduction, plus some tips and practice for familiarization. Do come even if you have no clue or have not read up.

All the best! If you have any feedback for the cases, please email Kennedy Ng at kennedy.ng@gmail.com.

Sincerely,

Your seniors (Medicine Class of 2016)*

Contributors (authors and facilitators) include:*

Nigel Fong, Wilnard Tan, Joel Soon, Daniel Lim, Kennedy Ng, Gilbert Soh, Nicholas Ngiam, Liang Sai, Eugene Gan
## SUMMARY OF CASES

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<th>Stem</th>
<th>Conditions / Diagnosis</th>
<th>Learning Point</th>
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• Diagnosis and Management of Small Bowel Obstruction  
• Diagnosis and Management of Cholecystitis |
| Case 2 | 55 year-old woman with blood in her stool | Colorectal cancer complicated by large bowel obstruction | • Approach to Lower Gastrointestinal Tract Bleeding  
• Diagnosis and Management of Colorectal Cancer |
| Case 3 | 45 year-old woman with black stools | Gastric cancer presenting with upper gastrointestinal bleed | • Approach to Upper Gastrointestinal Tract Bleeding  
• Diagnosis and Management of Gastric Cancer |
| Case 4 | 58 year-old man with jaundice | Pancreatic cancer presenting with obstructive jaundice | • Approach to Jaundice  
• Diagnosis and Management of Pancreatic Cancer |
| Case 5A | 2 day-old boy with jaundice | Physiological jaundice of newborn | • Approach to Neonatal Jaundice  
• Differentiating between physiological and Pathological Jaundice |
| Case 5B | 1 month-old boy with jaundice | Biliary atresia presenting with obstructive jaundice | • Approach to Neonatal Jaundice  
• Diagnosis and Management of Biliary Atresia |
| Case 6 | 8 year-old girl with abdominal pain | Diabetic ketoacidosis | • Approach to Abdominal Pain in Children  
• Diagnosis and Management of Diabetic Ketoacidosis |
| Case 7 | 65 year old gentleman with nausea and headache | Post-operative hyponatremia | • Approach to hyponatremia  
• Treatment of hyponatremia |
| Case 8 | 25 year-old gentleman with generalized weakness | Thyrotoxic Periodic Paralysis | • Approach to hyperkalemia and hypokalemia |
| Case 9 | 60 year-old gentleman with shortness of breath | Chronic Obstructive Pulmonary Disease complicated by Type 2 Respiratory Failure | • Interpreting arterial blood gas  
• Management of COPD exacerbation |
| Case 10 | 78 year-old female who presents with functional decline, delirium and fever | Pyelonephritis complicated by Septic Shock | • Recognizing atypical presentations of diseases  
• Septic and hypovolemic shock  
• Principles of management in sepsis and hypovolemic shock |
| Case 11 | 70 year-old gentleman with | Hospital-acquired Pneumonia | • Approach to fever in a post-operative patient |
| Case 12 | 50 year-old woman with joint pain | Rheumatoid Arthritis | • Approach to polyarthritis  
• Diagnosis and Treatment of Rheumatoid Arthritis  
• Principles in the usage of Diagnostic Criteria (Sensitivity and Specificity) |
| Case 13 | 52 year-old gentleman with joint pain | Gout | • Approach to Monoarthritis  
• Diagnosis and Treatment of Gout |
| Case 14 | 54 year-old woman with back pain | Metastatic Cancer to Vertebrae | Application of basic science to develop a mechanistic understanding of clinical problems  
• Understanding the mechanisms behind ‘pain’  
• Correlating an etiology to clinical presentation via a pathophysiological explanation. |
| Case 15 | 32 year-old woman with obesity | Cushing’s Disease | • Approach to Obesity  
• Diagnostic Workup of Cushing’s Syndrome |
| Case 16 | 85 year-old gentleman who presented with a fall | Head injury secondary to fall complicated by epidural hematoma | • Approach to Weakness  
• Approach to Falls  
• Management Principles of raised intracranial pressure |
| Case 17 | 65 year-old Chinese gentleman with weakness and numbness of his left arm and both legs | Cervical myelopathy secondary to cervical spondylosis | • Approach to weakness with sensory loss  
• Approach to spinal pathologies  
• Management of cervical spondylosis |
| Case 18 | 13 month-old girl with an episode of abnormal jerking of her limbs. | Febrile seizure | • Approach to seizure in children  
• Differentiating benign and pathological etiologies of seizures  
• Emergent management of seizure |
| Case 19 | 70 year-old Malay gentleman with a change in personality | Dementia with lewy body Onset of delirium after surgery complicated by neuroleptic malignant syndrome (secondary to administration of antipsychotics) | • Approach to personality / behavioural changes (dementia)  
  o Reversible etiologies  
  o Non-reversible etiologies  
• Approach to delirium (altered mental state)  
• Management of neuroleptic malignant syndrome |
| Case 20 | 50 year-old Chinese gentleman with | Neurosyphilis | • Approach to forgetfulness  
• Management of syphilis |
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<th>Treatment</th>
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<td>Severe Dengue Fever leading to Acute Kidney Injury (pre-renal)</td>
<td>• Approach to Acute Kidney Injury&lt;br&gt;• Diagnosis and Management of Severe Dengue Fever</td>
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<td>Acute Myocardial Infarction&lt;br&gt;Acute Pulmonary Embolism</td>
<td>• Approach to Chest Pain&lt;br&gt;• Diagnosis and Management of Acute Myocardial Infarction&lt;br&gt;• Diagnosis and Management of Pulmonary Embolism</td>
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<td>Case 24</td>
<td>13 year-old girl with bruises and pallor</td>
<td>Von Willebrand Disease</td>
<td>• Approach to abnormal bleeding&lt;br&gt;• Diagnosis and Management of Von Willebrand Disease</td>
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CASE 1: 40 YEAR-OLD MAN WITH ABDOMINAL PAIN

Mrs Lee is a 40 year old lady who is mildly obese. She presents to the A&E with a fever and a 2-day history of pain in the RHC that is worsening. There is no jaundice, but the pain radiates to the right tip of scapula. Prior to this she has had intermittent episodes of sharp but milder RHC pain associated with meals but they often relieve after a while.

Q1 What is the most likely diagnosis and what are the possible differentials for Mrs Lee?

- Acute cholecystitis
- Relating to the HPB system: biliary colic, choledocholithiasis, cholangitis
- Perforated peptic ulcer
- Acute peptic ulcer exacerbation
- Amoebic liver abscess
- Acute amoebic liver colitis
- Acute pancreatitis
- Acute intestinal obstruction
- Renal colic
- Acute retro-colic appendicitis

It would be useful to consider why the other possibilities are less likely. Discuss with the participants.

Q2 What further history would you ask Mrs Lee?

- Nature, pattern and severity of pain
- Consider cholecystitis: establish risk factors, history of gallstones, etc.
- Rule out the other differentials: e.g. jaundice, stool colour, urine colour, other medical and surgical history
- Constitutional symptoms
- Complications of cholescystitis

She did not have jaundice, but the pain radiates to the right tip of scapula. Prior to this she has had intermittent episodes of sharp but milder RHC pain associated with meals but they often relieve after a while. She had no significant Past Medical History or Surgical History. She was not on long term drug intake and had no drug allergies.

Q3 What would you elicit in physical examination

- Check vital signs (make sure patient is stable, not in shock)
- Check for jaundice and pallor
- Rule out an acute abdomen (no board like rigidity, etc.)
- Tenderness at RHC
- Feel for masses/palpable gallbladder
- Try to elicit Murphy’s sign
- Digital Rectal Examination to make sure there is no pale stools

Q4 What are some investigations you would want to order? Name 5 and explain your choice.

- Laboratory
  - Full Blood Count
  - Liver Function Test
  - Renal Panel
• Imaging
  o Ultrasound
  o Abdominal X-ray / Chest X-ray
  o Computed Tomography Scans

An HBS ultrasound was done for Mrs Lee, and this is what it shows:

Q5 Describe what you see on the ultrasound. What other sign would you elicit during this examination?

• Thickened GB wall
• Gall stones seen
• Pericholecystic fluid
• Would try to elicit the sonographic Murphy’s sign

Q6 How would you manage this patient? What are the complications of the condition?

• NBM, bowel rest or low fat diet if possible
• IV fluids
• IV Analgesia
• Anti-pyretics
• Early Laparoscopic Cholecystectomy (Within 7 days of symptoms) or Interval Cholecystectomy (>6 weeks after resolution of symptoms)*
  o Evidence suggests early laparoscopic may be equally effective and safe as compared to delayed
  o In the past, surgeons felt that it was dangerous to operate when the entire gallbladder is inflamed
• Emergency cholecystectomy needed if complications such as
  o Gangrene (tissue death) from GB hydrops; if infected, GB empyema
  o Perforation (a hole that forms in the wall of the gallbladder)
  o Severe haemorrhagic pancreatitis
  o Persistent bile duct blockage
  o Inflammation of the common bile duct

*Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR. Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg. 2010 Feb;97(2):141-50. “This systematic review with meta-analysis of RCTs found no significant difference in complication or conversion rates whether laparoscopic cholecystectomy had been performed at presentation with acute cholecystitis or 6–12 weeks after the symptoms had settled. The early strategy had the advantage of decreased hospital stay and avoided the risk of emergency surgery for non-resolved or recurrent symptoms with a high rate of conversion to open cholecystectomy. Open cholecystectomy is associated with an increase in morbidity, pain and time to return to work.”

Q7 What is the pathogenesis of gallstones?

• Pure stones (cholesterol or Ca bilirubinate of CaCO3, or can be mixed or combined) radiolucent unless it is mixed with Ca content.
• Cholesterol stones: increase with age, female sex hormones, oral contraception and pregnancy; obesity, inborn disorders of bile acid metabolism, and hyperlipidemia. They form as a result of supersaturation of the cholesterols in the gall bladder.
• Pigment stones: haemolytic anemia, biliary infection like ascaris or liver flukes
Mdm Lim was feeling much better after 3 days and was discharged. However she came back into the A&E 2 days later complaining of severe abdominal pain, with bloating, vomiting and constipation. This is her supine AXR.

Q8 Describe the AXR. What is the cause of her of presentation?

- Multiple air-fluid levels, supine AXR
- Note the stack of coins, indicative of SBO (differentiate from large bowel)
- Pneumobilia
- Given the history, the most likely cause is gallstone ileus.

Q9 How else may gallstones present in a patient like Mrs Lee?

- Asymptomatic (manage expectantly unless immunocompromised or chronic hemolysis) symptomatic sequelae include biliary colic,
- Acute cholecystitis,
- Mirizzi with OJ,
- Mucocele/empyema gall bladder,
- Choledocholithiasis with OJ,
- Ascending cholangitis,
- Pancreatitis,
- Fistula/gallstone ileus.

Q10 If a stone had been found in Mrs Lee’s common bile duct, what are some of the strategies to remove it?

- ERCP (therapeutic as well) can do stone removal with basket, sphincterotomy or stenting. But has high level of complications: pancreatitis, cholangitis, perforation of bile duct into duodenum.
• PTC (percutaneous transhepatic cholangiography) if stone cannot be removed from below.
• Failure of which would then require CBD Exploration and placement of Biliary T-tube; removal is with stone grasping forceps, flushing or dredging with baskets; T-tube used to prevent leakage as CBD will swell and take a while to heal (‘pressure release valve’).
CASE 2: 55 YEAR-OLD GENTLEMAN WITH BLOOD IN HIS STOOL

Mr Tan is a 55yo Chinese man who comes into your GP clinic saying that he has been feeling more tired lately, complaining that he gets breathless after climbing two flights of stairs over the past 3 months. He has lost 10kg in the last month and has poor appetite. He has no previous history of hypertension, diabetes, hyperlipidemia or heart disease. He also notes that his stools are smaller in calibre and is intermittently mixed with fresh red blood.

Q1 What are the differentials for Mr Tan’s condition?

- This is LBGIT, so causes of bleeding should be from anatomical causes distal to the ligament of treitz. Though an exception may be made for a torrential UBGIT, it is not applicable in this case because of the chronic history.
- We can divide causes anatomically and use large headings to help generate differentials:

<table>
<thead>
<tr>
<th>Anatomical location</th>
<th>Inflammation/Infection</th>
<th>Tumour</th>
<th>Vessels</th>
<th>Trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small intestines</td>
<td>Terminal ileitis (Salmonella or Crohn’s disease, jejunitis)</td>
<td>SI tumours (rare)</td>
<td>AV malformations</td>
<td>Any previous surgery? Any recent significant trauma? Bleeding tendency?</td>
</tr>
<tr>
<td>Colon</td>
<td>Ulcerative colitis, Colitis (Shigella, E coli, pseudomembranous, entamoeba histolytica)</td>
<td>Colon cancer (left-sided or right sided) Polyps</td>
<td>Angiodysplasia Diverticular disease Ischemic colitis</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>Solitary rectal ulcer Proctitis (usually an STD)</td>
<td>Rectal cancers Rectal Polyps</td>
<td>Haemorrhoids Rectal Varices</td>
<td></td>
</tr>
<tr>
<td>Anus</td>
<td>Anal cancers</td>
<td></td>
<td></td>
<td>Anal fissures</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
<td>Aorto-enteric fistula (rare and catastrophic)</td>
</tr>
</tbody>
</table>

Q2 What are some other important aspects in history and physical examination?

History

- How much blood: how often? Stains the toilet bowl, or only on toilet paper?
- Symptoms of anaemia
- Associated symptoms to consider specific etiologies as listed above (e.g. history of chronic constipation predisposes formation of haemorrhoids; travel history might suggest chronic traveller’s diarrhoea)
- Constitutional symptoms

Physical examination

- Vital signs
- Abdominal examination (masses, tenderness, etc) – to look for etiology and TRO complications like bowel perforation causing acute abdomen.
- CVS exam targeted at looking for signs of anaemia (tachycardia, collapsing pulse, conjunctival pallor, ESM)
- Digital rectal examination and proctoscopy (low-lying rectal masses, haemorrhoids, solitary rectal ulcer, anal fissures, anal cancers, confirms blood in stools
He has lost 10kg in the last month and has poor appetite. He has no previous history of hypertension, diabetes, hyperlipidemia or heart disease. Mr Tan’s vitals are stable. On physical examination you note Mr Tan to be slightly pale, but the rest of the examination is otherwise unremarkable. DRE and proctoscopy show an empty rectum with brown stools. Mr Tan’s vitals are stable. On physical examination you note Mr Tan to be slightly pale, but the rest of the examination is otherwise unremarkable. DRE and proctoscopy show an empty rectum with brown stools.

Q3 What are some investigations you would want to order? Name 5 and explain your choice.

- **Laboratory**
  - Full Blood Count
  - Renal Panel
  - Liver Function Test
  - PT/PTT/INR
  - GXM
  - Cardiac Enzyme
- **Imaging**
  - Abdominal X-ray
  - CT Abdomen / Pelvis
- **Others**
  - Colonoscopy
  - Electrocardiogram

You are still worried and do some blood tests for Mr Tan. The results are as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>7.6</td>
</tr>
<tr>
<td>Plt</td>
<td>253</td>
</tr>
<tr>
<td>TW</td>
<td>170</td>
</tr>
<tr>
<td>MCV</td>
<td>70</td>
</tr>
<tr>
<td>Hct</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Renal panel and liver function tests were otherwise normal.

**Q5 How would you interpret the full blood count?**

- Microcytic anemia, likely iron deficient, which suggests chronic blood loss. Note that hematocrit is low, suggesting renal compensation for plasma volume.
- This result is worrying given Mr Tan’s age group and presenting complaint. Unexplained anaemia is suspicious of malignancy and Mr Tan should be referred for further work-up.

Mr Tan was arranged to see a general surgeon, who then advised him to go for colonoscopy to evaluate the cause of his anemia.

**Q6 What could be the possible reasons if nothing was found on colonoscopy?**

- Poor bowel preparation (stool obscures the surgeon’s view)
- Inadequate air sufflation or missed lesions
- Obsolete bleed (from the small intestine)
Q7 A large mass was seen in the sigmoid colon, which prevented the scope from going beyond the lesion. The rest of the bowel could not be evaluated, but a biopsy of the lesion was taken. What would you expect the lesion be histologically? What is its pathogenesis?

- Adenocarcinoma
  - Adenoma-Carcinoma sequence (APC suppressor gene, failure to break down beta-catenin which accumulates to active MYC and cyclin D1, K-ras mutation and loss of tumour suppressors at p53 and 18q21) → shows a progression from localised epithelial proliferation to small adenoma to large dysplastic adenoma to Carcinoma-in-situ to invasive cancer.
  - Alternative pathway is microsatellite instability (DNA mismatch repair) involving MSH2, MLH1, etc. And this does not correlate with adenoma formation, but has a better prognosis than APC pathway tumours.
  - Grossly, left-sided tumours tend to be obstructive, “apple core/napkin ring” circumferential lesions and often presents with constipation and bleeding. Right sided tumours tend to be polypoid and exophytic (more space to grow) and present with unexplained anaemia rather than constipation.
The surgeon then carried out the necessary investigations and imaging to stage the tumour and planned for an operation to be carried out for Mr Tan next week. However, Mr Tan into the A&E 3 days later complaining of abdominal pain, bloating, vomiting and constipation. He has not passed flatus in the last day. His supine AXR is as follows

Q8 Describe this AXR. What is the diagnosis, what are its complications and discuss the emergent management of this condition?

AXR

- AXR is supine so air fluid levels can be seen (not the best XR to show this)
- Note the differences between large and small intestines and recognise this to be a large bowel obstruction
- No gas in the sigmoid colon might indicate that it is the level of obstruction
- Rectal gas suggests that the obstruction is incomplete
- This is a closed-loop obstruction (suggesting the ileo-caecal valve is competent)
- There is a risk of complications such as bowel perforation, peritonitis from translocation of bacteria across gut wall, resulting in septic shock

Management

Mr Tan should be treated for IO:

- Urgent Surgical Consult
- NBM
- IV fluids
- NG-tube decompression (“Drip and suck”)
- Prophylactic antibiotics
- Decompression
Emergency Surgery: Transverse Loop Colostomy or Primary Resection with End Colostomy

Endoscopic Stenting

Fortunately, Mr Tan survived the acute event. He eventually had a Hartmann’s procedure which removed his tumour completely. Mr Tan is still worried about his cancer coming back, and also notes that his family has a strong history of colon cancer and is very worried, wondering if he has passed on these “bad genes” to his children.

Q9 What can be done for surveillance in Mr Tan’s case for cancer recurrence?

• There are many different guidelines out there from Professional Groups.
  o Main modalities are the same, but timings may be slight different
Q10 What are some of the risk factors for colorectal cancer and what advise can you give Mr Tan and his children?

- Genetic syndromes: Genetic syndromes include FAP (yearly colonoscopy recommended) and its variants like Gardner (+ sebaceous cysts) and Turcot’s syndromes; other polyposis syndromes like Peutz jegher’s (hamartomatous, juvenile polyps) have smaller increased malignant potential. HNPCC (3 yearly colonoscopy) is non polyposis but is more common than FAP, accounting for 8% of cancers.
• AMSTERDAM CRITERIA for HNPCC 3,2,1: >3 family members from same side with CRC or HNPCC related cancer, one of which is 1st degree relative of the other 2; 2 successive generations and 1 of the CRC before age 50; FAP is excluded.

• Other non-modifiable risk factors: Age, male gender, family history, personal history

• Modifiable risk factors: NSAIDs are protective, UC (start screening 10 years after UC), adenomatous polyps, environment (diet: obesity, red meat, nitrosamines, low fibre, vitamins/mineral deficiency), smoking

• SCREENING is via early FOBT after 50 yo (or 10 years before first CRC in family); or colonoscopy every 5-10 years
CASE 3: 45 YEAR-OLD WOMAN WITH BLACK STOOLS

Mdm Lim is a 45yo Chinese lady. She is a chronic smoker of 20 pack years and presents to the gastroenterologist because of sticky and foul smelling black stools for the last month. She has no known history of liver disease, and is not on any long-term medications but was recently started on a pain-killer for her knee pain in the last 2 months. She has no other complaints except an occasional feeling of bloatedness and notes that she has been eating less lately.

Q1 What are the differentials for Mdm Lim’s black stools?

- One might consider iron supplements, bismuth (or even squid ink!) but not in this case as the question states that she is “not on any long-term medications”.
- Malaena is likely due to UBGIT and anatomical lesions proximal to the ligament of treitz may be considered.

<table>
<thead>
<tr>
<th>Anatomical location</th>
<th>Inflammation/Infection</th>
<th>Tumour</th>
<th>Vessels</th>
<th>Trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth/Oral cavity</td>
<td>Oral/dental infections (Rarely present with malaena)</td>
<td>Oral cavity tumours</td>
<td>Hereditary haemorrhagic telangiectasia (rare)</td>
<td></td>
</tr>
<tr>
<td>Oesophagus</td>
<td>Oesophagitis</td>
<td>Oesophageal Cancer</td>
<td>Oesophageal varices</td>
<td>Boerhaave syndrome (alcoholics, severe vomiting) Mallory-weiss tear</td>
</tr>
<tr>
<td></td>
<td>Reflux oesophagitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>Gastric ulcer</td>
<td>Gastric cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastritis</td>
<td>Gastric polyp</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute gastric erosions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenum</td>
<td>Duodenal ulcer</td>
<td>Tumor in the small intestines (rare)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duodenitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Meckel’s diverticulum (though not in the UGI, may produce the HCl needed to cause malaena)</td>
<td>NPC (atypical presentation)</td>
<td>Epistaxis (atypical presentation) Aorto-oesophageal fistula (rare)</td>
<td>Consider bleeding tendencies or acute trauma damaging structures</td>
</tr>
</tbody>
</table>
The gastroenterologist is concerned and decides to do an OGD for Mdm Tan. This lesion near the antrum is what he sees on the scope, and he takes a biopsy.

Q2 Describe the image. What is the diagnosis and pathogenesis of this lesion? What will the biopsy of the lesion show?

- Haemorrhage, describe punched edges, slough at the base characteristic of a peptic ulcer. Penetrates muscularis mucosae and may even perforate; with ruggae pulling towards it.
- May be useful to know Forrest classification
- Caused by H. Pylori, NSAIDs and other factors like smoking, alcohol, steroids/anticoagulants (not increased risk of ulcer formation, but risk of bleeding from existing ulcer). This is due to imbalance in protective and damaging factors that damage gastric mucosa. Protective factors include the mucus layer, epithelial layer, prostaglandins, etc; damaging factors include acid production, smoking, alcohol, drugs, etc.
- May present incidentally on OGD, with dyspepsia (ulcer like (upper abdominal pain), dysmotility like (bloating), or unspecified (worse when eating if gastric, better when eating when duodenal)), bleed or perforation (acute abdomen).
- On histopathology, there are 4 layers seen. (1) layers of necrotic debris, (2) non-specific acute inflammation, (3) granulation tissue, (4) fibrosis. This is chronic inflammation and healing.

Q3 Mdm Lim tests positive for H pylori. How would you manage her condition?

- Gastroprotection with PPI (20mg OM) or antacids
- H pylori eradication (triple therapy: amoxicillin, clarithromycin, PPI; or metronidazole if allergic to penicillin).
- Confirm eradication by endoscopy with CLO or urea breath test
- Gastric ulcers must be re-soped to document healing in 6 weeks as need to exclude malignancy.
However, Mdm Lim felt better and defaulted her follow-up with the gastroenterologist. 3 years later, Mdm Lim presents to the A&E complaining of severe projectile vomiting. She vomits everything that she eats and has not passed stools in the last 2 days. The vomitus is undigested food, mixed with some blood. This is a clinical picture of Mdm Lim:

Q4 What is the diagnosis? What are the possible causes in this case, and what other physical signs can you elicit?

- Gastric outlet obstruction
- May be due to pyloric stenosis from chronic peptic ulcer, or malignant change, where a tumour in the pyloric antrum can obstruct it.
- Other clinical signs may include succussion splash, or to observe for visible peristalsis. May also look for Virchow’s node if it is a gastric cancer.

The doctor in the A&E urgently does an arterial blood gas for Mdm Lim. The results are as follows:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.51</td>
</tr>
<tr>
<td>pO2</td>
<td>100mmHg</td>
</tr>
<tr>
<td>pCO2</td>
<td>50mmHg</td>
</tr>
<tr>
<td>HCO3</td>
<td>30</td>
</tr>
<tr>
<td>Na</td>
<td>130</td>
</tr>
<tr>
<td>K</td>
<td>3.0</td>
</tr>
<tr>
<td>Cl</td>
<td>83</td>
</tr>
</tbody>
</table>

Her urine dipstick also showed that her urine was acidic.

Q5 How would you describe Mdm Lim’s test results? What is the pathophysiology?

- Hypokalemic, hypochloremic, hyponatremic metabolic alkalosis (with some respiratory compensation) with paradoxical aciduria
• The renal physiology to account for this complication is complex but can be simply understood that gastric juices contain HCl. With prolonged vomiting, H+ and Cl- is lost and thus accounts for the alkalosis and hypochloremia.

• The loss of fluid contracts the ECF and further causes contraction alkalosis at the level of the renal tubules and thus further worsens the alkalosis. With the RAAS working to retain plasma volume, there is hypokalemia, (Na exchanged for K). With increased bicarbonate regeneration and reclamation from the tubular lumen, there is “paradoxical” aciduria.

• Activation of ADH because of volume depletion reclaims water without the Na and can result in the hyponatremia.

Mdm Lim then had another OGD done to investigate the condition. It was found that she had a malignancy at the pylorus.

Q6 What is the most likely histological diagnosis? What are the other possibilities?

• Adenocarcinoma

• It may be the Intestinal type (more common, occurs in high risk population, a/w erbB2 and erbB3 receptor stimulation) or diffuse type (linitis plastica, worse prognosis, in low risk population a/w K-sam oncogene).

• Non adenocarcinomas can be SCC, neuroendocrine, leiomyosarcoma, GIST, MALT lymphoma.

Q7 How can this cancer spread? What are the associated clinical signs?

• Spread of cancer can be by direct invasion – may perforate and give acute abdomen

• Lymphatic spread to regional nodes, umbilical (sister joseph node) or supraclavicular node (virchow’s node, troisier’s sign) – these nodes are palpable

• Haematogenous spread (Liver lung bone brain) – assess these organs for signs

• Peritoneal seeding (e.g. to ovaries (krukenberg’s tumour), pouch of douglas (blumer’s shelf, noted on PR exam)

Mdm Lim does not understand how she can have cancer. She wants to better understand her condition, and to explain it to her children as well so they do not end up in the same situation as her.

Q8 What are some of the risk factors for gastric cancer?

• Diet (preserved food, polycyclic hydrocarbons),

• Smoking

• Alcohol

• Occupational exposure to asbestos, heavy metals, rubber;

• Low socioeconomic status;

• Genetic factors include blood type A, HNPCC Lynch II, p53 mutation, germline E-cadherin mutation

• Family history

• Other high-risk conditions:
  o partial gastrectomy for benign disease (especially bilroth II because of biliary reflux),
  o gastric polyps (highest risk if inflammatory polyp vs adenomatous or villous);
  o chronic atrophic gastritis like pernicious anemia
• hypertrophic gastritis (Menetrier’s disease, inflammation of gastric epithelium),
• PUD (<1% risk), H. Pylori infection (3-6x added risk)

Q9 What are some surgical options to manage Mdm Lim?

• Surgery involves wide resection of tumour to negative margins (at least 6cm) and en-bloc resection of regional lymph nodes. Total or subtotal gastrectomy is done, with reconstruction (1) Bilroth I: end-to-end gastroduodenostomy: rarely done as duodenum is difficult to mobilise up to residual stomach (2) Bilroth II: gastrojejunostomy – no protection against biliary reflux but less change of leak. (3) Roux-en-Y which prevents biliary reflux, involves 2 anastomoses so higher chance of leak.
• Neoadjuvant or adjuvant chemotherapy with 5-FU, etc.
• Late presentations may require palliation. endoscopic laser ablation for obstruction, embolisation for bleeding, etc.

Q10 Describe some surgical complications of the operation?

• Bleeding, infection,
• anastomotic leak, biliary reflux,
• early satiety,
• dumping syndromes (early: due to increased osmotic load (so has bloating, vomiting); late dumping: due to reactive hyperinsulinemia and hypoglycaemia, so has dizziness/sweating);
• Afferent limb syndrome (mechanical kinking/obstruction of afferent jejuna loop);
• nutritional deficiency (intrinsic factor, less iron absorption as less Fe+++ to Fe++ via gastric acid) – Fe deficiency/B12 anaemia.
CASE 4: 58 YEAR-OLD GENTLEMAN WITH JAUNDICE

Ahmad is a 58 years old Malay gentleman who presents with jaundice of 2 weeks’ duration.

Q1) Describe the pre-hepatic, hepatic and post-hepatic causes of jaundice. Name 4 per categories.

- **Pre-Hepatic (Unconjugated Hyperbilirubinemia)**
  - Intrinsic hemolytic anemia
  - Hemoglobinopathies (e.g. Thalassemia)
  - Membranopathies (e.g. Hereditary Spherocytosis)
  - Enzyme deficiency (e.g. G6PD deficiencies)
  - Extrinsic hemolytic anemia
  - Autoimmune (e.g. Evan’s syndrome, Lupus)
  - Disseminated intravascular coagulopathy
  - Infections (e.g. Malaria)

- **Hepatic (Unconjugated Hyperbilirubinemia)**
  - Inability of liver to conjugate bilirubin – Crigler-Najjar, Gilbert’s syndrome

- **Hepatic (Cholestasis)**
  - Infections – Hepatitis virus, CMV, EBV
  - Autoimmune hepatitis
  - Metabolic – Non-alcoholic steatohepatitis, Fatty liver disease, Hemochromatosis, Wilson’s disease
  - Neoplasms
  - Drugs – OCP, Chlorpromazine, Penicillin
  - Inability of liver to excrete conjugate bilirubin – Rotor syndrome, Dubin-Johnson syndrome

- **Obstructive**
  - Intra-luminal
    - Stones
    - Bile slough
    - Parasites
  - Intra-mural
    - Cholangitis
    - Neoplasms
    - Strictures formation
    - Primary Sclerosing Cholangitis
    - Primary Biliary Cirrhosis
  - Extra-mural
    - Neoplasms
    - Pseudocyst

Q2) How would you take a history of this man? Describe 10 questions.

- Obstructive versus non-obstructive
- Pre-hepatic causes –
  - Symptoms of anemia
  - Family history/Past medical history
  - Episodic?
- Hepatic causes –
  - Infections
  - Risk factors
  - Symptoms – Fever, RHQ pain, diarrhea, sudden onset
  - Alcohol consumption/Lifestyle
He describes having tea-coloured urine and loss of weight over the last 1 month of 5kg. He does not have fever, abdominal pain.

Q3) What would you look for in the physical examination?

• Signs of jaundice – sclera icterus, jaundiced skin, scratch marks
• Signs pointing to etiology
  o Peripheries – Stigmata of chronic liver disease, duptyren contracture and parotidomegaly, xanthelesma, conjunctiva pallor, lymph nodes, needle track and tattoo
  o Abdomen – Presence of hepat- or splenomegaly, masses or ascites
• Signs pointing to complications
  o Purpura – Coagulopathy
  o Consciousness level – Encephalopathy
  o Ascites and pedal edema – Third spacing

Q4) What is Courvoisier’s law?

• States that in the presence of an enlarged gallbladder which is nontender and accompanied with mild jaundice, the cause is unlikely to be gallstones.
• Exceptions?
  o The exceptions to the law are stones that dislodge and acutely jam the duct distally to the hepatic/cystic duct junction:
    o Gallstone falling and blocking the Ampulla of Vater
    o Gallstone falling and blocking the cystic/hepatic duct junction
    o Mirizzi’s syndrome

On physical examination, the patient appears jaundiced and has sclera icterus. The gall bladder is palpable and is not tender. No other masses or organomegaly.

Q5) Name 5 differentials and your reasoning.

Malignancies are the top on the list of differentials.

• Pancreatic Adenocarcinoma
• Ampullary Adenocarcinoma
• Cholangiocarcinoma
• Gall Bladder Cancer

Others

• Mirizzi’s syndrome
Primary Sclerosing Cholangitis

Q6) How would you investigate? Name 5 investigations and your reasoning.

• Bloods
  o Full Blood Count
  o Liver Function Test
  o Prothrombin/Partial Thromboplastin Time
  o Renal Panel

• Imaging
  o U/S Hepatobiliary System
  o CT Abdomen Pelvis
  o Magnetic Resonance Cholangiopancreatography

• Procedure
  o Endoscopic Ultrasound or Endoscopic Retrograde Cholangiopancreatography

The Liver Function Test reveals the following:

Total Bilirubin – 150 umol/L
Conjugated – 130 umol/L
ALP – 480 U/L
ALT – 70 U/L
AST – 80 U/L
Albumin – 28 g/L
The Computed Tomography shows the following images.

Q7) Describe and interpret the images. What is your likely diagnosis?

- Focal hypoattenuating mass at the head of pancreas with atrophy of distal gland
- Dilated biliary tree
- Pancreatic adenocarcinoma

An Endoscopic Ultrasound Guided (EUS) Fine needle aspiration cytology is done and the patient is diagnosed with Pancreatic Adenocarcinoma with hepatic metastasis.

Q8) What are the treatment options available for this patient? Describe 3 options.

- Surgical bypass – Triple Bypass
  - Hepatico- or Choledocho-jejunostomy
  - Gastrojejunostomy
  - Jeju-jejunostomy
- Endoscopic
  - Biliary Stenting
  - Duodenal Stenting
  - Combination

The patient decides for ERCP insertion of biliary stent.

Q10) How will you prepare this patient for the procedure?

- Nil-by-mouth, Maintenance Fluids
• IV Antibiotics (Ceftriaxone and Metronidazole)
• Group Crossed Match and Standby Platelet / Fresh Frozen Plasma (if patient has thrombocytopenia or impaired clotting)
• Correct impaired coagulation if needed

Q11) What are the complications of this procedure? Describe 5 and the steps you would take to manage these complications.

• Complications related to sedation
  o Hypoventilation due to oversedation
  o Allergic reaction to sedative
• Complications related to procedure
  o Post-procedure Pancreatitis
  o Cholangitis
  o Biliary Duct Perforation
  o Bleeding
CASE 5A: 2 DAY-OLD BOY WITH JAUNDICE

Huang Huang is 2 days old and his mother is worried because he is becoming increasing yellow.

The serum bilirubin was analyzed and revealed the following:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bilirubin</td>
<td>150μmol/L</td>
</tr>
<tr>
<td>Conjugated Bilirubin</td>
<td>9μmol/L</td>
</tr>
<tr>
<td>Unconjugated</td>
<td>141μmol/L</td>
</tr>
</tbody>
</table>

Q1) What is the pattern of hyperbilirubinemia? What are the possible etiologies? Name 6.
Discussion Point: Jaundice in Children versus Adults
• There is physiological jaundice.
• Neonates are more susceptible to kernicterus.
• Etiologies are slightly different.
  o Congenital, hemolytic anemia, in-born error of metabolism are more common in children
  o Malignancy, stones and liver cirrhosis (all the various causes) are more common in adults

Discussion Point: Physiological versus Pathological

• Physiological
  o Commonest cause of jaundice in the first week of life
  o Onset usually on the 2nd day, Peaks at 5th, Resolves by 10th day
  o Levels usually <12mg/dl (205umol/L)
  o Baby is well otherwise (diagnosis of exclusion)
  o No treatment is required
  o Cause – Increase in RBC amount, shortened RBC lifespan, Immature hepatic uptake and conjugation, increase in enterohepatic circulation
• Pathological
  o 1st 24 hours, >2 weeks of duration
  o Rapidly rising (>85 umol/L per day) or TSB > 300 umol/L
  o Any levels of Conjugated Hyperbilirubinemia

Q2) How will you evaluate this child – history and physical examination?

• History
  o Family history of severe neonatal jaundice
  o Maternal illness during pregnancy (e.g. gestational diabetes, maternal flu-like symptoms/rash) – Children of mothers with gestational diabetes have higher risk of neonatal jaundice
  o Mother and child’s blood groups
  o Birth injuries (cephalhematoma, bruising)
  o Gestational age, birth weight, Cord G6PD and thyroid status
  o Feeding, voiding, and stool pattern
  o Growth and weight-gain
  o General appearance and well-being

• Physical Examination
  o Confirmation of jaundice and severity
  o Signs of Complications
    ▪ Kernicterus – Abnormal tone and posturing, lethargy
  o Etiologies
    ▪ Evidence of neonatal sepsis and source of infection – omphalitis
    ▪ Extra-vascular blood: Cephalohematoma, bruising
    ▪ Hemolysis: Pallor, splenomegaly
    ▪ Intrauterine infection: Petechiae, growth retardation, microcephaly, hepatosplenomegaly
    ▪ Dysmorphisms: Triangular facies
    ▪ CVS abnormalities

Q3) What are the investigations you will order?

  o Severity
    o Serum bilirubin
    o Transcutaneous bilirubin
Etiology
  - Hemoglobin and reticulocyte count, Blood film
  - Blood group and Rh
  - Coomb’s test
  - G6PD and Cord TSH

Q4) What is the likely diagnosis in this patient?
  - Jaundice in the first week, Consider these:
    - Physiological
    - Breast milk Jaundice
    - Breast non-feeding jaundice (dehydration)
    - Other pathological causes
CASE 5B: 1 MONTH-OLD BOY WITH JAUNDICE

Heng Ya Low is a 1 month old boy who is in hospital for evaluation due to jaundice.

Q1) How will you take a history in this patient?
See above.

History revealed that the child had pale stools and dark urine. He was feeding well on breast milk, and thriving (gained about 1kg). He was born full term, 3 kg via normal vaginal delivery. No significant antenatal history. Cord TSH and G6PD status were normal. No previous history of jaundice in his siblings.

He had no fever, lethargy, irritability or smelly urine.

Q2) What is the likely pattern of hyperbilirubinemia? What are your differentials? Name 6.

Q3) What will you look out for in the physical examination?
See above

Q4) How will you investigate?
- If you suspect cholestasis…
- Biochemical and Blood tests
  - Urine C/S + Dipstick
  - FBC
  - Liver Function Test
Gamma-glutamyltransferase
- PT/PTT
- Metabolic screens (serum amino acids, etc)
- Imaging
  - Biliary ultrasound
  - Hepatobiliary imino-diacetic acid scan (HIDA)

Investigations showed:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total/Conjugated/Unconjugated</td>
<td>180/155/25 umol/L</td>
</tr>
<tr>
<td>ALP</td>
<td>755 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>70 U/L</td>
</tr>
<tr>
<td>ALT</td>
<td>60 U/L</td>
</tr>
</tbody>
</table>
Hepatobiliary Scintigraphy @ 24 hours

Q5) What is your likely diagnosis?

Biliary Atresia

Q6) What are the treatment options in this child?

- Kasai procedure – Hepatopancreaticoenterostomy
  - Should be done within 2 months for best outcomes
- Liver Transplantation

_Heng Ya Low underwent a Kasai Procedure._

Q7) What are the complications you must look out for in this patient? Name 5.

- Ascending cholangitis
  - Fat-soluble vitamin deficiencies
- Failure of treatment → Hepatic cirrhosis
  - Portal hypertension
  - Varices
  - Coagulopathy
- Encephalopathy
- Ascites
CASE 6: 8 YEAR-OLD GIRL WITH ABDOMINAL PAIN

Lisa is a 8 year-old girl who presents with paraumbilical abdominal pain that started yesterday.

Q1) Name 6 possible etiologies.

- Abdominal Causes
  - Gastroenteritis
  - Inflammatory Bowel Disease
  - Intestinal obstruction
  - Intussusception
  - Meckel’s Diverticulum
  - Appendicitis (Early)

- Non-abdominal Causes
  - Henoch-Schonlein Purpura
  - Diabetic Ketoacidosis

Q2) Describe how you will evaluate her through history-taking and physical examination.

**History reveals**

*Pain was dull, ill-localized, started acutely and becoming worse, no radiation. Pain score of 6.*

*Associated with 2 weeks’ duration of polyuria, nocturia and weight loss.*

**Physical examination**

*Vitals: Tachycardic with tachypnea, afebrile, normotensive; drowsy.*

*Peripheries: Dry mucous membrane, decrease in skin turgor*

*Abdomen: Generalized tenderness, but no guarding or rebound tenderness*

*Patients weights around 25kg previously.*

Q3) What investigations will you perform? Describe your rationale for each investigation.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary Blood Glucose</td>
<td></td>
</tr>
<tr>
<td>Full Blood Count</td>
<td></td>
</tr>
<tr>
<td>Renal Panel</td>
<td></td>
</tr>
<tr>
<td>Arterial Blood Gas</td>
<td></td>
</tr>
<tr>
<td>Urine Glucose</td>
<td></td>
</tr>
<tr>
<td>Urine Ketones</td>
<td></td>
</tr>
<tr>
<td>Abdominal Ultrasound</td>
<td></td>
</tr>
<tr>
<td>Abdominal Radiograph</td>
<td></td>
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</table>
Investigations show

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>31.0 mmol/L</td>
</tr>
<tr>
<td>pH</td>
<td>7.046</td>
</tr>
<tr>
<td>Sodium</td>
<td>132</td>
</tr>
<tr>
<td>Potassium</td>
<td>5.3</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>8</td>
</tr>
<tr>
<td>Chloride</td>
<td>96</td>
</tr>
<tr>
<td>pCO2</td>
<td>19</td>
</tr>
<tr>
<td>Blood Ketones</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Q4) Interpret the Arterial Blood Gas, Renal Panel and Capillary Blood Glucose. What is the likely diagnosis?

**Arterial Blood Gas**

- There is High Anion Gap Metabolic Acidosis with adequate respiratory compensation
- Calculate the
  - Anion gap = Na – Cl – HCO3 = 132 – 96 – 8 = 28
  - Delta ratio = Delta AG/Delta HCO3 = (28-12)/(24-8) = 1
- Evaluate respiratory compensation using Winter’s formula = 1.5 x HCO3 + 8 = 1.5 x 8 + 8 = 20 (near the measured PCO2)

**Renal Panel**

- Hyperkalemia
- Pseudohyponatremia (corrected = [Na] + (Glucose – 10)/3) = 139 mmol/L

*Do you use the corrected sodium to calculate anion gap? No. The anion gap reflects the balance between positively and negatively charged electrolytes in the extracellular fluid. Glucose is electrically neutral and does not directly alter the anion gap. However, glucose is osmotically active so water is pulled into the extracellular fluid. This has a dilutional effect on all extracellular electrolyte concentrations, both positive or negative, and so the anion gap is minimally altered.

Q5) What are the diagnostic criteria for DKA?

- There are different criteria with slightly different values
- Diagnostic Criteria (American Diabetes Association – 2006)
  - Hyperglycemia > 11.0 mmol/L
  - HAGMA – pH < 7.3, HCO3 < 15 and below
  - Ketonemia (> 5 mmol/L)
Q6) Explain the patient’s symptoms/ signs

- Altered mental status: hypoperfusion of brain due to hypovolemia (note: in HHS, osmolality changes affect brain cells too)
- Polyuria & resultant polydipsia: hyperglycemia exceeds renal glucose threshold, result in osmotic diuresis
- Weight loss: insulin deficiency → cells cannot use glucose → lipolysis BUT more importantly massive amounts of water loss both intravascularly and intracellular
- Fruity breath odor: ketogenesis
- Abdominal pain: relative gut ischemia
- Clinically dry, tachycardic, hypotensive: volume depletion
- Tachypneic: Kussmaul breathing, due to metabolic acidosis → respiratory compensation

Q7) What is the severity of dehydration in this patient? What fluid replacement will you order?

- Severe(10% Loss)
  - Usually do not replace more than 10% for deficit in pediatric patients with DKA
- Fluid Replacement
  - Ongoing Losses + Deficit + Maintenance
  - Deficit = 10% x 25kg x 1000 = 2500 mL
  - Maintenance for two days – (1.5 litres + 5 x 20mL) x 2 days = 3200 mL
- Rate – Over 48 hours (IV fluid replacement is calculated over 48 hours, i.e. infusion at a slower rate, as risk of cerebral edema is higher in patients with DKA)
  - 5700 mL / 48 hours = 118.76 mL/Hr
- Solution –
  - Normal Saline
  - Change to Half strength Saline + 5% Dextrose when Glucose < 12mmol/L

Q8) Other than fluid replacement, what else will you do for this patient?

What do I need to know prior to starting management?

- Acute issue of shock
- Fluid loss – Described earlier
- Hyperglycemia - Insulin
- Acidosis – Bicarbonate in certain situations*
- Expected decrease in K and glucose after treatment – K and dextrose replacement
- Underlying etiology (the “I”s)

Q9) Name at least 5 conditions that can precipitate DKA.

- Infection – sepsis
- Infarction – stroke, AMI
- IUP(pregnancy)
- Infraction (non compliance)
- Illegal (substance abuse)
- Iatrogenic (drug interactions)
- Idiopathic (new onset DM)
CASE 7: 60 YEAR-OLD CHINESE GENTLEMAN WITH HEADACHE AND NAUSEA

You are the House Officer on duty. You are called to review Mr Ng, a 60 year old Chinese gentleman, due to an abnormal renal panel.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>120 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.8 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>110 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>4.5 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>80 umol/L</td>
</tr>
</tbody>
</table>

Q1) Please interpret this renal panel.

This is the result of a renal panel of this 60 year-old Chinese gentleman. The most obvious derangement is hyponatremia. The other values are within normal limits.

I would like to take a history, perform a PE and order relevant investigations before making a conclusion about the diagnosis and etiology.

Q2) What are the etiologies of hyponatremia? How can you classify the etiologies?

- PseudohypoNa (Hyperglycemia, Hyperlipidemia)
- Hypovolemic
  - Gastrointestinal fluid loss
  - Renal loss
  - Addison disease
- Euvolemic
  - Hypothyroidism
  - Hypocortisolism
  - Psychogenic Polydipsia
  - SIADH
- Hypervolemic
  - Heart Failure
  - Liver Cirrhosis
  - Chronic Renal Failure

Q3) Name some signs and symptoms that a patient with hyponatremia may experience. Describe the pathophysiology.
Acute (Medical Emergency)
Nausea, headache, vomiting, encephalopathy, seizure, brainstem herniation, coma, death
There can be normocapnic respiratory failure due to neurogenic pulmonary edema
Chronic
Vomiting, nausea, confusion
Subtle gait and cognitive defects, increasing risk of fall
Pathophysiology
Cerebral edema due to movement of fluid from the interstitial space to the intra-cellular space.

Q4) How will you take a history and perform a physical examination to elicit the underlying etiology of the hyponatremia?

Further history taking and physical examination reveals that he has just undergone a total knee replacement two days ago. He still experiences pain over the surgical site and has poor appetite. He has some headache and nausea. He has a past medical history of diabetes mellitus type 2, chronic renal failure and ischemic heart disease.

On physical examination, you noticed that he is euvoletic and he is receiving a 5% dextrose infusion. You checked the input and output chart (positive fluid balance). He weights 60kg.

Q5) Post-operative hyponatremia is a common post-operative problem and can be due to many causes. What are the 3 most likely etiologies in this patient?

- SIADH (e.g. post surgery, pain can stimulate ADH production)
- Iatrogenic (e.g. infusion of hypotonic fluids)
- Congestive heart failure, nephrotic syndrome, chronic renal failure

Q6) Name 3 investigations (other than the renal panel) that you would like to perform to help you find the cause of the derangement. Explain your rationale.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capillary blood glucose</td>
<td>Rule out pseudohyponatremia due to hyperglycemia. Correction factor:</td>
</tr>
<tr>
<td>Lipid panel</td>
<td>Rule out pseudohyponatremia due to hyperlipidemia.</td>
</tr>
<tr>
<td>Serum Osmolarity</td>
<td>Assess for pseudohyponatremia (serum osmolarity is usually normal or increased).</td>
</tr>
<tr>
<td>Urine Sodium</td>
<td>Helps determine if there is renal loss of sodium or</td>
</tr>
</tbody>
</table>
extra-renal loss of sodium.

| Urine Osmolarity | Helps distinguish between excessive water retention (urine osm will be high) or excessive water intake (urine osm will be low) as a cause of the hyponatremia. |

Q7) **You decided to replace the sodium as he has symptoms of acute hyponatremia (e.g. nausea, headache). How will you replace his sodium? Write out your order.**

- Replacement of sodium
  - Na Deficit = 0.6 x 60 kg x (135 – 120) = 540 mmol
  - Replacement fluid = 3% Normal Saline (Can be given in 50 – 100mL boluses, re-assess symptoms and renal panel after 1 to 2 boluses)
  - Rate = 1 – 2 mmol/L per hour (max 4 – 6 mmol/L in a day)
- Restrict oral intake of fluids
- Stop hypotonic solution infusion (5% dextrose)
- Strict Input / Output charting
- Renal panel after 2 – 4 hours to check levels
- *Note that 3% Normal Saline is usually only administered by the Endocrinologist/Nephrologist under very close supervision. Refer patients in such cases.

Q8) **In a patient with prolonged duration (chronic) hyponatremia, it is essential not to replace the sodium levels too quickly. What is the feared complication? Describe signs and symptoms of this complication and the proposed pathophysiology?**

Osmotic Demyelination Syndrome.
CASE 8: A 25 YEAR-OLD GENTLEMAN WITH WEAKNESS

You are the doctor in the emergency department.

John, a 25 year-old Chinese Gentleman, was brought in by his mother as he experienced fatigue and generalized weakness which occurred suddenly over the past one day.

Q1) What are the etiologies of generalized weakness?

- Electrolyte imbalances
- Myopathy (e.g. Cushing’s syndrome, Thyrotoxicosis)
- Neuromuscular junction disorder (e.g. Myasthenia gravis)
- Peripheral nerves (e.g. Guillain-Barre syndrome)
- Cord lesion (e.g. Tranverse myelitis)

*How to approach? Proximal versus Distal. Sensory vs No Sensory involvement

Q2) How will you take a history and physical examination?

History reveals that this is the first time he is experiencing such symptoms. The weakness started in the morning and became progressively worse and affects all 4 limbs, particularly the proximal muscles. There is no numbness or other neurological deficit. He recalled having a particularly intense weight lifting training session the previous day.

Physical examination shows flaccid paralysis in all 4 limbs. Power is MRC Grade 3; Deep Tendon Reflexes 1+. Sensory is intact (pinprick and proprioception). Babinski’s reflexes are absent in both lower limbs. There are no cranial nerves deficits. Vitals are stable.

Q3) What investigations will you order?

- Full blood count
- Renal Panel
- ECG
- CT Brain
- Nerve conduction test
- Electromyogram
Investigations are performed:

Renal Panel

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>1.2 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>120 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>5 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>80 umol/L</td>
</tr>
</tbody>
</table>

Electrocardiogram

Q4) Interpret the Renal Panel and Electrocardiogram.

- Hypokalemia with ECG changes
  - ST depression
  - T-wave inversion
  - Prominent U-waves

You note the hypokalemia and the associated ECG changes. Immediately, you place a medication order to replace his potassium. He weighs 60kg.

Q5) How will you replace his potassium?
K deficit = 0.6 x Body Weight (kg) x (4-\([K]\)) = 100 mmol

- Replace with 20 mmol packets (3 – 5 packets)
  - Rate should not exceed 60 mmol/hour
  - Do a repeat renal panel and ECG after infusion

Q6) What are the etiologies of hypokalemia? How can you broadly classify the etiologies?

- Refer to slides (51 – 60)

Q7) How will you take a history and physical examination to elicit the underlying cause?

- Refer to slides (51 – 60)

He shares that he has been losing weight over the last 3 months even though he is eating a lot. He has heat intolerance and difficulty sleeping at night as well. He noted that he has been experiencing fine tremors of his hands.

Q8) What is the likely diagnosis? Name one investigation you will order to confirm your diagnosis.

Thyroid Function Test (Free T4/T3, TSH).

You diagnose him with Thyrotoxic Periodic Paralysis and proceed to replace his potassium and provide beta-blockers. Just as you are completing your shift, a nurse ran over and show you the repeat Electrocardiogram.
Q9) Interpret the Electrocardiogram. What is the diagnosis?

- Hyperkalemia
- T-tented T-waves with widening of QRS leading to formation of sine pattern

You order an immediate iSTAT and the serum potassium was 8.0 mmol/L. You realize that you and your colleague had placed a duplicate order for Potassium Chloride infusion.

Q10) How will you manage this patient? Outline your steps.

- Calcium Gluconate
- Beta-agonist or Insulin or Sodium Bicarbonate
- Resonium A (15g per rectal or oral)
CASE 9: 60 YEAR-OLD MALAY GENTLEMAN WITH SHORTNESS OF BREATH

You are the House Officer on duty.

Mr Chee is a 60 year-old Malay gentleman who presents with shortness of breath over the last 2 days. He appears very breathless and the nurse informs you that his oxygen saturation is 85%. He has a past medical history of chronic pulmonary obstructive disease, hypertension and hyperlipidemia.

Q1) What are the etiologies of shortness of breath?

- Respiratory
- Cardiovascular
- Hematological
- Metabolic (e.g. acidosis)

Q2) How will you take a history and perform a physical examination?

He shares that he developed cough and an increase in the amount of sputum produced over the last 2 days. He has a decrease in effort tolerance and is breathless even after using the toilet. There is no chest pain, fever, orthopnea, or leg swelling.

He is tachypneic (25 breaths/min), tachycardic (105bpm) and using his accessory muscles of respiration. Respiratory examination reveals barrel chest with equal chest expansion, symmetrical breath sounds that are slightly diminished, normal percussion and vocal resonance. There is no trachea deviation. Normal heart sounds are heard. There is no pedal edema.

Q3) What is your most likely differential? Explain your choice.

Infective exacerbation of COPD

Q4) How will you resuscitate him?

You give him a venturi mask for him and set the FiO2 at 35%. His oxygen saturation improved to 94%. You also order salbutamol and ipratropium nebulization.

Q5) What investigations will you order? Explain your rationale.
Q6) You performed an ABG, but along the way the ABG results got mixed up. Which ABG is likely to belong to your patient?

a. pH 7.2, pO2 60, pCO2 60, HCO3 33
b. pH 7.2, pO2 60, pCO2 15, HCO3 18

Q7) What could be the reasons for COPD exacerbation?

Q8) How do you manage COPD exacerbation?

• Treat the exacerbation
• Pharmacological
  o Nebulised salbutamol, ipatropium
  o Oral prednisolone
• Non-pharm
  o NIV: BiPAP (not CPAP)
  o Worst case: intubation
• Treat the precipitant
  o If infection: antibiotics
  o If AMI, stroke, other stressors → treat accordingly
CASE 10: 78 YEAR-OLD FEMALE WITH FUNCTIONAL DECLINE AND DELIRIUM

Mdm Tan is a 78 year-old Chinese female who is staying in the nursing home. She is not able to ambulate on her own, but is able to feed herself. She craves attention and presses the call bell all the time. 3 days ago, the nurses noted that she became progressive quiet and pressed the bell less often. They were surprised, but glad at the same time. After all, it meant less work! She also had a decrease in appetite. They noticed that her attention fluctuates; she was more alert at times and less at other times. Today, they decided to bring her in after realizing she is very lethargic, is almost unresponsive and have not eaten or drank anything for 2 days.

Q1) What is the definition of delirium? What are the possible etiologies for Mdm Tan’s presentation? Name at least 6 different etiologies

- Stroke
- Acute Myocardial Infarction
- Infection
  - Pneumonia
  - Urinary Tract Infection
  - Intra-abdominal
  - Meningitis
- Drug interaction

Q2) How will you evaluate this patient through history and physical examination?

You are unable to obtain a history from the patient as she is very confused. You manage to check the records in the hospital and find out that she has the following past medical history: (1) Hypertension, (2) Hyperlipidemia, (3) Ischemic Heart Disease, EF of 45%, (4) Chronic Kidney Disease secondary to hypertension (CKD Stage 3). Her current medications include: (1) Atenolol, (2) Aspirin, (3) Lovastatin.

Her vitals are: T 36.6 degree Celcius, Blood Pressure 70/50 mmHg, Pulse 90 beats per minute, SpO2 95% on room air.

Normal heart sounds are heard with no murmur. There is adequate breath sounds bilaterally with no adventitia breath sounds heard. The patient’s abdomen is soft with no masses felt. Pupils are reactive to light and 3mm large. The neck is not stiff. The patient appears dehydrated as the skin turgor is lost and the mucous membrane are dry. Calves are supple and there is no pedal edema.

Q3) Your medical student thinks that this patient may be hypotensive. What are the possible causes for hypotension in this patient?

Hypotension (shock) can be classified as (1) cardiogenic, (2) obstructive, (3) septic, (4) anaphylactic, (5) hypovolemic/hemorrhagic.

In this patient, (1), (3) and (5) are most likely.

Cardiogenic shock can be due to acute myocardial infarction, myocarditis, congestive heart failure. Septic shock can be due to infections. Common sources of infection in the elderly include: intra-
abdominal sources, urinary tract infection, cutaneous infection, pneumonia. Hypovolemia shock can be due to either low intake (via oral or IV routes) or high output. High output can be due to renal losses, GIT losses, bleeding (from various sites). If water is lost into extravascular spaces it is known as third-spacing. Hemorrhagic shock can be due to sources of bleeding in the patient (e.g. gastrointestinal tract).

Q4) You suspect that the patient may be suffering from a severe infection. Your medical student thinks that it is unlikely as the patient does not have a fever. Does the lack of a febrile response preclude the possibility of an infection in this patient? What are some common features of infection that may be not present in the elderly?

Q5) What are some investigations you will perform? Name 8 and describe your rationale.

You order various investigations and these are the results:

**Full Blood Count**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>12.0 g/L</td>
</tr>
<tr>
<td>TW</td>
<td>18.0</td>
</tr>
<tr>
<td>Plt</td>
<td>350</td>
</tr>
<tr>
<td>Differential count (N/L)</td>
<td>90% / 5%</td>
</tr>
</tbody>
</table>

**Renal Panel**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>123</td>
</tr>
<tr>
<td>Potassium</td>
<td>5.4</td>
</tr>
<tr>
<td>Chloride</td>
<td>88</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>14</td>
</tr>
<tr>
<td>Urea</td>
<td>33.0</td>
</tr>
<tr>
<td>Creatinine</td>
<td>341 (baseline: 150)</td>
</tr>
<tr>
<td>Glucose</td>
<td>7.0</td>
</tr>
</tbody>
</table>

**Arterial Blood Gas**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.10</td>
<td>7.35 – 7.45</td>
</tr>
<tr>
<td>PaCO2</td>
<td>48</td>
<td>40 mmHg</td>
</tr>
<tr>
<td>Parameter</td>
<td>Values</td>
<td></td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------------</td>
<td></td>
</tr>
<tr>
<td>Urine Formed Element Microscopy Examination</td>
<td>WBC 15/hpf Bacteria seen RBC 2/hpf Nitrite (+)</td>
<td></td>
</tr>
<tr>
<td>Urine Culture</td>
<td>Pending</td>
<td></td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>No consolidation seen</td>
<td></td>
</tr>
<tr>
<td>CT Abdomen</td>
<td>Radiological feature of pyelonephritis</td>
<td></td>
</tr>
</tbody>
</table>

**Microbiology**

**Electrocardiogram and Cardiac Enzymes**

Raised with signs of ischemia.

Q5) What are the complications of hypovolemia? Which of these complications is the patient suffering from?

Classified by organ systems, hypovolemia affects the **Heart (NSTEMI)**, Brain (stroke), **Kidney (AKI)**, Gut (ischemia). The key concept is that the “watershed” areas are affected the most! E.g. subendocardial area of heart, watershed between MCA and ACA, splenic flexure of colon.

You should look out for the more commonly affected organs such as the heart, brain, kidney as part of the history and PE before deciding to investigate.

I would like to perform investigations to confirm my diagnosis, rule out differentials, ascertain etiology and to guide my management of the patient.

This patient is suffering from the possible complications.

- Acute Kidney Injury: Urea ↑↑ and Cr ↑ (electrolyte changes possible, we’ll see later)
- Lactic Acidosis (HAGMA with raised lactate)
- Non-ST-elevated Myocardial Infarction (NSTEMI)
*Use this as an exercise to go through the interpretation of the investigations.

Q6) What is your diagnosis? Summarize your problem list.

Septic Shock secondary to pyelonephritis complicated by: (1) Acute kidney injury, (2) Lactic acidosis, (3) NSTEMI.

*Clarify the concept of septic shock.

Q7) How will you resuscitate the patient?

I would like resuscitate the patient by managing her airway, breathing and circulation

- A – Ensure patency
- B – Give supplementary oxygen
- C – 2 large bore IV cannula (esp in trauma cases) for blood taking and fluid resuscitation

Fluid challenge followed by

- Adults: 500ml over 30 mins
- Paeds: 10-20ml/kg over 30-60mins
- If responsive e.g. HR↓ or BP↑ or urine o/p↑,

*In this case, the patient has chronic renal failure and care must be taken to monitor the fluid status (e.g. strict input / output charting with the use of urine catheter). Patient must be monitored for signs of fluid overload as well and fluid resuscitation should not be as aggressive.

Q8) What is your subsequent management plan? Describe the key steps of managing a patient with septic shock.

<table>
<thead>
<tr>
<th>Principle</th>
<th>Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early antibiotics administration</td>
<td>IV Ceftriaxone, 2g, STAT and OM Blood Culture, Urine Culture Change antibiotics according to response and sensitivity results</td>
</tr>
<tr>
<td>Aggressive fluid therapy</td>
<td>IV Normal Saline (30mL / kg) fast infusion over 1 hour when there is hypotension on top of maintainence drip. Monitor for fluid overload</td>
</tr>
<tr>
<td>Close Monitoring</td>
<td>Paras q2h, I/O strict, call if HR&gt;110, BP&lt;90 [signs of hypotension, monitor ongoing losses &amp; assess progress]</td>
</tr>
<tr>
<td>Vasopressor support if needed to maintain MAP &gt; 65mmHg</td>
<td>IV Noradrenaline infusion</td>
</tr>
</tbody>
</table>

*Source: Surviving sepsis campaign
**CASE 11: 70 YEAR-OLD GENTLEMAN WITH POST-OPERATIVE FEVER**

Mr Lee is a 70 year old gentleman with poorly controlled diabetes mellitus, peripheral vascular disease and history of diverticular disease. He was admitted 1 week ago with severe abdominal pain and underwent an emergency laparotomy. Intra-operatively, a perforation of the sigmoid colon was found and he underwent a recto-sigmoid resection and a Hartman’s procedure.

Post-operatively, he was transferred to the surgical high dependancy unit with continuous hemodynamic monitoring via central venous pressure catheter monitoring and urinary catheter for monitoring of urinary output. He was placed on intravenous ceftriaxone and metronidazole.

Today is post-operative day 7 and the nurse informs you that the patient spiked a fever of 38.5 degrees celsius overnight.

**Q1) What are broad etiologic categories of fever in a patient?**

A high temperature is interpreted as a fever, but essentially a high temperature in any patient should be divided as such:

1. Fever (Inflammation leading to release in inflammatory mediators - prostaglandins resulting in change in hypothalamic set point)
   - Tissue injury (e.g. DVT)
   - Foreign antigens (Infection, Blood transfusion reactions)
   - Self antigens (Autoimmune disease, Malignancy)

2. Hyperthermia (Heat gain > heat loss, no change in hypothalamic set point)
   - Heat injury
   - Hypermetabolic state (Hormonal - Thyroid crisis, Drugs)

Should take into consideration these broad categories when seeing a patient for fever, suited to the context.

*What aspects of the history will you take to ascertain the causes of fever in this patient?*

Main idea here is to have an organised manner of history taking.

**Pattern/Trend of fever**

**Surgery related**

Operative site
- Laparotomy wound (pain at wound site)
- Intra-abdominal - Rectal stump abscess/Intra-abdominal collection. (Abdominal pain, PR bleed). He had a colonic perforation which will spill GIT contents into the abdomen – GIT contents are considered ‘dirty’. At operation the team would have attempted to clean up as much as possible but there is high risk for residual intra-abdominal abscess.

**Immobility related**

Systemic review
- Pneumonia (Cough, purulent sputum, Breathlessness, pleuritic chest pain)
- Urinary Tract infection (Suprapubic tenderness, blood in urinary bag. On IDC so won’t have dysuria, frequency)
- Deep Vein Thrombosis (Calf tenderness)
- Infected Bed sores

**Patient related**
- Any pain in the feet? (PVD and poorly controlled DM predisposes to diabetic foot ulcers and non-healing wounds)

Drug related – any new drugs started? E.g. haloperidol given for agitation: can cause neuroleptic malignant syndrome and fever

The patient mentions that this is his first episode of high fever since the operation and he is feeling especially lethargic today.

There is still pain at his operative site but there is no abdominal pain or suprapubic pain otherwise. He does not have any per-rectal bleeding.

He mentions that he is feeling more breathless, though unable to cough or breathe deeply due to the significant pain from his laparotomy wound. There is no chest pain.

There is no leg swelling and he does not have any pain in his calves.

Otherwise, he has just begun to tolerate small feeds without any vomiting.

*What are your differential diagnoses for his chief complaint at this point?*

Breathlessness may be due to the fact that there is a lung/CVS pathology or simply tachypnea as a response to sepsis.

Breathlessness can be classified according to airway, parenchyma (pneumonia, pulmonary edema), pleura (effusion?), vessels (pulmonary embolism?). Physical examination should pay attention to whether signs are bilateral or unilateral.

In this patient’s case where the surgery was of a “contaminated” nature, there should be a continuous suspicion for an intra-abdominal collection/abscess which may not manifest in signs of an acute abdomen until later.

*How would you assess the patient to make a diagnosis and assess the complications?*

Guide the student to explain the signs they will look out for to assess each possible cause listed above.

The learning point here is to also pay attention to the general examination. Watch for a septic patient.

- Alert vs. Drowsy
- Respiratory Rate (Respiratory rate? Sign of systemic inflammatory response/sepsis)
- Heart rate and blood pressure

Mr Lee appears lethargic with a heart rate of 98 bpm, BP of 115/90, respiratory rate of 26 and saturation of 99% on room air. There is conjunctival pallor and he is not jaundiced.

Respiratory examination reveals dullness to percussion, reduced breath sounds and crepitations over the right lung base. Heart sounds are S1 S2 with no additional heart sounds or murmurs.

Abdominal examination reveals no guarding on deep palpation or rebound tenderness, and the laparotomy wound is clean with presence of granulation tissue and no discharge of pus. There is no tenderness or blood on PR examination.

There is no blood in the In-dwelling catheter bag.

The calves are supple, there is no pedal edema and there are no ulcers on the feet.

*List and explain the rationale for the investigations that you will carry out for this patient.*
Sample Answer

<table>
<thead>
<tr>
<th>Category</th>
<th>Investigation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Capillary blood glucose monitoring</td>
<td>Poorly controlled diabetic requires constant monitoring.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Infection provokes a sympathetic response, adrenaline release causes glucose levels to rise predisposing to DKA/HHS.</td>
</tr>
<tr>
<td></td>
<td>Full Blood Count</td>
<td>Look for a neutrophil predominant leukocytosis and left shift which suggests a bacterial infection</td>
</tr>
<tr>
<td></td>
<td>Renal Panel</td>
<td>Cr &amp; Urea are markers of end-organ perfusion in view of the concern of sepsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acute Kidney Injury is a complication of sepsis and hypoperfusion</td>
</tr>
<tr>
<td>Diagnostic</td>
<td>CXR</td>
<td>Look for consolidation correlating with clinical findings</td>
</tr>
<tr>
<td></td>
<td>Urine FEME, Urine Gram Stain &amp; Culture</td>
<td>The other possible source of infection that is not symptomatic due to IDC.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*Note – do a clean catheter or in/out, do not take urine culture from the bag!</td>
</tr>
<tr>
<td></td>
<td>Blood Cultures</td>
<td>Done at two separate sites, to look for bacteremia</td>
</tr>
<tr>
<td></td>
<td>Inflammatory markers (CRP, Procalcitonin)</td>
<td>No need to go into detail, but can discuss how CRP can be used to trend the progress of treatment, and how procalcitonin is more specific for a bacterial infection</td>
</tr>
</tbody>
</table>

What are your initial steps of management and your plan for definitive management?

1. Resuscitate - Fluids if hypotensive
2. Management of suspected pneumonia

- Encourage ventilation/clearance of secretions - Chest Physiotherapy, Incentive Spirometry use, Early ambulation
- This is likely hospital acquired pneumonia which may be multi-drug resistant. Start Broad spectrum antibiotics - e.g. IV pip-tazo; add IV vancomycin (if MRSA).
- Modify choice of antibiotics based on culture results, and what he has already been given (he is already on ceftriaxone – so whatever is growing is likely ‘R’ to ceftriaxone!) Check for drug allergy!

3. Further preventive measures
- Pneumatic calf pumps (DVT prophylaxis)
- Remove IDC and CVP lines once not required

Objectives for the case

<table>
<thead>
<tr>
<th>Competence in clinical skills</th>
<th>What a doctor is able to do - “Doing the right thing”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Be able to narrow down a diagnosis based on an understanding of the broad aetiologies of fever.</td>
<td></td>
</tr>
<tr>
<td>Be able to take a good history of fever, especially how to characterise the fever</td>
<td></td>
</tr>
<tr>
<td>Understand how to conduct a good systemic review in context of the clinical case to narrow down the possible sources of sepsis</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Competence in investigating a patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understand the components of a septic work-up and the rationale behind it</td>
</tr>
<tr>
<td>Understand the role of various inflammatory markers in diagnosis and monitoring of treatment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Competence in patient management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods of measuring temperature in a patient</td>
</tr>
<tr>
<td>How to manage pyrexia, high temperature in a patient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How the doctor approaches their practice - “Doing the thing right”</th>
</tr>
</thead>
<tbody>
<tr>
<td>With understanding of basic, clinical and social sciences and underlying principles</td>
</tr>
<tr>
<td>Understand the pathophysiology behind a raised temperature</td>
</tr>
</tbody>
</table>
CASE 12: 50 YEAR-OLD WOMAN WITH JOINT PAIN

A 50 year old woman comes to see you for longstanding pain in her hands and wrists and knees for the past year. On examination, they are painful, swollen, warm and red. She says they are stiff in the morning.

Q1) What are some possible differential diagnoses?

Joint pain can be classified into various large groups – acute versus chronic (usually more than 6 weeks), monoarticular vs polyarticular. Each of these large groups (acute monoarticular, acute polyarticular, etc) has different differentials.

This patient has chronic polyarticular pain. (One year) The differential diagnosis include:

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystal-induced</td>
<td>• Gout</td>
</tr>
<tr>
<td></td>
<td>• Pseduogout (Calcium pyrophosphate deposition disease)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>• Rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>• Systemic lupus erythematous</td>
</tr>
<tr>
<td></td>
<td>• Polymyositis/Dermatomyositis</td>
</tr>
<tr>
<td></td>
<td>• Systemic sclerosis</td>
</tr>
<tr>
<td></td>
<td>• Sjogren’s syndrome</td>
</tr>
<tr>
<td></td>
<td>• Behcet’s syndrome</td>
</tr>
<tr>
<td></td>
<td>• Polymyalgia rheumatic</td>
</tr>
<tr>
<td></td>
<td>• Mixed Connective Tissue Disease (MCTD)</td>
</tr>
<tr>
<td></td>
<td>• Spondyloarthropathies: Ankylosing spondylitis, psoriatic arthritis, reiter’s syndrome</td>
</tr>
<tr>
<td></td>
<td>• Vasculitis: Schönlein-Henoch purpura, polyarteritis nodosa</td>
</tr>
<tr>
<td>Malignancy</td>
<td>• Metastatic solid tumours</td>
</tr>
<tr>
<td></td>
<td>• Hematological malignancies: Leukemia, lymphoma, multiple myeloma</td>
</tr>
<tr>
<td>Degenerative</td>
<td>• Osteoarthritis</td>
</tr>
<tr>
<td>Infection*</td>
<td>• Viral</td>
</tr>
<tr>
<td></td>
<td>o Human parvovirus, enterovirus, adenovirus, EBV, CMV, HIV</td>
</tr>
<tr>
<td></td>
<td>o Bacterial (Reactive)</td>
</tr>
<tr>
<td></td>
<td>o Group A Streptococci (Rheumatic fever), Campylobacter spp, Chlamydia spp, Borrelia burgdorferi (Lyme disease)</td>
</tr>
<tr>
<td></td>
<td>o Bacterial (Direct infection)</td>
</tr>
<tr>
<td></td>
<td>o N.gonorrhoeae, S.aureus</td>
</tr>
<tr>
<td></td>
<td>• Mycobacterial</td>
</tr>
<tr>
<td></td>
<td>o M. tuberculosis</td>
</tr>
<tr>
<td></td>
<td>• Fungal</td>
</tr>
</tbody>
</table>

Q2) What are some essential elements in a rheumatological history?

A rheumatology history asks for nearly everything on earth, because rheumatology diseases can have multiple organ manifestations and can overlap. Also note that there can be co-existent associated pathology e.g. occult malignancy with adult dermatomyositis, inflammatory bowel disease with enteropathic arthritis.

The goals of history taking include:
- Diagnosis and Differentials
- Severity
- Complications (other systemic manifestations)
- Function and QOL
- Management and response to management
- Psychosocial and others
Diagnosis and Differentials

There are 7 main clinical factors to ask to help determine the diagnosis:

- Patient demographic
- Disease chronology
- Presence of inflammation
- Distribution of joint pain (Pattern, Symmetry, Axial Involvement)
- Extra-articular manifestations
- Disease course
- Others

**Patient demographic**

- **Gender**
  - Before menopause, women are more likely to develop SLE and RA
  - Gout is more common in men
- **Age**
  - Young: Rheumatic fever, systemic lupus erythematosus, rheumatoid arthritis, spondyloarthropathies
  - Old: Osteoarthritis, polymyalgia rheumatica

**Disease chronology**

- Acute: < 6 weeks, Chronic: 6 weeks or more
- Acute polyarticular joint pain can be a sign of self-limiting disorder (reactive to viral or bacterial infection) or a harbinger of chronic disease.

**Inflammation**

- Cardinal signs of inflammation include erythema, warmth, pain and swelling
  - Synovitis can be a sign of chronic inflammation
- Morning stiffness lasting longer than one hour suggests underlying inflammation

**Distribution**

- **Pattern:**
  - Osteoarthritis – DID and PIP joints, first CMC joint, large weight bearing joints
  - Rheumatoid arthritis – PIP, MCP joints and wrists
  - Spondyloarthropathies typically involve the large joints (e.g. sacroiliac, spine, knee)
- **Symmetry**
  - Systemic diseases such as rheumatoid arthritis, SLE, viral arthritis tend to present with symmetrical joint involvement
  - Psoriatic arthritis, gout, CPPD tends to be present with asymmetric involvement
- **Axial involvement**
  - Typically more common in spondyloarthropathies

**Disease Course**

- Intermittent versus Migratory
  - Intermittent (acute flares) suggests conditions like gout and pseudogout
  - Migratory arthritis (characterized by rapid onset of swelling in one or two joints, with resolution over a few days and as symptoms resolve, similar symptoms emerge in another joint) suggests conditions such as rheumatic fever, Lyme disease

**Extra-articular involvement**

- Every system can be affected
- Ask about muscles (any pain, trigger points)
- Ask about integument (any rash, nodules, nail problems e.g. pitting, hair problems e.g. alopecia)
- Any fever, fatigue, loss of weight, loss of appetite, Raynaud’s phenomenon, lymphadenopathy
- Any eye problems (redness, dry eyes, BOV, other symptoms)
- Any mouth problems (ulcers, dry mouth, other symptoms)
- Any GI problems (swallowing difficulty, vomiting, diarrhea, constipation, blood in stool)
- Any HPB problems (jaundice etc.)
- Any hematological problems (symptoms of cytopenia)
- Any nephro problems (hematuria, frothy urine etc)
- Any respiratory problems (pleuritic pain, hemoptysis)
- Any cardiac problems (chest pain)
- Any neurological problems

For a more complete list, look at the reference article.

**Summary of Common Diseases**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Chronology</th>
<th>Inflammation</th>
<th>Distribution</th>
<th>Extra-articular manifestations</th>
<th>Demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Chronic</td>
<td>Yes</td>
<td>Small joints (PIPJ, MCPJ) and large joints</td>
<td>Cervical</td>
<td>Subcutaneous nodules, interstitial lung disease, others</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Chronic</td>
<td>Yes</td>
<td>Small joints</td>
<td>No</td>
<td>Malar rash, oral ulcers, serositis</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>Chronic</td>
<td>Yes</td>
<td>Large and small joints</td>
<td>No</td>
<td>Psoriasis, dactylitis, tendonitis</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>Chronic</td>
<td>Yes</td>
<td>Large joints (e.g. Sacral, spine, hip)</td>
<td>Yes</td>
<td>Uveitis, tendonitis, aortic regurgitation, enthesitis, (inflammation of the muscular or tendinous insertion)</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Chronic</td>
<td>No</td>
<td>Small joints (DIPJ, PIPJ, First CMC joint), lower extremities</td>
<td>Yes / No</td>
<td>Cervical and lumbar</td>
</tr>
<tr>
<td>Gout</td>
<td>Acute</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Urate nephropathy</td>
</tr>
<tr>
<td>Human Parvovirus B19</td>
<td>Acute</td>
<td>Yes</td>
<td>Small joints</td>
<td>Yes</td>
<td>Lacy rash, malar rash</td>
</tr>
</tbody>
</table>

*The list is not exhaustive

**Others**
- Any trauma
- Travel history (impt for infective causes e.g. Lyme disease)
- Sexual history (impt for gonococcal arthritis, reactive arthritis, others e.g. Hep B)
- Intravenous drug abuse
- Family History of autoimmune and rheumato disorders
- Past Medical History
Complications
See under “extra-articular” manifestations

Function
• Ask about function (walking, climbing stairs, overhead work, putting on bra for ladies, doing fine motor work)
• Ask how condition affects the patient’s quality of life

Management and Response
• Non-pharmacological, pharmacological, surgical
• Any medications taken
  o Side effects experienced?
• Response to treatment?


Her daughter is accompanying her. She tells you that “old folks always complain of aches and pains, probably it is just bone degeneration like osteoarthritis”.

Q3) What features distinguish rheumatoid arthritis from osteoarthritis?

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rheumatoid arthritis</th>
<th>Osteoarthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary joints affected</td>
<td>Metacarpophalangeal</td>
<td>Distal interphalangeal</td>
</tr>
<tr>
<td>Heberden's nodes</td>
<td>Absent</td>
<td>Frequently present</td>
</tr>
<tr>
<td>Joint characteristics</td>
<td>Soft, warm, and tender</td>
<td>Hard and bony</td>
</tr>
<tr>
<td>Stiffness</td>
<td>Worse after resting (eg, morning stiffness)</td>
<td>If present, worse after effort, may be described as evening stiffness</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td>Positive rheumatoid factor</td>
<td>Rheumatoid factor negative</td>
</tr>
<tr>
<td></td>
<td>Positive anti-CCP antibody</td>
<td>Anti-CCP antibody negative</td>
</tr>
<tr>
<td></td>
<td>Elevated ESR and CRP</td>
<td>Normal ESR and CRP</td>
</tr>
</tbody>
</table>

(this is from Uptodate)

You have examined the patient’s arms and hands.

Q4) What do you expect to see if there is rheumatoid arthritis? How would you distinguish from the other causes you have listed above?

Joint
• Bilateral symmetrical deforming polyarthritis affecting MCP and PIP
• swan neck, boutonniere, Z thumb, ulnar deviation of fingers
• MCPJ subluxation, piano key sign
• +/- active arthritis
• synovial thickening

Muscle and Tendons
• Muscle wasting (may also be due to carpal tunnel syndrome)
• Dropped fingers from tendon rupture
• Extensor tendon subluxation
Others

- vasculitic lesions and nail fold infarcts
- palmar erythema
- look for rheumatoid nodules
- any carpal tunnel syndrome
- look for gouty tophi (gout)
- look for nail changes e.g. pitting and skin changes of psoriasis (ddx)
- look for SLE skin changes (SLE)
- feel for muscle pain (myositis of RA, polymyalgia rheumatica)

Function

While this is not used to distinguish between your differential diagnosis, it is used to evaluate the quality of life for the patient and should be done for all hand examination.

Gross: Grip strength
Fine: Ability to write, to pick up small objects (e.g. coins, key), ability to button clothes

Reference: Jenson Koh’s Notes / Derek Aw’s Notes

As a thorough physician, you also examine the rest of the patient.

**Q5) What other signs are you looking out for?**

**Eyes**
- Conjunctiva - keratoconjunctivitis sicca (dry eyes from lacrimal gland involvement), pallor (from anemia, various etiologies e.g. anemia of chronic disease, Felty syndrome, comorbid pernicious anemia, drug induced aplasia - gold, penicillamine)
- Sclera - episcleritis, scleritis (can be hard to distinguish)
- Retina - vasculitic lesions
- Extraocular nerve palsies 2 to mononeuritis

**Respiratory**
- Creps from pulmonary fibrosis, pneumonitis
- Effusion

**Cardiac**
- Murmurs and rubs - Pericarditis, myocarditis, coronary artery disease
- Atrial fibrillation

**Peripheral vessels**
- Peripheral vascular disease, stroke

**Neuro**
- Peripheral neuropathies, mononeuritis multiplex, atlantoaxial subluxation +/- cervical myelopathy

**Abdomen**
- Splenomegaly - Felty syndrome

After a thorough history and physical examination, you make a diagnosis of rheumatoid arthritis in this patient.

**Q6) What are some investigations you will order? What is your rationale?**

The investigation results are out.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Value</th>
<th>Reference*</th>
</tr>
</thead>
</table>

Rheumatoid Factor          30 IU/mL   <15 IU/mL
Anti-citrullinated protein antibodies (ACP antibodies)  15 EU/mL   < 20 EU/mL

Q7) Your medical student looks at the results (without correlating with the history) and concludes that the patient has rheumatoid arthritis. Do you agree?

No.

Q8) What is the difference in terms of specificity between rheumatoid factor and ACP antibodies? What is the advantage of ACP antibodies?

Anti-cyclic citrullinated peptide antibody is more specific for rheumatoid arthritis. It aids in ruling in the disease. It is also present in the early stages of rheumatoid arthritis, allowing for earlier diagnosis.

Extra information:
- The most common test for anti-CCP2 has a sensitivity of 61.6-75.2% for rheumatoid arthritis and specificity of 94-99%
- Rheumatoid factor (RF) is used in the diagnosis of rheumatoid arthritis (RA). RF results are positive in approximately 75% of patients with RA, although RF is not etiologically related to RA.[6]
- High RF titers indicate a poorer prognosis, as patients with higher RF levels tend to have more severe disease. Patients with nodules or clinical evidence of vasculitis usually have positive RF results.
- Low levels of RF can even be found in healthy patients, and the test is positive in up to 20% of older individuals.

Q9) What is the diagnostic criteria for rheumatoid arthritis (ACR 2013)? What are some key principles behind the formulation of diagnostic criteria?

1. Standardization
Autoimmune conditions vary in phenotype and may at times be difficult to differentiate from one another. One means of diagnosing patients is to classify them via various criteria. This allows standardization of recruitment into trials and provide the basis for a common approach to disease definition that can be used to compared across centers.

2. Factors more predictive of the condition are given a higher weight

3. Designed to allow earlier diagnosis
The 1987 classification was criticized for being too strict and hence, not helpful in identifying patients who would benefit from early effective interventions.

THE 2010 ACR-EULAR CLASSIFICATION CRITERIA FOR RHEUMATOID ARTHRITIS

<table>
<thead>
<tr>
<th>Target population (Who should be tested?): Patients who</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. have at least 1 joint with definite clinical synovitis (swelling)¹</td>
</tr>
<tr>
<td>2. with the synovitis not better explained by another disease²</td>
</tr>
</tbody>
</table>

Classification criteria for RA (score-based algorithm: add score of categories A - D; a score of ≥6/10 is needed for classification of a patient as having definite RA)³
<table>
<thead>
<tr>
<th>A. Joint involvement&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 large joint&lt;sup&gt;5&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without involvement of large joints)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with or without involvement of large joints)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least 1 small joint)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Serology (at least 1 test result is needed for classification)&lt;sup&gt;8&lt;/sup&gt;</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative RF and negative ACPA</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF or low-positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>High-positive RF or high-positive ACPA</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Acute-phase reactants (at least 1 test result is needed for classification)&lt;sup&gt;9&lt;/sup&gt;</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. Duration of symptoms&lt;sup&gt;10&lt;/sup&gt;</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
</tr>
</tbody>
</table>

1 The criteria are aimed at classification of newly presenting patients. In addition, patients with erosive disease typical of rheumatoid arthritis (RA) with a history compatible with prior fulfillment of the 2010 criteria should be classified as having RA. Patients with longstanding disease, including those whose
disease is inactive (with or without treatment) who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA.

2 Differential diagnoses vary among patients with different presentations, but may include conditions such as systemic lupus erythematosus, psoriatic arthritis, and gout. If it is unclear about the relevant differential diagnoses to consider, an expert rheumatologist should be consulted.

3 Although patients with a score of <6/10 are not classifiable as having RA, their status can be reassessed and the criteria might be fulfilled cumulatively over time.

4 Joint involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis. Distal interphalangeal joints, first carpometacarpal joints, and first metatarsophalangeal joints are excluded from assessment. Categories of joint distribution are classified according to the location and number of involved joints, with placement into the highest category possible based on the pattern of joint involvement.

4 "Large joints" refers to shoulders, elbows, hips, knees, and ankles.

5 "Small joints" refers to the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists.

6 In this category, at least 1 of the involved joints must be a small joint; the other joints can include any combination of large and additional small joints, as well as other joints not specifically listed elsewhere (e.g., temporomandibular, acromioclavicular, sternoclavicular, etc.).

7 Negative refers to IU values that are less than or equal to the upper limit of normal (ULN) for the laboratory and assay; low-positive refers to IU values that are higher than the ULN but ≤3 times the ULN for the laboratory and assay; high-positive refers to IU values that are >3 times the ULN for the laboratory and assay. Where rheumatoid factor (RF) information is only available as positive or negative, a positive result should be scored as low-positive for RF. ACPA = anti-citrullinated protein antibody.

8 Normal/abnormal is determined by local laboratory standards. CRP = C-reactive protein; ESR = erythrocyte sedimentation rate.

9 Duration of symptoms refers to patient self-report of the duration of signs or symptoms of synovitis (e.g., pain, swelling, tenderness) of joints that are clinically involved at the time of assessment, regardless of treatment status.

Reference: https://www.rheumatology.org/practice/clinical/classification/ra/ra_2010.asp#fn_09

Q10) What are some of the management options? What are the adverse effects?

Pharmacological

Anti-inflammatory

NSAID (PUD, N/V, Renal papillary necrosis)
Steroid (Cushing’s, DM, osteoporosis, immunosuppression)

Nonbiologic DMARD
Methotrexate (BM suppression, teratogen, ulcer, pneumonitis, hep fibrosis)
Hydroxychloroquine (ocular toxicity, N/V, dyspepsia)

Biologic DMARD (if nonbiologic fails)
Anti –TNFa e.g. adalimumab, infliximab, etanercept (infection, cancer, allergy)
Anti-IL-1R, IL-6 etc etc

Non pharmacological

General
Patient education, psychosocial support
Smoking cessation
Immunization

Lifestyle
Rest, exercise, PT, OT, Nutrition and diet advice

Surgery
Release of carpal tunnel, fix atlantoaxial instability
Joint replacement
CASE 13: 52 YEAR-OLD MAN WITH JOINT PAIN

This lady’s 52 year old husband presents to you some months later with acute onset of pain and swelling in his left 1st metatarsophalangeal joint lasting over the past few hours. There was no trauma to the foot, but the pain is so severe that he cannot walk. He says that he had a previous episode while he was on holiday recently on a luxury wine and dine cruise, but that it resolved within a few days.

Q1) What is your differential diagnosis?

This patient has acute monoarticular joint pain. The key differentials are: Septic arthritis, gout, pseudogout, other rheumatological disease (the first presentation of rheumatological diseases which can lead to chronic joint pain).

Q2) How will you investigate this patient? Describe your rationale.

You send him for a joint aspirate. Interpret the results.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Value</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint Fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>15 000/μL</td>
<td>Predominant neutrophil</td>
</tr>
<tr>
<td>Gram stain</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Glucose</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>
Serum Uric acid 0.75 mmol/L 0.18 – 0.48 mmol/L

Crystal microscopy shows:

Q3) What is the crystal seen? What is your diagnosis?

Strongly negative birefringent, needle-shaped crystal. Gout.

Q4) If the serum uric acid was normal. Will you still treat this patient for gout? Explain your reasoning.

Yes. The presence of hyperuricemia in the absence of symptoms of symptoms is not diagnostic of gout. (~25% of the population has a history of elevated serum uric acid, but only a minority of patients with hyperuricemia develop gout)
In addition, as many as 15% of patients with symptoms from gout may have normal serum uric acid levels at the time of their attacks.

The diagnosis of gout is made by the presence of urate crystals in the synovial fluid or soft tissue.

Q5) What are some risk factors for this condition? What are some of the complications?

Conditions increasing serum urate - dehydration, drugs (e.g. thiazides, loop diuretics, aspirin), alcohol, fatty food, meat, seafood, dairy, starvation
Proinflammatory conditions - trauma, surgery
Obesity
Local joint trauma

Complications:
Joint deformity, skin tophi, nephrolithiasis, urate nephropathy

Q6) What are some principles of management of this patient?

Treat the acute attack (NSAID +/- colchicine, glucocorticoids if NSAIDS or colchicine not suitable.
NO ROLE for urate lowering therapy but if patient is already on, continue dose)
Address risk factors
Urate lowering therapy indicated if patient has frequent disabling attacks, has renal complications, tophaceous gout, or joint destruction.
Urate lowering therapy includes uricosurics (e.g. probenecid), xanthine oxidase inhibitors (e.g. allopurinol, febuxostat), uricases (rasburicase, pegloticase). Gradually titrate up as an attack can occur during initiation of uricosurics and stones can also form. Hydrate well +/- urinary alkalization. Can do under cover of NSAIDS or colchicine.
Q7) Are there any medications this patient should be careful of?
There is a small increased risk of gouty attack with thiazide diuretics as they increase urate absorption in the proximal tubule. However, thiazides are cheap and good drugs for hypertension and they still can be used. Concurrent administration of ACE-I or ARB can ameliorate this effect.

Aspirin increases urate levels and increases risk of attacks. Allopurinol or probenecid can ameliorate this effect.

If patient needs allopurinol, beware drugs that are purine analogues (e.g. azathioprine, 5 mercaptopurine) as they are metabolized via xanthine oxidase and breakdown will be inhibited.

Allopurinol itself is infamous for being one of the top causes of Stevens-Johnson syndrome.
CASE 14: 54 YEAR-OLD WOMAN WITH BACK PAIN

Objectives

1. Application of basic science to develop a mechanistic understanding of clinical problems
   - Understanding the mechanisms behind ‘pain’
   - Correlating an etiology to clinical presentation via a pathophysiological explanation.

2. Developing Clinical Reasoning
   - Diagnostic approach to back pain
   - Integrating causes of back pain across clinical disciplines (medicine, surgery, orthopaedics)
   - A basic understanding of threshold for investigation and management

3. Effective communication and presentation

Case

PART I: Pathophysiology

Mdm Tan is a 54 year old Chinese lady who is a housewife. She comes to your clinic complaining of back pain, saying that the past week of packing the house and moving boxes around has probably strained her back severely.

Question 1:
What are possible causes of back pain? What are the different ways of classifying them?

Students should aim for categories that encompass all possible causes of back pain and be able to ask questions that clearly delineate one category from another

Muscloskeletal and Spine (Back sprain, Vertebral lesion - fracture, spondylosis, spondylolisthesis Prolapsed Intervertebral disc/cauda equina syndrome, Cord compression, Ankylosing Spondylitis) Vascular (Aortic Dissection) Thoracic/Retroperitoneal/Pelvic (Lower lobe pneumonia, Duodenal Ulcer, Body of Pancreas cancer, Invasive rectal cancer, Renal stones, Pancreatitis)

(To look at the pros and cons of each method of classification later)

Question 2:
Can you explain how each of these aetiologies lead to back pain?

Question 3:
What are the different types of pain and what are their characteristic features?

It is important to know how to differentiate between the types of pain mechanisms as the choice of pharmacotherapy differs.

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Neuropathic</th>
<th>Nociceptive</th>
<th>Somatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Example</td>
<td>Nerve or cord compression</td>
<td>Constipation Colic</td>
<td>MSK injury</td>
</tr>
<tr>
<td>Site</td>
<td>Along distribution of a nerve or dermatome</td>
<td>Poorly localised, referred to a particular region</td>
<td>Well localised</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Neuropathic</td>
<td>Nociceptive</td>
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<tr>
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<td></td>
</tr>
<tr>
<td></td>
<td>Visceral</td>
<td>Somatic</td>
<td></td>
</tr>
<tr>
<td>Timing</td>
<td>Constant</td>
<td>Intermittent</td>
<td>Constant/Upon movement of injured area</td>
</tr>
<tr>
<td>Character</td>
<td>Burning, shooting, gnawing</td>
<td>Cramping, squeezing</td>
<td>Aching, sharp</td>
</tr>
<tr>
<td>Associated symptoms</td>
<td>Parasthesia, Hyperalgesia, Allodynia</td>
<td></td>
<td>Localised swelling, tenderness</td>
</tr>
</tbody>
</table>

PART II: Diagnosis and differentials

Question 4: How would you take a history from Mdm Tan? (Facilitator can act as patient while students take history, go through with the students how to convert patient’s complaints into definite symptoms - abstract semantic qualifiers)

Define a case as an acute, chronic or an acute-on-chronic situation. In this case, this is acute - new onset, 1 week history.

Rule out trauma or a fall, of which the cause of pain is obvious and the suspicion for a fracture or to screen for other injuries is higher.

Characterise the type of back pain with a SOCRATES history, to differentiate between a non-mechanical or a mechanical type (think degenerative, muscle strain) of back pain. Non mechanical back pain can be an infiltrative type (Malignancy, Abscess) or an inflammatory type (Ankylosing spondylitis)

<table>
<thead>
<tr>
<th></th>
<th>Mechanical</th>
<th>Pathological</th>
<th>Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Course</td>
<td>Not related to time of day</td>
<td>Throughout the day, may wake patient from sleep</td>
<td>Worst at start of day, gets better through the day, occasional flares of pain</td>
</tr>
<tr>
<td>Exacerbating factors</td>
<td>Movement</td>
<td>Variable</td>
<td>Movement</td>
</tr>
<tr>
<td>Relieving</td>
<td>Rest</td>
<td>Variable</td>
<td>Movement</td>
</tr>
<tr>
<td>Character</td>
<td>Sharp localised pain</td>
<td>Burning, gnawing pain</td>
<td>Generalised stiffness</td>
</tr>
</tbody>
</table>

Ask for a history of neurological symptoms (weakness, numbness, shooting pain) and attempt to differentiate between cord (bilateral, sensory level) and peripheral nerve (unilateral, radicular pain, numbness in specific dermatome or nerve distribution) Bladder and bowel symptoms are red flags for either Cauda Equina syndrome or a Cord compression. Constitutional symptoms suggest systemic inflammation, such as malignancy, TB infection, autoimmune conditions e.g. Ankylosing Spondylitis. Systemic review to screen for other causes of back pain (retroperitoneal GI), secondary causes (e.g. primary source of a cancer) and screen for complications of her medical problem (e.g. sites of mets, systemic complications of autoimmune disease)
Past Medical History and Family history (Malignancy, back conditions, autoimmune disease)

Medication history (Painkillers) can give you an idea of severity and guide your pain management.

Pre-morbid functional history is important, ask for occupation, ADLs, bADLS, ambulation in community, walking aids if any.

*She tells you that she has been having severe back pain over the past 1 week. She denied any trauma to her back or fall recently.*

*Her pain is in the midline. She describes it as a persistent burning pain that occurs at rest and is not relieved or exacerbated by movement or lack thereof. The pain wakes her up in the middle of the night and she rates it as 8/10. Taking paracetamol and diclofenac has not helped the pain.*

*She has not experienced any numbness or weakness of her limbs and has not had any change in urinary and bowel habits recently. She also tells you that she has lost about 8 kg of weight in the recent 3 months. Her appetite has not been as good as before. She does not have any fever or night sweats. The systemic review reveals no headache, blurring of vision, nausea or vomiting, no cough or breathlessness, no abdominal pain.*

*She has no past medical history of Hypertension & Hyperlipidemia, cancer or other systemic illness. She is not on any regular medication and does not have any drug allergies. She does not smoke or drink. She is ADL independent, community ambulant and does not use any walking aids.*

**Question 5:**
What are your differentials at this point and how will you examine her?

**Differentials include**
- Pathological fracture, possible malignancy (most life threatening)
- Back sprain, Spondylosis (most common)

To share with the student that in offering differentials a helpful tip in general is to offer the most common and the most life threatening possibilities to demonstrate that he is thinking comprehensively, realistically and is a safe doctor.

**Physical Examination**
- General examination (Vitals, Temperature, body habitus - cachexia?)
- Examine the spine. Step deformities and spinous process tenderness suggest pathological fracture, spondylolisthesis, paravertebral tenderness more a musculoskeletal problem. Range of motion assesses for stiffness and whether pain is due to a disc problem or facet joint problem.
- Neurological examination and examination of anal tone (tight - UMN or lax - LMN)
- Abdominal exam to rule out AAA.
- Relevant systemic examination based on differential

*Her physical examination had the following significant findings. There was pain on palpation of the spinous processes along the thoracic region, no step deformities noted. Range of motion limited, pain in all directions of movement. Lower limb neurological examination normal, anal tone intact.*

**Vitals were stable, she was not febrile. However you took a closer look at her and noticed that she had a lump in the right supraclavicular region.**

**PART III: Principles of Investigation & Management**

**Question 6:**
What are your thoughts and how will you investigate her?

Such a patient will usually first present to the GP clinic, ED or orthopaedic clinic since back pain is the presenting complaint.
Blood investigations: FBC, UECr
Radiological: Routine Spine X ray with AP and Lateral view. Go through how to read spine x ray systematically. Look for signs suggestive of pathological fracture, and signs of infiltration (winking owl, loss of pedicle markings)

![Spine X-ray images](image-url)

X ray shows winking owl sign, loss of T11 pedicle. Considerations of such a sign - Malignancy - Primary (Bone, Myeloma, Lymphoma) vs. Secondary (Lung, Breast, Prostate), Infection - TB, Abscess.

Supraclav node may be malignant (primary – lymphoma or secondary – SCC of head and neck region or lung) or infective (e.g. TB). Consider further investigation such as LN biopsy, decompression and biopsy of vertebral lesion. Relevant investigations to search for a primary in a cancer case.

Question 7:
How will you manage her pain before any definitive management is instituted?

Application of the WHO pain ladder. Given failure of paracetamol and NSAIDS, should consider an opioid such as Pethidine, Codeine for example. Be aware that opioids cause constipation and nausea, the maxim is that ‘the pen that prescribes opioids should also order something for constipation and nausea)

Consider adjuncts like steroids to reduce inflammation.

Surgical options of pain relief can include decompression laminectomy and fusion, drainage if it is an abscess.
Question 8: What are the principles of management of her condition?

At M3 level, students are expected to outline broad principles of management. Try to get them to focus on highlighting broad principles rather than dwelling into the specifics of each type of treatment.

For example, for a possible cancer case like this. The first key is to get tissue diagnosis and stage the patient. If the LN is indeed malignant, then this is probably a stage IV cancer with spread to lymph nodes and bone. The management principles are: Decide on a curative or palliative intent. The modalities for cancer management are multidisciplinary, and include surgical, systemic therapy and radiotherapy.

Each of these modalities are employed to fit the intent. e.g. in a palliative setting, radiotherapy can be applied to reduce pain from bone mets, and decompression surgery performed. In a curative setting, surgery is to achieve resection of primary tumour with clearance of margins, while chemotherapy either eliminates residual systemic disease i.e. micrometastases (post-op chemo: adjuvant) or reduces tumor size to facilitate surgical resection (neoadjuvant).
CASE 15: 32 YEAR-OLD WOMAN WITH OBESITY

You are an MO in the outpatient medical clinic.

Ms TK is an obese 32-year-old Chinese lady, referred to you from an aesthetic physician. Ms TK has unfortunately misplaced the referral letter, but you gather that a month ago, she had visited the aesthetic physician seeking liposuction to decrease her large abdominal girth. However, the aesthetic physician declined to perform liposuction and instead suggested that she see you. Ms TK has always been on the plump side, and has had impaired fasting glucose since 25 years of age. She presents now because has noticed increased weight gain in the past 6 months despite restricting her food intake and signing up for a gym membership. You note that her weight was 75kg when she visited the aesthetic practitioner a month ago, and it has since increased to 78kg. Her height is 1.60m.

1. What history would you take?

Possible differentials are

- common obesity due to diet, metabolic syndrome
- fluid retention from cardiac, renal, or hepatic disease
- cushing’s syndrome
- hypothyroidism
- polycystic ovary syndrome
- drug-induced

History to take includes

- history of body weight, tempo of weight gain.
- past medical history esp. cardiac, renal, hepatic, endocrine disease
- dietary history and exercise over last few months
- drug history, especially intake of steroids, traditional medicines and supplements
- menstrual history: oligomenorrhoea (PCOS), menorrhagia (hypothyroid)
- symptoms of thyroid disease e.g. cold intolerance, constipation

2. What signs would you look for on physical examination?

- Cushingoid features as below. Also complications e.g. proximal myopathy, cataracts, and hypertension
- Goitre, slow-relaxing reflexes
- Pedal edema, S3 heart sound, basal lung creps, elevated JVP.

Physical examination indeed reveals central obesity, facial plethora, severe acne, supraclavicular fat pads, abdominal striae, and thin skin. She has no goitre, no pedal edema, elevated jugular venous pressure, or basal lung crepitations. Muscle power is 5/5. Clinic blood pressure is 145/90.

3. What is the most likely diagnosis?

Cushing’s syndrome

As you examine her, she shares with you that liposuction was her mother’s idea. She explains that she is under pressure from traditional Chinese parents to find a boyfriend, and thinks that she has not been successful thus far because she is too plump, ‘unattractive’ and ‘too manly’. She has had recurrent problems with acne, for which she has seen multiple dermatologists over many years, been treated with doxycycline and isotretinoin, which have failed to fully resolve the acne. She is also concerned that she has thick axillary hair and has to shave regularly. Her parents have also commented on her deep voice as ‘not feminine’. Due to all this, she has felt sad, and was prescribed an antidepressant by her GP.
4. Comment on her concerns

This is a picture suggestive of virilization – need to consider adrenal tumor (produces corticosteroids and androgens) especially if tempo of onset is rapid.

You explain that to confirm your diagnosis, you would like her to take 1mg of methasone at 11pm tonight, and return at 8am tomorrow morning for a blood test. Ms TK complains, ‘this is so troublesome, can I just do the blood test now’? The 8am blood test confirms your diagnosis. You explain to Ms TK that this is necessary, and in fact, she will still require further investigation to determine the cause of her diagnosis.

5. How would you answer Ms TK’s concern?

Random blood test is not informative as (1) Cortisol secretion follows a diurnal rhythm, to test for hypercortisolism, blood should be drawn at the expected trough level i.e. midnight. (2) a dynamic test i.e. dexamethasone suppression is more useful. The principle for this is that dexamethasone should exert negative feedback on cortisol secretion normally; if cortisol is not suppressed, then it is oversecreted.

6. Are there any alternative tests to confirm your diagnosis?

24h urinary cortisol or midnight cortisol levels.

7. What are the possible sites of overproduction of cortisol

** First rule out exogenous steroid intake **

ACTH independent: adrenal adenoma or carcinoma

ACTH dependent: pituitary hypersecretion from pituitary tumor (Cushing’s disease), or ectopic ACTH secretion (e.g. by a lung cancer)

8. How would you distinguish between these sites? Hence or otherwise, what further workup would you order for Ms TK?

- Skin hyperpigmentation (implies high ACTH as ACTH precursor has melanocyte stimulating component
- ACTH levels
- High-dose dexamethasone suppression test - failure to suppress with low-dose diagnoses Cushing’s syndrome. High-dose distinguishes pituitary from ectopic and adrenal causes - pituitary tumors do not respond to low dose dexamethasone but still respond to high dose dexamethasone (i.e. cortisol will be suppressed).

Workup for localization

- Adrenal CT
- Pituitary MRI
- Chest X ray or CT
- [Further tests e.g. CRH test, inferior petrosal sinus samping]

Workup for complications
• Blood pressure
• Fasting blood glucose, HbA1c
• Renal panel (see later)

The first test results to return reveal:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>143 mmol/L</td>
<td>8am cortisol</td>
</tr>
<tr>
<td>K</td>
<td>3.3 mmol/L</td>
<td>ACTH</td>
</tr>
<tr>
<td>Urea</td>
<td>4.4 mmol/L</td>
<td>Testosterone</td>
</tr>
<tr>
<td>Cr</td>
<td>50 mmol/L</td>
<td>DHEA-SO4</td>
</tr>
</tbody>
</table>

Fasting blood glucose: 9.0 mmol/L

Adrenal CT: no adrenal mass detected

Chest X-ray: normal

9. Please interpret the results above.

- 8am cortisol – not suppressed by dexamethasone. Hence, Cushing’s
- ACTH is “normal” – this is actually abnormal. If cortisol is so high, ACTH should be suppressed. A “normal” ACTH is suspicious for ACTH secretion (either pituitary or ectopic)
- Normal testosterone, DHEA (adrenal steroid), and adrenal CT is reassuring that there is no virilizing adrenal tumor
- Renal panel – cortisol has some adrenocorticoid effect, so this promotes Na reabsorption and K secretion, leading to the borderline high Na and low K.
- Impaired fasting glucose – complication of Cushing’s
- Chest X-ray – quick screen for source of ectopic ACTH i.e. lung CA

Ms TK is instructed to take 2mg of dexamethasone 6-hourly for 2 days, and return for a blood test at 8am on the third day. This time, cortisol is 260 nmol/L (reference range: <50% of original result).

10. Please interpret this result

This is the high dose dexamethasone suppression – see earlier explanation. Shows that the steroids are due to pituitary ACTH secretion.

Pituitary MRI finds a small mass lesion in the pituitary. There is no headache, visual field defect, or cranial nerve impairment. Thyroid function test, FSH and LH is normal. Ms TK receives further tests and undergoes trans-sphenoidal resection of pituitary.

Post-operatively, the ICU nurses notice that she has been passing large quantities of dilute urine for the past 4 hours. A renal panel shows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na</td>
<td>152 mmol/L</td>
<td>Urine Na</td>
</tr>
<tr>
<td>K</td>
<td>5.0 mmol/L</td>
<td></td>
</tr>
<tr>
<td>Urea</td>
<td>8.4 mmol/L</td>
<td></td>
</tr>
</tbody>
</table>
11. What has happened post-operatively? How would you manage this?

Diabetes insipidus, a known complication due to damage or stunning of the posterior pituitary.

Management is with fluids, DDAVP (a synthetic ADH analogue that has been modified in some ways), and close monitoring for urine output and serial renal panel.
CASE 16: 85 YEAR-OLD GENTLEMAN WHO PRESENTED WITH A FALL

DISCUSSIONS

Mr Tan, a 85 year old gentleman, presents to the ED immediately after a witnessed fall.

Q1) What are the possible etiologies to the fall that you must rule out. Describe the symptoms and signs that you will ask for of three possible etiologies.

Stroke – Risk factors as defined in CHAD2-VA2Sc, Acute onset, Hemiparesis, Facial droop, Cranial nerve signs, Clumsiness

Hypoglycemia – Hyperacute onset, history of reduced food intake, excessive insulin use, Fever, Lack of aura, LOC, post-ictally normal.

Seizure – Hyperacute onset, history of seizures/epilepsy, stroke before, pre-ictal symptoms, jerking of limbs, injury to tongue, uprolling of eyes, post-ictally lethargy/altered mental status.

Q2) What are possible complications that you need to evaluate for?

Head injury

Fractures

Intracranial bleeding

Further history taking from his caregiver reveals:

He was trying to get up from his bed to use the toilet when the fall happened. Mr Tan loss consciousness briefly but regained it soon after. After which he was able to call for help. He complained of pain over the back of his head. He has a past medical history of hypertension, hyperlipidemia and diabetes and is currently on medications for all of them. He also had ischemic stroke five years ago.

History taking taken from the patient reveals:

There was no giddiness or light-headedness prior to the incident. There was no loss of consciousness. He mentioned that he fell because he felt weak. After the incident, there was no nausea/vomiting. He was oriented to time and place and person.

Q3) What would you look out for the in the physical examination?

General examination: Look for signs of injury, score GCS, assess for orientation, nutritional status/hydration status of patient

Neurological examination

UL/LL: Tone, reflexes, power. Observe the distribution of weakness

Cranial nerves: Look for facial droop, localizing signs for cranial nerves

Cerebellar examination
Physical examination yield the following:

- **Consciousness** – Oriented to time, place and person. Slightly lethargic.
- **Vitals** – T 36.5 degrees Celsius, Supine BP 110/70, Standing BP 100/65, PR 85, SpO2 98%
- **General inspection** – Hematoma noted over the right temporal region
- **Neurological examination** – Pupils were equal and reactive to light.
  - Left upper and lower limb power was reduced: 4/5
  - Right upper and lower limbs power normal
  - Patient was hyporeflexic and had decreased tone on the left.
  - Slight facial droop on right
  - Cerebellar examination was grossly normal.
  - His speech was coherent. He was able to comprehend information given to him. Eyes were in a neutral position.
  - Pronator drift absent
- No tenderness or deformities over his extremities were noted

Q4) Where can the lesion be?

Internal capsule

Brainstem

Q5) What are some investigations you would perform? Describe 3 and your rationale.

Bloods: FBC, Renal Panel, Hypocount, INR

Imaging: CT brain

CT brain was done and the results were normal

Q6) Why must you perform a CT brain scan in this case?

To rule out acute bleed secondary to the head injury.

You also checked his full blood count, renal panel and hypocount and the results are as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>12 g/dL</td>
<td>12-16 g/dL</td>
</tr>
<tr>
<td>MCV</td>
<td>96 fL</td>
<td>96-108 fL</td>
</tr>
<tr>
<td>Hct</td>
<td>38%</td>
<td>38-52%</td>
</tr>
<tr>
<td>Sodium</td>
<td>120 mmol/L</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>2.5 mmol/L</td>
<td>3.5-5.5 mmol/L</td>
</tr>
<tr>
<td>Urea</td>
<td>6.5 mmol/L</td>
<td>2.7-6.9 mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>99 µmol/L</td>
<td>54-µmol/L</td>
</tr>
<tr>
<td>CBG</td>
<td>3.5 mmol/L</td>
<td>7.0-11.1 mmol/L</td>
</tr>
</tbody>
</table>
MRI revealed a hypodense lesion noted on the right brainstem

Q7) What are possible differentials for his fall now? Name 4.

Previous brainstem stroke leading to weakness, Hyponatremia, Hypoglycemia, Anemia

Q8) What is an important complication that you must look out for in this patient?

Epidural hemorrhage

Q9) How would you treat the patient? Describe 4 broad management principles.

Immediately:

Correct the correctable: Hyponatremia (3% sodium), hypokalemia (replace 10 mmol/h), have dextrose replacement,

Prevent falls

Input/output monitoring

Q30mins – Q1h vitals monitoring

Subsequently:

Consider referral to PT/OT for rehabilitation of his stroke

After 1 hour, the patient suddenly loss consciousness. His vitals are as follows:

T: 36.9°C, BP: 170/80, HR: 45 bpm, SpO2: 96% RA.

On examination, he had labored and irregular breathing. GCS: 3/15.

A repeat CT brain showed the following:
Q10) Describe 2 abnormalities seen in the scan above.

The scan above shows a lens shaped hyperdense lesion on the right, together with a midline shift. The above is suggestive of epidural hemorrhage complicated by raised intracranial pressure.

Q11) What will the definitive management be for this patient?

Definitive management of this patient will be immediate neurosurgical decompression. This patient already shows Cushing’s triad of High blood pressure (SBP>160 mmHg), Bradycardia (<50 bpm) and Irregular breathing, indicating that this patient is likely to be coning.

Q12) What will your advice be for this patient should he recover? Describe 3 that will improve the outcome for this patient in the long run.

Advise the family to consider getting an OT to go down to help assess family environment if this hasn’t already been done.

Caregiver training to help caregiver better understand what she needs to watch out for.

Consider PT to help Mr Tan regain balance and strength, both of which are the top two factors that are positively correlated with falls prevention.
CASE 17: 65 YEAR-OLD CHINESE GENTLEMAN WITH WEAKNESS AND NUMBNESS OF HIS LEFT ARM AND BOTH LEGS

LEARNING POINTS

- Approach to weakness with sensory loss
- Approach to spinal pathologies

DISCUSSIONS

Mr Ng is a 65 year old Chinese retiree presenting with weakness and numbness of his left arm, as well as both his legs.

Q1) What are possible causes that can account for Mr Ng’s symptoms? Describe 3 causes.

Weakness can be broadly classified into upper motor neuron, lower motor neuron or mixed.

Upper motor neuron weakness pathologies begin proximally from the anterior horn cell up to the cortex of the brain while lower motor neuron pathologies are distal from the anterior horn cell.

Examples of upper motor neuron pathologies include spinal cord pathologies (cervical myelopathy, syringomyelia, epidural abscess), brainstem, cerebellar, subcortical areas and cortex (stroke, abscess, tumours). In addition, it is useful to consider conditions that attack CNS in general such as multiple sclerosis.

Lower motor neuron pathologies has three broad classes: the peripheral nerves, the NMJ and the muscle itself.

Anterior horn cell pathologies may present as mixed signs of upper motor neuron and lower motor neuron weakness. Similarly, disseminated conditions like vitamin B12 deficiency or taboparesis in syphilis patients.

In Mr Ng’s case, he has both weakness and sensory loss on his left arm, which is also observed in his legs. If weakness and sensory loss occurs together, it effectively rules out muscular involvement, NMJ involvement and motor neuron disease. This limits it to mainly upper motor neuron pathologies, unless there are disseminated lesions that attack both sensory nerves and motor nerves. It is then important to consider which part of the CNS is hit, by taking a proper history and doing a physical examination.

Q2) What are some important things that you will ask for in the history?

History should be geared towards establishing the time course of the condition and distribution of the motor and sensory loss. Consider also autonomic dysfunction. Concomitant symptoms such as fever, pain, imbalance, cranial nerve symptoms etc should be asked.

Preceding events should be explored too, while also considering risk factors for the respective pathologies such as cardiovascular risk factors, trauma, previous spinal surgeries, previous infections, LOW/LOA etc.

On further history taking, you find that Mr Ng’s symptoms have been going on for 8 months. He also experienced some difficulty in walking as he felt unbalanced and undexterous. No respiratory difficulties were noted. His medical and family histories are unremarkable and he is currently not on any medications.
Q3) What are some things you will look out for on physical examination? Describe 4 and elaborate on how it can help you in your diagnosis.

The neurological examination is arguably the most important to rule out or rule in conditions. Use this to look for signs of UMN/LMN conditions. It is important to correlate the signs to the time course of the disease, as an UMN lesion may present with hyporeflexia and hypotonia in the hyperacute setting (few hours) and may progress subsequently to hyperreflexia. In chronic cases, the hyperreflexia may disappear and become hyporeflexic, although this typically only happens many years down the road.

Characterise the sensory deficits into spinothalamic or DCML tracts and note the distribution.

Look for possible etiologies too such as spinal tenderness which may be suggestive of an infective/inflammatory process going on in the spine.

On physical examination, the following was noted:

- **Vitals:** Afebrile, BP 120/75, PR 85 bpm SpO2 99% RA
- **Inspection:** General wasting of muscles in his left upper limb. Stooped posture, limited neck mobility
- **Neurological examination:**
  - Left UL: Global hypotonia, power 3/5, diminished biceps and triceps reflexes. Impaired pain and light touch in all dermatomes
  - Bilateral LL: Global hypertonia, power 3/5, exaggerated knee jerk and ankle reflexes, positive Babinski response, impaired pain and vibration in all dermatomes
  - **Gait:** Spastic gait was observed
  - Pain shooting down left hand on neck extension
  - No other neurological deficits or abnormalities
  - No localized tenderness of spine

Q4) In view of the above, suggest three possible differentials that can explain the symptoms above.

- Cervical myelopathy, epidural abscess, syringomyelia

Q5) What are some investigations that you will do? Name 2.

- Lateral C-spine X ray, Cervical MRI, somatosensory motor potential (SSMP)

Lateral C-spine X ray showed the following:
Q6) What is the most likely diagnosis? Describe your reasoning.

Cervical myelopathy. In his age group, it is likely to be cervical spondylolytic myelopathy, the most common cause of myelopathy in his age group. This is supported also by his history, which revealed a more subacute course to his condition. The difficulty in walking with an impairment in dexterity supports this diagnosis too. The physical examination findings of limited neck mobility further strengthens this diagnosis. On lateral C-spine X ray it shows loss of IV disc height with osteophytic changes in C5/C6.

Q7) How will you counsel Mr Ng about the management of his condition?

Conservative management vs surgical management. In these patients, surgical management has been shown to be superior in neurological outcome compared to those on conservative treatment. Since Mr Tan has no significant risk factors that weigh against surgery, it should be the first line for him. Consider conservative management as an adjunct to the surgery while he awaits surgery (collar, analgesics).
CASE 18: 13 MONTH-OLD GIRL WITH ABNORMAL JERKING OF HER LIMBS

Baby Sara is a 13 month-old baby who presents with an episode of abnormal jerking of her limbs.

Q1) How would you take a history of this patient?

History is the most important part of the evaluation

Differentiate from other mimics

Determine the type of seizure

Pre-ictal, ictal and postictal

Semiotics of seizure history

On history taking, the mother revealed that the child was febrile and had running nose for a day. She became irritable minutes before the seizure episode. During the episode, there was uprolling of eyes, jerking of all 4 limbs and no response to her mom’s call. The entire episode lasted for 30s. After that, the child was drowsy and cried, no paralysis of limbs

Antenatal/Birth Hx

- No fever or any infections during pregnancy
- Normal birth, 3.5kg, Apgar Score of 9 at birth and 5 minutes

PMHx and Drug Hx: Nothing significant

Vaccination Hx: Up to date

Developmental Hx: Normal

Q2) What type of seizure is this? What are other conditions that may mimic seizures? Name 3 conditions.

Generalized Tonic-Clonic Seizure

Others:

Breath-holding spell

Syncope

Night terror

Q3) What are some etiologies of seizure? Name 5.

Febrile

Cryptogenic (no overt cause in neurologically normal child)

Remote symptomatic

Acute symptomatic

Infections (CNS)
Electrolyte imbalances

Intra-cranial bleed

Trauma

Progressive encephalopathy

Epilepsy syndrome

Neurocutaneous/Metabolic diseases

Q4) What are some neurocutaneous stigmata you would look out for in the physical examination? Name 4 stigmata and the conditions they are associated with.

Tuberous sclerosis – Angiofibroma, shagreen spots

Sturge-Weber syndrome – Port-wine stains

Cafè au-lait spots, axillary – Neurofibromatosis

Q5) What other things would you look out for in the physical examination?

Neurological exam – hypotonia, hypertonia, hemiplegia

Rule out meningitis

Physical examinations was performed.

Vitals

- Temperate: 38.0 degree Celsius
- BP: 75/40
- PR: 150
- SpO2: 100%
- 50% for Height, weight and head circumference

Neurological

- No dysmorphism or neurocutaneous stigmata
- No neck stiffness, Kernig’s or Brudzinski’s sign
- Normal tone
- Reflexes 2+ Bilateral
- Moving all 4 limbs
- Normal plantar reflex

Others: Normal

Q6) What preliminary investigations would you do? Describe 3 and your rationale.

FBC

Electrolyte

Glucose

Investigations: No abnormalities found
Q7) What is your working diagnosis? Outline your reasons.

Simple Febrile Seizure secondary to URTI.

The child was diagnosed with upper respiratory tract infection and febrile seizure by the paediatrician in charge.

She had another episode of seizure in the wards. You were called to see her. The nurses ask you how they should react if another such episode occur.

Q8) What is status epilepticus? Describe how you would manage this medical emergency.

Different definition: > 10 minutes or > 30 minutes of continuous seizure or two or more sequential seizures without full recovery of consciousness between seizures

Management

- ABC, Position patient away from danger and to the side
- Check glucose early along with other investigations
- 1st line
  - If seizures last more than 5 minutes, administer IV Lorazepam 0.1 mg/kg or rectal diazepam 0.5 mg/kg
- 2nd line
  - IV phenytoin 15 – 20 mg/kg
  - IV phenobarbitone 20mg/kg
- 3rd line
  - ICU + IV midazolam, thiopentone, propofol

Baby Sara recovered and had no further episodes of febrile seizure. The parents asked if their child has epilepsy, and whether this would affect her development.

Q9) How would you educate the parents on the topic of febrile seizure? Highlight 5 important points regarding the following areas. (Prognosis, management, red flags)

Definition

- Epileptic seizure occurring in childhood after age of 1 month,
- Associated with febrile illness (other than CNS infections)
- Without previous neonatal seizures or a previous unprovoked seizure
- Not meeting criteria for other acute symptomatic seizures

Classification

Simple versus Complex (Duration, No. of episodes with 24 hours, other complications or focal)

Prognosis and statistics

- Risk of epilepsy is same as standard population in absence of neurological disease, delayed developments or cerebral palsy
- Approximately one in every 25 children will have at least 1 febrile seizure and more than one-third of these children will have additional febrile seizures

Risk factors for increased recurrence of febrile seizure
• Onset < 15 months
• Family history of febrile fits and epilepsy
• Complex febrile seizure
• Frequent febrile episodes

How to manage

• Airway, Breathing, Circulation
• Observe – Take a video
• Anti-pyretics – Paracetamol or ibuprofen
• Rectal diazepam: dose 0.5mg/kg or Intra-nasal/buccal midazolam
• Red flags to look out for:
  o Different form of seizure from Generalized Tonic Clonic
  o Todd’s paralysis
  o Status epilepticus
  o Developmental delay

Q10) What is the definition of epilepsy?

Epilepsy occurs when 2 or more epileptic seizures occur unprovoked by any immediately identifiable cause. Must be 24 hours apart.
CASE 19: 70 YEAR-OLD MALAY GENTLEMAN WITH A CHANGE IN PERSONALITY

Mr Ahmad is a 70 year old Malay gentleman. He stays on his own. He is brought to the clinic by his son, who complains that his father has been behaving increasingly more oddly over the past year. He says that he has noticed his father making mistakes with his personal accounts, and occasionally having times when he speaks unrecognizable words or stares into space. He says that his father of late does not recognise him and thinks that he is someone else. Mr Ahmad has stopped driving because he gets lost and has also bumped his car several times while parking over the past 2 years.

Q1) Classify your differential diagnosis (no need to elaborate on specific causes). What are some cardinal features of these classes? Suggest how these classes may be distinguished.

Dementia vs Delirium vs Depression.

Q2) State 5 physical signs that you would look for which are not from the neurological system. Justify your answer.

Can examine cardio system, abdominal system (for signs of liver/renal failure), endocrine system (thyroid, cushing’s). This list is not exhaustive.

Q3) Suggest 3 bedside tests that would aid your assessment.

AMT, MMSE, tests of frontal lobe function
Postural blood pressure
Urine dipstick, capillary glucose, ECG

Q4) State 5 relevant investigations. Justify your answer.

Dementia = need to rule out super a lot of things because there are reversible causes
FBC, Renal Panel, LFT, TFT, Calcium panel
VDRL/other syphilis screen, B12, folate, CXR,
Brain imaging (CT scan will suffice for older people to look for SDH, for younger pt consider MRI)
+- EEG

Mr Ahmad’s son also complains that that his flat is cluttered with dishes of uneaten food, and cups of undrunk tea. On questioning, Mr Ahmad describes how many guests have come to his home and he has prepared food for them. However, Mr Ahmad also complains of small children and animals invading his home at times throughout the day.

When Mr Ahmad gets up, you notice that he has a slow unsteady gait. The tone in his limbs is rigid and is fairly symmetrical.

Q5) Suggest 3 most likely differential diagnosis. Suggest how they may be distinguished.

Dementia with Lewy bodies, Parkinson dementia, coexistent Parkinsonian disease and neurodegenerative disease.
Mr Ahmad is given a referral to neurology. Several months later, you are called to see a patient at night and are surprised to see him again. He had been admitted for a right hip fracture after a fall and is post op day 3 after a right hemiarthroplasty. He is agitated and confused, and has a fever of 40°C.

Q6) What is Mr Ahmad’s current problem? What is the aim of treatment?
Delirium, address underlying cause.

Q7) What are some possible etiologies in a post operative patient such as Mr Ahmad?

- Fluid / Electrolytes abnormalities
  - Hyponatremia
  - Hypovolemia
  - Hemorrhage
- Infections
  - Surgical sites
  - Other hospital-acquired infections
- Intra-cranial:
  - Cerebrovascular accident (hemorrhage or ischemic)
- Etiologies of hypoxia
  - Acute myocardial infarction
  - Pulmonary embolism
- Pain

You notice that both of Mr Ahmad’s hands have severe tremors and that he is very stiff. The nurse tells you that Mr Ahmad had been given haloperidol the night before by the on-call MO, as Mr Ahmad had been complaining of hearing voices and seeing small animals.

Q8) What condition would you like to exclude?
Neuroleptic malignant syndrome

Q9) Suggest some other differential diagnosis.
CNS infection, Systemic infection, Seizures, Thyrotoxicosis, Serotonin syndrome,

Q10) How would you manage this condition?
Call senior, stop haloperidol
Draw bloods - FBC, RP, LFT, CK
Supportive therapy - fluids, electrolytes, cooling blankets.
Cardiorespiratory support - antiarrhythmics, ventilation, pacing, blood pressure lowering
DVT prophylaxis
May need BZD for agitation
CASE 20: 50 YEAR-OLD CHINESE GENTLEMAN WITH FORGETFULNESS

Mr Wong is a 50 year old Chinese gentleman. He presents to your clinic with the chief complaint of forgetfulness. He says that his job as an investment banker is not going well as he has lost the bank several hundred thousand dollars from poor transactions. You notice that he has problems with pronouncing the words he is saying and his hands tremble when he reaches out to shake yours. Sitting outside in the waiting room is a gentleman called Mr Tan, whom Mr Wong describes as his ‘life partner’. Your diligent questioning reveals that he is in a steady relationship with Mr Tan, but had ‘a few dalliances here and there’ when he was in his 30s. He had painless genital sores during that period but they had resolved on their own.

Q1) What is the most likely diagnosis, and what is the causative organism? What other differentials would you consider?

Neurosyphilis, Treponema pallidum.
Consider HIV and associated CNS infection.
Consider intracranial pathology e.g. brain tumour
Consider neurodegenerative disease e.g. Huntington

Q2) What is a characteristic ocular sign?

Argyll Robertson Pupil - nonreactive to light but can accommodate

Q3) What are some confirmatory investigations?

Serum FTA-Abs or EIA or TPPA
Serum RPR
CSF VDRL, WBC, Protein

Q4) What is the most appropriate therapy?

IM Benzathine penicillin G 2.4 million units q1week for 3 weeks

Q5) What complications may arise from the therapy?

Jarisch Herxheimer reaction
Complications of penicillin - allergy
Complications of injection - pain, muscle hematoma, infection

Q6) What are some other neurological syndromes of syphilis?

Tabes dorsalis
General paresis of the insane
CASE 21: 70 YEAR-OLD GENTLEMAN WHO PRESENTS WITH LOWER LIMB SWELLING

LEARNING OBJECTIVES

- Approach to Edema
- Approach to Chronic Kidney Disease

DISCUSSIONS

A 70 year old man, Mr Lim, presents with lower limb swelling. The swelling started 2 weeks ago and has been bothering him since.

Q1) What are the etiologies of lower limb swelling?
Refer to discussion in Q2.

Q2) What will you ask on history taking?

Key considerations:

a) Unilateral versus bilateral

<table>
<thead>
<tr>
<th>Unilateral</th>
<th>Bilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generally due to localized causes.</td>
<td>Generally due to systemic causes (e.g. poor heart function, hypoalbuminemia state)</td>
</tr>
<tr>
<td>Cellulitis, DVT, venous insufficiency (varicose veins), lymphoedema, necrotizing fasciitis, Pelvic tumour compressing the iliac veins, orthopaedic causes: ruptured Baker’s cyst, septic arthritis, compartment syndrome</td>
<td>Cardiac failure, Renal failure, Liver failure, Nephrotic Syndrome, Protein losing entraphathy, allergy (angioedema), hypothyroidism (myxedema)</td>
</tr>
</tbody>
</table>

b) Painful versus Painless

In a patient with painful pedal edema, it suggests the following: fast onset (deep vein thrombosis leading to stretching of fascia and cutaneous tissue), infection (cellulitis, necrotizing fasciitis), inflammation (Henoch Schlooein Purpura).

In a patient with painless pedal edema, the etiology is likely to cause slow accumulation of the fluid, hence, allowing the cutaneous tissue to stretch without much pain.

c) Temporal History – onset and duration

d) Approach by Organ Systems

- Cardiac: Heart failure (Orthopnoea, paroxysmal nocturnal dyspnea)
- Hepatic: Liver failure (Jaundice, bruising, pruritus, history of hepatitis)
- Renal:
  - Renal failure (History of renal failure, on dialysis? How often does he go for dialysis? Urine output, History of diabetes)
  - Nephrotic syndrome (Frothy urine, urine tests done before showing abnormal protein levels)
  - Nephritic syndrome (Hematuria)
- Local causes: History of immobility, long travel, local tenderness etc.
e) Rule out Iatrogenic Causes

- Drugs: Calcium channel blockers (nifedipine, amlodipine, rosiglitazone), newly started drugs

f) Effect on function

- Effect on walking, ADLs

Some discussion points: (Pathophysiology)

<table>
<thead>
<tr>
<th>Question</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>How does cellulitis cause oedema?</td>
<td>Infection, Release of cytokines and other inflammatory markers to recruit immune cells, inflammatory reaction, blood vessels vasodilate, become more permeable</td>
</tr>
<tr>
<td>How does nephrotic syndrome cause oedema?</td>
<td>Hypoalbuminemia, Intravascular oncotic pressure decreases, imbalance of Starling’s forces, fluid leaves blood vessel and enters interstitial fluid compartment</td>
</tr>
<tr>
<td>How does cardiac failure cause oedema?</td>
<td>What is the definition of heart failure? Back pressure effect from the heart, intravascular hydrostatic pressure in the veins leading to the heart increases, imbalance of Starling’s forces</td>
</tr>
<tr>
<td>Differentiate between transudate and exudate (not relevant in pedal edema, but useful in pleural effusion)</td>
<td>What is Light’s criteria?</td>
</tr>
</tbody>
</table>

He reveals that he has this leg swelling for the last 2 months, and they got progressively worse. Currently, it is up to the level of his knee bilaterally. It is not painful, nor erythematous.

Upon review of systems, he has frothy urine, polyuria and polydipsia. There is no chest pain, exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, jaundice, bruising and abdominal distension.

He is unclear about his past medical history, but vaguely remembering having diabetes mellitus type 2, hypertension and hyperlipidemia for the last 10 years. His last appointment with the doctor was 2 years ago and he defaulted the other appointments (citing the high costs of each consultation).

He has no known drug allergies. He is on various oral medications and is uncompliant to them. He cannot remember what medications he is on.

He smokes approximately 10 cigarettes a day for the last 30 years. He stays with his friend in a rental apartment.

Q2) Which features would you look out for on physical examination?

- Vitals especially SpO2 (DVT/PE causing hypoxia)
- General inspection- jaundice, pallor, respiratory distress, sallow appearance, lines
- Peripheries- Palmar erythema, asterixis, diabetic dermopathy, other signs e.g. peripheral amputations, diabetic ulcers, AV fistula
- Conjunctiva- Scleral icterus, conjunctival pallor
- Neck- Jugular venous pulse elevated, double lumen central venous catheters (suggestive of renal replacement therapy)
Lungs - Crepitations
Heart - Murmurs, S3 heart sound, deviation of apex beat, murmurs
Abdomen - organomegaly, ballotable kidneys, ascites, stigmata of chronic liver disease, Tenckoff catheters
CNS: peripheral neuropathy (absent reflexes, reduced sensation, paraesthesia)
Lower limb - pitting or non-pitting edema, unilateral or bilateral swelling, signs of inflammation, varicose veins

This is a systematic way of performing the physical examination. It will help you to be complete in your examination. After the physical examination, it will be good to consolidate your findings to answer the following questions:

- What is the clinical diagnosis? Any possible differentials?
- What is the underlying etiology?
- What is the severity? Are the any complications?

**His vitals signs are:**

<table>
<thead>
<tr>
<th>BP</th>
<th>160/110mmHg</th>
<th>PR</th>
<th>80bpm</th>
<th>RR</th>
<th>518</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO2</td>
<td>100% (room air)</td>
<td>Temp</td>
<td>Afebrile</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Physical examination**

- **General appearance:** Obese gentleman who is comfortable and alert; conjunctiva pallor present, no asterixis or pronator drift
- **Cardiovascular:** Normal heart sounds heard with no deviated apex beat, no murmur/gallops/rubs heard, jugular venous pressure not raised
- **Lungs:** Equal breath sounds heard with no adventitia breath sounds
- **Abdomen:** Soft and nontender with no organomegaly; normal bowel sounds heard; no shifting dullness; no renal bruit heard
- **Neurological:** Peripheral neuropathy (gloves and stocking distribution)
- **Extremities:** Pedal edema up to the knee, diabetic dermopathy seen over the shins

**Q3) What is your diagnosis? Explain your answer.**

Chronic renal failure secondary to diabetic nephropathy

**Q4) What investigations would you like to order?**

**Laboratory (Blood)**

- **Full blood count**
  - Raised TW (local infection or DVT)
  - Anemia (secondary to CKD)
- **Liver function Test** – Marker of liver function
- **PT/PTT** – Estimate of liver function
  - However, note that this is deranged only in late stages of liver diseases.
- **Renal panel** – Creatinine raised in renal failure, Complications of renal dx (Electrolyte imbalance) or cardiac disease (Hypervolemic hyponatremia)
- **Pro-BNP** – raised in heart failure
- **Thyroid function test** – pretibial myxedema
- **Calcium/ phosphate/ parathyroid hormone levels:** hypocalcemia plus hyperphosphatemia (Secondary hyperparathyroidism)

**Urine**
• Dipstick
  o Proteinuria
• Albumin/Creatinine ratio (ACR) or Protein/Creatinine ratio (PCR)
  o These are done in spot urine test (random samples)
• 24-hour urine creatinine or protein levels
  o For assessment of creatinine clearance (for estimation of GFR) and assessment of proteinuria
• Urine formed element microscopy examination
  o Looks for casts, WBC, RBC
• Urine phase-contrast microscopic examination
  o To differentiate between glomerular or non-glomerular bleeding
  o Isomorphic (non-glomerular), dysmorphic (glomerular)

Radiological

• Transabdominal Ultrasound – pelvic masses, shrunken kidneys
• Doppler studies – renal artery stenosis, renal vein thrombosis

Others

• 2D Echocardiography: Cardiac function
• OCG/ colonoscopy: Protein-losing enteropathies

His laboratory results read:

<table>
<thead>
<tr>
<th>Hb</th>
<th>10.3</th>
<th>Na</th>
<th>142</th>
<th>LDL</th>
<th>5.2</th>
<th>Ca</th>
<th>1.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>7</td>
<td>K</td>
<td>5.2</td>
<td>HDL</td>
<td>0.8</td>
<td>PO4</td>
<td>3.2</td>
</tr>
<tr>
<td>Plt/</td>
<td>280</td>
<td>CT</td>
<td>99</td>
<td>TG</td>
<td>2</td>
<td>PTH</td>
<td>↑</td>
</tr>
<tr>
<td>MCV</td>
<td>75</td>
<td>HCO3</td>
<td>20</td>
<td>HbA1c</td>
<td>8.3 %</td>
<td>Vit D</td>
<td>low</td>
</tr>
<tr>
<td>Cr</td>
<td>300</td>
<td>Urea</td>
<td>8</td>
<td>Urea</td>
<td>300</td>
<td>PTH</td>
<td>↑</td>
</tr>
</tbody>
</table>

His baseline Cr (2 years ago): 150.

Q5) Interpret the laboratory findings.

• Raised Creatinine
• Raised HbA1C (Diabetes Mellitus)
• Hypocalcemia with raised phosphate, PTH, Vitamin B

Q6) What is the definition of CKD?

Irreversible deterioration in renal function for more than 3 months – GFR < 60ml/min for > 3 months.

Q7) What is the aetiology of CKD in this patient? What other aetiologies can you think of? Name 4 more.

• Diabetes Mellitus (61.7%)
• Primary glomerulonephritis (18.8%)
• Hypertension and renovascular disease (10%)
• Autoimmune disease/ GN with systemic manifestations (2.2%)
• Polycystic kidney disease (1.8%)
• Obstruction (1.6%)
• VUR/ Chronic pyelonephritis (0.7%)
Discussion Points:

We can presume DM if there is a longstanding history of poorly controlled DM. But be aware that this clinical presumption is occasionally wrong. In a younger patient, you will want to work up more carefully. May I add a compare and contrast with two other clinical scenarios:

a) If the same pt presents with a 2-day history of rapidly worsening bilateral LL edema, what would your approach be?
   - ? Acute cardiac event causing fluid overload
   - ? Acute kidney injury: prerenal vs renal vs postrenal
   - DVT becomes more worrying

b) If the patient is 30 yrs old and has no past medical hx, how would your approach differ?
   - Workup for glomerulonephritis.
   - Exact workup depends on whether nephrotic vs nephritic picture.
   - Baseline
     - FBC, UECr, LFT,
     - Urine dipstick, total protein, UFEME and phase contrast microscopy, cultures
   - Etiology workup
     - Exclude post-renal obstruction, renal vasculopathy (Renal Ultrasound/Doppler)
     - HepB/C/HIV
     - ANA, ANCA, anti dsDNA C3, C4
     - Hx of recent URTI etc
     - HbA1c
     - Myeloma panel in older patient (serum and urine protein electrophoresis for M bands, bence jonce protein)
     - Eventually renal biopsy

Q8) What are the complications of renal failure? For each complication, explain the pathophysiological basis of these complications.

Complications of renal disease

<table>
<thead>
<tr>
<th>System</th>
<th>Complication</th>
<th>Associated Conditions</th>
<th>Discussion of pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Anemia</td>
<td></td>
<td>Deficiency of EPO, Diminished erythropoiesis due to toxic effects of uraemia on marrow precursor cells, anemia of chronic disease</td>
</tr>
<tr>
<td></td>
<td>Hypercalcemia / hypocalcemia, Bone diseases/ fractures</td>
<td></td>
<td>Cause: (1) loss of renal 1 alpha hydroxylase enzyme which converts cholecalciferol (vitamin D) to active metabolite 1,25 dihydroxycholecalciferol, causing hypocalcemia; (2) Phosphate accumulation leading (1) + (2) lead to secondary hyperparathyroidism and bone disease</td>
</tr>
<tr>
<td>Uremia</td>
<td>Pericarditis, Encephalopathy Metabolic acidosis Peripheral neuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electrolyte</td>
<td>Hyperkalemia</td>
<td></td>
<td>Accumulations of metabolic waste</td>
</tr>
</tbody>
</table>
imbalances | Acidosis | products which are acidic
---|---|---
Infection | Pneumonia, Line access infections | Cellular and humoral immunity impaired in CKD.
Cardiac | Fluid Overload | Hypertension Cardiac failure | Noncompliance with fluid restriction
Cardiac comorbid | | | Higher risk in CKD
Access issues | |

- Primary hyperparathyroidism: Inappropriate secretion of PTH causing hypercalcemia, usually due to hyperfunctioning parathyroid glands from adenoma, hyperplasia
- Secondary hyperparathyroidism: Low calcium, causing high PTH. It is an appropriate homeostatic response. Seen in renal failure and vitamin D deficiency
- Tertiary hyperparathyroidism. After long-term secondary hyperparathyroidism from hyperplasia of parathyroid glands. (Loss of response to calcium levels, PTH secreted even though calcium levels are increased) Seen in end-stage renal failure

<table>
<thead>
<tr>
<th>Primary Hyperparathyroidism</th>
<th>Secondary Hyperparathyroidism</th>
<th>Tertiary Hyperparathyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>↑</td>
<td>↓/N</td>
</tr>
<tr>
<td>PTH</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Phosphate</td>
<td>↓</td>
<td>↑/N</td>
</tr>
</tbody>
</table>

Q9) How would you manage Mr Lim’s chronic kidney disease? Outline the key management principles. Name 5.

<table>
<thead>
<tr>
<th>Goals</th>
<th>Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure control</td>
<td>Lifestyle</td>
</tr>
<tr>
<td>• Goal: &lt; 130/80 mmHg</td>
<td>• Exercise, Salt-reduction</td>
</tr>
<tr>
<td>Pharmacological</td>
<td>• Use of ARBs/ACE-I plus other anti-hypertensive agents</td>
</tr>
<tr>
<td>Glycemic control</td>
<td>Lifestyle changes</td>
</tr>
<tr>
<td></td>
<td>• Exercise, decrease calorie in-take, food with low glycemic index</td>
</tr>
<tr>
<td>Pharmacological</td>
<td>• Metformin (for type 2 DM), oral hypoglycemic agents, insulin (if needed)</td>
</tr>
<tr>
<td>Avoidance of nephrotoxins / renal-dosing</td>
<td>Avoid drugs such as gentamicin, non-steroidal anti-inflammatory drugs.</td>
</tr>
<tr>
<td></td>
<td>Use GFR adjusted dosages for drugs that are excreted by the kidney.</td>
</tr>
<tr>
<td>Decrease of proteinuria</td>
<td>ACE-Inhibitors or/and ARBs</td>
</tr>
<tr>
<td>Management of anemia</td>
<td>Replace iron</td>
</tr>
<tr>
<td>Erythropoietin injection (only if there is persistent anemia despite sufficient iron)</td>
<td></td>
</tr>
<tr>
<td>Management of renal bone disease</td>
<td>Lifestyle</td>
</tr>
<tr>
<td></td>
<td>• Avoid food high in phosphate</td>
</tr>
<tr>
<td>Electrolyte imbalances</td>
<td>Lifestyle</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Avoid food high in potassium (e.g. oranges and orange juice, nectarines, Kiwis, raisins or other dried fruit, bananas, cantaloupe, honeydew, prunes, and nectarines, asparagus, avocado, potatoes, tomatoes or tomato sauce, winter squash, pumpkin, avocado, and cooked spinach)</td>
<td></td>
</tr>
<tr>
<td>Pharmacological</td>
<td></td>
</tr>
<tr>
<td>• Insulin, Beta-agonist</td>
<td></td>
</tr>
<tr>
<td>• Sodium Polystyrene Sulfonate (Kalexate)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fluid Status</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid restriction</td>
<td></td>
</tr>
<tr>
<td>Diuretic</td>
<td></td>
</tr>
<tr>
<td>Dialysis if necessary</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Control of other cardiovascular risk factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>In most CKD patients, statin is indicated regardless of levels of LDL. There is no target to aim for as statin decreases the risk of CVS morbidity and mortality regardless of the existing LDL levels as CKD patients are already high risk of such events. This is the concept of “fire and forget” as compared to conventional “treat to target”.</td>
<td></td>
</tr>
<tr>
<td>Reference: KDIGO Clinical Practice Guideline for Lipid Management in CKD.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Dialysis</td>
<td></td>
</tr>
<tr>
<td>• Transplant (Living donor, cadaveric)</td>
<td></td>
</tr>
</tbody>
</table>

**Q10) What are the types of dialysis?**

- Hemofiltration: Filtration of water from plasma to ultrafiltrate across a more porous semipermeable membrane **down a pressure gradient** with removal of solutes by convection
- Hemodialysis: Bidirectional diffusion of solutes between plasma and dialysate across a semipermeable membrane **following concentration gradients**.
- Peritoneal dialysis: Uses peritoneum as a semipermeable dialysis membrane. Solute moves down a concentration gradient and water down an osmotic gradient achieved by using an osmolar compound typically glucose in the dialysis fluid.

**Q11) What are the complications associated with transplantation?**

- Complication: Infection, rejection, complications from immunosuppression
CASE 22: 35-YEAR OLD INDIAN WITH FEVER AND RASH

LEARNING OBJECTIVES

- Approach to Acute Kidney Injury
- Diagnosis and Management of Severe Dengue Fever

DISCUSSIONS

Mr Ravi is a 35-year old construction worker from India with no significant past medical history. He presents with a 3-day history of high fever (Tmax = 39.5), polyarthritis, and a confluent erythematous rash with islands of sparing.

Q1) State the most likely diagnosis

Dengue

Q2) What confirmatory tests would you like to do

- Platelets
- Dengue NS1Ag
- Dengue IgG/IgM

Four days later, his fever subsides. However he now complains of abdominal pain and his BP is 92/50. He was transferred to ICU and aggressively resuscitated. 12h later, the nurse calls you for ‘poor urine output’ – 30ml in 12 hours via catheter.

Q3) What would you do at the bedside, and what investigations would you order?

- Check catheter, percuss for bladder
- Take vitals
- Assess fluid status for signs of volume overload or dehydration
- Investigations:
  - FBC, Renal panel, Calcium panel, ABG, CXR
  - ECG, cardiac enzyme – possible cardiac event
  - PT/PTT, GXM – coagulopathy, transfusion
  - LFT – may have rise
  - Fibrinogen, fibrin degradation products – haemorrhagic fever

You order some preliminary blood tests and the results are:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>13.5</td>
</tr>
<tr>
<td>Na</td>
<td>125</td>
</tr>
<tr>
<td>WBC</td>
<td>10</td>
</tr>
<tr>
<td>K</td>
<td>6.5</td>
</tr>
<tr>
<td>Plt</td>
<td>70</td>
</tr>
<tr>
<td>HCO3-</td>
<td>18</td>
</tr>
<tr>
<td>Hct</td>
<td>55 %</td>
</tr>
<tr>
<td>Cl-</td>
<td>95</td>
</tr>
<tr>
<td>Urea</td>
<td>12</td>
</tr>
<tr>
<td>Cr</td>
<td>240</td>
</tr>
<tr>
<td>(baseline Cr 70)</td>
<td></td>
</tr>
</tbody>
</table>

Q4) Interpret the blood tests and formulate a problem list.

- Low platelets – dengue.
• Raised hematocrit, urea – dehydration
• Raised creatinine, hyperkalemia – renal failure (RIFE – F)
• Hyponatremia – likely third spacing.

Problem list:
• Hyperkalemia secondary to acute renal failure
• Acute renal failure secondary to dengue shock syndrome
• Dengue shock syndrome

Q5) Suggest three possible causes for the rise in creatinine and your approach to differentiate them.

Prerrenal – hypovolemia, hypotension
Renal – acute tubular necrosis secondary to ischemia
Postrenal – catheter blockage

Approach
• Postrenal cause can be clinically excluded – percuss for bladder, if in doubt do renal ultrasound
• Fluid challenge – urine output should increase
• UFEME – brown granular casts suggest acute tubular necrosis
• Urea: creatinine ratio – much higher in prerenal than in renal causes as urea is reabsorbed
• Urine electrolytes – high urine osmolality, low urine Na, high urine Cr : plasma Cr suggest prerenal dx

Q6) How would you manage this patient?

Goals of management
• Emergent management of hyperkalemia
• Restore circulating volume
• Supportive management for ATN and dengue

Steps
• Paras, fluids, activity, monitoring
• Close clinical monitoring Q1h KIV central line insertion
• Fluid challenge - 1L IV normal saline stat
• Normal diet
• Investigations
  o FBC, Renal panel, UFEME, urine electrolytes
• Stop nephrotoxic management
• Management of Hyperkalemia
  o 10ml 10% calcium gluconate IV
  o 10 units insulin + 50mL IV dextrose
  o Resonium PO (15 – 30g)

Q7) What are the indications for emergent dialysis in this patient?

Pulmonary edema
Hyperkalemia refractory to medical treatment
Severe acidosis

Symptomatic uremia e.g. pericarditis
CASE 23: 56 YEAR-OLD WOMAN WITH ACUTE ONSET OF CHEST PAIN

LEARNING OBJECTIVES

- Approach to Chest Pain
- Diagnosis and Management of Acute Myocardial Infarction
- Diagnosis and Management of Pulmonary Embolism

DISCUSSIONS

A 56 year-old woman presents to the emergency department complaining of severe pain in her chest over the last 1 hour.

Q1) What are the differential diagnoses for her chest pain that you would have in mind?

6 Most Dangerous differential diagnoses for chest pain that must be thought of first and ruled out:

- Acute Myocardial Infarction
- Aortic Dissection
- Pulmonary Embolism
- Tension Pneumothorax
- Unstable Angina
- Esophageal Rupture

Other important but not life-threatening diagnoses:

<table>
<thead>
<tr>
<th>Systems</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>Stable angina, Pericarditis, Myocarditis</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Simple pneumothorax, Pneumonia with pleurisy</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Reflux oesophagitis</td>
</tr>
<tr>
<td>Referred pain</td>
<td>Gastritis, peptic ulcer disease, biliary disease, subphrenic abscess</td>
</tr>
</tbody>
</table>

Q2) Take a history of her chest pain. What are the questions that you would like to ask?

SOCRATES (Site, Onset, Character of Pain, Radiation of Pain, Temporal History, Alleviating and Exacerbating factors, Score, Associated features: heartburn or indigestion associated with nausea)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Important Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Character</td>
<td>• Visceral (Pressure-like, compressing, squeezing, discomfort, chest pain cannot be localized with one finger). Usually cardiac causes</td>
</tr>
<tr>
<td></td>
<td>• Pleuritic (Sharp Pain on inspiration). Usually respiratory causes</td>
</tr>
<tr>
<td></td>
<td>• Somatic (Sharp chest pain that can be precisely localized with one finger) Usually musculoskeletal causes</td>
</tr>
<tr>
<td>Onset</td>
<td>• Stable Angina Pectoris: occurs on exertion, relieves within 3-5 min of rest or sublingual GTN</td>
</tr>
<tr>
<td></td>
<td>• Unstable Angina Pectoris: Occurs at rest or with minimal activity, unlike previously</td>
</tr>
<tr>
<td></td>
<td>• Acute MI: Can occur at rest or with exertion</td>
</tr>
</tbody>
</table>

Discussion Point:
How do you piece these pieces of information together to rule in or rule out diagnosis? A suggested approach will be to think of the differentials you have provided in part 1 and think of the features in the history that would rule in or rule out the diagnosis.

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Features Ruling in the Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Myocardial Infarction</td>
<td>Nature of Pain: Pressure over the sternal area, Radiation of chest pain to the either arm, both arms or angle of jaw accompanied by diaphoresis, associated with exertion and relieved by rest</td>
</tr>
<tr>
<td></td>
<td>Rationale for asking question: Usually, in the case of stable angina, the pain reports that the nature of pain this episode will be same as that in previous episodes. In the case of unstable angina or acute myocardial infarction, the nature of pain this episode will be worse than the patient’s usual angina or similar to that experienced during a prior MI.* This observation supported by data from a Multicenter Chest Pain Study. (MCPS)</td>
</tr>
<tr>
<td></td>
<td>Also, AMI pain is crescendo in nature. It reaches maximal intensity after a few minutes. Compare and contrast this to aortic dissection pain, which is maximal at onset.</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>Angina at rest, Worsening or Increasing pain, Not relieved by nitrates, New-onset angina (new onset angina is considered as unstable angina).</td>
</tr>
<tr>
<td>Stable Angina</td>
<td>Occurs on exertion, relieved within 3-5 mins of rest or sublingual nitrates (note the route of administration of nitrates).</td>
</tr>
<tr>
<td>Aortic dissection</td>
<td>Chest pain maximal at onset, radiating to the back (interscapular region), Unequal pulses bilaterally on both arms (if suspected, confirm with bilateral blood pressure measurement)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Pleuritic Chest pain, Tachypnoea, Dyspnoea of sudden onset. Usually associated with a low SpO2 and tachycardia.</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>Pain worse on lying down, relieved by sitting up or leaning forward</td>
</tr>
</tbody>
</table>

She describes the pain as a pressure that is not relieved by rest or by changes in position. She took ibuprofen at home without relief. She also complains of nausea that began shortly before the onset of jaw and neck pain. On further questioning, she admits to a heavy feeling in her chest, which she describes as a squeezing or crushing sensation. She had previous episodes before, but each resolved spontaneously. Pain this time is significantly worse.

**Q3) Perform a relevant physical examination. What would you like to look out for?**

**Salient features**

- General inspection: Alertness (tells us about end organ perfusion), Significant respiratory distress
- Vital signs: Tachycardia, Hypotension (Cardiogenic shock as a complication), Arrhythmia (AMI can lead to arrhythmia and arrhythmia can precipitate an AMI)
- Signs of heart failure (JVP, S3S4 heart sound, Bibasal crepitations, pedal oedema)
- Myocardial complications (new onset pansystolic murmur suggestive of papillary muscle rupture leading to mitral regurgitation)

**On Physical Examination**

- General inspection
Patient is conscious, but slightly lethargic
Vitals: BP 100/60, PR 120, RR 30

- Peripheries
  - Sweaty palms, slight trembling
  - Cold peripheries
  - Pulses are weak and irregular
  - JVP is elevated
- Auscultation
  - Holosystolic murmur heard
  - Bibasal crepitations heard

Q4) How would you investigate this patient?

Suggested mean of classification:
- ECG
- Chest X-ray
- Blood investigations: FBC, UECR, PT/PTT, GXM, Cardiac Enzymes

Other investigations:
- PE
  - Determine if it is likely or unlikely
    - Likely: proceed straight to do a spiral CT pulmonary angiogram
    - Unlikely: do a D-dimer test to rule out PE if negative; proceed to CT-PA if positive
- High suspicion of pneumonia
  - Cultures (sputum, blood)
- Referred pain from abdomen
  - LFTs, serum lipase/amylase, CTAP
- 2D Echocardiography

Discussion Points: Cardiac enzymes

- What to take?
o 3 sets principle (6-8 hours interval after patient’s presentation to ED)

• Progression
  o Rises within 3-12 hours from onset of chest pain
  o Peaks at 24-48 hours
  o Return to baseline over 5-14 days

• When is it a positive?
  o cTn with at least one value above the 99th percentile upper reference limit

• Types
  o Myoglobin: First cardiac enzyme to rise but not specific for cardiac muscle. Useful in ruling out AMI early as myoglobin is raised in nearly all AMIs.
  o Creatinine-kinase MB: Serologic gold standard of AMI.
  o Troponin T and I. Most widely used cardio-specific marker but not necessarily due to MI. By 2-3 hours after onset of AMI, up to 80% of AMI will have troponin elevations in the high-sensitivity assays. Hence the high-sensitivity assays are useful to rule out NSTEMI. Other causes of raised troponins include: Acute cardiopulmonary conditions e.g. pulmonary embolism, myocarditis, heart failure.

Discussion Points: Definition of AMI

According to the third universal definition, any one of the following criteria meets the diagnosis of MI:

• Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin [cTn] with at least one value above the 99th percentile upper reference limit [URL]) and with at least one of the following:
  o Symptoms of ischemia
  o Development of pathologic Q waves in the electrocardiogram (ECG)
  o New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB).
  o Identification of an intracoronary thrombus by angiography or autopsy
  o Imaging evidence of new loss of viable myocardium or a new regional wall motion abnormality.

• Cardiac death with symptoms suggestive of myocardial ischemia and presumed new ischemia ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased.

• Percutaneous coronary intervention (PCI)-related MI was defined by elevation of biomarker values (cTn is preferred) >5 x 99th percentile URL) in patients with normal baseline values (<99th percentile URL) or a rise of values >20 percent if the baseline values are elevated but stable or falling. In addition, either (i) symptoms suggestive of myocardial ischemia, (ii) new ischemic ECG changes or new LBBB, (iii) angiographic loss of patency of a major coronary artery or a side branch or persistent slow - or no-flow or embolization, or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required.

• Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarkers with at least one value above the 99th percentile

• Coronary artery bypass graft surgery (CABG)-associated MI was defined by elevation of cardiac biomarker values >10 x 99th percentile URL in patients with normal baseline cTn values. In addition, either (i) new pathologic Q waves or new LBBB, (ii) angiographic documented new graft or native coronary artery occlusion, or (iii) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Q5) Interpret this ECG. What are the abnormalities?

- ST elevation in lead 2, 3, aVF
- ST Depression in lead V1, V2, V3, V4, I, avL
- Inferior STEMI with reciprocal changes in the anterior-lateral leads

Discussion Point: Concept of Localisation of infarct

<table>
<thead>
<tr>
<th>Site of Infarction</th>
<th>ST-elevation</th>
<th>Reciprocal changes (ST depression)</th>
<th>Arterial Supply</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Inferior           | Leads II, III, aVF | Leads I, aVL | • Right coronary artery (80% of the time)  
• Dominant Left circumflex artery (18% of the time) | Look for a right ventricular infarction and/or posterior infarction |
| Posterior          | Leads V7, 8, 9 | Leads V1, 2, 3 | Usually found in the context of an inferior (more common) or lateral infarct. Suggests a poorer prognosis due to the larger area of myocardium involved. |
| Right Ventricle    | Leads V4R, 5R, 6R | Leads I, aVL | Found in the context of patients with inferior STEMI (~40% of patients with inferior STEMI) |
| Anterior           | V1, V2 | Leads 2, 3, aVF | Left Anterior Descending | Anterior |
| Septal             | V3, V4 | Leads 2, 3, aVF | Left Anterior Descending | Anterior |
| Lateral            | V5, V6, aVL, I | Leads 2, 3, aVF | Left Circumflex artery branch of left coronary artery |
Right Ventricular Infarction
• If ST Depression seen in lead V1, V2, V3, request to do a right sided ECG
• If inferior STEMI, look for rhythm disturbance. Up to 20% of patients with inferior STEMI will develop rhythm disturbances (bundle branch block, second- or third-degree AV block). This is because the RCA supplies the SA node of the heart.
• In patients with RV infarction, usage of GTN is not recommended as GTN leads to vasodilation, which can result in decreased venous return → worsening of cardiogenic shock

Left Ventricular Infarction

• In patients with LV infarction, fluid usage has to be done conscientiously as they are likely to run into trouble with pulmonary edema if they are overloaded with fluids

Discussion Point: Stages of ECG change

• Hyperacute ST elevation: 0-2 hours
• Fully evolved ST elevation: past 24 hours. Tombstone appearance of ST segment, Deepening Q waves.
• Resolution: 24-48 hours. ST segment goes down, Q wave more prominent, T waves invert
• Chronic: more than 48 hours. Q wave present

Discussion Point: Distinguish between Unstable Angina, NSTEMI and STEMI

<table>
<thead>
<tr>
<th></th>
<th>Unstable Angina</th>
<th>NSTEMI</th>
<th>STEMI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ECG</strong></td>
<td>ST depression, T wave inversions</td>
<td>ST depression, T wave inversion</td>
<td>ST elevation</td>
</tr>
<tr>
<td><strong>Cardiac Enzymes</strong></td>
<td>No increase</td>
<td>Increase</td>
<td>Increase</td>
</tr>
</tbody>
</table>
Q6) What treatment would you offer for this lady?

STEMI

- Morphine (give in titratable doses)
- Oxygen therapy
- Nitrates-sublingual. If pain persist, can consider IV GTN (not for STEMI with right ventricular involvement)
- Anticoagulation and dual antiplatelet therapy (aspirin + clopidogrel)
- Beta blockers
- Emergent revascularisation (Thrombolysis or Percutaneous Coronary Intervention)

NSTEMI

- Low molecular weight Heparin
- Beta-blockers
- Glycoprotein IIb/IIIa inhibitors
- ACE-inhibitors
- Statins
- Early but no immediate reperfusion and revascularisation

You have diagnosed STEMI. A PCI was subsequently done for this patient. On POD4, while in the coronary care unit, the patient develops chest pain worse on inspiration, associated with coughing. The pain was localised. She also complains of difficulty breathing. The Sp02 is now 88% on RA. Her BP is 140/80 mmHg, HR 120 beats per minute. RR was 25.

Q7) What differential diagnosis do you think of now?

- Pulmonary embolism
Q8) What would you look out for in your physical examination?

- New murmurs
- JVP elevation, Pedal edema
- Calf pain, swelling
- Radial-radial delay or radial-femoral delay

Physical examination revealed: normal heart sounds heard with no murmur, gallops or rubs. There were no radial-radial or radial-femoral delay. There was equal breath sounds heard with no adventitial breath sounds. There was no pedal edema or tenderness of the lower extremities.

Q9) What investigations would you order?

- Chest Radiograph
- Electrocardiogram
- Cardiac Enzymes
- Doppler ultrasound of lower limbs
- CT-PA (Possible discussion on when to do CT-PA, V-Q scan)

DO not order D-dimer- not a useful investigation as there is a high pre-test probability of DVT in this case.

ECG was performed.

![ECG Image]

Troponins 0.09 (< 0.01 ng/mL)

Q10) What is the most likely diagnosis? What are other ECG findings in patients with this condition?

Pulmonary embolism.

S1Q3T3. S-wave in Lead I, Q=wave in Lead III and inverted T-wave in Lead III
Q11) Why are troponins raised?

In patients with suspected PE, serum troponin I and T levels are neither sensitive nor specific diagnostically. However, as markers of right ventricular dysfunction, troponin levels are elevated in 30 to 50 percent of patients who have a moderate to large PE. Consequently, they can be used to assess prognosis in patients diagnosed with PE. Troponin elevations usually resolve within 40 hours following PE, in contrast to the more prolonged elevation after acute myocardial injury.

Emergency CT Pulmonary Angiogram confirmed the diagnosis of Pulmonary Embolism.

Q12) What are the treatment options for Pulmonary embolism?

Hemodynamic Stable

- Pharmacological: Empiric anticoagulation with low molecular weight heparin
- Inferior Vena Cava Filter (for certain patients)

Hemodynamic Unstable

- Pharmacological: Empiric anticoagulation with low molecular weight heparin
- Embolectomy
  - Surgical
  - Catheter-based

Your medical student wonders if there are antidotes to heparin and warfarin.

Q13) How would you treat a heparin overdose? A warfarin overdose? How do these therapies work?

Heparin overdose is treated with protamine sulphate. It has a lot of positive charges and hence binds heparin which has a lot of negative charges.

Warfarin overdose is treated with IV vitamin K and fresh frozen plasma. IV vitamin K is used to inundate the production pathway of coagulation factors to overcome the effect of warfarin. However, this takes time so replacement of coagulation factors with FFP is also needed.
CASE 24: 13 YEAR-OLD GIRL WITH BRUISES AND PALLOR

LEARNING OBJECTIVES

- Approach to abnormal bleeding
- Diagnosis and Management of Von Willebrand Disease

DISCUSSIONS

A 13 year old girl presents to the clinic with symptoms of fatigue, exertional dyspnea, and palpitations. Her symptoms have been getting worse over the past 6 months. You notice that she has many bruises on her body and that she is very pale.

Q1) What are some possible differential diagnoses?

- Consider symptomatic anemia, and all its causes.
- Consider other systemic illness e.g. chronic liver disease, chronic kidney disease, complex congenital heart disease, autoimmune diseases e.g. SLE, cancer, collagen diseases
- Consider nutritional deficiency, abuse, neglect
- Consider drug induced problems e.g. NSAIDs

You wonder whether she has a bleeding disorder.

Q2) What types of bleeding disorder are there? What questions would you ask to distinguish between the different types of disorder?

Can classify as problem with platelet/blood vessel vs coagulation factors

<table>
<thead>
<tr>
<th>Platelet/blood vessel</th>
<th>Coagulation factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>skin bleeding (petechiae, superficial ecchymoses)</td>
<td>muscle bleeding (hematoma)</td>
</tr>
<tr>
<td>mucous membrane bleeding (epistaxis, gum bleeding, hemorrhagic bullae)</td>
<td>joint bleeding (hemarthrosis)</td>
</tr>
<tr>
<td>tends to have problem with immediate hemostasis</td>
<td>skin bleeding (deep ecchymoses)</td>
</tr>
<tr>
<td></td>
<td>tends to have problem with delayed hemostasis</td>
</tr>
</tbody>
</table>

Q3) What other relevant history would you ask for?

- Ask for other bleeding manifestations e.g. heavy menstrual bleed, GI bleed, intracranial bleed
- Ask for response to hemostatic challenges (e.g. wounds, minor surgery, major surgery)
- Ask for onset of disease
- Ask for any medications e.g. NSAIDs
- Ask for family history of any bleeding diathesis

You find out that her onset of menarche was 9 months ago. Her periods have come every 28 days for the past 6 months and have been very heavy, lasting for over 1 week and overflowing her sanitary pads. She has experienced easy bruising since a young age. Sometimes, when she knocks herself hard there develop painful hard masses in her muscles. There are no other bleeding manifestations. The fancy new POCT you have in your clinic gives her Hb as 7.5g/dL.
Her mother tells you that her mother (the child’s grandmother) also had easy bruising. She passed away at 40 years old from ‘brain bleeding’ after an apple falling from a tree knocked her head. Her mother mentions that out of the 8 children she has (4 boys and 4 girls), only this child and one of her brothers have experienced easy bruising. No other members of the extended family have been similarly afflicted (Her husband, husband’s parents, and husband’s sister are well. Her brother and sister are both well).

Q4) What are some possible differential diagnoses?

Suspicion for inherited coagulation disorder e.g. Hemophilia, vWD

Q5) Draw a family tree. What mode of inheritance is this?

[Diagram of a family tree showing autosomal recessive inheritance]

Autosomal Recessive

Your MO tells you that this patient might have von Willebrand disease type 2N. He says that the main differential is Hemophilia A but that ‘it does not affect girls’.

Q6) What is von Willebrand disease? What is Hemophilia A? What is the difference between the two? Can Hemophilia A affect girls?

vWD involves a quantitative or qualitative defect of vWF, which is involved in platelet aggregation AND prevents breakdown of FVIII. Different forms of vWD (not required knowledge for MBBS) can present with bleeding more similar to platelet disorders or coagulation disorders. It is the most common inherited bleeding disorder and is inherited in an Autosomal Recessive fashion.

Hemophilia A involves a deficiency of FVIII (and hence vWD can present similarly). It is inherited in a X-Linked Recessive fashion. Hemophilia B (deficiency of FIX) and Hemophilia C (deficiency of FXI) are much less common.

Hemophilia can be expressed fully in girls if both X chromosomes have the defective FVIII gene, although this is a very rare scenario. Girls with the defective FVIII gene are more commonly carriers, or heterozygotes. They are expected to have about 50% of the normal FVIII levels, which is able to ensure normal hemostasis. However, this may not be the case for all carriers as they may have unfavourable lyonisation patterns, or they may have other concomitant inherited disorders of hemostasis.

Q7) What are some principles of management of this patient?

Investigate with a view to
1. Making a diagnosis (coagulation screen, FBC for platelet. Other workup based on results, beyond scope of medical school)
2. Determining extent of anemia (FBC for Hb)
3. FBC is useful as it will help to screen for pancytopenia (which is worrisome for leukemia)
   Advise patient on risks of bleeding in different situations (e.g. surgery)

Give therapeutic medication - for vWD, can give DDAVP, replacement vWF, antifibrinolytics, OCPs to stop menses if this is her main problem