Lecture 16&17

Editing file

MED438
KING SAUD UNIVERSITY

PRIMARY HEALTHCARE TEAMWORK

Data Interpretation I & II

Objectives:

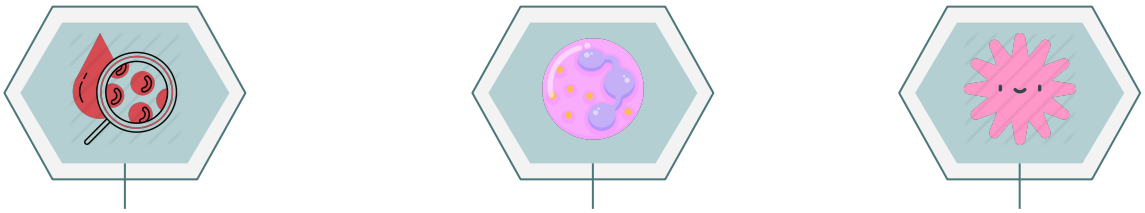
- ★ Safe CBC interpretation
- ★ Approach to Anemia
- ★ Diagnosis and highlight about polycythemia
- ★ Diagnosis and highlight about thrombocytopenia
- ★ Diagnosis and highlight about Thrombocytosis
- ★ Diagnosis and highlight about neutropenia and leukopenia.
- ★ Diagnosis and highlight about Pancytopenia
- ★ Explain different presentation of Hepatitis B markers.
- ★ Explain different types of thyroid disorder.
- ★ Recognize the likely explanations for hypocalcemia or hypercalcemia.

Color index:

Original text Important Doctor's notes Golden notes Extra

CBC Interpretation

The Major Components Of CBC Are:



Hb **WBC** **Platelets**

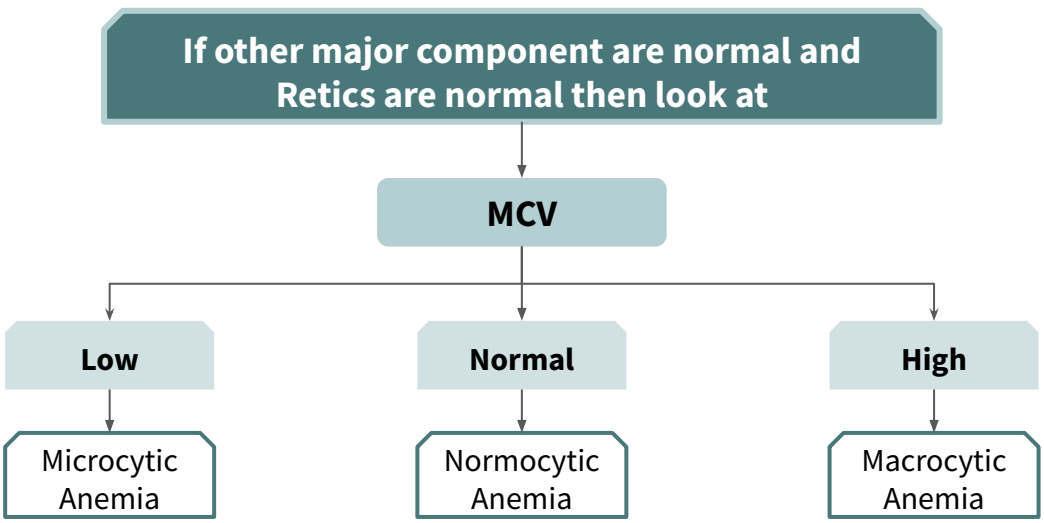
★ **If all major components are normal, then it is very less likely you miss a serious disease.**

Safe CBC Interpretation

1. Look at **Hb** >>**if low** >> look at other major components (**WBCs and Platelets**) to not miss bone marrow disease (Bone marrow suppression, Pancytopenia).
2. If there is no striking abnormality of WBC and platelet then **check MCV** to classify the anemia into **Microcytic, Normocytic or Macrocytic.**
3. Some references recommend to check reticulocyte before MCV to not miss hemolytic anemia but not practical.

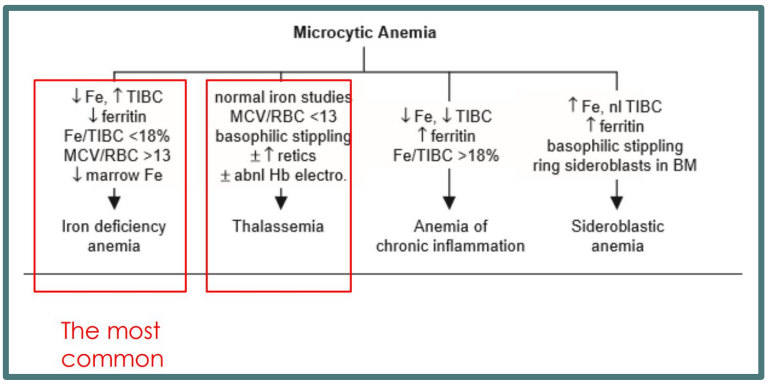
Anemia

- **Anemia is a symptom** not a disease. So, look for underlying cause.
- Helpful parameters to diagnose the underlying cause of anemia:
  - **Size of red blood cells** (**MCV**): (small/ normal/ big)
  - Abnormal cells on microscopic examination (like blast cells in leukemia (>5%))
  - Status of leukocytes and platelets (Bone marrow function)
  - **Reticulocyte count** (ability of marrow to respond to anemia)>> can help in hemolytic anemia (if high) and in marrow suppression (if low).
  - **Evidence of destruction(hemolysis)** >> (elevated LDH and indirect bilirubin and low haptoglobin)



Anemia

Approach To Microcytic Anemia



- **Most Important causes of microcytic anemia are:**
  - Iron deficiency anemia
  - Thalassemia
- Anemia of chronic disease is usually normocytic and can be microcytic.

Iron Deficiency anemia (IDA)

- Iron studies – Low serum iron.
- High total iron binding capacity (TIBC, transferrin concentration).
- Low % transferrin saturation.
- Low ferritin (the most sensitive test esp if < 15).

Features might help in distinguishing between IDA and Thalassemia

Feature	IDA	Thalassemia
RBC	Low, Low normal Not good production	High, High normal Trys to compensate
MCV **Normal: (80-100)**	Mild to moderate low (most likely above 70) ~80	Very low (< 70) ~60
RDW	Mostly High	Mostly Normal
Mentzer index: MCV/RBC	> 13	< 13

Normocytic anemia

Anemia of chronic inflammation or disease like:

- Chronic kidney disease , autoimmune disorders , chronic infection , malignancy or patients with B12 deficiency & IDA

Macrocytic anemias

Megaloblastic Common	Non-Megaloblastic
Vitamin B12 deficiency	Liver disease
Folate deficiency	Myelodysplastic syndrome
-	Increased reticulocyte count
-	Alcoholism causing: BM suppression & macrocytosis independent of folate/B12 defic.or cirrhosis

Other Blood Disorders

Polycythemia:

Polycythemia approach:

- What is the most important test to approach polycythemia?
  - Erythropoietin
- **Low erythropoietin**
  - Most likely primary polycythemia (polycythemia vera)
  - Polycythemia vera sometimes combined with high WBC and/or platelet.
- **High erythropoietin**
  - Most likely secondary polycythemia (smoking , COPD,hypoxia ..)

Thrombocytopenia:

- Thrombocytopenia (ie, platelet count <150,000/microL [150 x 109/L])
- **Severe spontaneous bleeding is most likely with platelet counts <20,000 to 30,000/microL**, especially below 10,000/microL.
- Surgical bleeding generally may be a concern with platelet counts <50,000/microL
- DDx is wide and including bone marrow malignancy.

Thrombocytosis:

- Patients with elevated platelet counts, the initial diagnostic question is whether their thrombocytosis is :
  - Reactive phenomenon (infection, post surgery or Trauma..)
  - Marker for the presence of a hematologic disorder (chronic myeloproliferative neoplasms..).

Neutropenia Vs leukopenia:

- Leukopenia = low WBCs
- Neutropenia = low absolute neutrophils count (ANC)
- Leukopenia ≠ Neutropenia
- Febrile Neutropenia is a medical emergency
- Causes of neutropenia:
  - Autoimmune, malignancy, chemotherapy.

Neutropenia classification is based on Absolute Neutrophil count (ANC)	
Mild	< 1.5 K/uL (1500 cells / MicroL)
Moderate	<1.0 K/uL (1000 cells / MicroL)
Sever	< 0.5 K/uL (500 cells / MicroL)

Pancytopenia DDx

- Bone marrow malignancy
- Viral infection
- Drug induced

CBC Interpretation Cases

Case Study 1

A 25 year- old lady, presented with 2 months H/O dizziness and fatigue.

NOTE: Consider upper and lower GI endoscopy for any males (esp. elderly) and postmenopausal women to R/O GI malignancy.
Anemia: Hypochromic Microcytic Anemia
Most likely: Iron Deficiency Anemia (IDA)
What do expect the following results?

- Ferritin: low (Especially if <15)
- TIBC: High
- Fe: Low
- Transferrin saturation: low

Treatment:

- **How much Hb increment is excepted with treatment?**
  - Around 2 to 4 g/dL every three weeks.
  - If Hb increased in slower rate, check for ongoing bleeding?
  - Possible causes: Heavy menstruation, PUD, malnutrition, celiac, malignancy or IBD)
- **How long the treatment course is expected?**
  - Oral Fe TID (or less if not tolerated (GI upset))
  - Around 6 wk to correct anemia;and 6 months to replete Fe stores.

Test 1	Results	Normal range
WBC	7. 0	4 – 11 x10.e9/L
RBC	**3.7 (Low)**	4.2 – 5.5 x10.e12/L
HGB	**90 (Low)**	120 – 160 g/L
HCT	**28 (Low)**	42 – 52 %
MCV	**73 (Low)**	80 – 94 fl
MCH	**23.6 (Low)**	27 – 32 pg
MCHC	320	320 – 360 g/L
RDW	**15.8 (High)**	11.5 – 14.5 %
PLT	330	140 – 450 x10.e9/L

Case Study 2

65 years old gentleman presented with Hx of SOB and generalized weakness

Diagnosis: Hypochromic Microcytic Anemia
Need Urgent Blood transfusion.

★ Generally The Hb threshold for blood transfusion for asymptomatic patient **is <7 g/L and 10 for heart failure patients.**

Test 2	Results	Normal range
WBC	7. 9	4 – 11 x10.e9/L
RBC	**3.1 (Low)**	4.2 – 5.5 x10.e12/L
HGB	**5.7 (Low)**	120 – 160 g/L
HCT	**24 (Low)**	42 – 52 %
MCV	**74 (Low)**	80 – 94 fl
MCH	**23.9 (Low)**	27 – 32 pg
MCHC	319	320 – 360 g/L
RDW	**16.9 (High)**	11.5 – 14.5 %
PLT	410	140 – 450 x10.e9/L

Case Study 3

A 31 year old man came for pre-marital check up .

Anemia: Hypochromic Microcytic Anemia
Diagnosis: Most likely Thalassemia
What you will order to confirm Dx?

- Hemoglobin electrophoresis (HE).

What do you expect in HE?

- If HB A2 is > 3.5% most likely B-Thalassaemia Minor
- If HB A2 is normal (< 3.5%) most likely alpha Thalassaemia Minor

Test 3	Results	Normal range
WBC	8.5	4 – 11 x10.e9/L
RBC	5.9	4.7 – 6.1 x10.e12/L
HGB	**122 (Low)**	130 – 180 g/L
HCT	**39 (Low)**	42 – 52 %
MCV	**63.5 (Low)**	80 – 94 fl
MCH	**20.4 (Low)**	27 – 32 pg
MCHC	**317 (Low)**	320 – 360 g/L
RDW	14	11.5 – 14.5 %
PLT	177	140 – 450 x10.e9/L

CBC Interpretation Cases

Case Study 4

A 55 years old gentlemen complain of CKD came for follow up

Creatinine: 188 (53-106 µmol/L)
Urea : 7 (2.5 to 7.1 mmol/L)
eGFR: 34 mL/min/1.73 m2

What is the Dx:

- Normocytic Normochromic Anemia most likely secondary to CKD.
- When urea/creatinine ratio is 2/1 that indicate pre-renal azotemia. The most common cause of dehydration in children is gastroenteritis.

What is the stage of CKD?

- G3b

Test	Results	Normal range
WBC	8.9	4 – 11 x10.e9/L
RBC	5.1	4.7 – 6.1 x10.e12/L
HGB	**111 (Low)**	130 – 180 g/L
HCT	**41(Low)**	42 – 52 %
MCV	88	80 – 94 fl
MCH	30	27 – 32 pg
MCHC	352	320 – 360 g/L
RDW	14	11.5 – 14.5 %
PLT	199	140 – 450 x10.e9/L

Case Study 5

A 41 years old alcoholism complain of fatigue

Diagnosis: Macrocytic Hyperchromic Anemia
What lab you will order for this patient?

- Vit b12
- Folate

Test	Results	Normal range
WBC	9.6	4 – 11 x10.e9/L
RBC	5.5	4.7 – 6.1 x10.e12/L
HGB	**121 (Low)**	130 – 180 g/L
HCT	**41 (Low)**	42 – 52 %
MCV	**99 (High)**	80 – 94 fl
MCH	**38 (High)**	27 – 32 pg
MCHC	362	320 – 360 g/L
RDW	13	11.5 – 14.5 %
PLT	320	140 – 450 x10.e9/L

Case Study 6

14 years old c.o generalized weakness and yellowish discoloration of skin for 2 days

LFT:

- Total bilirubin: 48 H (3- 17 umol/L)
- Direct bilirubin: 4 (0 – 5 umol/L)
- Total protein: 73 (60-80 g/L)
- Albumin: 38 (35-50 g/L)
- Alkaline phosphatase: 55 (50-136u/L)
- Alanine aminotransferase: 40 (20-65 u/L)
- Aspartate aminotransferase: 22 (10-31 u/L)
- G.G. Transferase: 40 (5-55 u/L)

What you will order to confirm hemolysis?

- Reticulocyte (>4%) is the most important (it will be high).
- LDH will be high, Haptoglobin will be low and Hemoglobinuria (if intravascular hemolysis)

What are the +ve acute phase reactant?

- CRP, ESR, albumin, ferritin, WBC, platelets.

What's the difference between ESR and CRP?

- Peak: CRP peaks faster and ESR is later.
- Duration: ESR lasts longer and CRP is shorter.

Test	Results	Normal range
WBC	9.2	4 – 11 x10.e9/L
RBC	5.5	4.7 – 6.1 x10.e12/L
HGB	**9.5 (Low)**	130 – 180 g/L
HCT	**41 (Low)**	42 – 52 %
MCV	81	80 – 94 fl
MCH	28	27 – 32 pg
MCHC	322	320 – 360 g/L
RDW	14.4	11.5 – 14.5 %
PLT	188	140 – 450 x10.e9/L

Case Study 7

A 51-year-old man presents with 2 month H/O of headache

Diagnosis:

- Polycythemia.

Test	Results	Normal range
WBC	**20.8 (High)**	4 – 11 x10.e9/L
RBC	**8.33 (High)**	4.7 – 6.1 x10.e12/L
HGB	**201 (High)**	130 – 180 g/L
HCT	**62.6 (High)**	42 – 52 %
MCV	82	80 – 94 fl
MCH	28.9	27 – 32 pg
MCHC	329	320 – 360 g/L
RDW	14	11.5 – 14.5 %
PLT	300	140 – 450 x10.e9/L

Case Study 8

32 years old gentleman came for regular check up

Diagnosis:

- Thrombocytopenia.

Test	Results	Normal range
WBC	10.9	4 – 11 x10.e9/L
RBC	6	4.7 – 6.1 x10.e12/L
HGB	14.6	130 – 180 g/L
HCT	51	42 – 52 %
MCV	81	80 – 94 fl
MCH	30	27 – 32 pg
MCHC	340	320 – 360 g/L
RDW	12.8	11.5 – 14.5 %
PLT	**86 (Low)**	140 – 450 x10.e9/L

Case Study 9

A 48 years old lady c.o leg redness and hotness (cellulitis)

Diagnosis:

- Thrombocytosis (Most likely reactive)

Test	Results	Normal range
WBC	10.2	4 – 11 x10.e9/L
RBC	5.7	4.7 – 6.1 x10.e12/L
HGB	15.6	130 – 180 g/L
HCT	50	42 – 52 %
MCV	91	80 – 94 fl
MCH	30	27 – 32 pg
MCHC	360	320 – 360 g/L
RDW	12.6	11.5 – 14.5 %
PLT	**665 (High)**	140 – 450 x10.e9/L

CBC Interpretation Cases

Case Study 10

A 28 y old gentleman k/c of AML on chemotherapy c.o Fever

Diagnosis:

- Febrile Neutropenia
- Top emergency

Test Name	Result	Units	Flag	Reference Range
CBC W/ 5 PART DIFF. (X6)				Run by:
WBC	2.2	K/uL		4.0 - 11.2
RBC	4.35	M/uL		4.00 - 5.60
HGB	14.5	gm/dL		12.0 - 16.0
HCT	41.7	%VOL		35.0 - 50.0
MCV	96	fl		82 - 98
PLATELETS	210	K/uL		140 - 440
MCH	33.3	pg		26.0 - 36.0
MCHC	34.7	g/dL		27.0 - 36.0
RDW	12.0	%		9.0 - 18.0
MPV	7.4	fl		6.0 - 12.0
NEU%	42.3	%		45.0 - 65.0
LYMPH%	38.6	%		20.0 - 50.0
MONO%	14.3	%		0.0 - 11.0
EOS%	3.9	%		0.0 - 7.0
BASO%	0.9	%		0.0 - 3.0
NEUT#	0.91	K/uL		2.00 - 8.00
LYMPH#	0.83	K/uL		1.80 - 4.80
MONO#	0.31	K/uL		0.10 - 1.10
EOS#	0.08	K/dl		0.00 - 0.80
BASO#	0.02	K/dl		0.00 - 0.30

Neutrophil percentage ✗

Absolute neutrophil count ✓

When interpreting neutrophil data don't use neutrophil percentage, use the absolute neutrophil count

Case Study 11

19 years old lady c.o weakness.

Diagnosis:

- Pancytopenia (needs a careful management)

Test	Results	Normal range
WBC	**3.1 (Low)**	4 – 11 x10.e9/L
RBC	5.7	4.7 – 6.1 x10.e12/L
HGB	**105 (Low)**	130 – 180 g/L
HCT	**40 (Low)**	42 – 52 %
MCV	**90 (Low)**	80 – 94 fl
MCH	31	27 – 32 pg
MCHC	362	320 – 360 g/L
RDW	13.3	11.5 – 14.5 %
PLT	**117 (Low)**	140 – 450 x10.e9/L

CBC (quick review)

- Safe CBC interpretation
- How to Approach to Anemia
- What is the Hb level indicating blood transfusion?
- How to distinguish IDA from Thalassemia?
- What is DDX of normocytic and macrocytic anemia?
- What finding suggest hemolytic anemia and what laboratory orders can confirm it?
- How to distinguish primary Vs secondary polycythemia
- At what level spontaneous bleeding risk is very high in thrombocytopenic patient?
- What are the main two types Thrombocytosis?
- What medical emergency can occur in Neutropenic patient?.
- What is the main three DDx of Pancytopenia?

Urine Data Interpretation

Kidney Function Assessment

- Assessing kidney function is differ from screening for a kidney disease.
- Measured GFR is the best overall index of kidney function in health and disease.
- eGFR (estimated GFR) may be the best available way to assess kidney function despite having some limitations.

All-cause mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR ≥300
eGFR >105	1.1	1.5	2.2	5.0
eGFR 90-105	Ref	1.4	1.5	3.1
eGFR 75-90	1.0	1.3	1.7	2.3
eGFR 60-75	1.0	1.4	1.8	2.7
eGFR 45-60	1.3	1.7	2.2	3.6
eGFR 30-45	1.9	2.3	3.3	4.9
eGFR 15-30	5.3	3.6	4.7	6.6

Realtive Risk Mortality with eGFR stage and albumin creatinine ration(ACR)

GFR stages	GFR (mL/min/1.73 m²)	
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)

eGFR staging when there is evidence of kidney pathology (lab, image or histology)

Urinary Tract Infection (UTI):

What urine analysis finding could be seen in UTI:

- Positive WBCs :a number of leukocytes (WBCs) >10/microL indicate significant **pyuria.**
- Positive Nitrite.
- Positive leukocyte esterase.
- Positive RBCs (Sometimes).

Note: Presence of WBCs Cast indicate upper urinary tract infection (pyelonephritis).

Urine culture:

- If > 100.000 (CFU)/mL indicate a positive urine culture

Urine Analysis Clinical Tips

Microscopic Hematuria	• Microscopic hematuria (which is defined as **3 RBCs or more** per high power field)
RBC Casts	• Red blood cell (RBC) casts is suggestive of glomerular hematuria and an **underlying glomerulonephritis**
Microalbuminuria	• Protein in urine analysis can not detect microalbuminuria (early sign of kidney damage in some diseases like diabetic nephropathy). • To detect microalbuminuria we need to order urine **Albumin/creatinine ratio** (A/C ratio).
Nephrotic Pattern Proteinuria	• Nephrotic pattern is characterized by **proteinuria that is usually above 3.5 g/day** usually **by 24h urine collection.**

Urine Data Interpretation Cases

Case Study 1

A 42 year old lady presented with 2 days H/O lower abdominal pain and vomiting

Diagnosis:

- Lower Urinary tract infection.

Test	Results	Test	Results
NITRITE	**POSITIVE**	HEMOGLOBIN	3+
leukocyte esterase	negative	WBC	442
PH	8.3	RBCs	830
PROTEIN	1+	CAST	NIL
GLUCOSE	NIL	CRYSTAL	NIL
KETONE	TRACE	OTHERS	**BACTERIA ++**
BLOOD	3+	SPECIFIC-GRAVITY	1.025

Case Study 2

29 years old male c.o **fever**, chills, Rt **flank pain** and dysuria

Diagnosis:

- Acute pyelonephritis (upper urinary tract infection)
- The patient needs admission and IV Antibiotic.

Test	Results	Test	Results
NITRITE	negative	HEMOGLOBIN	3+
leukocyte esterase	**Positive**	WBC	512
PH	8.1	RBCs	671
PROTEIN	1+	RBC CAST	NIL
GLUCOSE	NIL	WBC CAST	**Positive**
KETONE	TRACE	OTHERS	**BACTERIA ++**
BLOOD	3+	SPECIFIC-GRAVITY	1.025

Case Study 3

45 years old gentleman c.o facial swelling in the morning and lower limb swelling ,The following urine analysis is shown below

Diagnosis:

- Heavy Proteinuria most likely nephrotic syndrome

Confirm:

- To Confirm it we need 24 urine collection If > 3.5 g/day.

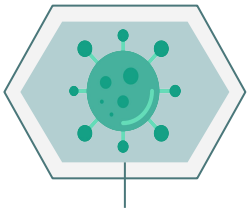
Test	Results	Test	Results
NITRITE	negative	CASTS	NIL
PH	5.8	ANTIBACTERIAL ACTIVITY	NIL
PROTEIN	**4+**	HEMOGLOBIN	NIL
WBC	10 / CMM	CULTURE	NO GROWTH
RBC	10 / CMM		

Urine (quick review)

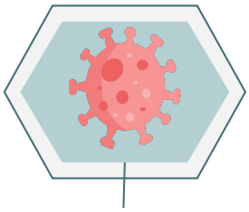
- How to assess kidney function?
- What are the urine analysis findings in UTI?
- What is the urine analysis finding indicating Pyelonephritis?
- What is the lowest abnormal value for RBC in microscopic urine analysis?
- At what level of protein nephrotic range start to be diagnosed?

Hepatitis B

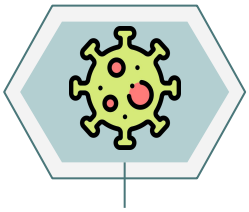
Three Major Structural Antigens



Surface (HBsAg)



Core (HBcAg)[1]



e antigen (HBeAg)

Transmission

Spread via:

- Infected blood
- Sexual intercourse
  - Can someone with hepatitis get married? Yes, by vaccinating the uninfected person and explaining all the risks and how to protect him/herself and check the antibody titers annually.
- From mother → newborn
  - If a known case of hepatitis gave birth to a child what to do in this case?
    - Give both vaccine and immunoglobulin within 24 h from delivery to the newborn.
- Human bites

Hepatitis B Characteristics

- **Incubation:**
  - 6– 23 weeks (average 17 weeks).
- **Presentation:**
  - Asymptomatic or fever, malaise, fatigue, arthralgia, urticaria, pale stools, dark urine, and/ or jaundice.
- **Prognosis:**
  - 10% become carriers/ have chronic hepatitis which may cause cirrhosis / liver cancer.
  - >85% recover fully.
  - <1% develop acute liver failure .

Investigations

- **LFTs:**
  - Hepatic jaundice
  - ↑ bilirubin
  - ↑ ALT/ AST
  - ↑ alkaline phosphatase
- **Serology:**
  - **HBsAg** Present from 1– 6mo after exposure. **Carrier if present >6mo**
  - **HBeAg** Present from 6wk– 3mo after acute illness. **Indicates high infectivity**
  - **Anti- HBs Antibodies** appear >10mo after infection; **imply immunity**

1- Antibody against the virus is divided into: IgM (acute) and IgG (chronic).

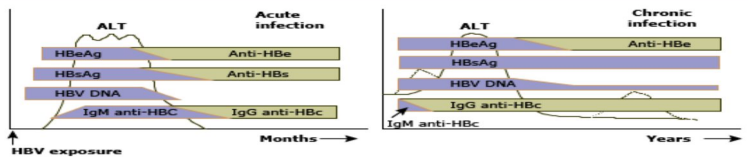
Hepatitis B High Risk Groups

Box 21.1 High-risk groups for hepatitis B and C infection

- Multiple sexual partners
- Men having sex with men (MSM)
- HIV +ve
- Intravenous drug users
- Prison inmates/workers
- Sex workers
- Healthcare workers
- Family contacts of a case/carrier
- Babies of hepatitis B/C +ve mothers
- Travellers to ↑ risk countries
- Adopted child from outside the UK
- Foster parents
- Blood transfusion before 1990
- People receiving regular blood products and their carers
- Patients on haemodialysis
- Staff/residents of residential homes for people with intellectual disability

Serologic Response To hepatitis B Viral Infection:

Serologic responses to hepatitis B virus infection



Schematic representation of the serologic responses to acute and chronic HBV infection in relation to the serum ALT concentration.
(Left panel) Acute infection is characterized initially by the presence of HBeAg, HBsAg, and HBV DNA beginning in the preclinical phase. IgM anti-HBc appears early in the clinical phase; the combination of this antibody and HBsAg makes the diagnosis of acute infection. Recovery is accompanied by normalization of the serum ALT, disappearance of HBV DNA, HBeAg to anti-HBe seroconversion, and subsequently HBsAg to anti-HBs seroconversion and switch from IgM to IgG anti-HBc. Thus, previous HBV infection is characterized by anti-HBs and IgG anti-HBc.
(Right panel) Chronic infection is characterized by persistence of HBeAg (for a variable period), HBsAg, and HBV DNA in the circulation; anti-HBs is not seen (in approximately 20% of patients, a non-neutralizing form of anti-HBs can be detected). Persistence of HBsAg for more than 6 months after acute infection is considered indicative of chronic infection.

HBV: hepatitis B virus; ALT: alanine aminotransferase; HBeAg: hepatitis B e-antigen; anti-HBe: antibody to hepatitis B e-antigen; HBsAg: hepatitis B surface antigen; anti-HBs: antibody to hepatitis B surface antigen; IgM: immunoglobulin M; anti-HBc: antibody to hepatitis B core antigen; IgG: immunoglobulin G.

UpToDate

Interpretation of the hepatitis B serologic panel

Tests	Results	Interpretation
HBsAg	Negative	Susceptible
anti-HBc	Negative	
anti-HBs	Negative	
HBsAg	Negative	Immune due to natural infection
anti-HBc	Positive	
anti-HBs	Positive	
HBsAg	Negative	Immune due to hepatitis B vaccination*
anti-HBc	Negative	
anti-HBs	Positive	
HBsAg	Positive	Acutely infected
anti-HBc	Positive	
IgM anti-HBc	Positive	
anti-HBs	Negative	
HBsAg	Positive	Chronically infected
anti-HBc	Positive	
IgM anti-HBc	Negative	
anti-HBs	Negative	
HBsAg	Negative	Four interpretations possible¶
anti-HBc	Positive	
anti-HBs	Negative	

HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody; IgM: immunoglobulin M; HBV: hepatitis B virus.
* Antibody response (anti-HBs) can be measured quantitatively or qualitatively. A protective antibody response is reported quantitatively as 10 or more milliinternational units (≥10 milliint. unit/mL) or qualitatively as positive. Postvaccination testing should be completed one to two months after the third vaccine dose for results to be meaningful.
¶ Four interpretations:
1. Might be recovering from acute HBV infection.
2. Might be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum.
3. Might be susceptible with a false positive anti-HBc.
4. Might be undetectable level of HBsAg present in the serum, and the person is actually chronically infected.

Centers for Disease Control and Prevention, Hepatitis B information for health professionals: Interpretation of hepatitis B serologic test results. Available from the CDC website. UpToDate

Hepatitis B Cases

Case Study 1

A patient that you follow has recently started volunteering at a drug treatment hospital and requires hepatitis B vaccination. You find that he is hepatitis B surface antibody positive. Which of the following would be the best guideline to follow in this case?

A. No vaccination is necessary based on his laboratory evaluation
B. Administer one dose of hepatitis B vaccine.
C. Administer two doses of hepatitis B vaccine, at least 1 month apart.
D. Administer two doses of hepatitis B vaccine, at least 6 months apart.
E. Administer three doses of hepatitis B vaccine at the appropriate time interval.

A

Case Study 2

You check serologies on a patient exposed to hepatitis B. His serologies are shown below:

Markers	Results
HBsAg	Negative
HBeAg	Negative
IgM anti-HBc	Negative
IgG anti-HBc	Negative
Anti-HBs	Positive
Anti-HBe	Negative

Which of the following terms best describes his disease status?

A. Acute infection, early phase
B. Acute infection, window phase
C. Acute infection, recovery phase
D. Previous exposure with immunity
E. Vaccination

E

Case Study 3

A 28 year old man, referred from Blood Bank because of being HBsAg positive. The following HB markers are shown

Markers	Results
HBsAg	Reactive
HBeAg	Nonreactive
IgG anti-HBc	Reactive
Anti-HBs	Nonreactive
Anti-HBe	Reactive

Disease status?

- Chronic infection

What is your next step?

- LFT, U/S liver, PCR (to check and monitor for the viral load)
  - Hepatitis B DNA Qualitative ➡ Positive
  - Hepatitis B DNA Quantitative ➡ 889796 IU/ML

How are you going to deal with any patient in general?

- Measures for the patient:
  - Request LFT, U/S liver, PCR Referral to hepatologist, No blood donation.
- Measures for Family Contacts:
  - Screen and Vaccinate the negative ones.
- Chronic HBV no cure only referral and viral load monitoring.

Case Study 4

A 35 year old man came to the clinic for screening, as one member in his family is HBV positive.

Markers	Results
HBsAg	Nonreactive
HBeAg	Nonreactive
IgG anti-HBc	Reactive
Anti-HBs	Reactive
Anti-HBe	Nonreactive

- **What is your diagnosis?**
  - Immune post exposure to HB virus
- **How are you going to deal with patient?**
  - Reassurance, No further actions could be taken

Thyroid Problems

1 Hyperthyroidism

- Affects 2% of females and 0.2% males.
- Peak age: 20– 49y

Causes:

- Graves' disease, Toxic nodular goiter older females with past history of goiter, Thyroiditis, Amiodarone[1], Kelp ingestion[2].

Presentation:

- Weight loss, Tremor, Palpitations, Hyperactivity, AF, Hyperhidrosis, Eye changes, Infertility, Alopecia
- In elderly patients, symptoms of hypo/hyper may be less obvious and include confusion, dementia, apathy, and depression. In ealderly the presentation is vaug these symptoms are actually more with hypo especially dementia as its a normal physiological changes in ealderly to decrease in thyroid function. Confusion is more with hyper.

2 Hypothyroidism

- Common: 10% females >60y
- Female: Male 88:1

Causes:

- Chronic autoimmune thyroiditis (Hashimoto), Post 131I or Thyroidectomy

Presentation:

- Onset tends to be insidious and may go undiagnosed for years.
- Always consider hypothyroidism when a patient has non- specific symptoms, depression, fatigue, lethargy, or general malaise.
- Other symptoms: ↑ weight, constipation, hoarse voice, or dry skin/ hair.
- Signs are often absent, there may be a goiter, slow- relaxing reflexes, or non- pitting edema of the hands, feet, or eyelids.

Screening thyroid functions in patients with :

- Persistent symptoms of tiredness/ lethargy without clear cause
- On amiodarone or with a history of 131I administration
- With hypercholesterolaemia, infertility, Turner's syndrome, depression, dementia, obesity, T1DM, celiac or other autoimmune disease

3 Subclinical Hypothyroidism

Indication of treatment:

- Clinical symptoms, Presence of goiter, TSH > 10 miu/l, High positive antithyroid antibodies.

If TSH < 10 and asymptomatic:

- Repeat TSH after 3 – 6 months.
- Request thyroid antibodies, if high +ve then treat.

Interpretation of thyroid function results[3]

Table 11.6 Interpretation of thyroid function test results

Results of TFTs	Interpretation	Notes
TSH ↓, T_4 ↑	Hyperthyroid (thyrotoxic)	Occasionally T_4 is normal but T_3 ↑; request T_3 levels if low TSH and normal T_4
TSH ↑, T_4 ↓	Hypothyroid	TSH ↓ if hypothyroidism is secondary to pituitary failure (rare)
TSH ↑, T_4 normal	Subclinical hypothyroidism	If any symptoms (including depression and non-specific symptoms or hypercholesterolaemia) consider a trial of treatment. If no symptoms, repeat after 3–6mo and then monitor annually

1- Amiodarone causes both hypo and hyperthyroidism, it causes disruption of the thyroid gland and depending on the body reaction it causes either of them.
2- Rich in iodine.
3- If both are low TSH and T4 its secondary hypothyroidism due to the pituitary.

Thyroid Disorders Cases

Case Study 1

A 50 year- old man presents to your office with 6 month H/O of fatigue and weakness.. O/E: no objective positive findings.

Test	Results
TSH (0.25—5)	12.2
FT4 (10.3—25 .8)	11.6

What is your diagnosis?

A. Primary Hypothyroidism
B. Subclinical Hyperthyroidism
C. Subacute Thyroiditis
D. Subclinical Hypothyroidism
E. Secondary Hypothyroidism

D

Case Study 2

A 32-year-old lady, nurse, single presented with one month H/O palpitation and loss of weight. O/E: pulse 116 / min, Bp 140 / 70. Apart from fine tremors nothing was significant. The following investigations are shown:

Test	Results
WBC	8.4
ESR	4
TSH (0.25—5)	< 0.01miu/l
FT4 (10.3—25 .8)	92.6 pmol/l
Thyroid scan	Reduced iodine uptake

Mention three causes of reduced iodine uptake:

1. Subacute thyroiditis
2. Post-partum thyroiditis
3. Factitious thyroiditis

Case Study 3

A 19-year-old lady presents with 3 weeks H/O a neck swelling discovered incidentally. The swelling move with deglutition and related to left lobe of thyroid and no Lymph Node swellings. She is euthyroid. TSH and T4 are within normal.

What is the most appropriate step in management?

A. Observation
B. Referral urgent to endocrine
C. Thyroglobulin antibodies
D. Technetium thyroid scan
E. U/S thyroid[1]

(Note: U/S to see its type solid or cystic, size, one nodule or more and also to localize the nodule for biopsy)

E

Case Study 4

A 42-year-old man booked recently in the clinic. Followed in a private psychiatry clinic because of depression mainly insomnia, weakness and fatigue, on 40 mg Paroxetine. Still not improving, so another antipsychotic drug was added. The patient has good insight and very cooperative.

Mention one investigation of importance for this patient?

- TSH : 329.0 H mIU/L (0.25 – 5)
- FT4: 2.87 L pmol/L (10.3 - 25.8)
- Cholesterol: 9.86 mmol/L
- Trig.: 3.12 mmol/L

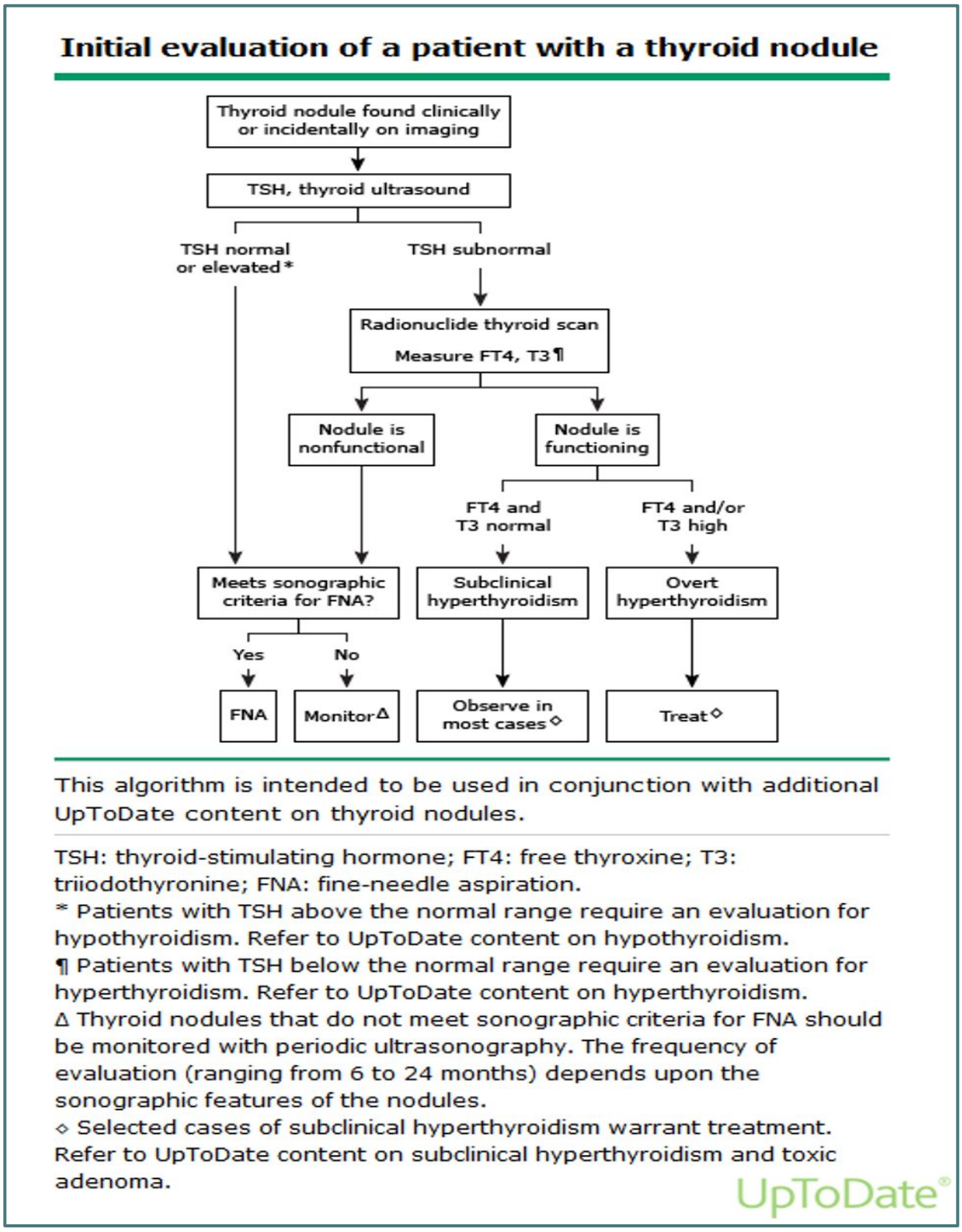
What is your diagnosis?

- Primary hypothyroidism
- Secondary hypercholesterolaemia

- It's mandatory to check thyroid function before starting lipid treatment.
- If a patient has subclinical hypothyroidism and hypercholesterolaemia which one you treat first?
  - Treat subclinical hypothyroidism before starting lipid treatment.

Thyroid Disorders

Initial Evaluation Of A Patient With A Thyroid Nodule.



- **For MCQ, always start TSH if there is a thyroid mass or nodule, but in practise we do both TSH and U/S together.**
- **Do thyroid scan when hyperthyroidism (↑ T4) to differentiate the cause.**

Thyroid Disorders Cases

Case Study 5

A 30-year-old lady with menstrual irregularities. desiring pregnancy

Initially	
Test	Results
TSH (0.25—5)	44.58 miu/l
FT4 (10.3—25 .8)	5.58 pmol/l

→

3 months later: (after 100 micgm thyroxin)	
Test	Results
TSH (0.25—5)	7.37 miu/l
FT4 (10.3—25 .8)	10.68 pmol/l

→

3 months later: (after 125 micgm thyroxin)	
Test	Results
TSH (0.25—5)	2.3 miu/l
FT4 (10.3—25 .8)	12.58 pmol/l

- Diagnosis: Primary hypothyroidism
- Treatment: thyroxine
- If the case was subclinical hypothyroidism, do we treat the patient? Yes with thyroxine as the patient is desiring pregnancy, also to increase the chance for pregnancy as TSH needs to be below 2.5

Case Study 6

A 27-year-old woman presents with one month H/O weight loss, sweating and tremors. She has diffuse neck swelling. Pulse: 124 bpm

What are the differential diagnosis?

1. Graves' disease
2. Subacute thyroiditis
3. Multinodular toxic goiter
4. Toxic nodule /adenoma

Mention one appropriate investigation to reach the diagnosis:

- Thyroid Scan (To identify the cause)

Test	Results
CBC	Normal
ESR	12 mm/h
TSH (0.25—5)	< 0.001miu/l
FT4 (10.3—25 .8)	139.2 pmol/l (sky high)

Case Study 7

A 28 year old woman presents to your office with 10 days H/O palpitation, sweating and neck discomfort. O/E: Wet hands and neck tenderness. Pulse: 116/m, temp. 37.7

1- What is the most likely diagnosis?

A. Graves' disease B. Subacute thyroiditis (Painful)
C. Hashimoto's thyroiditis D. Multinodular toxic goiter

2- Select one investigation to confirm your diagnosis:

A. Ultrasound neck B. Thyroid antibodies
C. Free T3 level D. Radioactive Iodine thyroid uptake
E. Fine needle aspiration

3- What is the treatment? Choose one or more.

A. L- Thyroxin B. Blockers (Relieve the symptoms)
C. NSAID (For the pain) D. Iodine therapy
E. Carbimazole

1: B, 2:D, 3: B+C

Test	Results
CBC	Normal
ESR	82 mm/h
TSH (0.25—5)	< 0.01miu/l
FT4 (10.3—25 .8)	89.2 pmol/l

Hypocalcaemia & Hypercalcemia

Hypocalcaemia

Hyper- and hypocalcaemia
If there is abnormality in calcium the first thing to check is **albumin**

⚠ **Checking Ca^{2+}** Take an *uncuffed* sample (to avoid falsely high readings) and correct for serum albumin—for every mmol/L less than 40, a correction of 0.02mmol/L should be added. For example:

Calcium 2.40	Corrected calcium	= (40 − 24) × 0.02 + 2.4
Albumin 24		= 0.32 + 2.4 = 2.72

- **↓ Serum calcium (<2.15mmol/ L).**
- **Presentation:**
  - Tetany
  - Irritability
  - Depression or psychosis
  - Perioral paraesthesia
  - Carpo- pedal spasm (wrist flexion and fingers drawn together)
  - Neuromuscular excitability: tapping over parotid causes facial muscles to contract (Chvostek's sign)
- **Apparent hypocalcaemia may be an artefact of hypoalbuminaemia.**
- **Management**
  - Check vitamin D levels. Supplement with calcium. Referral may be needed to investigate/ treat the underlying cause.

Causes of Hypocalcemia

High Phosphate

- CKD
- Hypoparathyroidism (may be congenital or 2° to thyroid or parathyroid surgery, or malignant infiltration)
- Pseudohypoparathyroidism (insensitivity to parathyroid hormone)

Normal or Low Phosphate

- Vitamin D deficiency (osteomalacia, rickets)
- Malabsorption
- Lack of calcium in diet
- Overhydration
- Pancreatitis

Hypercalcaemia

- **↑ level of serum calcium (>2.55mmol/ L) more common.**
- **Prevalence:**
  - Male: 81 in 500, Female 81:3, Rare <age 50y
- **Common causes (90%):**
  - Primary hyperparathyroidism
  - **Malignancy** (10% tumors usually myeloma, breast, lung, kidney, thyroid, prostate, ovary or colon)
- **Uncommon causes:**
  - Chronic renal failure, Familial benign hypercalcaemia, Sarcoidosis, Thyrotoxicosis, Milk alkali syndrome, Vitamin D treatment
- **Presentation:**
  - Often very non- specific. May be an incidental finding.
- **Symptoms:**
  - Bones, stones, groans, and abdominal moans

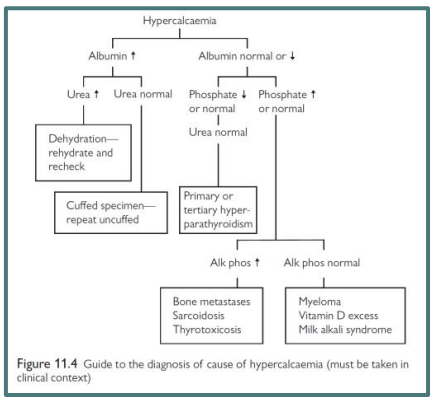
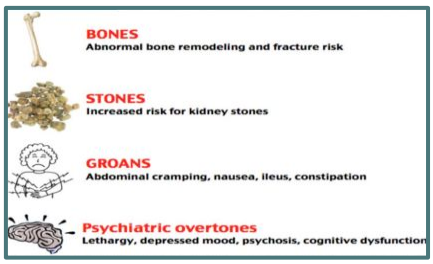


Figure 11.4 Guide to the diagnosis of cause of hypercalcaemia (must be taken in clinical context)



Hyperparathyroidism

1 Primary hyperparathyroidism

- **Incidence:**
  - 0.5/ 1000.
  - Peak age 40– 60y
  - Female :male 82:1
- Circulating level of PTH is inappropriately high
- Most patients are hypercalcaemic (but may be normocalcaemic if coexistent vitamin D deficiency). Due to ↑ secretion of PTH from one or both parathyroid glands.
- Sometimes lung cancer can secrete PTH, so in exam you might get a case where the patient is having high PTH + B symptoms of lung cancer.
- **Management:**
  - Treatment is usually surgical.
  - Drug treatment (e.g. with cinacalcet) may be an option if unsuitable for surgery.

2 Secondary hyperparathyroidism

- ↑ PTH in response to chronic hypocalcaemia or hyperphosphataemia.
- Management: Treat the underlying cause.

3 Tertiary hyperparathyroidism

- Inappropriately ↑ PTH ⟶ ↑Ca2+
- Follows prolonged secondary hyperparathyroidism.
- Most common in patients with chronic kidney disease **(especially if on dialysis)** or chronic malabsorption.
- **Management:**
  - Treatment may be either surgical or medical (e.g. with cinacalcet or paricalcitol)

Others:

Rickets / Osteomalacia	Hypoparathyroidism
Low calcium	**Low** calcium
Low or **Normal** phosphate	**High** phosphate
High alkaline phosphatase	**Normal** alkaline phosphatase

Hypocalcaemia & Hypercalcemia Cases

Case Study 1

A 70-year-old blind man known case of hypothyroidism, vitiligo and left ventricle dysfunction presents with 2m H/O SOB, bouts of dry and irritating cough, loss of appetite, hoarseness of voice and low mood.

What is your diagnosis?
- Primary hypoparathyroidism

What is the next investigation of choice?
- Parathyroid hormone: **0.353** pmol/L (1.65 – 6.9)
- Any abnormality in both Ca and Ph check PTH.

What is your management?
- Vitamin D
- Oral Calcium

What other organs or diseases you may screen for?
- Diabetes (FPG)
- Adrenal gland (Cortisol level)

Test	Results
TSH (0.25—5)	0.288 miu/L
T4 (10.3 – 25.8)	20.5 pmol/L
Ca. (2.10 – 2.55)	**1.4 mmol/L**
Ph. (0.74 – 1.30)	**1.67 mmol/L**
Alb. (30 – 50)	35 gm/L
Alk. Ph. (50 – 136)	86 u/l

Case Study 2

A 52- year- old woman presents to your office with 6 month H/O polyuria and lethargy. O/E: looks dehydrated and has a neck swelling (she has the swelling for years and informed to be a simple goitre)

What is your diagnosis?
- Hyperparathyroidism due to parathyroid adenoma

Which investigation of choice are you going to request?
- Nuclear scan for parathyroid glands
- Parathyroid hormone
- Unilateral selling is usually adenoma

Test	Results
Ca. (2.10 – 2.6)	3.4 mmol/L
Ph. (0.8 - 1.4)	0.62 mmol/L
Urea (2.6 - 6.6)	9.2 mmol/L
Chloride (95 - 105)	113 mmol/L

Case Study 3

A 48 year old woman presents with 5 month. H/O difficulty in raising from sitting position. The following investigation is shown below:

What is your diagnosis?
- Hypoparathyroidism

Which investigation of choice are you going to request?
- Nuclear scan for parathyroid glands
- Parathyroid hormone

Test	Results
Ca. (2.1 – 2.6)	1.65 mmol/L
Ph. (0.8 – 1.4)	1.52 mmol/L
Alb. (35 – 50)	38
Alk. Ph. (43 – 154)	134 mmol/L

Case Study 4

A 14-year-old girl presents with 1 year H/O pain in lower limbs. O/E: unremarkable. The following results are shown:

Test	Results
Ca. (2.10 – 2.55)	1.62 mmol/L **(low)**
Corrected calcium 2.10 – 2.55	1.6 mmol/L **(low)**
Inorganic Phosphorus 0.87 – 1.45	1.13 mmol/L
Albumin (35 – 50)	39 g/L
Alkaline phosphatase 195 – 476	1191 u/L **(high)**
Vit D	4.0 nmol/L

- **X-Ray showing:** Widened growth plate with fraying, splaying And cupping of the Metaphysis Involving both distal both Femurs and proximal Tibias and fibulas suggestive of Rickets

- **What is your diagnosis and management?**
  - **Diagnosis:** Rickets Disease.
  - **Management:** Vit D + Calcium Carbonate.

Vit D	
Deficiency	<25
Insufficiency	25 – 75
Sufficient	75 – 250
Toxicity	>250

- **She was put on Vit. D3 45000 U /week and calcium carbonate 600 mg BID for 2 months.**
- **The results are shown below:**

Calcium (2.10 – 2.55)	Corrected calcium 2.10 – 2.55
2.27	2.30
Inorganic Phosphorus 0.87 – 1.45	**Albumin (35 – 50)**
2.00 (High)	39
Alkaline phosphatase (195 – 476)	
687 (High)	

Summary

CBC Interpretation

CBC Interpretation

Look at **Hb** >>**if low** >> look at other major components (**WBCs and Platelets**) to not miss bone marrow disease (Bone marrow suppression, Pancytopenia).
If there is no striking abnormality of WBC and platelet then **check MCV** to classify the anemia into **Microcytic, Normocytic or Macrocytic.**
Helpful parameters to diagnose the underlying cause of anemia:

- **Size of red blood cells** (**MCV**): (small/ normal/ big)
- Abnormal cells on microscopic examination (like blast cells in leukemia (>5%))
- Status of leukocytes and platelets (Bone marrow function)
- **Reticulocyte count** (ability of marrow to respond to anemia)>> can help in hemolytic anemia (if high) and in marrow suppression (if low).
- **Evidence of destruction(hemolysis)** >> (elevated LDH and indirect bilirubin and low haptoglobin)

Microcytic anemia (low MCV)

Most Important causes of microcytic anemia are:

- Iron deficiency anemia
- Thalassemia

Iron Deficiency anemia (IDA):

- Iron studies – Low serum iron.
- High total iron binding capacity (TIBC, transferrin concentration).
- Low % transferrin saturation.
- Low ferritin (the most sensitive test esp if < 15).

Features might help in distinguishing between IDA and Thalassemia

Feature	IDA	Thalassemia
RBC	Low, Low normal Not good production	High, High normal Trys to compensate
MCV Normal: (80-100)	Mild to moderate low (most likely above 70) ~80	Very low (< 70) ~60
RDW	Mostly High	Mostly Normal
Mentzer index: MCV/RBC	> 13	< 13

Normocytic anemia (normal MCV)

Anemia of chronic inflammation or disease like:

- Chronic kidney disease , autoimmune disorders , chronic infection , malignancy or patients with B12 deficiency & IDA

Macrocytic anemia (high MCV)

- **Megaloblastic Common:** Vitamin B12 deficiency, Folate deficiency
- **Non-Megaloblastic:** Liver disease, Myelodysplastic syndrome, Increased reticulocyte count, Alcoholism causing: BM suppression & macrocytosis independent of folate/B12 defic.or cirrhosis

Polycythemia

Polycythemia approach:

- What is the most important test to approach polycythemia? Erythropoietin
- **Low erythropoietin**
  - Most likely primary polycythemia (polycythemia vera)
  - Polycythemia vera sometimes combined with high WBC and/or platelet.
- **High erythropoietin**
  - Most likely secondary polycythemia (smoking , COPD,hypoxia ..)

Thrombocytopenia

- Thrombocytopenia (ie, platelet count <150,000/microL [150 x 109/L])
- **Severe spontaneous bleeding is most likely with platelet counts <20,000 to 30,000/microL**, especially below 10,000/microL.
- Surgical bleeding generally may be a concern with platelet counts <50,000/microL, DDx is wide and including bone marrow malignancy.

Thrombocytosis

- Patients with elevated platelet counts, the initial diagnostic question is whether their thrombocytosis is :
  - Reactive phenomenon (infection, post surgery or Trauma..)
  - Marker for the presence of a hematologic disorder (chronic myeloproliferative neoplasms..).

Neutropenia Vs leukopenia

- Leukopenia = low WBCs
- Neutropenia = low absolute neutrophils count (ANC)
- Leukopenia ≠ Neutropenia
- Febrile Neutropenia is a medical emergency
- Causes of neutropenia: Autoimmune, malignancy, chemotherapy.

Neutropenia classification is based on Absolute Neutrophil count (ANC)	
Mild	< 1.5 K/uL (1500 cells / MicroL)
Moderate	<1.0 K/uL (1000 cells / MicroL)
Sever	< 0.5 K/uL (500 cells / MicroL)

Pancytopenia

DDX: Bone marrow malignancy, Viral infection, Drug induced

Summary

Urine Data Interpretation

Kidney Function Assessment

- Assessing kidney function is differ from screening for a kidney disease.
- Measured GFR is the best overall index of kidney function in health and disease.
- eGFR (estimated GFR) may be the best available way to assess kidney function despite having some limitations.

GFR stages	GFR (mL/min/1.73 m²)	
G1	≥90	Normal or high
G2	60 to 89	Mildly decreased
G3a	45 to 59	Mildly to moderately decreased
G3b	30 to 44	Moderately to severely decreased
G4	15 to 29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)

eGFR staging when there is evidence of kidney pathology (lab, image or histology)

Urinary Tract Infection (UTI)

- **What urine analysis finding could be seen in UTI:** Positive WBCs :a number of leukocytes (WBCs) >10/microL indicate significant **pyuria,** Positive Nitrite, Positive leukocyte esterase, Positive RBCs (Sometimes).
- **Note:** Presence of WBCs Cast indicate upper urinary tract infection (pyelonephritis).
- **Urine culture:** If > 100.000 (CFU)/mL indicate a positive urine culture

Urine Analysis Clinical Tips

- Microscopic hematuria (which is defined as **3 RBCs or more** per high power field)
- Red blood cell (RBC) casts is suggestive of glomerular hematuria and an **underlying glomerulonephritis**
- Protein in urine analysis can not detect microalbuminuria (early sign of kidney damage in some diseases like diabetic nephropathy).
- To detect microalbuminuria we need to order urine **Albumin/creatinine ratio** (A/C ratio).
- **Nephrotic pattern is characterized by proteinuria that is usually above 3.5 g/day** usually **by 24h urine collection.**

Hepatitis B

Characteristics

Three Major Structural Antigens: Surface (HBsAg), Core (HBcAg), e antigen (HBeAg).
Incubation: 6– 23 weeks (average 17 weeks).
Presentation: Asymptomatic or fever, malaise, fatigue, arthralgia, urticaria, pale stools, dark urine, and/ or jaundice.
Prognosis: 10% become carriers/ have chronic hepatitis which may cause cirrhosis / liver cancer, >85% recover fully, <1% develop acute liver failure .

Box 21.1 High-risk groups for hepatitis B and C infection

- Multiple sexual partners
- Men having sex with men (MSM)
- HIV +ve
- Intravenous drug users
- Prison inmates/workers
- Sex workers
- Healthcare workers
- Family contacts of a case/carrier
- Babies of hepatitis B/C +ve mothers
- Travellers to ↑ risk countries
- Adopted child from outside the UK
- Foster parents
- Blood transfusion before 1990
- People receiving regular blood products and their carers
- Patients on haemodialysis
- Staff/residents of residential homes for people with intellectual disability

Transmission

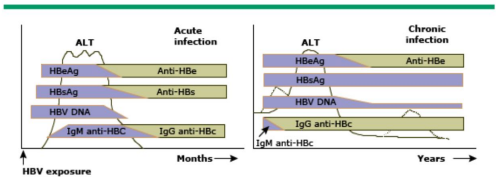
Spread via: Infected blood, Sexual intercourse, From mother ⟶ newborn, Human bites.

Investigations

LFTs: Hepatic jaundice, ↑ bilirubin, ↑ ALT/ AST, ↑ alkaline phosphatase.
Serology:

- **HBsAg** Present from 1– 6mo after exposure. **Carrier if present >6mo**
- **HBeAg** Present from 6wk– 3mo after acute illness. **Indicates high infectivity**
- **Anti- HBs Antibodies** appear >10mo after infection; **imply immunity**

Serologic responses to hepatitis B virus infection



Schematic representation of the serologic responses to acute and chronic HBV infection in relation to the serum ALT concentration.
(Left panel) Acute infection is characterized initially by the presence of HBeAg, HBsAg, and HBV DNA beginning in the preclinical phase. IgM anti-HBc appears early in the clinical phase; the combination of this antibody and HBsAg makes the diagnosis of acute infection. Recovery is accompanied by normalization of the serum ALT, disappearance of HBV DNA, HBeAg to anti-HBe seroconversion, and subsequently HBsAg to anti-HBs seroconversion and switch from IgM to IgG anti-HBc. Thus, previous HBV infection is characterized by anti-HBs and IgG anti-HBc. (Right panel) Chronic infection is characterized by persistence of HBeAg (for a variable period), HBsAg, and HBV DNA in the circulation; anti-HBs is not seen (in approximately 20% of patients, a non-neutralizing form of anti-HBs can be detected). Persistence of HBsAg for more than 6 months after acute infection is considered indicative of chronic infection.

HBV: hepatitis B virus; ALT: alanine aminotransferase; HBeAg: hepatitis B e-antigen; anti-HBe: antibody to hepatitis B e-antigen; HBsAg: hepatitis B surface antigen; anti-HBs: antibody to hepatitis B surface antigen; IgM: immunoglobulin M; anti-HBc: antibody to hepatitis B core antigen; IgG: immunoglobulin G.

UpToDate

Interpretation of the hepatitis B serologic panel

Tests	Results	Interpretation
HBsAg	Negative	Susceptible
anti-HBc	Negative	
anti-HBs	Negative	
HBsAg	Negative	Immune due to natural infection
anti-HBc	Positive	
anti-HBs	Positive	
HBsAg	Negative	Immune due to hepatitis B vaccination*
anti-HBc	Negative	
anti-HBs	Positive	
HBsAg	Positive	Acutely infected
anti-HBc	Positive	
IgM anti-HBc	Positive	
anti-HBs	Negative	
HBsAg	Positive	Chronically infected
anti-HBc	Positive	
IgM anti-HBc	Negative	
anti-HBs	Negative	
HBsAg	Negative	Four interpretations possible¶
anti-HBc	Positive	
anti-HBs	Negative	

HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody; IgM: immunoglobulin M; HBV: hepatitis B virus.
* Antibody response (anti-HBs) can be measured quantitatively or qualitatively. A protective antibody response is reported quantitatively as 10 or more milliinternational units (≥10 milliint. unit/mL) or qualitatively as positive. Postvaccination testing should be completed one to two months after the third vaccine dose for results to be meaningful.
¶ Four interpretations:
1. Might be recovering from acute HBV infection.
2. Might be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum.
3. Might be susceptible with a false positive anti-HBc.
4. Might be undetectable level of HBsAg present in the serum, and the person is actually chronically infected.

Centers for Disease Control and Prevention, Hepatitis B information for health professionals: Interpretation of hepatitis B serologic test results. Available from the CDC website. UpToDate

Summary

Thyroid Disorders

Hyperthyroidism

Affects 2% of females and 0.2% males.
Peak age: 20– 49y

Causes:

- Graves' disease, Toxic nodular goiter older females with past history of goiter, Thyroiditis, Amiodarone, Kelp ingestion.

Presentation:

- Weight loss, Tremor, Palpitations, Hyperactivity, AF, Hyperhidrosis, Eye changes, Infertility, Alopecia
- In elderly patients, symptoms of hypo/hyper may be less obvious and include confusion, dementia, apathy, and depression. In ealderly the presentation is vaug these symptoms are actually more with hypo especially dementia as its a normal physiological changes in ealderly to decrease in thyroid function. Confusion is more with hyper.

Hypothyroidism

Common: 10% females >60y ,Female: Male 88:1

Causes:

- Chronic autoimmune thyroiditis (Hashimoto), Post 131I or Thyroidectomy

Presentation:

- Onset tends to be insidious and may go undiagnosed for years.
- Always consider hypothyroidism when a patient has non- specific symptoms, depression, fatigue, lethargy, or general malaise.
- Other symptoms: ↑ weight, constipation, hoarse voice, or dry skin/ hair.
- Signs are often absent, there may be a goiter, slow- relaxing reflexes, or non- pitting edema of the hands, feet, or eyelids.

Screening thyroid functions in patients with :

- Persistent symptoms of tiredness/ lethargy without clear cause
- On amiodarone or with a history of 131I administration
- With hypercholesterolaemia, infertility, Turner's syndrome, depression, dementia, obesity, T1DM, celiac or other autoimmune disease

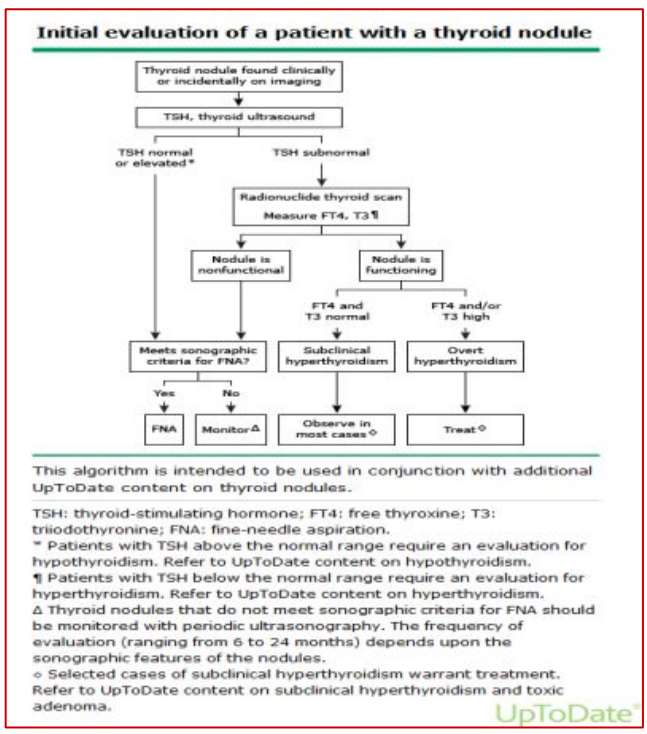
For MCQ, always start TSH if there is a thyroid mass or nodule, but in practise we do both TSH and U/S together.
Do thyroid scan when hyperthyroidism (↑ T4) to differentiate the cause.

Subclinical Hypothyroidism

Indication of treatment: Clinical symptoms, Presence of goiter, TSH > 10 miu/l, High positive antithyroid antibodies.
If TSH < 10 and asymptomatic: Repeat TSH after 3 – 6 months, Request thyroid antibodies, if high +ve then treat.

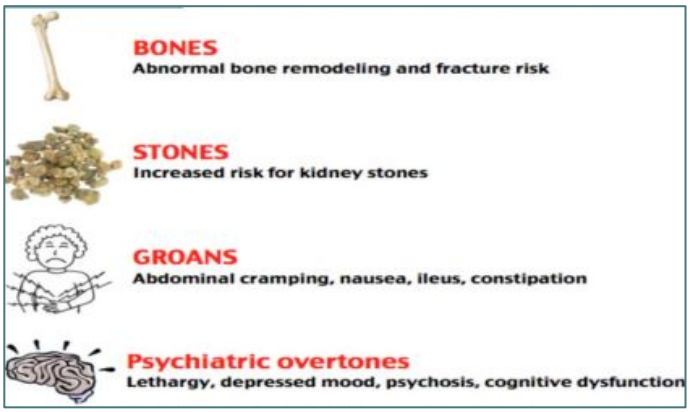
Table 11.6 Interpretation of thyroid function test results

Results of TFTs	Interpretation	Notes
TSH ↓, T_4↑	Hyperthyroid (thyrotoxic)	Occasionally T_4 is normal but T_3 ↑; request T_3 levels if low TSH and normal T_4
TSH ↑, T_4↓	Hypothyroid	TSH ↓ if hypothyroidism is secondary to pituitary failure (rare)
TSH ↑, T_4 normal	Subclinical hypothyroidism	If any symptoms (including depression and non-specific symptoms or hypercholesterolaemia) consider a trial of treatment. If no symptoms, repeat after 3–6mo and then monitor annually



Summary

Hypocalcaemia & Hypercalcemia	
Hypocalcaemia	• ↓ **Serum calcium (<2.15mmol/ L).** • **Presentation:**Tetany, Irritability, Depression or psychosis , Perioral paraesthesia, Carpo- pedal spasm (wrist flexion and fingers drawn together), Neuromuscular excitability: tapping over parotid causes facial muscles to contract (Chvostek's sign) • **Apparent hypocalcaemia may be an artefact of hypoalbuminaemia.** • **Management:** Check vitamin D levels. Supplement with calcium. Referral may be needed to investigate/ treat the underlying cause.
Hypercalcaemia	• ↑ **level of serum calcium (>2.55mmol/ L) more common.** • **Prevalence:** Male: 81 in 500, Female 81:3, Rare <age 50y • **Common causes (90%):** Primary hyperparathyroidism, **Malignancy** (10% tumors usually myeloma, breast, lung, kidney, thyroid, prostate, ovary or colon) • **Uncommon causes:** Chronic renal failure, Familial benign hypercalcaemia, Sarcoidosis, Thyrotoxicosis, Milk alkali syndrome, Vitamin D treatment • **Presentation:** Often very non- specific. May be an incidental finding. • **Symptoms:** Bones, stones, groans, and abdominal moans
Hyperparathyro -idism	**Primary hyperparathyroidism:** • **Incidence**: 0.5/ 1000, Peak age 40– 60y. Female :male 82:1. • Most patients are hypercalcaemic (but may be normocalcaemic if coexistent vitamin D deficiency). Due to ↑ secretion of PTH from one or both parathyroid glands, Sometimes lung cancer can secrete PTH, so in exam you might get a case where the patient is having high PTH + B symptoms of lung cancer. • **Management:** Treatment is usually surgical, Drug treatment (e.g. with cinacalcet) may be an option if unsuitable for surgery. **Secondary hyperparathyroidism:** ↑ PTH in response to chronic hypocalcaemia or hyperphosphataemia, management is by treating the underlying cause. **Tertiary hyperparathyroidism:** • Inappropriately ↑ PTH ⟶ ↑Ca2+, Follows prolonged secondary hyperparathyroidism. • Most common in patients with chronic kidney disease **(especially if on dialysis)** or chronic malabsorption. • **Management:** Treatment may be either surgical or medical (e.g. with cinacalcet or paricalcitol)



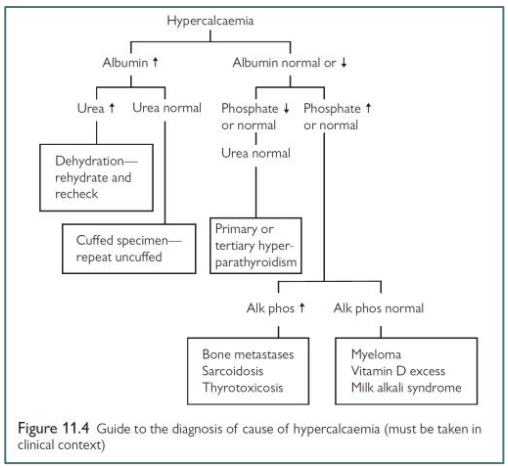


Figure 11.4 Guide to the diagnosis of cause of hypercalcaemia (must be taken in clinical context)

Rickets / Osteomalacia	Hypoparathyroidism
Low calcium	**Low** calcium
Low or **Normal** phosphate	**High** phosphate
High alkaline phosphatase	**Normal** alkaline phosphatase

Lecture Quiz

Q1: 47-year-old patient was not accepted by blood bank for donation because of low hemoglobin.the patient is asymptotic and physical exam is normal. his CBC are as follows (all normal but low RBC, HB, MCV low but not lower than 70 and low MCH). What will you do for the patient?

A. Give a course of iron and folate then repeat CBC
B. Reassurance and no need for further investigation
C. Tell the patient that he can go back to donate blood because he has nothing abnormal
D. Do further investigation to find the underlying cause

Q2: A 77-year-old woman presents with weight gain, constipation and lethargy initial tests show a hemoglobin of 114 g/L (120-160), MCV of 106 fl. (80-90) and ECG shows bradycardia. What is the most appropriate investigation of choice will help in diagnosis?

A. Echocardiogram
B. Serum iron
C. Thyroid stimulating hormone
D. Vitamin D level

Q3: A 46-year-old man is a known case of IBS for several years. He is controlling his symptoms by dietary advice. He is referred from blood bank, because of low hemoglobin and his blood donation was refused. He looked healthy but lost 2 Kgs over the last 2 months. His CBC result is shown:

RBC ..... 3.88 L 4.2 – 5.5 x10.e12/L
HGB .....110 L 120 – 160 g/L
MCV .....73.6 L 80 – 94 fl
MCH .....23.6 L 27 – 32 pg
RDW .....5.7 H 11.5 – 14.5 %
What is the most appropriate step in the management?

A. Refer him for endoscopy
B. Request for serum iron level
C. Request for serum B12 level
D. Start iron supplements and repeat CBC after 2 months

Q4: Sarah, a 32 year old woman, has come in for her anxiety. Sarah says that she is experiencing: excess sweating, can feel her heart beat faster than usual, and is also having diarrhea. It should be noted that Sarah appears to have puffy eyes, high blood pressure, and enlarged thyroid. and Thyroid scan showed High uptake what is the most likely diagnosis?

A. Gravis
B.Hashimoto thyroiditis
C.subacute thyroiditis
D.factitious

Answers: Q1:D | Q2:C | Q3:A | Q4:A

THANKS!!

The lecture is done by:

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Send us your feedback:
We are all ears!