

“Trying to Loose Bodyweight”

Endocrine Block-Case 3

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Learning Objectives:

By the end of this PBL package, students should be able to:

- Discuss the hormones involved in the metabolism of carbohydrates and fats and the mechanisms responsible for maintaining normal blood glucose level.
- Discuss the biochemical and physiological interactions between the different components of metabolic symptoms (such as obesity), and clinical findings (such as high blood pressure, dyslipidaemia, and impaired blood glucose tolerance).
- Understand the role of obesity in insulin-resistance and the development of type 2 diabetes.
- Use basic sciences to interpret clinical manifestations and investigations obtained from a patient with metabolic syndrome.
- Understand the role of changing the life style (including weight loss, low calorie diet and stopping smoking) in managing a patient with metabolic syndrome.

Trigger

Mohamed Ali a 50-year-old teacher, who has been successfully accepted for a job as a principal in a private high school in Riyadh, comes in for a medical check-up. This is part of the requirements for the new job. During the medical examination he is found to have a BMI of 33, a blood pressure in the range of 170/95- 175/93 mmHg measured over three separate occasions. During the medical consultation, Mohamed tells Dr. Khalid Al Sulayman, "About two years ago a blood test showed that I have high blood cholesterol but I was so busy and never worked on the medical advice recommended by my doctor."

Discussion Questions:

- Are there any difficult words you do not understand?
- List the key information about Mohamed.
- Identify Mohamed's presenting problems.
- For each problem, generate a list of possible causes (hypotheses).
- What further information would you like to know from history to refine your hypotheses?

Trigger

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New Terms/Difficult words

- *BMI.*
- *Cholesterol.*

Tutor: *Encourage students to use a medical dictionary resource to discuss the meaning of each of these words.*

Problems/Hypotheses

A BMI of 33:

- Simple obesity (Genetic + environmental causes).
- Increased caloric intake.
- Increased caloric intake + lack of exercising.
- Genetic causes.
- Metabolic disorders.
- Endocrine disorders.
- Cushing syndrome.
- Hypothyroidism.
- Type 2 diabetes mellitus.
- Metabolic syndrome.

Problems/Hypotheses

High blood pressure:

- Primary hypertension (Environmental + Genetic causes).
- Secondary hypertension (Renal, vascular, endocrine causes).
- Polycystic kidney disease.
- Chronic renal failure.
- Urinary tract obstruction.
- Renovascular hypertension.
- Renin-producing tumour.
- Coartication of aorta.
- Vasculitis.
- Collagen vascular disease.
- Hyperthyroidism.
- Hypercalcaemia.
- Acromegaly.
- Obstructive sleep apnoea.
- Pheochromocytoma
- Drugs (alcohol, cocaine, NSAIDs, Decongestants (ephedrine)).

Problems/Hypotheses

High blood cholesterol:

- Familial hypercholesterolaemia (Genetic defect).
- Obesity.
- Increased dietary calories.
- Diabetes mellitus-type 2
- Alcohol consumption.
- Nephrotic syndrome.
- Obstructive liver disease.
- Hypothyroidism.
- Cushing syndrome.
- Anorexia nervosa.
- Medication:
 - Thiazide diuretics.
 - Glucocorticoids.
 - Beta blockers.
 - Retonic acid.

Facilitation Questions

Discuss the role of the hypothalamus, liver, muscles, adipose tissues, stomach and pancreas in contributing to the mechanisms regulating body weight?

Normally we have our blood pressure maintained within a normal range. What are the physiological factors maintaining that control?

- Blood volume.
- Left ventricular function.
- Cardiac output.
- Regular heart rhythm.
- Autonomic nervous system.
- Elasticity of the aorta.
- Peripheral resistance.
- Hormonal balance (thyroxin, growth hormone, cortisol).

Facilitation Questions

What is BMI?

What are the factors responsible for increased BMI?

- Increased caloric intake.
- Increased food intake.
- Lack of exercising.
- Metabolic disorders.
- Endocrine/hormonal disorders.
- Genetic causes.

Further Questions

- Describe daily activities, any exercising.
- Describe what does he eat in each meal and in between meals.
- Any history of obesity during childhood?
- Any family history of obesity, hypercholesterolaemia?
- Any history of hospital admission, investigations, or treatment.
- Any history of urinary troubles or kidney problems?
- Any other symptoms?
- Any history of medication?
- Any history of smoking or drinking alcohol?

**Please Read
The History**

Mohamed has been overweight since childhood. Over the years, he tried several regimens to loose weight but with little benefit. About two years ago, his GP found Mohamed to have a high blood pressure. This has been confirmed on three occasions. Finally the GP commenced him on Enalapril (an ACE inhibitor) which he took for only five months. At that time his laboratory tests showed that his blood cholesterol was high and the liver function tests were a little raised. Further laboratory assessments for viral hepatitis were all negative. The doctor, at that time told him that the increases in the liver function tests are due to accumulation of fat in the liver cells. Mohamed was asked by his GP to start exercising and eat less calories, and low fatty food to control his bodyweight and the increased blood cholesterol. He did join a gym near his home and went for exercising regularly. However, this routine lasted only for a few weeks then he was back to eating fatty foods and stopped exercising. He prefers sitting at home and watching TV in the evenings.

Continue-History

Past medical history

No history of angina, surgery or hospital admissions. No past history of renal trouble.

Allergy and Medication

Nil.

Family history

No family history of hypercholesterolaemia or collagen-related disorders. His father was diagnosed with diabetes mellitus and he suffered a heart attack 5 years ago. He is still alive and on medication. His mother, two brothers and three sisters are all over-weight.

Continue-History

Alcohol and smoking

Mohamed smokes 20 cigarretes a day for the last 25 years. No history of alcohol consumption.

Social history

Mohamed has been married for the last 20 years. He has two grown up children. He has no hobbies and does very little exercise. He tried to reduce his body weight and even joined the local Body Masters gym but did not continue.

Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Identify patient's new problems. Provide hypotheses for each problem.
- What further information would you like to know through clinical examination?

New Terms

(Tutor: encourage students to use their medical dictionary to find out more about these words)

- Enalapril (an ACE inhibitor)
- Carlorie.

Tutor: Encourage students to use a medical dictionary resource to discuss the meaning of each of these words/phrases.

Key information

- Has been overweight since childhood.
- Tried to loose body weight but little benefit.
- Diagnosed with a high blood pressure (2 years ago)
- Was on Enalapril (an Ace inhibitor) for five months.
- High blood cholesterol and abnormal liver function tests (2 years ago).
- Viral hepatitis negative- diagnosed as fatty liver.
- Did not change his dietary habits or work on his bodyweight.
- No history of angina, surgery or hospital admission.
- No family history of hypercholesterolaemia.
- Father is on treatment for diabetes mellitus. Had a heart attack
- Smokes 20 cigarettes per day for 25 years.
- Has 2 grown-up children.

Problems/Hypotheses

A BMI of 33:

- Simple obesity (Genetic + environmental causes).?/++
- Increased caloric intake.++
- Increased caloric intake + lack of exercising.+++
- Genetic causes.++/+
- Metabolic disorders. ++
- Endocrine disorders.?
- Cushing syndrome.?/-
- Hypothyroidism. ?/-
- Type 2 diabetes mellitus.?/++
- Metabolic syndrome.+++ /++

Problems/Hypotheses

High blood pressure:

- Primary hypertension (Environmental + Genetic causes). ?/+++
- Secondary hypertension (Renal, vascular, endocrine causes).
- Polycystic kidney disease. ?/+
- Chronic renal failure. ?/+
- Urinary tract obstruction. ?--
- Renovascular hypertension. ?/++
- Renin-producing tumour. ?
- Coarctation of aorta. ?
- Vasculitis. ?
- Collagen vascular disease. ?
- Hyperthyroidism. ?/---
- Hypercalcaemia. ?
- Acromegaly. ?/--
- Obstructive sleep apnoea. ?/--
- Pheochromocytoma. ?/-/+
- Drugs (alcohol, cocaine, NSAIDs, Decongestants (ephedrine). ?/---

Problems/Hypotheses

High blood cholesterol:

- Familial hypercholesterolaemia (Genetic defect)./--
- Obesity./+++
- Increased dietary calories./+++
- Diabetes mellitus-type 2 /++
- Alcohol/----
- Nephrotic syndrome./----
- Obstructive liver disease./----
- Hypothyroidism./----
- Cushing syndrome./----
- Anorexia nervosa./---
- Medication:/----

 - Thiazide diuretics.
 - Glucocorticoids.
 - Beta blockers.
 - Retonic acid.

Problems/Hypotheses

High blood cholesterol:

- Familial hypercholesterolaemia (Genetic defect)/---
- Obesity./+++
- Increased dietary calories./+++
- Diabetes mellitus-type 2 ?/++
- Alcohol /---
- Nephrotic syndrome./---
- Obstructive liver disease./--
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- Medication:/---

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**Please Read
The Clinical
Examination**

Clinical Examination

The index and the middle fingers of his right hand have nicotine stains. Mohamed is 1.70 meters tall and his body weight is 96 kg. His BMI is 33 and his waist circumference is 105 cm. No evidence of central obesity or hypothyroidism.

His vital signs are summarized in the table below:

Vital signs	Mohamed	Normal range
Pulse rate	100 regular	60-100/min
Blood pressure	170/95 mmHg	100/60-120/80 mmHg
Temperature	37.0	36.6-37.2 °C
Respiratory rate	17	12-16/min

Continue- Clinical Examination

Cardiovascular and Respiratory Systems:

Normal, apart from his high blood pressure.

Abdominal Examination:

No abdominal tenderness or rigidity.

Liver is palpably enlarged with a liver span of 16 cm (normally less than 13 cm).

No abdominal swellings.

Auscultation of the abdomen is normal.

Discussion Questions

- Are there words that you do not understand?
- Summarize key information that you have obtained from this progress.
- Identify patient's new problems. Provide hypotheses for each problem.
- What further information would you like to know through investigations?

Difficult words

- Nicotine stains
- Waist circumference.
- Liver span

Problems/Hypotheses

A BMI of 33:

- Simple obesity (Genetic + environmental causes)/+++.
- Increased caloric intake./+++
- Increased caloric intake + lack of exercising./++++
- Genetic causes./++
- Metabolic disorders./++
- Endocrine disorders.?+
- Cushing syndrome./--
- Hypothyroidism./--
- Type 2 diabetes mellitus./++
- Metabolic syndrome./+++



Problems/Hypotheses

High blood pressure:

- Primary hypertension (Environmental + Genetic causes). ?/+++
- Secondary hypertension (Renal, vascular, endocrine causes).
- Polycystic kidney disease./--
- Chronic renal failure./---
- Urinary tract obstruction./---
- Renovascular hypertension./--
- Renin-producing tumour./--
- Coarctation of aorta./---
- Vasculitis./---
- Collagen vascular disease./--
- Hyperthyroidism./--
- Hypercalcaemia./--
- Acromegaly./--
- Obstructive sleep apnoea./--
- Pheochromocytoma./--
- Drugs (alcohol, cocaine, NSAIDs, Decongestants (ephedrine)./--

Problems/Hypotheses

Liver is enlarged:

- Congestion: e.g., congestive heart failure (less likely, as per clinical examination)
- Acute liver infection: e.g., viral hepatitis A (less likely as there is no fever, jaundice or tenderness).
- Chronic liver infections e.g., viral hepatitis (needs screening for viral hepatitis).
- Mechanical obstruction: e.g., cholestasis, biliary obstruction, biliary stones (needs LFTs, ultrasound examination, ERCP etc.)
- Masses: e.g., liver metastases (U/S examination).
- Accumulation of fats in the liver etc : e.g., fatty liver (We need to exclude all other causes first).

**Please Read the
Investigations**

Investigations

The doctor arranges for Mohamed some blood tests to check for his blood count, blood glucose level, lipid profile, blood biochemistry and a viral screening for hepatitis. He also arranges for an abdominal ultrasound to assess the enlarged liver. Because Mohamed has been smoking for 25 years and has high blood pressure for a number of years, the doctor decides to do a chest X-ray and an ECG. A summary of the investigation results are shown below:

Complete Blood Count (CBC)

Blood Test	Mohamed	Normal range
Haemoglobin	14 g/100ml	11.5-15.5 g/100ml
White blood cell count	8,000 mm ³	5,000 -10,000 mm ³
Platelet count	242,000 mm ³	160,000-500,000 mm ³

Continue- Investigations

Blood Biochemistry

Blood Test	Mohamed	Normal range
Fasting blood glucose	6.5	3.8-5.8 mmol/L
Total Cholesterol	6.1	<5.2 mmol/L
Blood Triglycerides	3.1	<1.7 mmol/L
HDL Cholesterol	0.89	>1.03 mmol/L
LDL Cholesterol	4.21	<2.84 mmol/L
Blood urea	2.9	2.5-6.7 mmol/L
Serum creatinine	101	79-118 μ mol/L

Continue- Investigations

Liver Function Tests

Test	Mohamed	Normal range
Serum bilirubin	5	0 - 19 $\mu\text{mol/L}$
Serum aspartate aminotransferase (AST)	40	0 - 34 IU/L
Serum alanine aminotransferase (ALT)	87	0 - 50 IU/L
Serum alkaline phosphatase (ALP)	120	0 - 120 IU/L
Serum albumin	39	35 - 50 g/L

Viral screening for hepatitis: Negative

Ultrasound Abdomen

There is an increased echogenicity of the liver tissue. No masses are found. The gallbladder and biliary tract are normal. Both kidneys are normal.

Continue- Investigations

Chest X-Ray

Shows bilateral hyperinflation of the lungs and a flat diaphragm.

Electro-cardiogram

Evidence of left ventricular hypertrophy

Discussion Questions

- Are there any terms that you do not understand?
- Summarize the key information that you have obtained from this progress.
- Identify if there are any new problems. Use the new information obtained to refine and rank your hypotheses.
- Work out with your group your “learning issues”.

New words

- Blood cholesterol
- Blood triglycerides.
- HDL Cholesterol
- LDL Cholesterol
- Left ventricular hypertrophy.

Question:

Do you know a Nobel prize laureate whose work has contributed to the advancement of our knowledge in physiology and/or pharmacology related to this case? What was exactly his/her work about? Give a summary.

Interpretation of findings

Test	Change	Interpretation/possible causes
Blood glucose	Raised	Obesity, increased fat in body cells, Insulin resistance
Blood cholesterol and triglycerides	Raised	Problem with fat metabolism, Problem with the liver (LDL receptor), others
Blood urea and creatinine	Normal	Renal failure is less likely a cause of his high blood pressure. There is no renal complications yet as a result of his high blood pressure.
Liver function tests	Mildly raised	? viral hepatitis, ? chronic liver disorders ? due to fat accumulation (He does not drink, no history of blood transfusion or operations)
Viral hepatitis screening	Negative	Excludes viral hepatitis
Ultrasound examination	Increased echogenicity of the liver	No masses, no stones, no gallbladder problems, no biliary system problems The findings are consistent with increased fat in the liver.
Chest X-ray	Bilateral hyperinflation of lungs + flat diaphragm	Changes consistent with COPD (he has been smoking for 20 years).
ECG	LV hypertrophy	Most likely related to increased load on the heart due to increased blood pressure.

Hypotheses: Ranking

Most likely:

- Several problems are occurring at the same time. These problems are related to increased body weight and are enhancing each other.

Evidence:

- Increased BMI
- High blood glucose level.
- Increased blood cholesterol and triglycerides.
- Increased fat in the liver cells (no evidence of viral hepatitis).
- Increased blood pressure.

Less likely/Excluded:

- Chronic renal failure.
- Polycystic kidney disease.
- Reno-vascular hypertension.
- Familial hypercholesterolaemia.
- Alcohol-related disorders.
- Obstructive jaundice.
- Chronic viral hepatitis
- Cushing syndrome./Increased cortisol secretion.
- Medication associated disorders.
- Increased growth hormone secretion.
- Hypothyroidism.

Learning Issues

(Tutor: Encourage students to identify their learning issues that reflect key issues raised in the case. They might need to edit their learning issues into sentences or questions. Usually learning issues are about 5-7 key principles. See examples shown below).

Learning Issues

- Hormones involved in the metabolism of carbohydrates and fats and their role in maintaining normal blood glucose level.
- Biochemical and physiological interactions between the different components of metabolic symptoms (such as obesity, dyslipidaemia, high blood pressure and impaired blood glucose tolerance).
- The mechanisms by which obesity causes insulin-resistance and the development of type 2 diabetes.
- Interpretation of the clinical manifestations and investigation results obtained from a patient with metabolic syndrome.
- Differences between HDL and LDL
- Role of changing life style (including weight loss, low calorie diet and stopping smoking) in managing metabolic syndrome.

Tutorial Two

Discussion Questions

After the students spent about 60 minutes addressing their learning issues. You might spent 10-15 minutes on these questions:

Discussion Questions:

- On the basis of the information provided, what is your final hypothesis? Justify your views.
- How would you explain to Mohamed the examination findings and the investigation results?
- What is your management goals and your management plan for Mohamed?





Do you know a Nobel prize laureate whose work has contributed to the advancement of our knowledge in physiology and/or pharmacology related to this case? What was exactly his/her work about? Give a summary.

Student: You could also after the completion of this case submit your work about the Nobel Prize laureate for this case to Professor Samy Azer at (sazer@ksu.edu.sa) or hand it to him.

**Please Read
Progress 1**

Progress 1

Mohamed comes in to see Dr. Khalid with the lab results. Dr. Khalid explains the results to Mohamed and tells him that he has gained a lot of body weight and is not doing enough exercise. This has caused an accumulation of fats in several places in his body such the abdomen, thighs, and body organs. The fat also accumulated in the liver cells causing an enlargement in the size of the liver and changes in the liver function tests. Also eating high calorie food, containing high fat contents contributed to these problems and caused increases in the level of blood cholesterol and blood triglycerides above normal limits. This also resulted in decreases in the good cholesterol also known as HDL below normal limits and increases in the bad cholesterol also known as LDL above normal limits. The accumulation of fat in the body cells also interfered with the uptake of glucose by body cells resulting in an increased blood glucose level. So there are several problems happening at the same time and they are all related to increased body weight and lack of exercising. Usually such problems are associated with increases in blood pressure as it is the case with you. The high blood pressure if left untreated causes a load on the heart function and hence the changes in your ECG.

Progress 1

As you can see there are a number of changes happening in your body and they are all triggered by your increased body weight and lack of exercising. So to reverse these changes you need to change your life style by decreasing the amount of fats and calories in your food, exercising regularly with the aim to reach a BMI in the range of 23 to 25.

Dr. Khalid outlines a management plan with Mohamed. He advises him to stop smoking and guide him to a program for smoking cessation. He also plans with him a plan for reducing body weight, and referred him to a dietitian to manage his daily calorie requirements. He commences him on Enalapril tablets for high blood pressure and asks him to review in 6 weeks.

Discussion Questions

• Write down a mechanism showing the pathogenesis of Mohamed's problems and highlighting his symptoms, clinical signs, and laboratory investigations results. Use knowledge you learnt from physiology, biochemistry and pathology to build your mechanism.

• In another diagram discuss how loss of body weight and changes in daily intake of calories could help Mohamed in reversing his symptoms, clinical signs, and lab investigations results. Use knowledge you learnt from physiology, biochemistry and pathology to build your mechanism. .

**Please Read the
Closure**

Case Closure

Six weeks later, Mohamed reviews Dr. Khalid for a check-up. He has been following a rigid regime to loose body weight and eat only low calorie foods. He swims three days a week and for the other three days he does cardio exercise on a treadmill. In the first week Mohamed lost 3 kg of body weight and in the last week he lost 1kg. Going to the gym requires from Mohamed a lot of motivation and his family is supporting his decision of starting a healthier life style. He feels much better. His BMI is 28 and his blood pressure is in the range of 135/80 to 130/80 mmHg.

Eighteen months later, Mohamed continues exercising regularly and follows a strict dietary regime. His BMI is 25 and his blood pressure is in the range of 120/75 to 120/70 mmHg. His blood lipids are within normal range and his liver function tests are back to normal.

Case Closure-feedback

Tutor's note:

In the last 10 minutes of the tutorial, you might encourage your group to discuss how they could work better as a group. What are the things they need to change and what things they need to improve? This discussion is very useful and will help the group to function better as they work on the next PBL case.