Past Papers (Medical Candidates)

This file contains 6 cases which have been presented to candidates for the Part 2 MRCPath oral examination in Clinical Biochemistry. Candidates are given half an hour to prepare their answers to the clinical case and a management case.

After each case, the notes for the examiners have been provided by the examiner who set the question. These are not intended to be exhaustive but provide some background for the case. More importantly, they provide some insight for candidates into what the examiners are looking for.

Note that the examiners expect candidates to interact diplomatically with their clinical colleagues not only to suggest diagnosis but also management and treatment.

Note also that examiners are more interested in candidates showing a logical progression from diagnosis to management and treatment than a list of causes spouted from textbooks (even if it is one the examiner wrote!).

In some cases, there are important clinical signs and urgent management issues. Failure to recognise the importance of these as the first matter requiring attention will count against candidates as the examiners are looking for evidence of safe practice.

Note that some cases are incomplete and in the ideal scenario, with candidates who are on top of the problem, the discussion should end up as a dialogue with the examiners who may also be looking for help with a difficult problem!

In preparing for this part of the examination, there is no substitute for regular discussion about clinical issues with senior consultant staff and, if possible, trying to arrange “mock” oral examinations with senior colleagues.

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Question 1

A 47 year old man presented to his GP with eruptive xanthomata over his elbows and hips. The GP arranged for fasting lipids to be measured:

Cholesterol	17.4 mmol/L
Triglyceride	28.8 mmol/L
HDL Cholesterol	0.5 mmol/L

He was referred to the local Lipid Clinic, and in the course of investigation for secondary causes of hyperlipidaemia he was found to have abnormal thyroid function tests:

Free T4	3 pmol/L	(10-24)
TSH	0.91 mIU/L	(0.5-6.0)

His identical twin brother was also screened and found to have very similar lipid and thyroid function test results.

How would you investigate these patients and what recommendations would you make about their management?

Question 1: Notes for Examiners

There are two aspects to this problem: the mixed hyperlipidaemia (which is reasonably straightforward) and the odd thyroid function tests (which we have still not explained satisfactorily).

Candidates should be aware of secondary causes of hyperlipidaemia and of the need to try lifestyle changes before considering pharmacological treatment. In fact both of these patients were still living with their mother and consuming a fairly unhealthy diet. Their weekly beer intake was around 14 pints each and they were not taking much exercise. They were advised accordingly and complied enthusiastically, so that drug treatment for the hyperlipidaemia was unnecessary. The xanthomata present in the first twin had virtually disappeared when I last saw him.

It is important to treat patients and not laboratory tests, so I would expect candidates to want more clinical information with regard to endocrine status. Neither man appeared to be hypothyroid. The only unusual points in their past medical history is that they both had Perthes disease as infants and they were considered to be 'educationally subnormal' and were educated in a special school. However, they both have engaging personalities and are both able to hold down jobs. They appear fit and well and have normal secondary sexual characteristics.

The first question thus seems to be are the thyroid results correct?

The TFTs were consistently abnormal using the in-house assay (Bayer Immuno 1), even when the samples were no longer lipaemic. Tests for heterophile antibody interference were negative. The Free T4s and TSHs were confirmed in another lab by a different commercial assay, and the Free T4 was also found to be low by an equilibrium dialysis method.

The TFT results seem to be genuine, so a pituitary cause seems to the next most likely explanation, even in the absence of any clinical evidence. Baseline pituitary hormones have all been normal, and response to intravenous Synacthen was also normal. This is as far as we have got to date – please note down any pertinent ideas from good candidates!

Question 2

Routine checking of the overnight emergency results reveals the following results obtained from an 80 year old woman admitted the previous evening. The clinical details are "? Obstruction".

Na	115	mmol/L	
K	2.8	mmol/L	
Urea	12.9	mmol/L	
Creatinine	81	umol/L	
ALT	26	IU/L	(9-52)
Alkaline Phosphatase	64	IU/L	(36-125)
Total Protein	67	g/L	
Albumin	42	g/L	
Bilirubin	18	umol/L	
Calcium	2.39	mmol/L	
Glucose	7.2	mmol/L	

A TSH had also been requested.

On contacting the ward, you discover the patient has a four week history of abdominal pain and has suffered from profuse vomiting for a week. She was admitted because she had become confused. The houseman had diagnosed SIADH, possibly secondary to gastric carcinoma and had put the patient on fluid restriction but the Registrar is not so sure and asks for your help.

How would you investigate this patient and what suggestions would you make about management?

Question 2: Notes for Examiners

I would expect the candidates to want to know her fluid status (put on Dextrose, saline 1L over 16 hours but had not yet passed urine, clinically rather flat but not markedly dehydrated).

The clinical picture is one of gastric outlet obstruction, which had been recognised by the medical team. They thought she might have a gastric carcinoma and this was causing SIADH and hence the fluid restriction therapy. However, this was unlikely as adenocarcinomas tend not to be associated with SIADH and her results suggested a degree of dehydration with a high albumin and urea for someone who had not been eating for weeks. Further, she has other reasons for low potassium concentration, from alkalosis due to loss of gastric acid and her drug therapy could cause the hypernatraemia. Finally if we accept she was significantly dehydrated, then she may have elevated ADH due to volume contraction from prolonged fluid loss enhancing water retention and causing relative hyponatraemia.

I would expect the candidate to:

1. Recognise this is unlikely to be SIADH and violates most of the principles underlying the definition of SIADH.
2. Suggest that the original therapy (fluid restriction) is potentially dangerous in a patient who has had significant fluid loss.
3. Be able to discuss the pathophysiology of the electrolyte response to prolonged vomiting.
4. Recognise the effects of drugs (and ask about them).
5. Recognise the need to suggest therapeutic changes to medical colleagues diplomatically!

I recommended checking her urine osmolality and sodium loss on a stat urine as I was sure she would be conserving it as much as possible given her drug therapy. I suggested she needed N saline with potassium IV to maintain her urine output and slowly raise her sodium. Fluid restriction was not indicated in a patient who was vomiting. If she had untoward sodium loss I would have measured a cortisol although this was not a typical picture of Addison's crisis and I checked the TSH as hypothyroidism could have complicated the picture.

Her TSH was normal. We never received a urine sample and her electrolytes approached normal in a couple of days on IV fluids alone, although her sodium has remained slightly low (they have now stopped her drugs so it may rise further). Her albumin dropped to 32 g/L once adequately hydrated emphasising her original fluid deficit may have been more than was apparent clinically. The gastroscopy showed severe erosive duodenitis but no malignancy and she stopped vomiting once her oral intake was stopped. She is now awaiting rehabilitation although it may be delayed as she slipped in the bathroom and banged her head!

Question 3

You are the most senior person in the laboratory when, at 5.15 pm on a Monday evening, the MLSO in your automated section brings you the following results on a 26 year old woman on a gynaecology ward.

Serum		
Sodium	108	mmol/L
Potassium	4.2	mmol/L
Urea	21	mmol/L
Creatinine	130	umol/L
Glucose	6.2	mmol/L
TSH	<0.1	mIU/L
Free T4	>50	pmol/L

You find the request form: the clinical details are ‘hyperemesis gravidarum, agitated’. The patient administration system records that she was admitted late that morning.

What action do you take?

Question 3: Notes for Examiners

This woman was admitted in July, under the circumstances described. There are a whole host of possible answers that we could consider acceptable but clearly candidates must appreciate first that this woman is gravely ill and second that she may not be in the best place. I rang the Gynae SHO whose bleep number was on the form and explained that (a) this woman was thyrotoxic (b) severely hyponatraemic and thus (c) should be referred immediately to the physicians with a view to further management in the ITU.

Having established this, the candidate could then be invited to discuss the principles of management: it might be, for example, that the physicians were busy in A&E and would be unable to see her for an hour. In that case, it could reasonably be expected that the Chemical Pathologist should initiate immediate treatment . If that is the case he or she must go and see the patient (I hope that they would want to anyway).

Although from the history the probability is that the hyponatraemia is secondary to vomiting and inadequate sodium intake, the candidate should think about whether the lab can measure her cortisol urgently.

Details of management will depend on clinical assessment of course and candidates should be able to consider the principles which are straightforward, eg. cessation of any hypotonic fluid, very careful provision of hypertonic saline with regular biochemical, physiological and neurological monitoring, drugs to control vomiting (and fitting if necessary) for the hyponatraemia and anti-thyroid drugs, iodine, dexamethasone and beta-blockade for the thyrotoxicosis (if confirmed clinically).

The discussion might then lead to the dangers of severe hyponatraemia and its treatment, and/or the nature of thyrotoxic crisis – often of very sudden onset, precipitated by intercurrent illness, vomiting, etc. in a patient who may not have been diagnosed as hyperthyroid before.

Question 4

A 24 year old woman weighting 60 kg is admitted to hospital with an acute abdomen. She is diagnosed as having superior mesenteric artery thrombosis. Attempts to restore perfusion are in vain and she develops irreversible bowel ischaemia, necessitating resection of the small gut from a point 20 cm distal to the duodenal-jejunal junction, to a point 50 cm proximal to the ileocaecal junction, with construction of the jejunoileal anastomosis.

You will be asked to advise on her immediate and longer-term management from the point of view of maintaining fluid and electrolyte balance, and ensuring maintenance of her (previously good) nutritional status.

You may further be asked how this management would differ from that of a patient who has had a jejunostomy constructed.

Question 4: Notes for Examiners

These notes are fairly comprehensive – but general principles more important than detail.

Note that this patient does not have a jejunostomy. Preservation of the colon allows considerable absorption of fluid and although IV fluid supplementation will be required until bowel sounds return, it may not be required long term. The preservation of the ileocaecal value is also significant, as it may delay transit and increase the time for absorption of fluid (an nutrients) in the small gut. Nevertheless, diarrhoea is often a problem, and patient's oral free fluid intake should be limited; drugs such as Loperamide (to reduce intestinal mobility) may be helpful.

With less than 50 cm of jejunum, this patient is likely to require long term parenteral nutrition, but it is important to introduce early enteral feeding as much as can be tolerated. This helps to preserve the integrity of the gut and promotes adaptation in the ileum.

Malabsorption is usually a continuing problem, and nutrient intake must take account of this. A diet high in polysaccharides is recommended. These undergo fermentation in the colon to short chain fatty acids, which provide a valuable source of energy (NB hazard of D-lactic acidosis). A high fat intake will cause steatorrhoea, reducing transit time and water and mineral absorption in the colon but medium chain fatty acids can be reabsorbed from the colon. Diarrhoea and steatorrhoea may significantly reduce the amount of food/enteral supplements that a patient is willing to consume.

Oxalate urinary calculi are a recognised hazard and the diet should be low in oxalate. Vitamin supplementation is usually required.

In patients with a jejunostomy, the major early problem is fluid loss. Intravenous replacement is always required – stoma output can be up to 8L/24h and is exacerbated if oral fluids containing inadequate sodium are given. The concentration of sodium in oral fluid should be 100-120 mmol/L and the addition of glucose facilitates sodium and water uptake. Loperamide and drugs to reduce secretion (Omeprazole, Octreotide) are often useful. Magnesium supplementation is usually required, potassium supplementation may be.

Long term parenteral nutritional support is always required with less than 75 cm of jejunum, but in addition to whatever enteral intake is possible. Patients with up to 200 cm jejunum usually require enteral supplementation (eg. overnight gastrostomy/ nasogastric) but can usually manage without parenteral support. Enteral supplements should be iso-osmolar and high in salt – note that elemental diets are usually the opposite – hyperosmolar, low salt, and may exacerbate fluid loss. Vitamin B12 supplementation is essential.

Question 5: For Medically Qualified Candidates

A man you discharged some years ago is referred by the GP back to your lipid clinic:

	Referral 1	Referral 2
Age	57	68
Presentation	Mixed hyperlipidaemia discovered during blood donation 13 years previously. Been on diet and Clofibrate in the past, but no treatment at present.	Lipid medication changed to Simvastatin a few months ago: lipids now worse.
Exercise tolerance	Walks for miles without ill effect. Occasional chest tightness and difficulty breathing brought on by jarring movements and eased by leaning forward.	Still a keen walker, but has noticed some chest tightness and 'fizziness' in his left arm when walking uphill during a monthly 8 mile hike with friends.
Past medical history	Has had attacks of gout in the past	Recent urological investigations after passing small blood clot in urine; no pathology found.
Medications	Nil at present.	Nifedipine m/r 30 mg bd Simvastatin 40 mg nocte
Smoking history	Non-smoker from age 18.	Non-smoker from age 18.
Alcohol intake	Six units per week.	One bottle of red wine per week.
Family history	Mother died of stroke at 65 after 4 year history of angina. Father has gout. One brother has peripheral vascular disease and hypertension. Sons of 29 and 27 not investigated.	As before, plus: elder brother died of MI at 68; younger brother of 65 had MI last year; sister of 60 on treatment for hypertension. Sons of 40 and 38 not investigated.
On examination	Well. No signs of lipid deposition. BMI 28.7.	Well, apart from a small amount of bilateral pitting ankle oedema. BMI 31.2.
BP mm/Hg	190/110	170/110 (140/82 earlier in the day on own BP meter!).
Fasting lipids (mmol/L): Cholesterol Triglyceride HDL cholesterol	 11.3 8.6 0.6	 7.8 16.0 0.7
Fasting plasma glucose mmol/L	5.5	9.6

On the first occasion he was discharged on Bezafibrate 400 mg nocte and Nifedipine 30 mg bd. His lipids then were cholesterol 6.5 mmol/L, triglycerides 3.9 mmol/L, HDL 0.8 mmol/L and LDL 3.9 mmol/L, his BMI was 27.8 and his blood pressure 144/84

How would you investigate and manage this patient now?

If the first referral was being made now, would your investigation and management be any different to what it was 11 years ago?

Question 5: Notes for Examiners

This clinical scenario is taken from a real case and should be familiar territory for anyone who has worked in a lipid clinic. However, there is a lot of material here, so it is important for candidates to prioritise their responses. I think the aspects to focus on first are as follows.

How would you investigate and manage this patient now?

The clinical history is suggestive of angina and needs further investigation. He had a positive exercise test, positive coronary angiography and is awaiting CABG.

Glucose: his fasting plasma glucose is in the diabetic range, although this was the first raised glucose on record and he was asymptomatic. Further biochemical evidence was sought (and readily obtained) to support the diagnosis. A dietitian gave appropriate dietary advice.

Lipids: the Simvastatin is clearly not keeping his lipids within ideal limits. It was stopped and he started Fenofibrate 267 mg nocte. After a couple of month he had managed to reduce his BMI to 29.4 and the combination of this and the Fenofibrate improved his lipids to:

Cholesterol	5.7 mmol/L
Triglyceride	3.3 mmol/L
HDL	0.9 mmol/L
LDL	3.3 mmol/L

This is encouraging, but in view of his very high risk, a small dose (10 mg) of Simvastatin was added back in (with appropriate warnings etc.), with further improvement in the profile (non-fasting cholesterol 4.8 mmol/L).

Blood pressure etc: Nifedipine may have been implicated in his ankle oedema.
Currently on:

Ramipril	2.5 mg daily	
Atenolol	50 mg daily	
Nicorandil	10 mg bd	
Lansoprazole	30 mg daily	
Aspirin	75 mg daily	
Nitrolingual spray	prn	plus lipid lowering drugs.

Family: his two sons should clearly be encouraged to have their lipids and other risk factors checked.

If the first referral was being made now, would your investigation and management be any different to what it was 11 years ago?

The way we assess risk, the evidence in favour of the benefits of risk factor management, the drugs available and the targets of treatment have all changed over the years, so it is not unreasonable to ask this question. It is more difficult for the author to be objective about his own practice! However, some possible topics for discussion are:

Should the patient have had an exercise test at the first referral?

The lipids at discharge are not as good as current practice would wish.

I have heard it argued that everyone with raised triglycerides should have a glucose tolerance test, irrespective of their fasting glucose. The rationale for this is that one would

be more likely to treat their hyperlipidaemia if the 2-hour glucose were raised. Since this patient was treated anyway, it does not seem an important consideration here.

The two sons should have had a CHD risk factor assessment before now.

There are other biochemical markers of CHD risk that could have been checked, although I am not convinced that the results would have made any difference to his management.

No one seems to have taken much interest in the management of his gout.

(NB. All the usual tests for secondary causes of hyperlipidaemia were negative).

Question 6

52 year old male bus driver presented with a 6 month history of increasing weakness.
He was previously healthy.
Weakness severe enough to require help.
He also complained of diarrhoea on and off for the past 4 months.
He also complained of generalised bone pain.
He is a non-smoker, does not drink alcohol.
Examination unremarkable except for muscle weakness – worse in proximal and lower limbs.

Investigations

Renal function tests – normal.
Liver function tests – normal.
FBC – normal.
Calcium 2.28 (2.15-2.55) mmol/L
Phosphate 0.40 (0.80-1.30) mmol/L
ALP 376 (<126) IU/L

What further investigations would you recommend?

ALP isoenzyme studies showed ALP to be predominately of bone origin
TmP/GFR 0.23 (0.7-1.3) mmol/L
Serum PTH 25 (10-65) ng/L
Serum 250HD 82 (50-150) nmol/L

How do you interpret these results?

Suggest a possible diagnosis.

What advice would you give regarding the management of this patient?

Question 6: Information for Examiners

What further investigations would you recommend?

First confirm the low phosphate to exclude a transient decrease in phosphate due to transcellular shift. Persistent low phosphate can cause muscle weakness.
Next step is to exclude vitamin D deficiency.
With a history of diarrhoea a malabsorption syndrome needs to be considered.
Faecal fat measurement was done and it was found to be normal.
Vitamin B12 and folate and full blood count were all normal.
Measurement of serum 250HD and PTH and renal tubular reabsorption of phosphate are necessary.

How do you interpret these results?

Low TmP/GFR indicates reduced reabsorption of phosphate.
In vitamin D deficiency secondary hyperparathyroidism will cause low TmP/GFR and low serum phosphate. Serum PTH and 250HD are within the reference range and this makes vitamin D deficiency unlikely.

Suggest possible diagnosis.

Inherited hypophosphataemic disorder is unlikely – age and recent onset .
Oncogenic osteomalacia is the most likely diagnosis.

What advice would you give regarding the management of this patient?

Attempts to find the tumour were made and these were initially unsuccessful.
Treatment: Calcitriol and phosphate supplements. These improved symptoms and serum phosphate increased to 0.7 mmol/L.