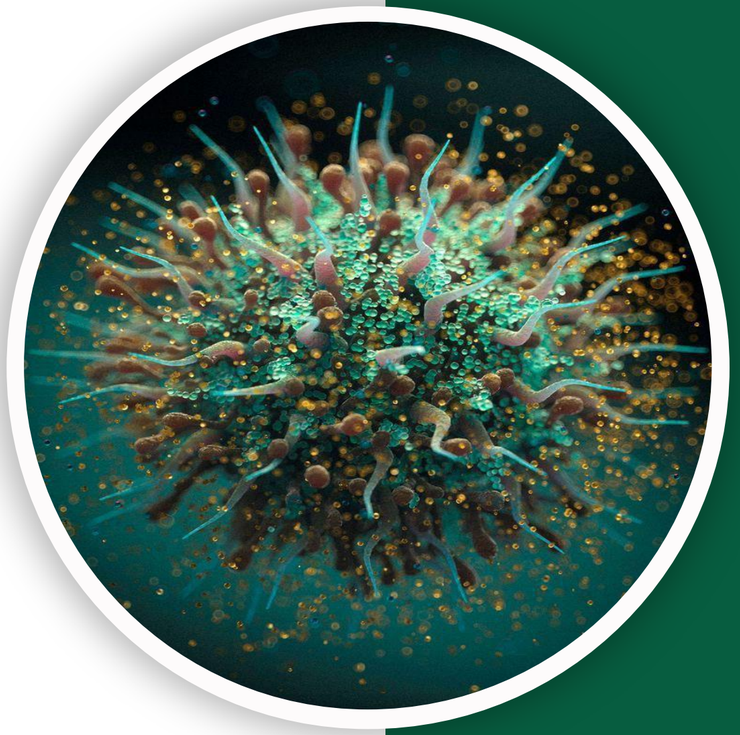
بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

HLS Pathology | FINAL 2

Anemia



Written by : DST

Reviewed by : Sara Qatatshah
NST member

PATHOLOGY OF BLOOD AND LYMPHATIC SYSTEM

Dr. Tariq Al-Adaily, MD
Associate Professor
Department of Pathology
The University of Jordan
Email: TNALADILY@ju.edu.jo

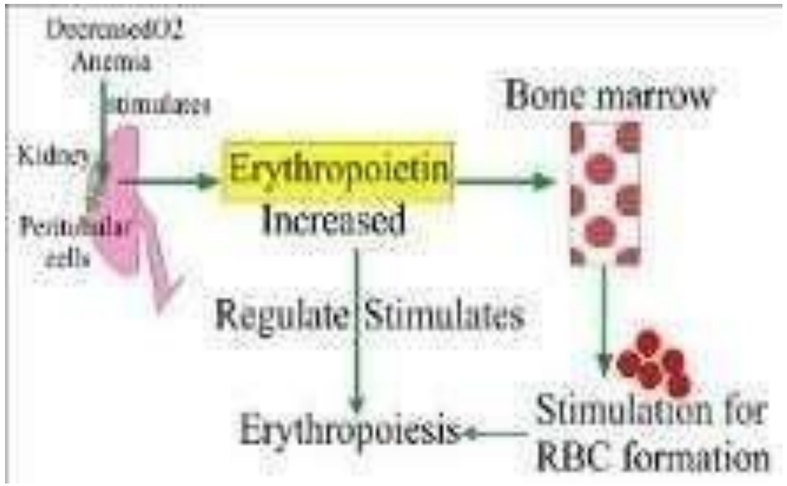
School of Medicine

ANEMIA

DEFINITION

- Definition of anemia is the opposite of polycythemia Anemia decrease in red blood cell mass below the normal level, which may lead to:
- Reduction of oxygen carrying capacity of blood to the systems.
- secondary to decrease in red cell mass.
- Leads to tissue hypoxia;
- Diagnosis by tests…again numeric diagnosis. (symptoms alone are insufficient).
- Practically, measure by Hemoglobin concentration (g/dL),
  and Hematocrit (Percentage of red cell to the whole blood)

ANEMIA AND ERYTHROPOIETIN



Anemia → hypoxia → sensed by kidneys→ erythropoietin → erythropoeisis

- Anemia triggers production of erythropoietin
- Causes compensatory erythroid hyperplasia in bone marrow (BM).
- In acute anemia, production can increase by 5x or more in healthy people .Healthy BM can produce x5 times the amount of RBC in normal conditions, and can effectively correct anemia.

- In severe cases (or congenital anemia); erythropoietin is high but cannot reverse the anemia, erythropoeisis takes place outside the BM causes extramedullary hematopoiesis in secondary hematopoietic organs (spleen, liver and lymph nodes) so the patient will develop large spleen and liver.
- Exceptions(erythropoietin is low, :(anemia of renal failure (kidneys don't function …they don't secrete erythropoietin) , anemia of chronic inflammation in the next lecture.

CLASSIFICATION ACCORDING TO CAUSE

1) Blood loss

2) Diminished RBC production (most common) ,decreased production from BM..BM is inactive and doesn't secrete enough amount from RBC.

- Iron deficiency anemia
- Anemia of chronicinflammation
- Megaloblastic anemia
- Aplastic anemia
- Pure red cellaplasia
- Myelophthisic anemia
- Myelodysplastic syndrome
- Anemia of renalfailure
- Anemia ofhypothyroidism

3)Increased destruction

(hemolytic anemia)

- Extrinsic factors (infection, antibody,mechanical)
- Intrinsic RBC abnormalities:

1) Hereditary (membrane, enzyme, Hgabnormalities.

1) Acquired (Paroxysmal nocturnal hematuria)

- BM produces RBCs but they are abnormal so they die early/immaturely and thus there will be shortage of RBC in circulation.
- That's mean RBC undergo premature destruction instead of complete their normal lifespan.

- In thalassemia, both reduced red cell production and increased destruction contribute to anemia.

We examine anemia according to the morphology in the blood film (remember! Diagnosed through numerical tests)

CLASSIFICATION ACCORDING TO MORPHOLOGY BLOOD FILM

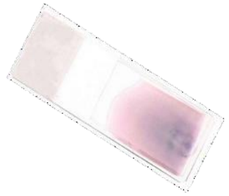
RBC is a bit smaller than lymphocyte nucleus

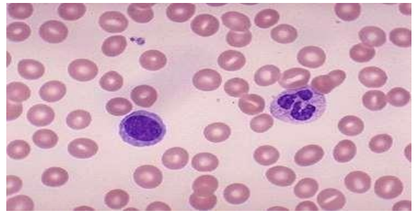
- Size of RBC: normo, micro, macrocytic (MCV)
- Color: normo, hypochromic (MCH) or hyper chromic by examining the central(thin) one third of RBC which allows light to pass through it, it will appear white.

And I can know without checking them by complete blood count that they give MCV…RBC HAVE NORMAL RANGE FROM 80 TO 100 fL… if it's less than 80 → micro …if more than 100
→macro and if it's between 80-100 → normo

- Shape: anisopoikelocytosis different shape and size(spherocytes, sickle, schistiocytes)
  (RBC distribution width)
- Hypochromic microcytic anemia usually reflects impaired Hg synthesis Hg consist of heme group(iron) and globin(protein from DNA)
- Macrocytic anemia reflects stem cell disease (in bone marrow) and maturation

It's very early disease…they can't mature enough like RBC



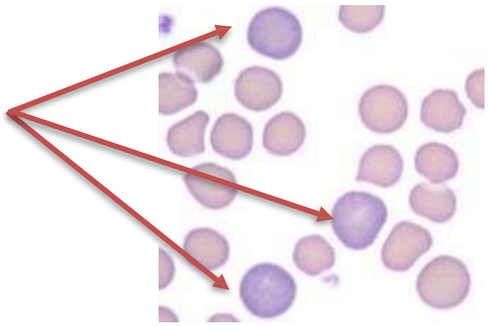


RBC INDICES

- Can be directly measured, or automated
- Slight variation is present between labs, geographic areas
- Sex, age, race, mobility status have effect
- Reticulocyte count: helps differentiate hemolytic anemia (high) from aregenerative anemia (low)

See the next slide

These are Reticulocyte they are large and blue in color because of streaks of DNA so you can count them from blood film



	Units	Men	Women
Hemoglobin (Hb)	g/dL	13.2–16.7	11.9–15.0
Hematocrit (Hct)	%	38–48	35–44
Red cell count	$\times 10^6/\mu L$	4.2–5.6	3.8–5.0
Reticulocyte count	%	0.5–1.5	0.5–1.5
Mean cell volume (MCV)	fL	81–97	81–97
Mean cell Hb (MCH)	pg	28–34	28–34
Mean cell Hb concentration (MCHC)	g/dL	33–35	33–35
Red cell distribution width (RDW)		11.5–14.8	

*Reference ranges vary among laboratories. The reference ranges for the laboratory providing the result should always be used in interpreting a laboratory test.

Reticulocyte count: helps differentiate hemolytic anemia (high) from aregenerative anemia (low)

Reticulocyte is an immature RBCs without nucleus. The differences between it and the mature RBCs; its size (is larger) and has streaks of residual DNA.

It is found in bone marrow and in peripheral blood, it's life as Reticulocyte is one day and then it will become a mature RBC.

The normal percentage of Reticulocytes is 1% if it's more this indicates that bone marrow is active and produce extra RBCs to compensate anemia (usually hemolytic anemia).

Anemia + reticulocytes → healthy (functional) BM. {RBCs are the problem/cause}
Anemia + x reticulocytes → nonfunctional BM. {BM is the problem/cause}

Additional Blood test to diagnose anemia (Not Required)

1. **Serum Iron Indices**
   - These tests help distinguish between **iron deficiency anemia, anemia of chronic inflammation, and thalassemia**, especially when the anemia is microcytic (low MCV).

A. Serum iron

- **What do we measure?**

✓ The amount of iron circulating in the blood, mostly bound to transferrin.

- **What does the result mean?**

✓ **Low:** Iron deficiency or chronic inflammation.
✓ **Normal or high:** May occur in thalassemia or other conditions, depending on the cause.

Not Required

B. Total iron-binding capacity (TIBC)

- **What do we measure?**

✓ The blood's capacity to bind iron, reflecting mainly the amount of transferrin available.

- **What does the result mean?**

✓ **High:** The body produces more transferrin to capture iron, commonly in iron deficiency.
✓ **Low:** Less transferrin is available, commonly in chronic inflammation.

C. Transferrin saturation (TSAT)

- **What do we measure?**

✓ The percentage of transferrin's iron-binding sites occupied by iron.

- **What does the result mean?**

✓ **Low:** Little iron is available for RBC production.
✓ **Normal or high:** May be seen in thalassemia or iron overload, depending on the condition.

D. Ferritin

- **What do we measure?**

✓ Ferritin reflects the body's stored iron.

- **What does the result mean?**

✓ **Low:** Strong evidence of iron deficiency.
✓ **Normal or high:** May indicate adequate iron stores, but ferritin can increase during inflammation even when iron availability is low.

Additional Blood test to diagnose anemia (Not Required)

2. **Tests for Hemolytic Anemia**
   - These tests investigate whether RBCs are being destroyed prematurely.

A. Plasma unconjugated (indirect) bilirubin

- **What do we measure?**
  - ✓ Bilirubin produced when hemoglobin heme is broken down.
- **What does the result mean?**

✓ **Increased:** More heme is being broken down, which can occur in hemolysis.
✓ May cause jaundice when sufficiently elevated.
✓ Remember: heme breakdown → unconjugated bilirubin.

Not Required

B. Haptoglobin

- **What do we measure?**

✓ The blood protein that binds free hemoglobin released into plasma.

- **What does the result mean?**

✓ **Low:** Haptoglobin is being consumed by binding free hemoglobin, supporting intravascular hemolysis.
✓ **Normal or high:** Does not completely exclude hemolysis; haptoglobin can rise during inflammation.
✓ Remember: more free hemoglobin → more haptoglobin consumption → lower haptoglobin.

C. Lactate dehydrogenase (LDH)

- **What do we measure?**

✓ The activity of an enzyme found inside many cells, including RBCs.

- **What does the result mean?**

✓ **Increased:** Can indicate cell destruction, including RBC destruction.
✓ Must be interpreted with other findings because LDH is not specific to hemolysis.
✓ **Typical hemolysis pattern:** ↑ unconjugated bilirubin + ↓ haptoglobin + ↑ LDH.
✓ These findings support hemolysis, but no single result proves it on its own.

Additional Blood test to diagnose anemia (Not Required)

3. Tests for Megaloblastic Anemia

- Megaloblastic anemia commonly results from vitamin B12 or folate deficiency, which impairs DNA synthesis in developing blood cells.

A. Serum vitamin B12

- **What do we measure?** The concentration of vitamin B12 circulating in the blood.
- ✓ **Meaning:** A low level supports B12 deficiency, which can impair DNA synthesis and cause macrocytic anemia. B12 deficiency can also cause neurological abnormalities.

B. Serum folate

Not Required

- **What do we measure?** Folate currently circulating in the blood.
- ✓ **Meaning:** A low level supports folate deficiency, which also impairs DNA synthesis.

C. Red-cell folate

- **What do we measure?** Folate contained within RBCs, reflecting folate availability during RBC formation over a longer period than serum folate generally does.
- ✓ **Meaning:** A low level supports folate deficiency. However, this test is used less routinely in some settings, and its interpretation has limitations.

❑ **Important distinction:**

- ✓ B12 deficiency → impaired DNA synthesis **and possible neurological damage**.
- ✓ Folate deficiency → impaired DNA synthesis, but does not typically cause the characteristic neurological injury of B12 deficiency.
- ✓ Both can produce macrocytosis (increased MCV).

4. Hemoglobin Electrophoresis

- **What do we measure?**
  - ✓ The types and relative proportions of hemoglobin present in the blood, separated according to their physical properties in an electric field.
- **What does the result mean?**
  - ✓ Detects abnormal hemoglobins, such as HbS in sickle cell disorders.
  - ✓ Helps identify abnormal hemoglobin proportions associated with thalassemia, such as increased HbA_2 in many cases of beta-thalassemia trait.
  - ✓ Helps distinguish hemoglobin disorders from uncomplicated iron deficiency.

Additional Blood test to diagnose anemia (Not Required)

5. Coombs Test (Antiglobulin Test)

- This test investigates whether the immune system is involved in RBC destruction.

Only the Coombs Test Required

1. **Direct Coombs test (DAT)**
   - **What do we measure?**
     - ✓ Whether antibodies and/or complement are attached to the patient's RBCs.
   - **What does the result mean?**
     - ✓ **Positive:** Supports immune involvement, such as autoimmune hemolytic anemia, in the appropriate clinical context.
     - ✓ **Negative:** Makes immune-mediated hemolysis less likely but does not exclude it completely.
     - ✓ **Indirect Coombs test**
   - **What do we measure?**
     - ✓ Antibodies in the patient's serum that can bind to RBC antigens.
   - **What does the result mean?**
     - ✓ It helps detect circulating RBC antibodies, particularly in pre-transfusion testing and pregnancy-related antibody screening.

   ❑ **Remember the difference:**
     - ✓ **Direct = antibodies/complement already attached to RBCs.**
     - ✓ **Indirect = antibodies circulating in serum that may bind to RBCs.**

6. When Is a Bone Marrow Examination Needed?

- The final part of your paragraph describes how the combination of abnormal blood-cell counts guides the investigation.
- **Why?**

✓ The bone marrow produces RBCs, platelets, and granulocytes. If anemia occurs alongside reduced platelets and/or granulocytes, the problem may affect the marrow itself rather than only RBCs.

✓ Examples include:

- **Marrow aplasia:** The marrow fails to produce sufficient blood cells.
- **Marrow infiltration:** Abnormal cells or other material occupy the marrow and interfere with normal blood-cell production.

- A bone marrow examination can help establish the diagnosis when indicated; these blood-count patterns raise suspicion but do not prove either

CLINICAL FEATURES OF ANEMIA

General symptoms for anemia:

The dizziness and headache here due to hypotension as the doctor said

- Dizziness (hypotension) In polycythemia hypertension
- Fatigue Loss of energy and tiredness as a result of hypoxia of skeletal system
- Pallor In polycythemia plethora which is the skin is red in color
  We can examine the pall skin in highly vascular areas like finger nails , oral , lips and tongue to make sure the patient is pallor
- Headache

Adaptive changes: the body tries to compensate the hypoxia

- Tachycardia Here the rate of heart beats becomes high to ensure that the oxygen will be delivered to the tissue in a short time to overcome the hypoxia
- Tachypnea Respiratory rate will rise to bring more oxygen inside the body
- Increased red cell 2,3-Bisphosphoglycerate This leads to decrease the strength of association between the oxygen and hemoglobin so it facilitates the oxygen releasing to the tissues

If the patient has heart or lung diseases, symptoms will be worse

CLINICAL SYMPTOMS IN SPECIAL TYPES OF ANEMIA

- Chronic hemolytic anemia:

The RBCs are destructed ,the concentration of hemoglobin will increase and will be metabolized into bilirubin (it's an insoluble compound elimenated through the biliary system), if the concentration of bilirubin is increased the liver can't handle it and will be deposited in the tissues.

jaundice, pigmented gall bladder stones, red urine

The sclera of the eye will be yellow cuz the deposited billirubin in the tissue

Because of the insolubility of bilirubin it will accumulate in the biliary system and cause black gallbladder stones

This red color of urine appear in sever case of hemolytic anemia when the body cannot recycle and handle with exessive amounts of hemoglobin anymore so the hemoglobin will leak through kidneys and goes out of the body in urine and this gives the red color to the urine not because the blood

CLINICAL SYMPTOMS IN SPECIAL TYPES OF ANEMIA

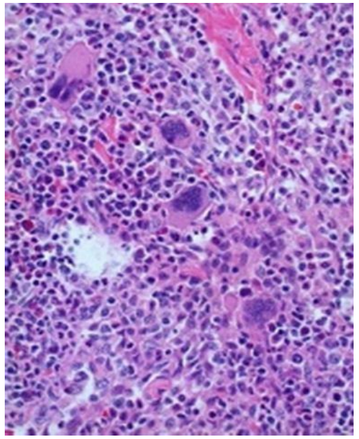
- Extramedullary hematopoiesis: splenomegaly, hepatomegaly
- Thalassemia major and sickle cell anemia : (they are Congenital - life long disease) the concentration of erythropoietin is chronically high which leads to extramedullary hematopoiesis, the patients are children because it's Congenital.

Persistent hypoxia even high erythropoietin can't reverse it, it's genetic, the body can't make Hb, it's persistent anemia.

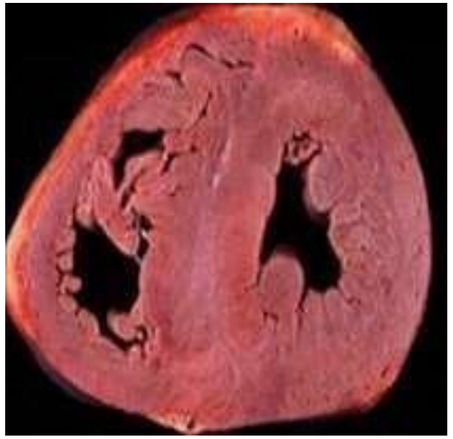
growth retardation, bone deformity especially cranial bones they are protruded and large regarding to increase erythropoietin so the bone marrow will increase.

secondary hemochromatosis as we know the
blood contains iron and it's difficult to rid from, so the only method is to shed epithelial cells, because if the iron accumulates in the tissues, it becomes toxic and causes
damage to heart (cardiomegaly as a result of hemochromatosis then heart failure and death)
endocrine glands (any gland can be destroyed by iron)

Large abdomen due to hepato/splenomegaly.
Growth retardation; they're short.
Skeletal deformities.



Bone biopsy; erythropoeitic cells.



Very thick wall

Sudden

ANEMIA OF ACUTE BLOOD LOSS

We lost hemoglobin in that sudden blood loss so make this is in your consideration

Fluids from the tissues shifted to the vascular compartment to handle with the sudden drop in the blood pressure so the hemoglobin molecules Will be diluted and this leads to worse the hypoxia and this is normally event so the hemoglobin concentration will low and this doesn't mean repeated hemorrhage this is just due to the dilution and for this this anemia called : Dilutional Anemia

Symptoms are related to decreased intravascular volume,

If loss is >20% of blood volume, patient might have hypovolemic shock especially vital organs like brain, kidney they suffer from **ischemia** and death

Body responds by shifting fluid from interstitial to intravascular space, causing dilutional anemia which cause decreasing in the concentration of hemoglobin and worse hypoxia (stays 2-3 days)

Erythropoietin secretion is stimulated, activating BM erythropoiesis (needs 5-7 days)

Iron is difficult to gain (the absorption is limited)and difficult to get rid of so if hemorrhage happened:

In internal hemorrhage, iron is restored from extravasated RBCs and used again in erythropoiesis

In external and GIT hemorrhage, iron is lost, and the patient may develop iron deficiency which complicates anemia

The anemia is normochromic normocytic, with reticulocytosis

Indication on the active bone marrow activity to restore the Normal levels of hemoglobin and RBCs count

Anemia of acute blood loss : The sudden loss of blood leads to decrease intravascular volume so this leads to sudden hypotension so we can say that

: If the blood loss more than (20%) this mean there is hypovolemic shock and this leads to necrosis of the organ then loss of the functions and finally death

If the blood loss less than (20%) this leads to the dilutional anemia as we explained above

This is anemia called : Iron deficiency anemia

ANEMIA OF CHRONIC BLOOD LOSS

Here there is always iron loss because the repetitive hemorrhage outside the body so the iron after the blood loss here will not be preserved and this leads to the iron deficiency anemia (Hypochromic microcytic anemia) will progress.

- Loss of small amount of blood but it is repeated
- Occurs when the rate of RBC loss exceeds regeneration.

Causes of hemorrhage in gastrointestinal diseases:

Peptic Ulcers, stomach and esophagus cancers, hemorrhoids,

- Mostly occurs in gastrointestinal diseases, also in excessive menstruation.
- Results in iron deficiency, anemia appears hypochromic and microcytic (depletion in iron stores → anemia starts to fully develop), low reticulocytes also due to ↓ iron stores, the BM can't produce RBCs.

Because there isn’t sufficient iron to push the chain of erythropoiesis to going on so the entire process will be impaired

Pathoma Summary of Anemia

I. BASIC PRINCIPLES

A. Reduction in circulating red blood cell (RBC) mass.

B. Presents with signs and symptoms of hypoxia.

1. Weakness, fatigue, and dyspnea
2. Pale conjunctiva and skin
3. Headache and light headedness
4. Angina, especially with preexisting coronary artery disease

C. Hemoglobin (Hb), hematocrit (Hct), and RBC count are used as surrogates for RBC mass, which is difficult to measure.

1. Anemia is defined as Hb < 13.5 g/dL in males and< 12.5 g/dL in females (normalHb is 13.5-17.5 g/dL in males and 12.5-16.0 g/dL in females).

D. Based on mean corpuscular volume (MCV), anemia can be classified as microcytic(MCV < 80 µm3), normocytic (MCV = 80-100 µm^3), or macrocytic (MCV > 100 µm^3).

Pathoma Summaries for all aneimia Types and the whole Blood System.

Pathology Quiz 2

shutterstock.com · 1751596670

رسالة من الفريق العلمي:

عندما تتمعَّن في القرآن الكريم، وأنت تمسك بيديك دفتيَ المصحف الشريف، وتتدبّرَ كلام الله تعالى، تدرك كم هي قصيرة هذه الحياة، وكم هي متعبة، وكم تشبهَ اختبارًا مفتوحًا؛ كُثبتَ فيه الأجوبة قبل الأسئلةَ، وأعطيت فيه للإنسان دلائل الإجابة، وهو تحت مراقبة الله تعالى، ويعلم الأجوبة، ومع ذلك فإنَ كثيرًا منَا لا يحسن الإجابة.

وكم أن وقت هذا الاختبار طويل في نظر الإنسان، لا يعلم مقداره إلا الله؛ وإن طال في نظرك، فهو عند الله قصير، يقول الحق سبحانه وتعالى:

كَأَنَّهُمْ يَوْمَ يَرَوْنَهَا لَمْ يَلْبَثُوٓا۟ إِلَّا عَشِيَّةً أَوْ ضُحَىٰهَا

ويقولَ سبحانه:

قَالَ كَمْ لَبِثْتُمْ فِى ٱلْأَرْضِ عَدَدَ سِنِينَ ﴿١١٢﴾ قَالُوا۟ لَبِثْنَا يَوْمًا أَوْ بَعْضَ يَوْمٍ،

واعلم أنه بقدر ما أن الله رؤوفٌ رحيمٌ بعباده، فهو كذلك دقيَق الحساب؛ فلا يظلم ربِك أحدًا، ولا يُنقص من عملك شيئًا. وعلى قدر ما قدّمت في اختبارك تكون درجتك.

فإن أجبتَ بالأجوبة التي علَّمك الله إياها، وأحسنت العملَ بما عرفت، فقد فزت بحظٍ عظيم. وإن عصيت وتمردت على أوامر الله، فحينها لا ينفع الندم، ولا تكون هناك عودة إلى الوراء، ولا فرصة لإعادة الاختبار؛ فقد انتهى زمن العمل، وقام الناس لرب العالمين.

فطوبى لمن أدرك أن هذه الدنيا اختبارٌ طويل في نظره، وأن الأجوبة قد كُتبت أمامه، وأن السؤال آتٍ لا محالة، وأن خيَر ما يفعله المرء أن يُحسن كتابةَ إجابته قبل أن تطوى صحيفته.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			