PHASE I INTEGRATED CLINICAL CASES

"Thinking through pathophysiology"

Prepared by: Yii Zheng-Wei
Germaine Loo
Cai Mingzhe
Wilbert Ho

Vetted by: Nigel Fong
Prof. Hooi Shing Chuan
A/Prof. Koh Dow Rhoon
A/Prof. Celestial Yap

Case 1

You are the house officer on call at the accident and emergency. Mr. Gerald Eng is a 65 year old Chinese gentleman who walks in with a 1 day history of vomiting, fever and abdominal pain. He complains that he vomits out everything that he tries to eat and drink. He says that his urine output has also decreased in the last 6 hours, and that he feels quite thirsty.

On examination, he is alert and reasonably comfortable. His blood pressure is 125/85mmHg, heart rate is 110bpm, respiratory rate is 12/min and temperature is 38.3°C.

Blood Test Results
Sodium: 135mEq/L (135-145)
Potassium: 3.3mEq/L (3.5-5.0)
Bicarbonate: 33mEq/L (22-26)
Chloride: 93mEq/L (95-105)
pH: 7.47 (7.35-7.45)
$PaCO_2$: 46mmHg (35-45)

Your consultant on call with you diagnoses him to have acute gastroenteritis.

1. Interpret and explain the blood test results in light of what has been happening to Mr. Eng.
(a) How does the body maintain a normal pH?

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(b) How does the body maintain potassium homeostasis?

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(c) Name this patient's acid-base status

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(d) Why is the potassium low?

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(e) Why is the chloride low?

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(f) Why is the bicarbonate high?

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2. What is the normal physiological response to dehydration?

(a) What problems are caused by dehydration? (BP and osmolarity)

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(b) What is the cardiovascular response to dehydration?

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(c) What is the renal response to fluid loss? (includes ADH)

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3. In light of the laboratory findings, do you agree with your consultant's diagnosis?

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Several minutes after discharging Mr. Eng, a 65 year old man by the name of Mr. Ding Kong An is rushed in the emergency department by ambulance. His son is with him, and says that his father had been having vomiting, diarrhoea, fever and abdominal pain for the past 24 hours. He has a history of type 2 diabetes mellitus, but has forgotten to take his insulin injections for the past 24 hours as well. The son also says that Mr. Ding has been getting progressively more agitated and drowsier over the past 12 hours.

On examination, Mr Ding is breathing deeply and rapidly, and he appears to be drowsy. His blood pressure is 90/60, heart rate 140, temperature 38.5o, respiratory rate 28, oxygen saturation 98% on room air.

Blood Results
Sodium: 128mEq/L (135-145)
Potassium: 5.2mEq/L (3.5-5.0)
Bicarbonate: 15mEq/L (22-26)
Chloride: 97mEq/L (95-105)
pH: 7.31 (7.35-7.45)
PaCO2: 31mmHg (35-45)
Serum Glucose: 22mmol/L (under 7.8 2hours postprandial)
His serum ketones are markedly elevated, and a dipstick shows high amounts of glucose and ketones in his urine.

4. What are the metabolic functions of insulin, cortisol and adrenaline? When are these hormones secreted?

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5. Why are there ketones and glucose in this patient's urine?

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6. Why might the serum glucose and ketones be high?

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7. Offer an explanation of the acid-base status of the patient, including the anion gap.

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8. Why is this patient hyponatremic and hyperkalemic?

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9. Interpret and explain the vital signs in this patient.

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Treatment Plan

Recognising that the patient is in diabetic ketoacidosis, he is treated with IV insulin and IV normal saline that is mixed with potassium. Sometime after treatment, his vitals are:

BP: 120/80
Heart Rate: 90
Temperature: 38.5o
Respiratory rate: 20
Oxygen Saturation: 98% on room air

Blood Results

Sodium: 138mEq/L (135-145)
Potassium: 4.0mEq/L (3.5-5.0)
Bicarbonate: 24mEq/L (22-26)
Chloride: 106mEq/L (95-105)
pH: 7.40 (7.35-7.45)
$PaCO_2$: 40mmHg (35-45)
Serum Glucose: 6.8mmol/L (under 7.8 postprandial)
Serum and urine ketones are negative, and dipstick no longer shows urinary glucose.

Mr Ding has become alert and comfortable at rest, though he still complains of the fever and resolving diarrhea.

10. What will happen if he is only treated with insulin and nothing else?

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11. How does IV normal saline with potassium make a difference?

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12. What advice might you give him and his family regarding the insulin therapy when he next falls sick?

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Case 2

A 40 year old woman comes into your clinic complaining of weight gain, weakness, constipation and feeling cold for the past 2 months. The weight gain puzzles her because she says she recently hasn't felt like eating much. Her husband, who is with her in clinic, complains that she has been very lethargic recently and seems to be less focused than usual. Her voice has also become somewhat hoarse.

On examination, she appears to be pale and her skin has a peaches and cream appearance. Her hair seems unusually thin and dry. Though her reflexes are intact, you find that they take a while longer to relax after contracting than normal. Her skin is cool to the touch and feels dry.

Vitals
HR: 50
RR: 18
BP: 110/70
T: 36.0
SpO2: 98%

1. What hormones are secreted by the thyroid gland? What are their functions?

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2. How is the secretion of thyroid hormones regulated?

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3. What is this patient's clinical thyroid status and why? What tests would you order to confirm this suspicion?

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You order a thyroid function test and it comes back as follows:
TSH: 0.8mIU/L (0.4-4.0)
Free T4: 0.5ng/L (0.8-1.8)
Free T3: 1.8pg/mL (2.3-4.2)

4. What is this patient's biochemical thyroid status?

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5. From the thyroid panel, what is the anatomic location of the lesion?

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6. What other signs and symptoms of her thyroid status did she not present with?

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As you are concluding the consult, she mentions that she has had 3 near-misses at the road recently. The first time round, she was turning a corner side by side with a bus and ended up side-swiping the bus. The second time, she nearly knocked down a motorcyclist overtaking her on the right. Most recently, she nearly got into an accident while trying to filter into the left lane because she could not see a car in her left blind spot.

She also says that she has not been pregnant or given birth recently, yet she has not had her period for the last 9 months. She attributes this to early menopause, but she does note that for some reason, she has been having white breast discharge recently.

7. Is this new information consistent with the suspected anatomical location of the lesion? Explain the physiology behind these symptoms.

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8. What are some signs on physical exam that might corroborate with this suspicion?

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9. What other hormonal deficiencies might you expect? What abnormalities would these deficiencies cause?

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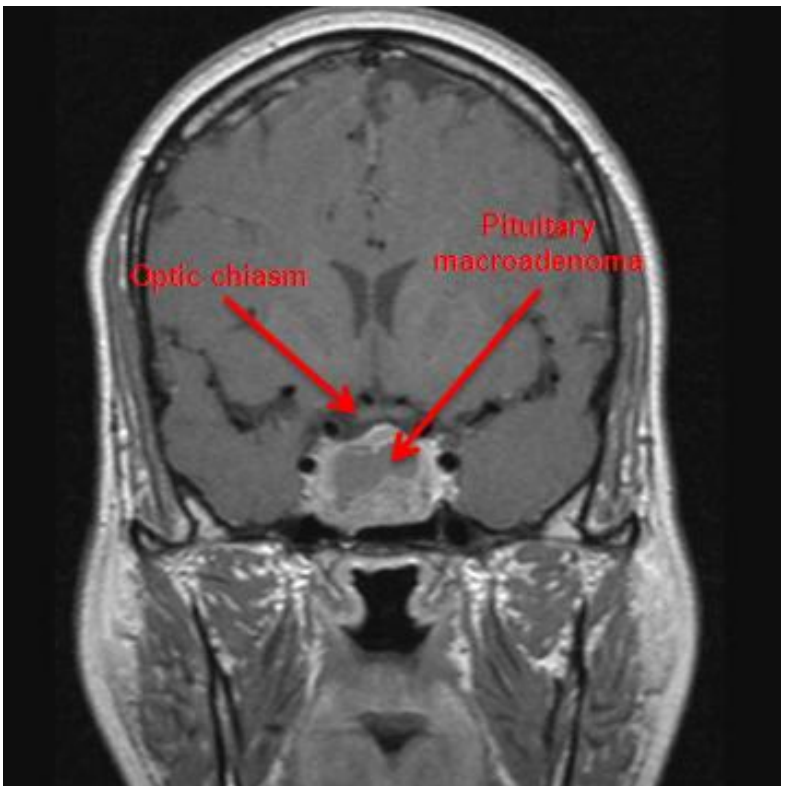
You suspect that there may be a pituitary tumor of some sort causing the endocrine and visual disturbances. To search for the tumor, you order an MRI of her brain. At the same time, you order other blood tests to help you workup the endocrine disturbances. They return as follows:



http://bestpractice.bmj.com/best-practice/monograph/363/resources/image/bp/3.html

<u>Prolactin Test</u>
Serum Prolactin: 12000mU/L (43-617)

<u>Electrolyte Panel</u>
Sodium: 133mEq/L (135-145)
Potassium: 4.2mEq/L (3.5-5.0)
Bicarbonate: 24mEq/L (22-26)
Chloride: 98mEq/L (95-105)

<u>Arterial Blood Gas</u>
pH: 7.4 (7.35-7.45)
$PaCO_2$: 40mmHg (35-45)

<u>Serum Glucose</u>
Serum Glucose: 3.4mmol/L (<4 is considered hypoglycemic)

10. Given that you suspect this patient might have deficiencies of other pituitary hormones and you have an MRI confirming a pituitary tumor, interpret these lab results.

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11. Summarise her pituitary hormone status.

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12. What treatments might be appropriate for her?

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You recognize that this is a prolactin secreting macroadenoma causing deficiencies of all other anterior pituitary hormones and compressing the optic chiasm. She is unlucky in this respect because most prolactinomas in women are microadenomas, and it's usually men that get macroadenomas. Nonetheless, you treat her with cabergoline (a synthetic dopamine agonist) with the intention of shrinking the tumor and restoring normal pituitary function.

3 years later, she returns to the clinic for followup. Repeat blood tests show that her electrolytes and glucose have normalized. Her visual fields are intact, and her menstrual cycle is regular. Her weight and appetite have returned to normal, and you note that her energy and presence of mind have greatly improved.

You give yourself a pat on the back as you reassure her that she is responding well.

Case 3

Mr. Sim Chong Peh is a 45 year-old Chinese taxi driver who has hypertension, hyperlipidemia and moderate obesity. He experiences occasional chest discomfort during his weekly badminton sessions with his family or when climbing multiple flights of stairs, which is relieved by resting.

1. What are the risk factors for coronary artery disease (CAD) that Mr. Sim has?

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2. Can you name additional 3 more risk factors for developing CAD?

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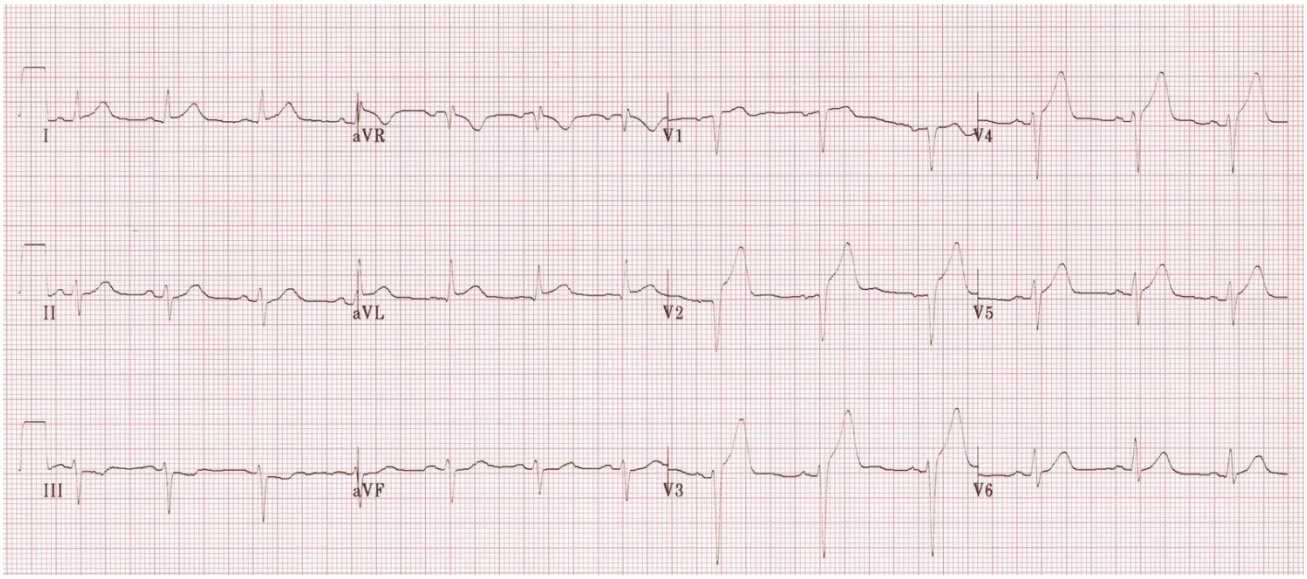
One day, while having lunch at a food court with his wife, Mr Sim suddenly felt a tight crushing sensation in his chest, radiating to his left arm and jaw. This was accompanied by profuse sweating and a nauseous feeling. Mr. Sim's wife noticed that his face had turned pale and he was also very breathless. She called 995 and was subsequently transferred to the hospital by the paramedics. At the hospital, an ECG was done for Mr Sim:



ECG taken from: lifeinthefastlane.com/ecg-library

3. What is the diagnosis for Mr Sim's symptoms?

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4. Explain the physiology behind the symptoms experienced by Mr Sim, specifically:

(a) What is the chest pain caused by?

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(b) Why did the pain radiate to the arm and jaw?

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(c) Why was there sweating and nausea?

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(d) Why was Mr Sim pale and breathless?

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5. What does the ECG show?

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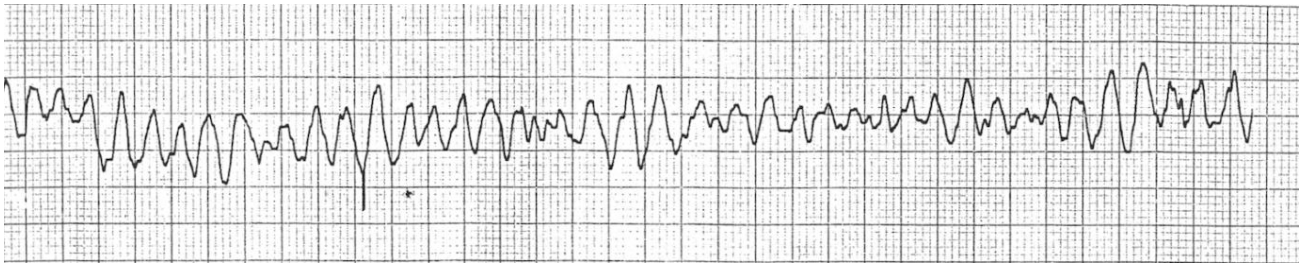
10 minutes after reaching the hospital, the cardiac monitor attached to Mr Sim started to beep very loudly. Mr Sim became unresponsive and his blood pressure was undetectable. His ECG shown on the cardiac monitor was:



ECG taken from: lifeinthefastlane.com/ecg-library

6. What has happened to Mr Sim? Give the ECG diagnosis and clinical diagnosis.

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7. Why did he become unresponsive with undetectable blood pressure?

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Electrical defibrillation was commenced, and after successful resuscitation by the medical team, Mr. Sim was transferred to the cardiac catheterization laboratory for immediate percutaneous coronary intervention to relieve the acute blockage in the coronary artery. He was subsequently warded in the coronary care unit (CCU).

At the CCU, Mr. Sim was examined by the medical officer and a medical student, who both noted the following findings on physical examination: normal first and second heart sound, with a pan-systolic murmur heard loudest at the apex of the heart. Inspiratory lung crepitations were also heard. The MO explained to the medical student, that the findings were consistent with mitral regurgitation and acute pulmonary edema.

8. With regards to the mitral regurgitation:

(a) What was the cause?

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(b) How did the mitral regurgitation result in a systolic murmur?

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(c) The potential complications of the mitral regurgitation include: left atrial enlargement, pulmonary hypertension and right heart failure. How would these complications arise?

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(d) Explain how Mr. Sim developed pulmonary edema (use the Starling forces). What are the complications of pulmonary edema?

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Mr. Sim was given supplementary oxygen support, and he was also treated with inotropic agents (to increase cardiac contractility) and furosemide in-patient. His echocardiography results on Day 5 of admission showed showed regional wall motion abnormality (reduced movement of one portion of the heart compared to the other), moderate mitral regurgitation, left ventricular apical thrombus and an ejection fraction of 35% (normal EF: 55% and above). In view of the thrombus formation, Mr. Sim was started on heparin.

9. What do you think resulted in the thrombus formation in the heart? Briefly describe, using your knowledge regarding the normal mechanisms in blood clot formation.

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10. What are the potential complications of the ventricular thrombus?

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11. Explain how heparin is effective in treating the thrombus.

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12. How does ejection fraction affect cardiac output? What is the clinical significance of knowing the ejection fraction of the heart?

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Mr. Sim was subsequently discharged from the hospital 3 days later. He was converted to warfarin instead of heparin treatment, and was also prescribed antihypertensive, lipid lowering agent, dual antiplatelet agents and referred for outpatient cardiac rehabilitation. He was given a 2 weeks clinic appointment to see his cardiologist for monitoring of his condition.

13. What are the possible long-term outcomes for Mr. Sim?

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Case 4

Mr. Mai Cheong Suah is a 51-year-old Chinese male. He has been smoking cigarettes since his army days, starting from "a few packs every day" when he picked the habit up, although he has managed to cut down to a one or two packs per day owing to financial constraints.

Mr. Mai works in the food catering industry. He and his team of men provide manual labour to set up buffets around Singapore; this mainly involves setting up the buffet line at event venues, which entails carrying heavy tables, chairs, food items and the drink containers around. Over the past two years, though, he noticed himself needing to stop and catch his breath much more frequently during such event setups. Whilst he once prided himself in being able to "tank" an entire event setup alone in his younger days, his 51-year-old self now wonders if this decrease in stamina is simply part of growing old. Regardless, he now has a team of younger men under him, on whom he increasingly relies for most of the manual work.

You have recently gotten to know Mr. Mai as a medical student in charge of catering food for a school event. In waiting for the buffet setup Mr. Mai, aware of your university major, talks to you about his condition as he is increasingly concerned about its impact on his job. On further questioning, he reveals he has been coughing intermittently for the past few years with significant phlegm production – enough to warrant clearing his throat onto the roadside every now and then. You wonder if he has Chronic Obstructive Pulmonary Disease (COPD).

1. COPD is classified as an "obstructive" lung disease. There are three important pathological components of COPD in reaction to prolonged exposure to cigarette smoke: chronic bronchitis (hypersecretion of mucus in airways), chronic bronchiolitis (inflammatory small airways thickening) & emphysema (progressive destruction of elastic alveolar walls). For each chronic bronchitis & emphysema, separately consider how the (a) airflow within the airways and (b) exchange of gas at the alveolar-capillary membrane are affected.

	Chronic bronchitis	**Emphysema**
(a) Airflow		
(b) Gas exchange		

2. COPD patients with predominant chronic bronchitis or emphysema are sometimes described as being "blue bloaters" or "pink puffers" respectively. Explain these terms and comment on the degree of respiratory failure present in these patients.

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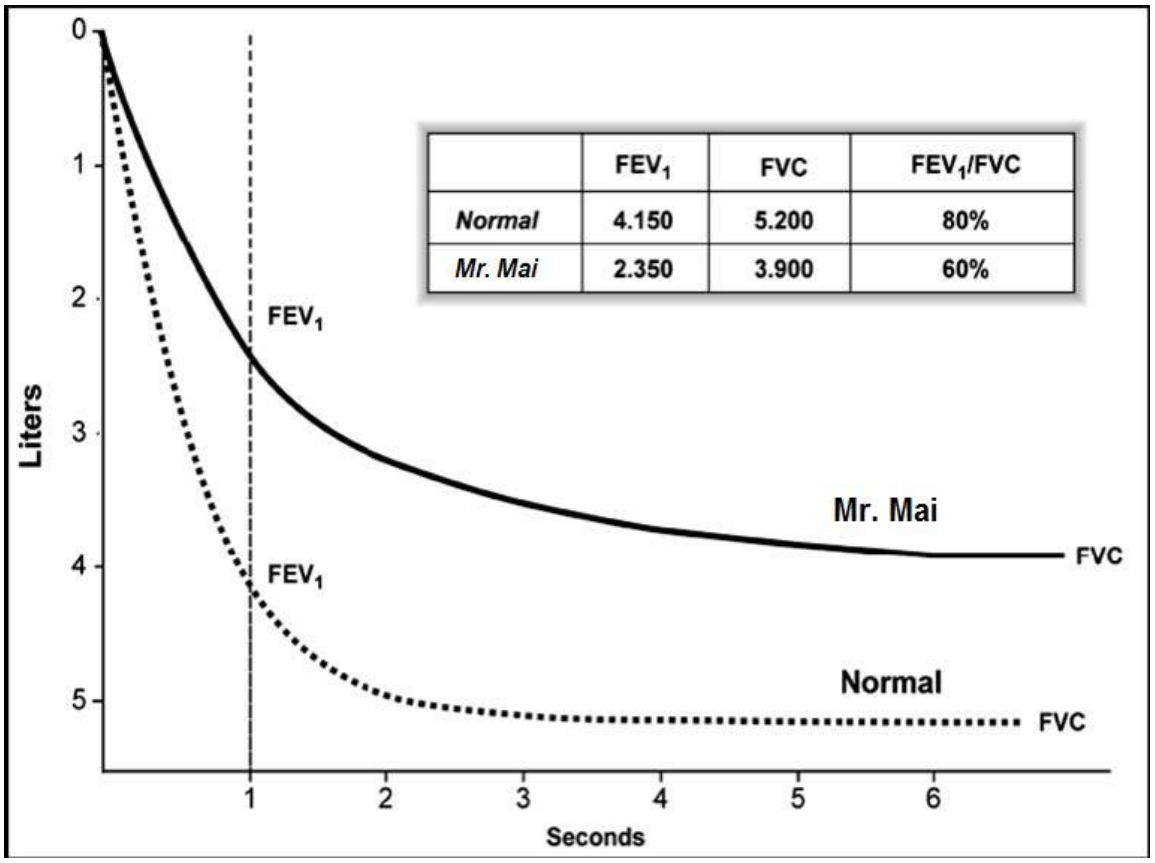
There are a number of parameters we can use clinically to assess lung function. The forced expiratory volume in 1 second/forced vital capacity ratio (FEV1/FVC) is an assessment of the degree of obstruction in airways. The diffusion capacity of carbon monoxide (DLCO) assesses the capacity for gaseous exchange at the alveolar-capillary interface.



	FEV_1	FVC	FEV_1/FVC
Normal	4.150	5.200	80%
Mr. Mai	2.350	3.900	60%

3. Shown here is Mr. Mai's FEV1/FVC curve. His DLCO (a measurement of total diffusion capacity) is at 50% of normal predicted. Explain (a) Mr. Mai's derangements in all the above parameters and (b) how they might differ in a patient with "restrictive" lung disease.

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You advise him to seek medical help from a qualified doctor, which he refuses to heed because of his inherent dislike to approach healthcare professionals in a daunting clinical setting. It is not until many years later that you, as a Medical Officer in the Emergency Department, with another medical student by your side encounter Mr. Mai again. He rehashes the same story of progressive worsening of his exercise tolerance over many years. However following a recent “flu” he caught over the past few days, his symptoms have dramatically worsened, and now experiences shortness of breath even at rest which made him seek medical attention. He also noticed that he has been catching the "flu" more frequently. You take a look at Mr. Mai.

4. With your knowledge of physiology, explain the following observations:

(a) His “barrel chest”, that appears larger compared to the thorax of a normal person

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(b) His pursed-lip breathing

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(c) A bluish appearance to his lips

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(d) Increased respiratory rate, pulse rate and use of other muscles (e.g. the sternocleidomastoid) to breathe, with his hands on his lap

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5. Suggest possible reasons for the increasing frequency of Mr. Mai's "flu".

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Being the good doctor that you are, you complete the rest of your physical examination and note the presence of wheezes with decreased air entry bilaterally and a prolonged expiratory phase when listening to his chest with your stethoscope.

The medical student attached to your clinic suggests administering 100% oxygen to Mr. Mai. However, with your years of clinical experience, you decide this is a bad idea, and instead administer oxygen at a lower dose. You explain to the medical student that COPD patients rely on oxygen, instead of carbon dioxide, as the main drive behind their respiratory rate.

6. In a normal person, how is the rate of ventilation regulated? Is oxygen or carbon dioxide normally the primary driver of a person's respiratory rate?

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7. Consider the effect of administering 100% oxygen to Mr. Mai. What physiological consequences are there to this decision?

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8. You also considered the option of putting Mr. Mai on positive pressure ventilation. How might this help?

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You make the choice to admit Mr. Mai to an inpatient setting, where he is formally diagnosed with COPD and started on therapy, and is counselled to stop smoking.

A few years down the road, Mr. Mai returns to the Emergency Department on your shift. This time, he complains of an acute-onset stabbing left-sided chest pain that began about an hour ago. This was accompanied by an onset of shortness of breath at rest too. Worried it may be a "heart attack", he called for a taxi to fetch him to the hospital.

You note a shift in his trachea towards the right side, as well as an apex beat at the left lower sternal edge. There was a visible decrease in chest expansion on the left side after Mr. Mai removed his shirt, together with hyperresonance on percussion and almost no breath sounds on the left. His blood pressure was also low. You recognise this as a tension pneumothorax.

9. Using your understanding of the anatomy of the thorax, explain:
(a) Tracheal deviation towards the right, with a shift in his apex beat in the same direction.

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(b) Hyperresonance on percussion with markedly decreased breath sounds on the left side.

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(c) Low blood pressure.

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10. Explain the acute onset of his shortness of breath. How is this different from the progressive dyspnea and decrease in exercise tolerance Mr. Mai first experienced when he was diagnosed with COPD?

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11. Why might a COPD patient be predisposed to a pneumothorax?

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Mr. Mai is once again admitted. Following the resolution of his tension pneumothorax, the House Officer overseeing his care notes some pitting edema bilaterally over his shins, together with a raised jugular pressure and signs suggestive of ascites. There was also a parasternal heave. You realise you have missed these signs owing to the urgent nature of Mr. Mai's tension pneumothorax. These signs are suggestive of right heart failure.

12. Right heart failure secondary to lung pathology, also known as cor pulmonale, may result from longstanding unresolved lung pathologies. Consider the physiology explaining how poor alveolar ventilation in the long-term may result in the development of right heart failure.

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On further history taking, it is realised that Mr. Mai has not been compliant with his discharge plans, in particular smoking cessation, resulting in a worsening of his COPD. After being scared by this acute pneumothorax episode, Mr. Mai vowed to quit smoking for good on further counselling by his primary team.