

GNT OSPE

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1- Malabsorption Analysis of Serum Amylase

Questions and Answers

Q1

What is amylase, and what are its sources in human body?

Answer: **Amylase** are a group of proteins found in saliva and pancreatic juice. They help to convert starch into sugar.

Q2

What is the physiological action of amylase?

Answer: **Amylase** hydrolyzes (breakdown) the dietary starch and glycogen into:

1- Short, branched oligosaccharides (e.g. maltotriose) 2- Disaccharides (maltose and iso-maltose).

Q3

Would you expect a high level of amylase in blood under a normal condition?

Answer: **No (Increase only in pathological conditions)**

Q4

A: What are the uses of amylase measurement in clinical practice?

Answer A: Acute pancreatitis

B: What other diagnostic marker that can be measured in this clinical condition?

Answer B: Serum lipase

Serum Lipase More specific and more sensitive than Serum Amylase but we don't use it more in Labs because lipase measurement is not easy and more expensive.

Serum amylase vs. Serum lipase for acute pancreatitis

Female Dr: you have to memorize these values

	Serum amylase	Serum lipase
Levels start rising	2-12 hrs	4-8 hrs
Levels peak	12-72 hrs	24 hrs
Levels return to normal	One week	8-14 days
Normal range: adults < 60yrs	25-125 IU/L	10-140 IU/L
Normal range: adults > 60yrs	24-151 IU/L	18-181 IU/L

- Values more than three times (**not just 180 IU/L, three times more like 250,350,400**) the normal range along with the clinical picture is considered positive for acute pancreatitis.
- Even though the specificity and sensitivity of serum amylase are lower than those of serum lipase, serum amylase is widely used for Adults > 60 yrs diagnosing pancreatitis because it is relatively inexpensive.

1- Malabsorption Analysis of Serum Amylase

Questions and Answers

Q4

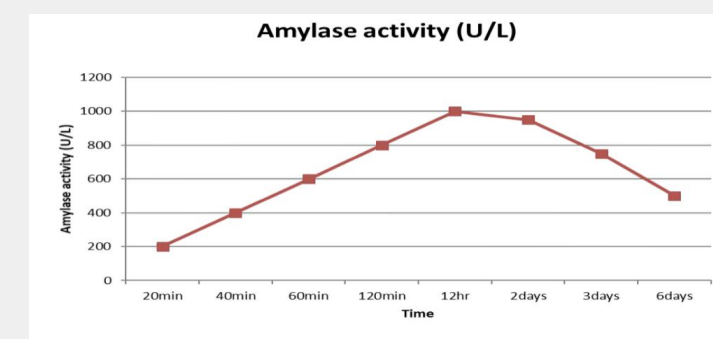
C: If a patient has an elevated amylase levels, does this always mean that he has a pancreatic condition?

Answer: No, Amylase levels may also be significantly increased in patients having conditions other than pancreatic disease.

Example: (we differentiate them from acute pancreatitis by other clinical diagnosis)

- 1- Gallbladder diseases
- 2- Acute appendicitis
- 3- Intestinal obstruction
- 4- Perforated intestinal ulcer

Changes in serum amylase activity during course of an injury (time course), Amylase levels will be increasing over time and will reach a peak within 12-72 hours. It will return to normal in few days (~ a week).



Q5

A: What are the possible factors responsible for these changes in the curve above?

Answer:

Why does amylase level increase?

Acute pancreatitis → damage of the exocrine part of the pancreas → release of the pancreatic enzymes into the circulation (α -Amylase is one of the pancreatic enzymes released).

Why does it decrease?

1. The condition is self-limited
2. The circulating amylase will be excreted in urine
3. The circulating amylase will be degraded (protein turnover)

Q5

B: With knowledge about amylase activity overtime, what is the clinical application?

Answer: Three points can be derived from such a curve:

1. Measurement of α -amylase in the serum is limited by the time elapsed since the initiation of acute inflammation of the pancreas. If the patient presented late, and the condition was self limited, the diagnosis of acute pancreatitis based on the enzyme level at time of presentation could be missed.
2. The measurement of α -amylase in serum should not be interpreted on its own (it's not enough for diagnosis); it has to be evaluated in association with the clinical picture (e.g. the nature of abdominal pain).
3. The rising trend of the levels of serum α -amylase as the acute inflammation is taking place is more clinically significant than one single high reading.

1- Malabsorption Analysis of Serum Amylase

Sources of Variation in Test Results

For adequate interpretation of laboratory test results, you have to completely understand different reasons for variation in test results:

1- Analytical factors: e.g., **accuracy (reliability) and precision (reproducibility)**

2 -Biological factors: e.g., sex, age, diet, drugs ..

3- Pathological factors: e.g., progression of the disease, complications



Accuracy (reliability)

Means how close to the target results



- The reliability of the method in determining the true value of the analyte.
- The extent to which the mean measurement is close to the true value.
- It is useful for comparison of original, gold standard method with other methods.



Precision (reproducibility)

Means every time we repeat the test the results will be the same.



- The reproducibility of the method when it is run **repeatedly** under identical conditions.

1- Malabsorption Analysis of Serum Amylase



SOURCES OF VARIATION IN TEST RESULTS:

Accuracy & Precision موضع اسئلة

Accuracy

VS

Precision

They are independent, e.g., an inaccurate result can be extremely precise

مالهم علاقة ببعض يعني ممكن شي يكون very accurate ولكن not precise والعكس

The relation between accuracy and precision can be easily illustrated by its analogy to shooting at a target or 'dartboard'

Examples of Accuracy & Precision:

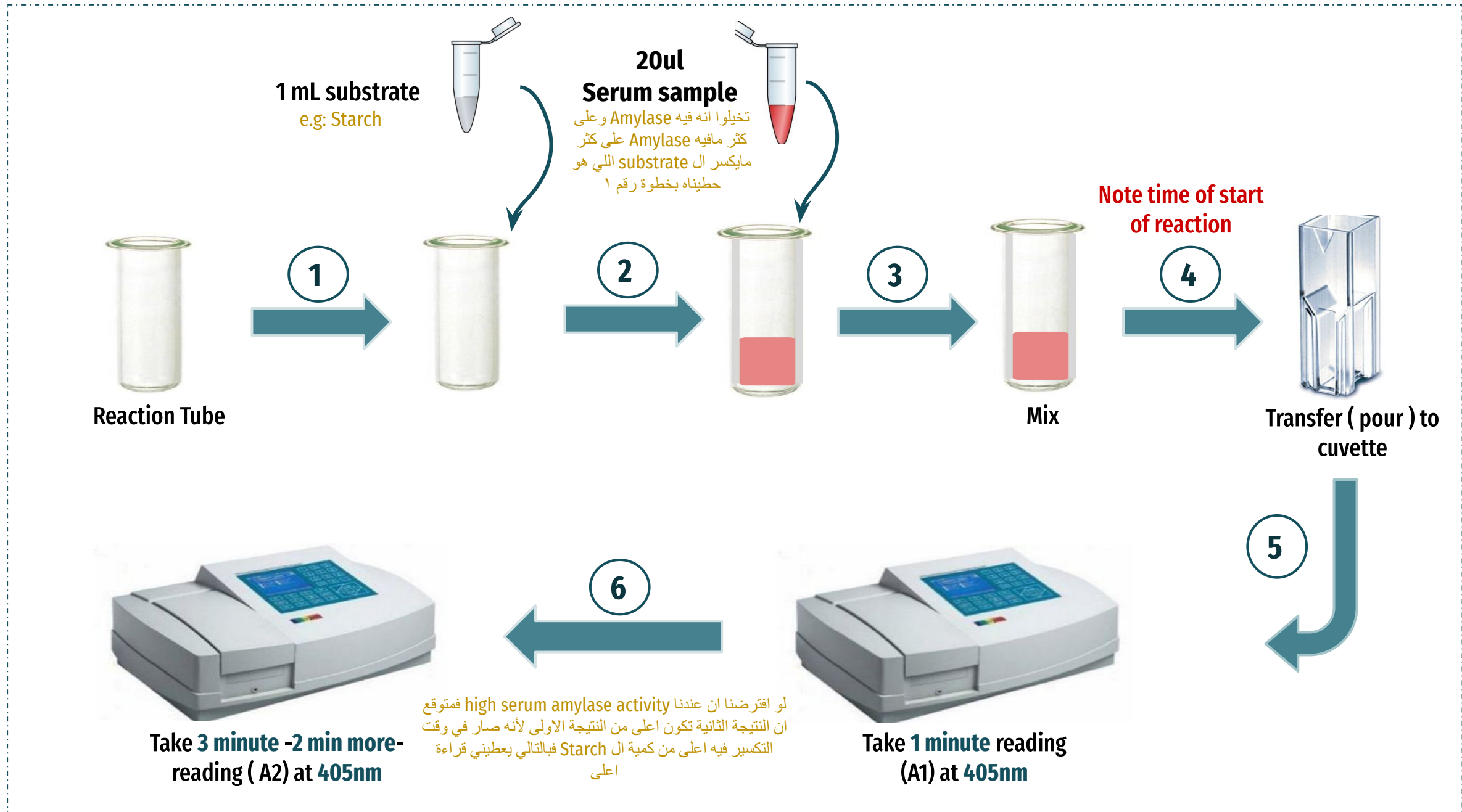
Accurate and Precise	Accurate but not Precise	Inaccurate but Precise	Both inaccurate and imprecise

Accurate Precise	Not Accurate Precise	Accurate Not Precise	Not Accurate Not Precise

1- Malabsorption Analysis of Serum Amylase

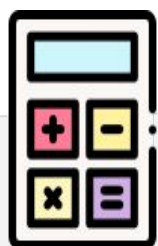
Measurement of Serum Amylase:

Female Dr: You don't have to memorize anything here, just know the procedure how we do it.



Calculation & Interpretation:

Very important



Serum amylase (U / L) =

$$\Delta A = \frac{A2 - A1}{3} \quad (A = \text{Reading})$$

$$\text{Serum amylase (U/ L)} = 4712 \times \Delta A$$

Results: **U/L** DON'T FORGET WRITE THE UNIT

You don't have to memorize this number because it will be given in the example and it may change.

Normal serum amylase reference values:
Serum: up to 125 U/L (at room temperature)
Normal range: 25 - 125 U/L

If the value is above the normal range you have to say that is (high).
 If in the case they give you a clinical picture of acute pancreatitis and the values come three times above the normal range you can say the diagnosis could be **Acute pancreatitis** otherwise you just have to say the value is high.

2- Liver Function Tests (Measurement of total bilirubin)

What are the liver function tests (LFTs)?

Liver Chemistry Test	Clinical Implication Of Abnormality
Alanine aminotransferase (ALT)	Hepatocellular damage e.g viral hepatitis
Aspartate aminotransferase (AST)	Hepatocellular damage e.g viral hepatitis
Bilirubin	Cholestasis, impaired conjunction. Or biliary obstruction
Alkaline phosphatase	Cholestasis, impaired conjunction. Or biliary obstruction
Prothrombin time	Synthetic function
Albumin	Synthetic function
-γ- glutamyl transferase	Coolestasis or biliary obstruction
Bile acids	Coolestasis or biliary obstruction

Liver Chemistry Test	Clinical Implication Of Abnormality
(AST) OR (ALT)	Hepatocellular damage e.g viral hepatitis
bilirubin, alkaline phosphatase, -γ- glutamyl transferase, OR bile acids	Cholestasis, or biliary obstruction
Prothrombin time OR albumin	Synthetic function

Questions And Answers

Q1 What is bilirubin, and how is it produced in the body?

Answer: Bilirubin is a yellow bile pigment, It is produced from the degradation of heme; which is one of the breakdown products of red blood cells.

Q2 A: Which form of bilirubin is carried to the liver and How?

Answer A: The unconjugated form of bilirubin is carried to the liver, Unconjugated bilirubin forms a complex with albumin to be transported.

B: From the picture On the right,★ mark the intracellular location for the process of conjugation + How and why is bilirubin conjugated?

Answer B: In the **Smooth Endoplasmic Reticulum**, Bilirubin is conjugated with UDP-glucuronic acid by UDP-glucuronyl transferase to make it more soluble for excretion as it is a toxic substance.

Q3 How is bilirubin eliminated from the body?

Answer: From the figure in the next page:

Q4 What are the fates of bilirubin in the intestine?

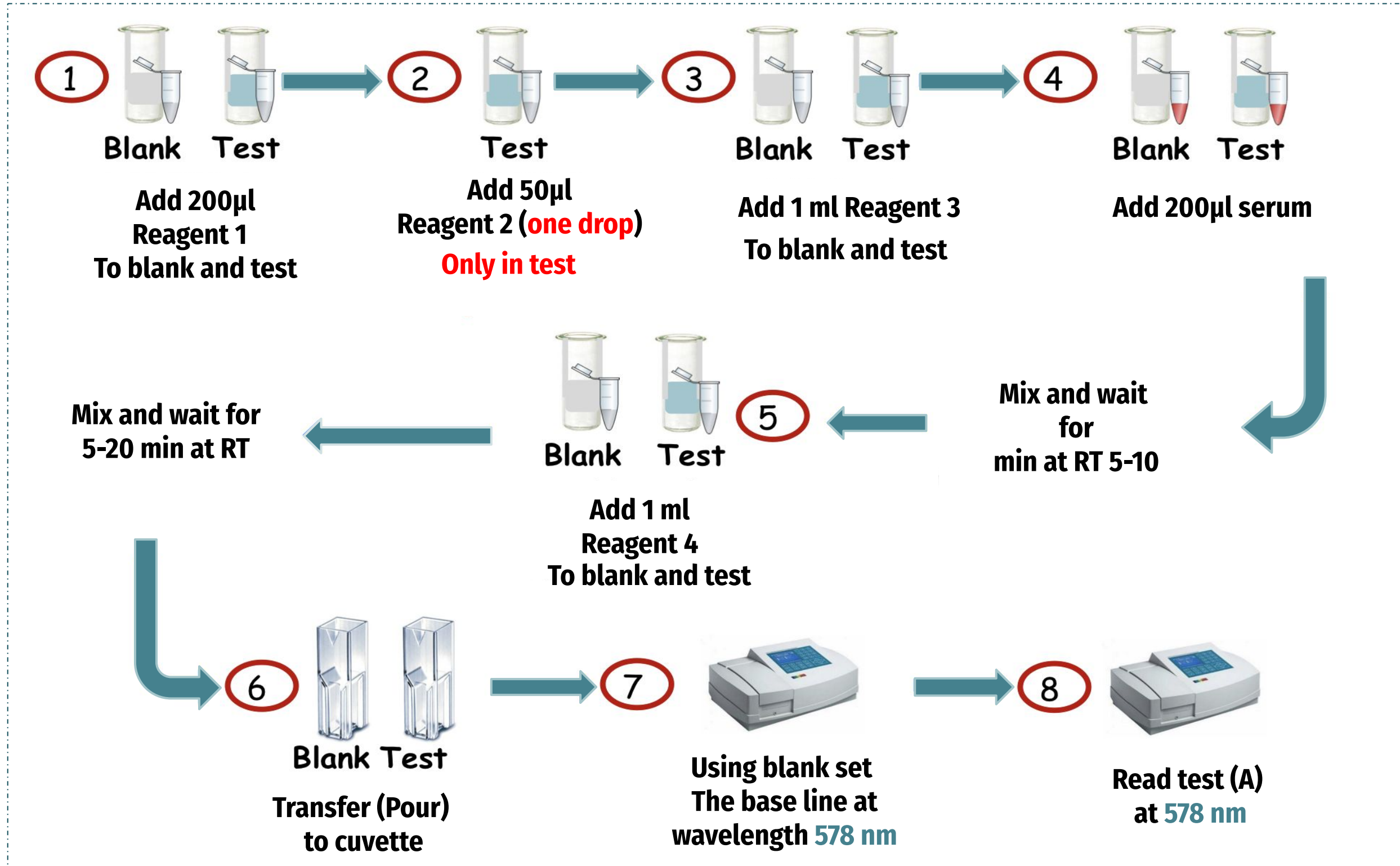
Answer: From the figure in the next page:



2- Liver Function Tests (Measurement of total bilirubin)

Measurement of Total Bilirubin

Female Dr: You don't have to memorize anything here, just know the procedure how we do it.



Calculation of total bilirubin concentration:

Very important



Conc. of total serum bilirubin ($\mu\text{mol/L}$) =

$$A \text{ (test result)} \times 185 = \dots\dots\dots \mu\text{mol/L}$$

You don't have to memorize this number because it will be given in the example and it may change.

DON'T FORGET WRITE THE UNIT

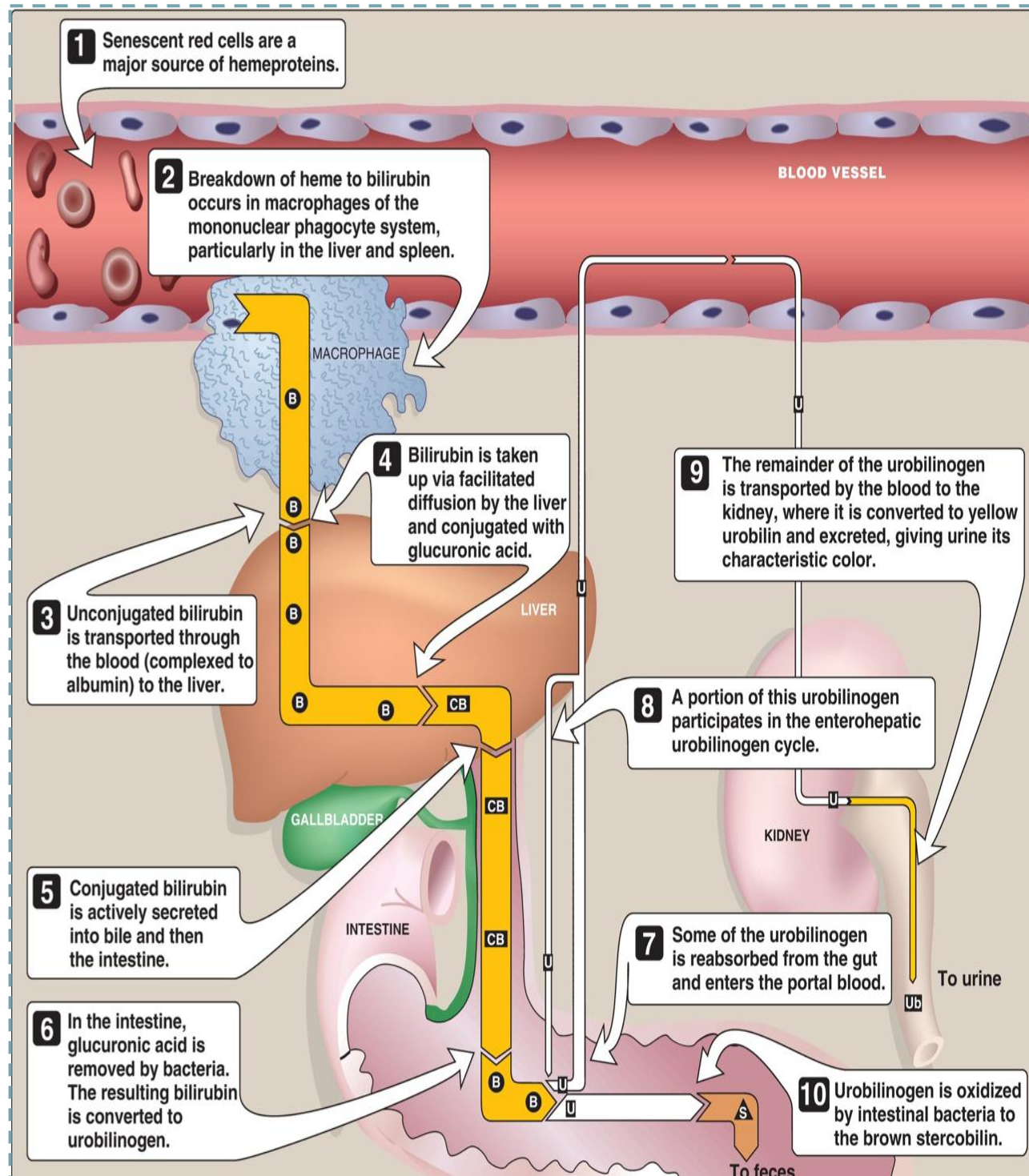
Normal Conc. of total serum bilirubin:

(reference range: 2 – 17 $\mu\text{mol/L}$)

Female dr: You have to memorize the normal range you may be ask you calculate the conc of billirune and may have to comment about it is it normal or high

2- Liver Function Tests (Measurement of total bilirubin)

The Figure



Explanation # team 438

- 1- Rupture of RBCs lead to release of heme
 - 2- Heme is converted to biliverdin catalyzed by microsomal heme oxygenase which is reduced to bilirubin
 - 3- bilirubin is complexed with albumin (bilirubin-albumin complex), from the blood it's taken up to the liver (unconjugated bilirubin).
 - 4- Bilirubin is conjugated with UDP-glucuronic acid.
 - 5- Conjugated bilirubin is secreted into bile and then into the intestine.
 - 6- Bacteria utilize glucuronic acid so it remove it from bilirubin converting it into urobilinogen.
- Fate of urobilinogen:**
- 7- Some enter the portal circulation where:
 - 8- Returns back to the liver.
 - 9- filtered by the kidney as urobilin
 - 10- majority is excreted with feces as stercobilin (gives the feces its characteristic color)

Defective enzymatic conjugation of bilirubin

Example of clinical conditions due to congenital deficiency of the conjugating enzyme (Bilirubin UDP-glucuronyl transferase)

- Crigler-Najjar syndrome
- Gilbert syndrome

2- Liver Function Tests (Measurement of total bilirubin)

Sensitivity

Sensitivity answers the following question:

If a person has a disease, how often will the test be positive. (**true positive rate**)?
 i.e.: if the test is highly sensitive and the test result is negative you can be nearly certain that the individuals don't have disease.

Rules out disease

-A **Sensitive** test helps **rule out** disease (when the result is negative).
Sensitivity rule out or "Snout"

Exclude the presence of the disease (i.e usually used for screening of large groups to exclude the disease)

in case of **Sen**: true positive "rule out/snout"



Calculation of The Sensitivity

Very important

Sensitivity

$$\frac{\text{True Positive (TP)}}{\text{True Positive (TP) + False Negative (FN)}} \times 100$$

The **true** positive rate usually refers to the number of people **who are infected** and get positive results
 The **false** positive rate usually refers to the number of people **who are not infected** but get positive results

2 X 2 Contingency Table:

Male Dr :You should to memorize this table cause not be given in exam

Test	Disease	
	+	-
+	True Positive (TP) (Positive result in diseased person)	False Positive (FP) (Positive result in normal person)
-	False Negative (FN) (Negative result in diseased person)	True Negative (TN) (Negative result in normal person)

For your info:

To convert $\mu\text{mol/L}$ to mg/dl , multiply by 0.0113. To convert mg/dl to $\mu\text{mol/L}$, multiply by 88.4.

2-Liver Function Tests (Measurement of total bilirubin)

Specificity

Specificity answers the following question:

-If a person does not have the disease how often will the test be negative
(true negative rate)?

i.e., if the test result for a highly specific test is positive you can be nearly certain that the individuals actually have the disease.

Rules in the disease

-A very **specific** test **rules in** disease with a high degree of Confidence (when the result is positive).
Specificity rule in or "Spin".

Ensure the presence of the disease (i.e usually after we finish screening with a sensitive test we use a specific test to diagnose)

in case of Sp: true negative "rule in/spin"



Calculation of The Specificity

Very important

Specificity

True Negatives (TN)

True Negatives (TN) + False Positives (FP)



100

The **true** positive rate usually refers to the number of people **who are infected** and get positive results
The **false** positive rate usually refers to the number of people **who are not infected** but get positive results

Male Dr :You should memorize this table cause not be given in exam

2 X 2 Contingency Table:

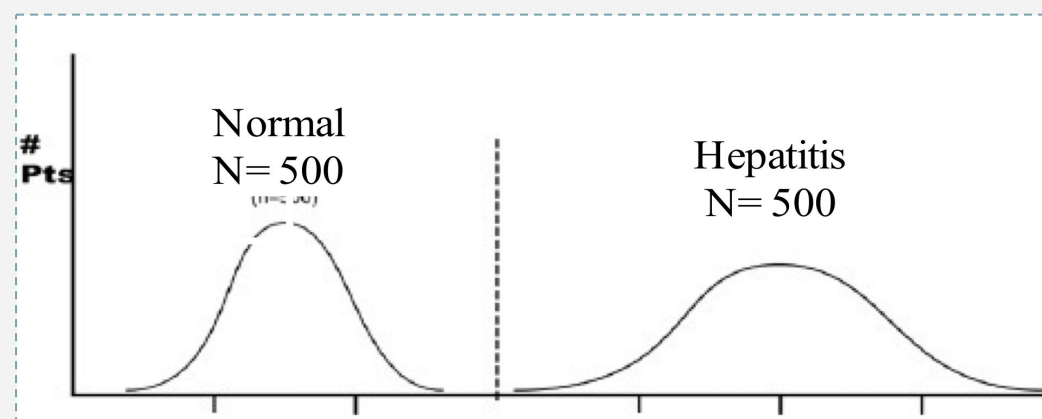
Test	Disease	
	+	-
+	True Positive (TP) (Positive result in diseased person)	False Positive (FP) (Positive result in normal person)
-	False Negative (FN) (Negative result in diseased person)	True Negative (TN) (Negative result in normal person)

For your info: To convert $\mu\text{mol/L}$ to mg/dl , multiply by 0.0113. To convert mg/dl to $\mu\text{mol/L}$, multiply by 88.4.

2-Liver Function Tests (Measurement of total bilirubin)

An ideal diagnostic lab test results for many subjects (normal and patients)

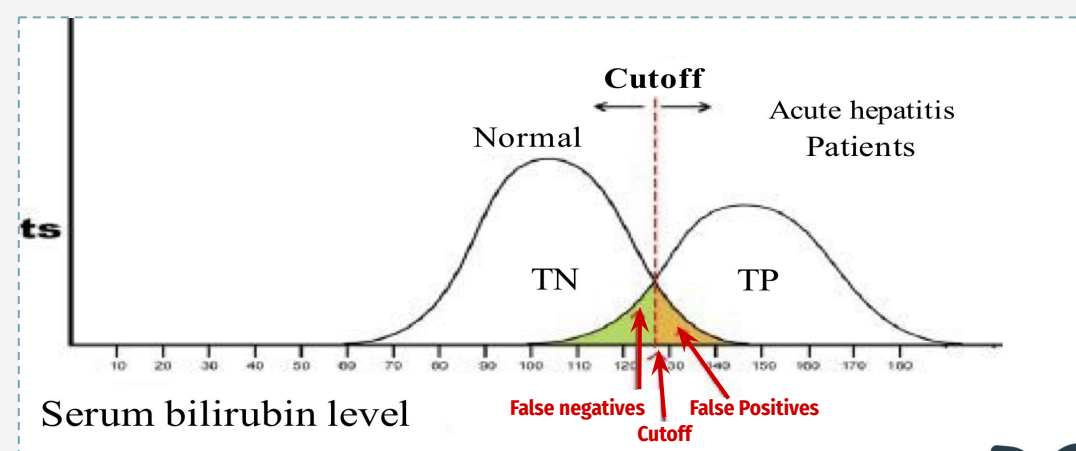
An Ideal diagnostic lab test results for many subjects (normal and patients) will **identify ALL patients with disease and All subjects without disease 100%** of the time. This is shown in the following graph:



- A **perfect test** for acute hepatitis: The test identifies ALL patients with disease and All subjects without disease 100% of the time. *إذا ما فيه تداخل بين الموجات ف هو Perfect Test*

In most diagnostic lab tests

- In most diagnostic lab tests this is not the case, and there is some overlap as shown in the following graph.



- **The lab test with the best specificity and sensitivity should be the one requested by physicians.**
- The lab test results in normal and disease conditions overlap.
- To increase the overall accuracy of the test, the centermost point of overlapping is chosen as the cutoff value.
- There are some normal subjects who will have a positive results(False positives).
- There are some patients who will have negative results (False negatives).

2-Liver Function Tests (Measurement of total bilirubin)



Example of calculation: Very Very important !!!

A Lab test to measure serum bilirubin was performed on 1000 individuals. The test gave the following results:

- Number of positive results in patients with acute hepatitis: 440
- Number of positive results in normal subjects: 50
- Number of negative results in normal subjects: 450
- Number of negative results in patients with acute hepatitis: 60
- For this Serum bilirubin test, calculate the following quality measures:

1- The sensitivity

2- The specificity



1-draw a 2 X 2 Contingency Table:

Test	Disease	
	+	-
+	440	50
-	60	450

Test	Disease	
	+	-
+	True Positive (TP)	False Positive (FP)
-	False Negative (FN)	True Negative (TN)

2-Calculate the Sensitivity and Specificity :

$$\text{Sensitivity} = \frac{\text{True Positive (TP)}}{\text{True Positive (TP) + False Negatives (FN)}} \times 100 \rightarrow \frac{440}{440+60} \times 100 = 88\%$$

$$\text{Specificity} = \frac{\text{True Negatives (TN)}}{\text{True negative (TN) + False Positive (FP)}} \times 100 \rightarrow \frac{450}{450+50} \times 100 = 90\%$$

NOTE: since the specificity of this test is higher than the sensitivity; this test is better for a diagnosing purposes (to rule in)

كل مازادات النسبه ال-Test يكون افضل

Handout Quiz

1- What is amylase, and what are its sources in the human body?

Answer: **Amylase** are a group of proteins found in saliva and pancreatic juice. They help to convert starch into sugar.

2- What is the physiological action of amylase?

Answer: **Amylase** hydrolyzes (breakdown) the dietary starch and glycogen into:

1- Short, branched oligosaccharides (e.g. maltotriose)

2- Disaccharides (maltose and iso-maltose).

3- Would you expect a high level of amylase in blood under normal conditions?

Answer: **No**

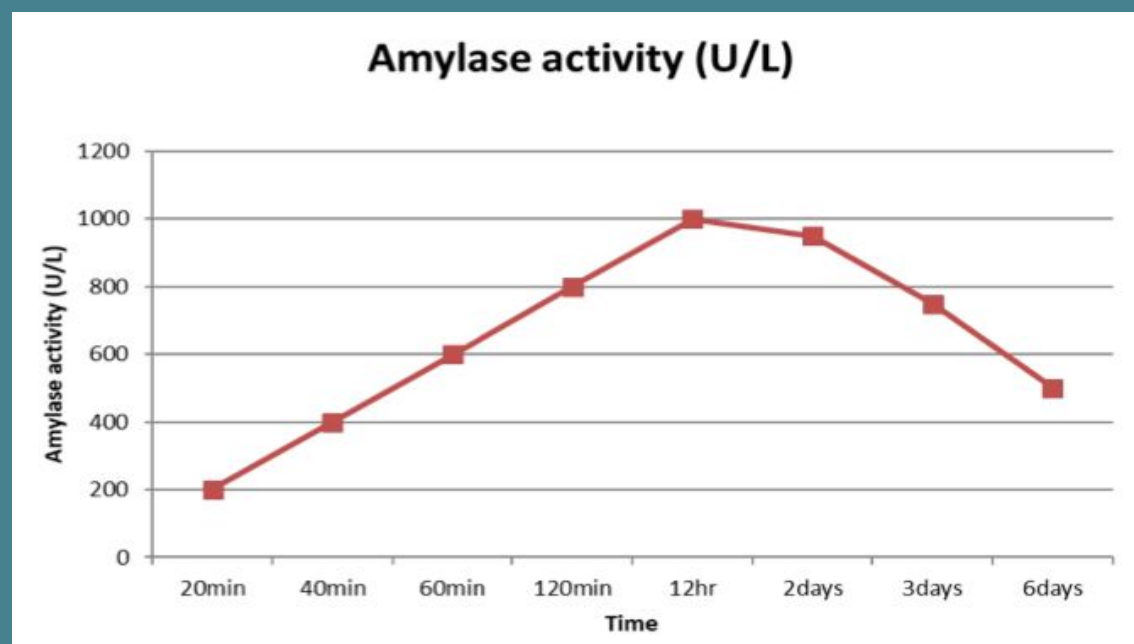
4A- What are the uses of amylase measurement in clinical practice?

Answer A: Acute pancreatitis

4B- What other markers can be used in a case of acute pancreatitis?

Answer B: Serum lipase

5- Changes in serum amylase activity during course of an injury (time course)?



5A- What are the possible factors responsible for these changes in the curve?

Answer A: Slide 3

5B- With knowledge about amylase activity overtime, what is the clinical application?

Answer B: Slide 3

Handout Quiz

1- What are the liver function tests (LFTs)?

Answer: Slide 7

2- What is bilirubin and how is it produced in the body?

Answer: Slide 7

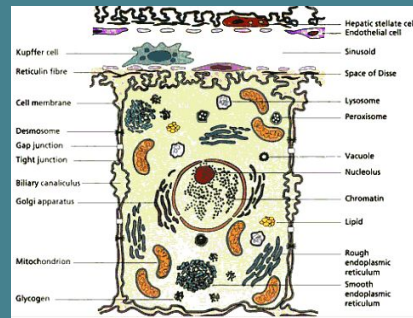
3- Which form of bilirubin is carried to the liver and how?

Answer: Slide 7

4A- How and why is bilirubin conjugated?

Answer A: Slide 7

4B- On the picture below, mark the intracellular location for the process of conjugation?

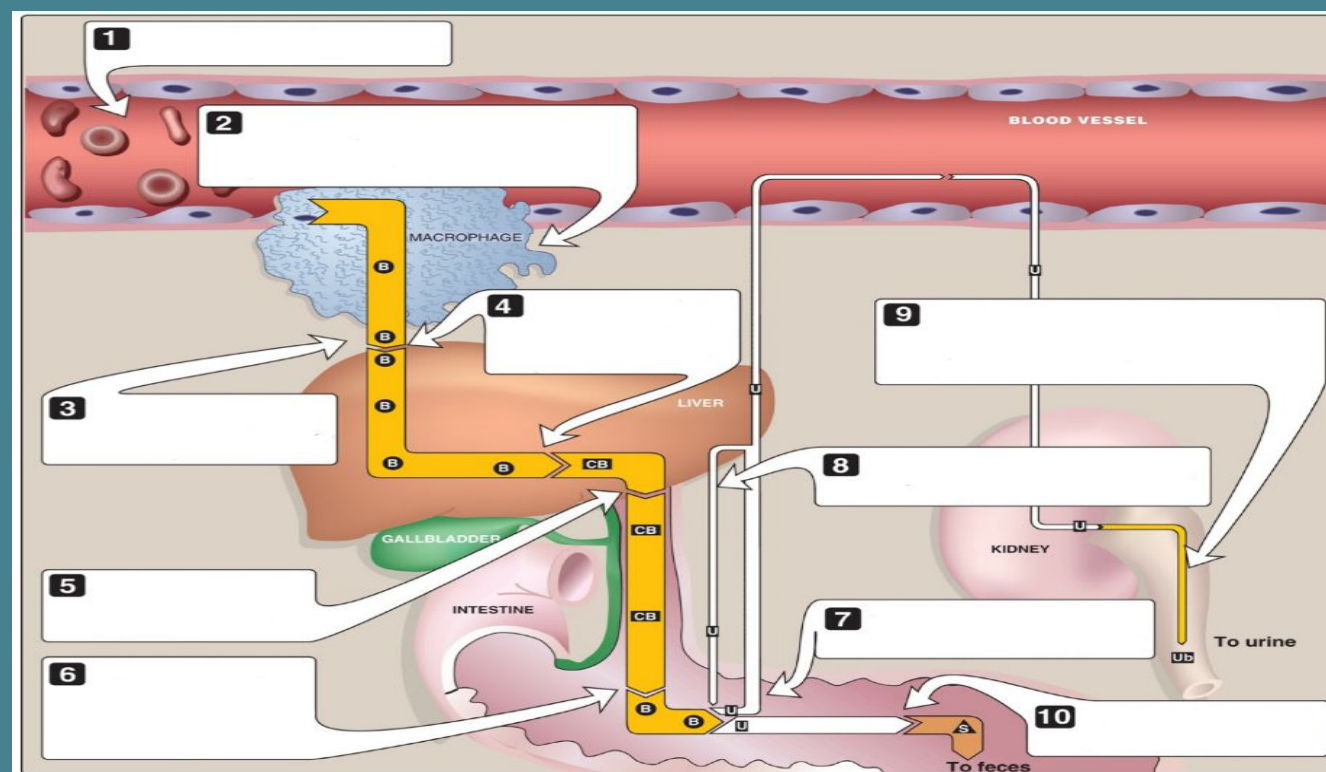


Answer: Slide 7

4C- Mention 2 syndromes due to congenital deficiency of the conjugating enzyme (bilirubin glucuronyl-transferase)?

Answer: Slide 9

5-



5A- How is bilirubin eliminated from the body?

Answer A: Slide 9

5B- What are the fates of bilirubin in the intestine?

Answer B: Slide 9

Quiz

Thanks for: 438 Biochemistry Team

- 1)

A) Calculate **serum amylase** when **A1= 0.122** and **A2= 0.219** and give the diagnosis with the normal range?
B) Name three conditions where serum amylase levels increase?
C) Give two reason how can serum amylase decrease after an acute injury?
- 2)

A) What are the factors for variation in test results?
B) Defined accuracy and precision?
C) Explain the figures?
- 3)

- Name two test that can be used when we suspect Cholestasis?
- 4)

A) Calculate the total serum bilirubin when A= 0.126 and give the diagnosis with the normal range?
B) What is the fate of bilirubin and how it's excreted out of the body?
C) Name one clinical condition for (bilirubin UDP-glucuronyl transferase) deficiency?
- 5)

A) Calculate the sensitivity, the specificity and draw a 2 X 2 Contingency Table:
for this lab tests for serum bilirubin in 1000 individuals.
▪ Number of positive results in patients with acute hepatitis: 350
▪ Number of positive results in normal subjects: 28
▪ Number of negative results in normal subjects: 570
▪ Number of negative results in patients with acute hepatitis: 42
B) What is the role of specificity and sensitivity tests in testing for A disease?

Ans.1:

A) 152.35 U/L, Acute Pancreatitis, NR= 25-125 U/L

B) 1- Gallbladder Diseases 3-Acute Appendicitis 2-Intestinal Obstruction

C) The Condition Is Self-limiting and The Circulating Amylase Will Be Excreted In Urine

Ans.2:

A) Analytical Factors, Biological Factors And Pathological Factors.

B) Accuracy Is The Reliability Of The Method In Determining The True Value Of The Analyte And Precision Is The Reproducibility Of The Method When It Is Run Repeatedly Under Identical Conditions

C) 1. Not Accurate But Precise 2. Accurate Not Precise

Ans.3: Bilirubin And Alkaline Phosphatase.

Ans.4: A) 23.31 $\mu\text{mol/L}$, Hyperbilirubinemia, 2 – 17 $\mu\text{mol/L}$

B) From the figure slide 8: Converted to urobilinogen then Excreted into the feces as stercobilin, Into urine as urobilin, Or back to liver through enterohepatic circulation.

C) Gilbert Syndrome.

Ans.5:

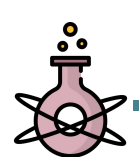
A) The Sensitivity = 89.3% and The Specificity= 95.3%

B) Sensitive Test Helps Rule Out Disease And Specificity Test Rules In Disease.

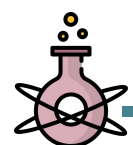
	Test	Disease
	+	-
+	350	28
-	42	570



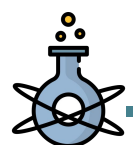
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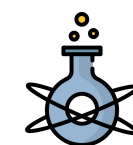
- **Albandari Alanazi**



- **Sara Alharbi**



- **Abdulaziz Alrabiah**



- **Abdulaziz Alghuligah**



Special thanks to Fahad AlAjmi for designing our team's logo.