ACUTE BREATHLESSNESS EVALUATED BIOCHEMICALLY

DR. SANJEELA NAHREEN CHOWDHURY

DEPARTMENT OF BIOCHEMISTRY

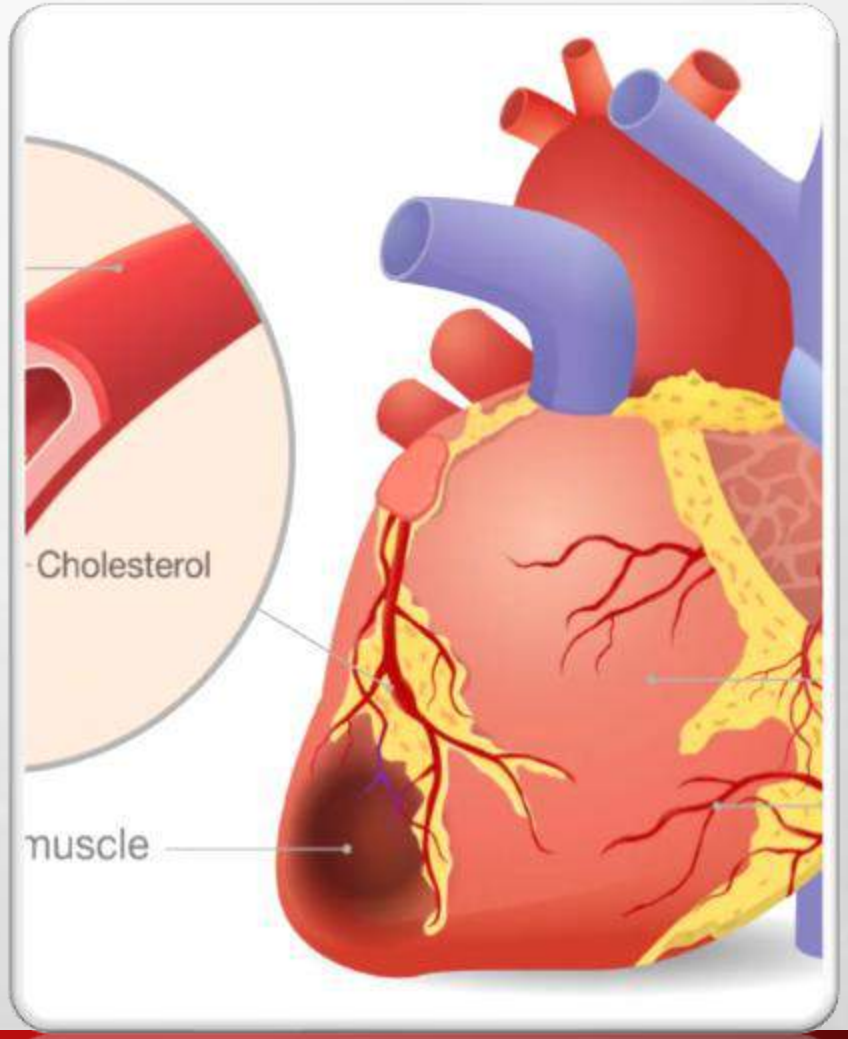
THE CLINICAL CHALLENGE

Acute breathlessness-

One of the most common and critical presentations in emergency medicine. The differential diagnosis is broad, primarily distinguishing between cardiac and pulmonary causes.

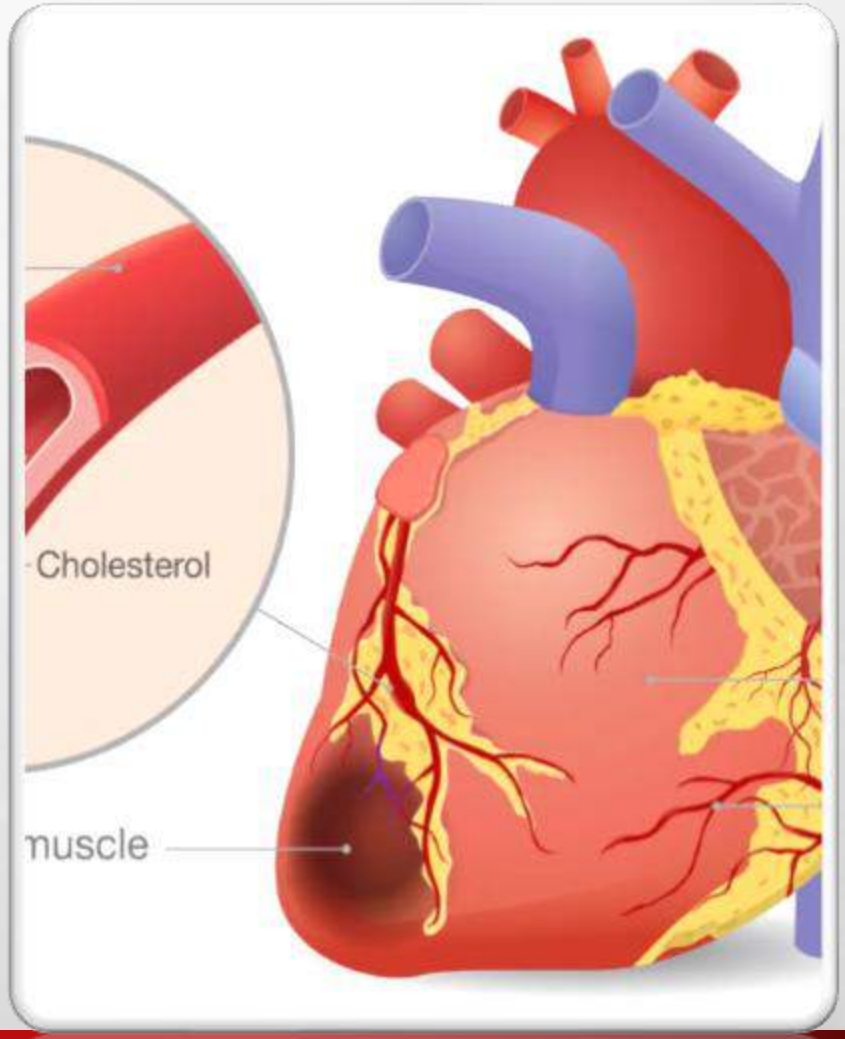
CASE SCENARIO 1

- A 48-yr old man presented to Emergency department with repeated attack of severe retrosternal crushing chest pain that was radiating to the left arm and not relieved by rest.
- It was associated with shortness of breath, nausea & excessive sweating. He had similar episodes of mild chest pain over the past 4 months when he walked at a fast pace or climbed stairs. Each time, the pain lasted for 1-5 minutes & was relieved by rest.



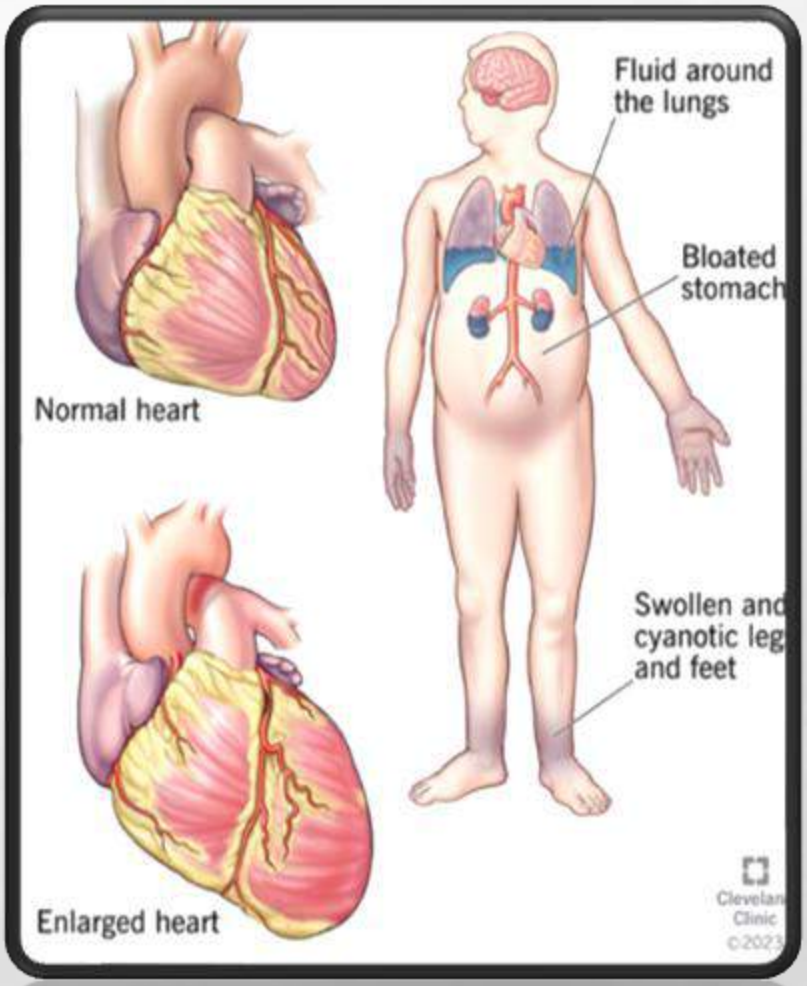
CASE SCENARIO 1

- ✓ The pain has been occurring more frequently and lasting longer over the past 2 weeks & sometimes occurring at rest.
- ✓ He had no prior health problems. He was not on any regular medication & had no allergies. He had an elder brother with similar complaints. He has a history of smoking (20 sticks per day)



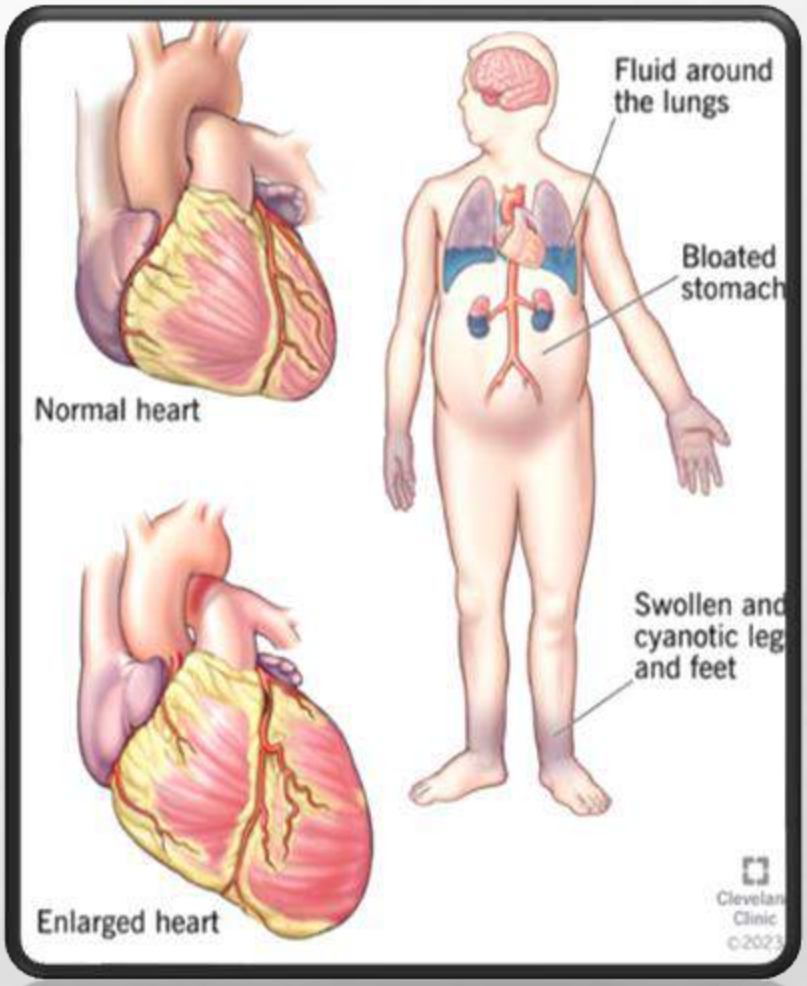
CASE SCENERIO 2

- A 70-year obese old man is brought into the Emergency department in the early hours of the morning with acute shortness of breath. He is pale, clammy, sweaty and very distressed.
- This is associated with ankle oedema and fatigue. He also complained about palpitation & cough with pink frothy sputum.



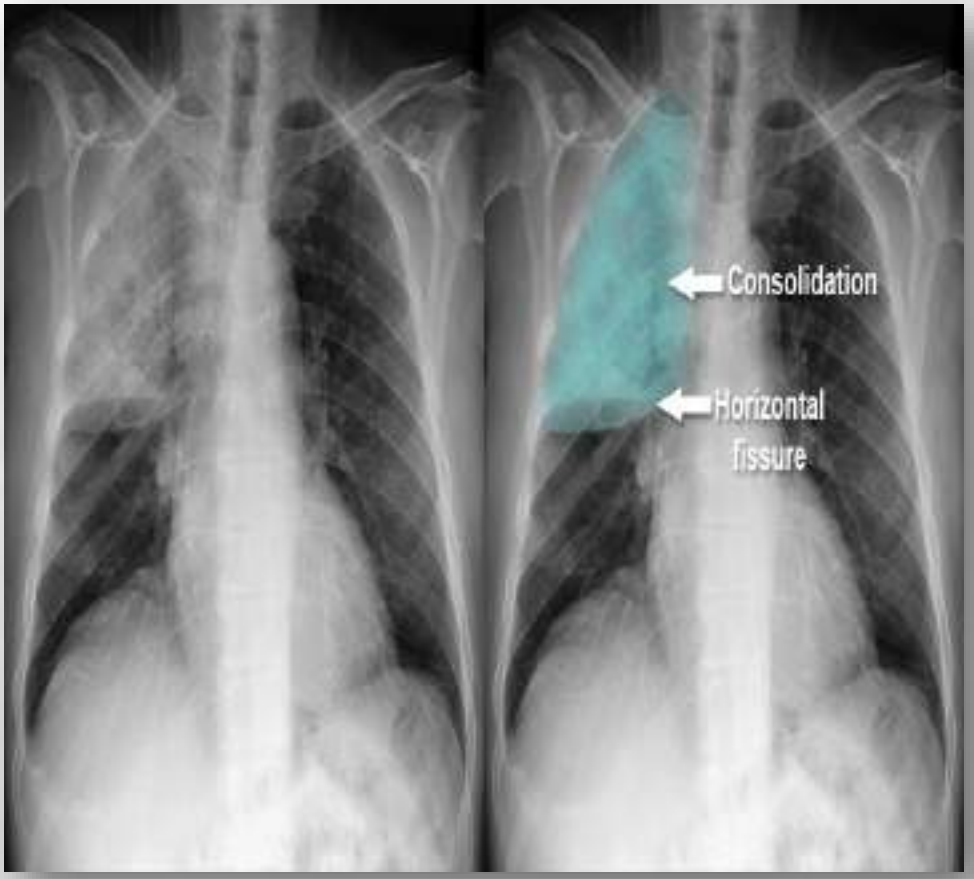
CASE SCENERIO 2

- He had episodes of difficulty in breathing on exertion & when lying down. He is a known case of uncontrolled diabetes & hypertension. He had a previous history of MI. He had a strong family history of heart disease. He is nonsmoker.



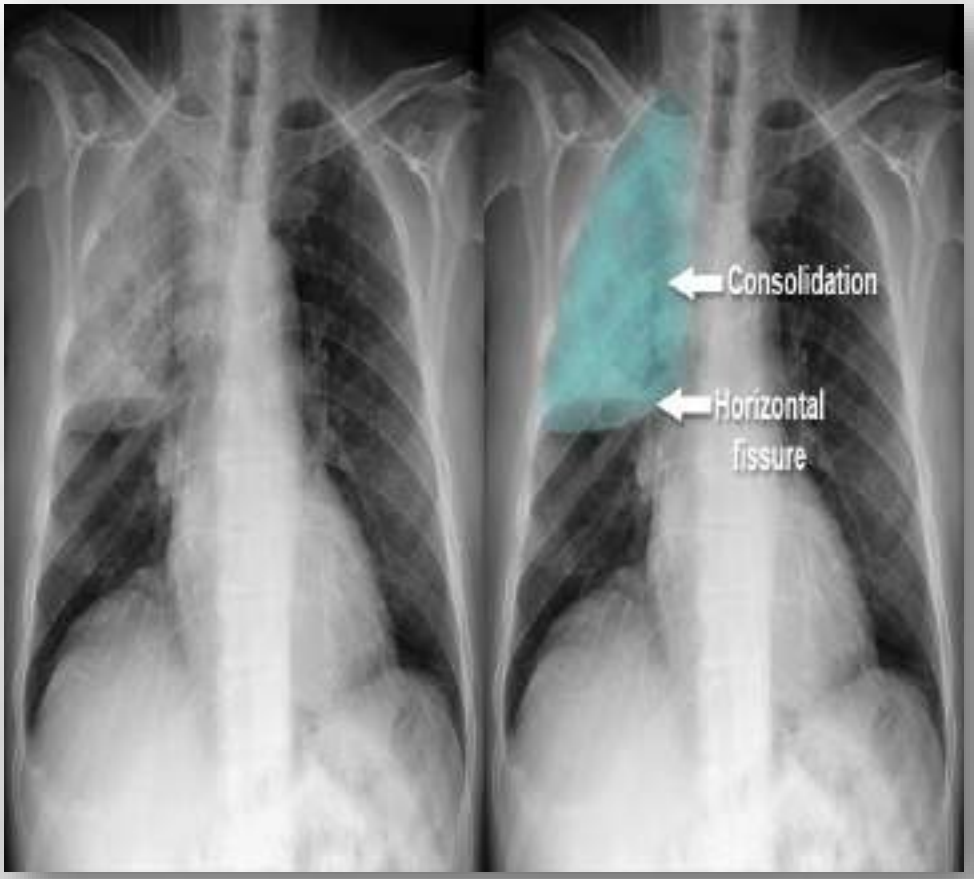
CASE SCENARIO 3:

- 45-year-old lady was seen in the outpatient clinic owing to sudden onset of fever 3 days prior with chills, cough with mucopurulent expectoration which is rust in color, and progressive breathlessness even at rest. She also complained of pain in the chest.



CASE SCENARIO 3:

- There was no history of recurrent sinusitis, diarrhea, and any soft tissue infection. She had no history of diabetes mellitus, bronchial asthma or steroid intake. She had neither herself history of tuberculosis nor in the family.
- Radiograph and CT scan of the chest revealed right upper lobe consolidation.



DYSPNEA

A subjective experience of uncomfortable breathing, is a symptom that typically results from cardiac, pulmonary, and neurologic etiologies that cause an increased drive to breathe, increased work of breathing, and/or stimulation of specific receptors in the heart, lungs, or vasculature.

DYSPNEA

- ✓ A common challenging symptom requiring a systematic diagnostic approach.
- ✓ Biochemical tests provide crucial information to differentiate between major organ systems involved.
- ✓ Laboratory tests, particularly specific biomarkers, can quickly help to determine the origin of dyspnea, aiding rapid and appropriate treatment.

DIFFERENTIAL DIAGNOSIS OF DYSPNEA

Cardiac cause

- ✓ Acute Coronary Syndrome
- ✓ Unstable Angina
- ✓ Acute Myocardial Infarction
- ✓ Left ventricular failure

Pulmonary cause

- ✓ Pneumonia
- ✓ Pulmonary embolism
- ✓ Bronchial Asthma
- ✓ Acute exacerbation of COPD

Hematologic and metabolic cause

- ✓ Severe anemia
- ✓ Metabolic acidosis

Renal cause

- ✓ Acute renal failure

DYSPNEA INVESTIGATIONS

A thorough history, physical examination and initial diagnostics are the first steps.

Initial tests:

- ✓ Pulse oximetry
- ✓ Urgent ECG
- ✓ hs Troponin I
- ✓ NT pro BNP
- ✓ Serum Creatinine
- ✓ Random Blood glucose
- ✓ Arterial blood gas analysis (ABG)
- ✓ Chest x-ray (CXR)

BIOCHEMICAL TOOLKITS

Cardiac injury

hs Troponins I and CK-MB are markers of myocardial necrosis, essential for identifying Acute Coronary Syndrome.

Hemodynamic stress

NT-proBNP are released in response to ventricular stretch, volume overload serving as the gold standard for Heart Failure.

Infection/Inflammation

Procalcitonin (PCT) and CRP help distinguish bacterial pneumonia from viral or non-infectious cause. lactate is an indicator of tissue hypoperfusion or shock due to sepsis.

Pulmonary embolism

Elevated level of D-dimer indicate the presence of a blood clot, which is a common marker for PE.

Metabolic Acidosis

Arterial Blood Gas (ABG) for pH status and Lactate/Ketones for metabolic acidosis

BIOCHEMICAL INVESTIGATION

Test	Result	Reference range
hs Troponin I	**34ng/ml**	< 10 ng/ml
CK-MB	**45 U/L**	<25U/L
NT pro-BNP	**180 pg/ml**	65-75 yrs < 325 pg/ml
Creatinine	**1.4 mg/dl**	0.6-1.3 mg/dl

Diagnosis

Acute Coronary Syndrome (ACS)

CARDIAC CAUSE: ACUTE CORONARY SYNDROME (ACS) BIOCHEMICAL EVALUATION

Inadequate blood flow to the heart muscle.

Diagnostic Evaluation: Initial ECG

Laboratory Results: Crucial values

- ✓ Serial estimation of hs cTroponin I,
- ✓ Serum Creatinine and eGFR
- ✓ NT proBNP
- ✓ hs C-reactive protein,
- ✓ Lipid profile
- ✓ Random blood sugar
- ✓ ABG

- **Imaging**
  - ✓ Chest X-ray (CXR)
  - ✓ Echocardiogram

CARDIAC CAUSES : BIOCHEMICAL EVALUATION

Marker	Role in ACS	Interpretation
hs-cTnI	Primary Diagnostic marker	Gold standard biomarker for diagnosing **Acute Myocardial Infarction**.
Creatine Kinase-MB (CK-MB)	Secondary Markers	Useful for diagnosing a **re-infarction**.
Myoglobin	Secondary Markers	**Sensitivity, but low specificity. Negative result** indicates no source of muscle injury.

CARDIAC CAUSES: BIOCHEMICAL EVALUATION (HS CTNI)

hs-cTnI has taken the center of the stage for diagnosing and classification myocardial infarction.

Mechanism: Released into the bloodstream following myocardial injury.

Normal level:

hs cTnI:0-0.034 ng/ml

high risk group:> 0.034-0.12 ng/ml

AMI: >0.12 ng/ml (Method: CMIA; VITROS)

ADVANTAGES OF HIGH-SENSITIVITY TROPONIN I TESTING

- ✓ **Rapid diagnosis:** can provide results in as little as 15 minutes, facilitating immediate clinical decisions.
- ✓ **Improved accuracy:** the precision of these tests reduces the false negatives and ↑ the ability to detect micro infarctions.
- ✓ **Broader applications:** Assess the risk of future cardiac events in patients without acute symptoms.

CARDIAC CAUSES: BIOCHEMICAL EVALUATION

- ✓ Markers of **risk stratification,** other ACS pathophysiology (inflammation, plaque instability) and prognosis

Marker	Interpretation
hs CRP	Elevated level associated with ↑ed risk of CAD
Homocysteine	Independent risk factor associated ↑ed risk of early inherited cardiovascular event.
Lipid Profile	Dyslipidemia reflects underlying risk factor for atherosclerotic CAD
Electrolytes	Hypokalemia or hyperkalemia can cause arrhythmias.
Interleukins (IL-6)	Reflect the inflammatory process.

BIOCHEMICAL INVESTIGATION

Test	Result	Reference range
Pro-BNP	26326 pg/ml	65-75 yrs< 325 pg/ml
troponin I	590ng/ml	< 10 ng/ml
Creatinine	1.4 mg/dl	Male:0.66-1.2 mg/dl Female:0.52-1.04 mgdl

Diagnosis

Acute left ventricular Failure with
Old Myocardial Infarction, Chronic kidney disease, Diabetes Mellitus, Anemia and Hypertension

CARDIAC CAUSES

Congestive Heart Failure (CHF):

Heart's inability to pump blood effectively due to structural or functional impairments.

The most common cause of CHF

- ✓ Coronary artery disease
- ✓ hypertension, valvular disease, and myocarditis.

Increased hydrostatic pressure leads to pulmonary edema.

BIOCHEMICAL MARKER: NT-proBNP , hs-cTn I

- ✓ **NT-proBNP** released from the ventricles in response to myocardial stretch and volume overload.
- ✓ Elevated level correlate **strongly with severity of heart failure.**
- ✓ Lowered level indicates a **positive response to therapy.**
- ✓ NT-pro BNP Level should interpreted according to age, sex and renal function.

hs-cTroponin I

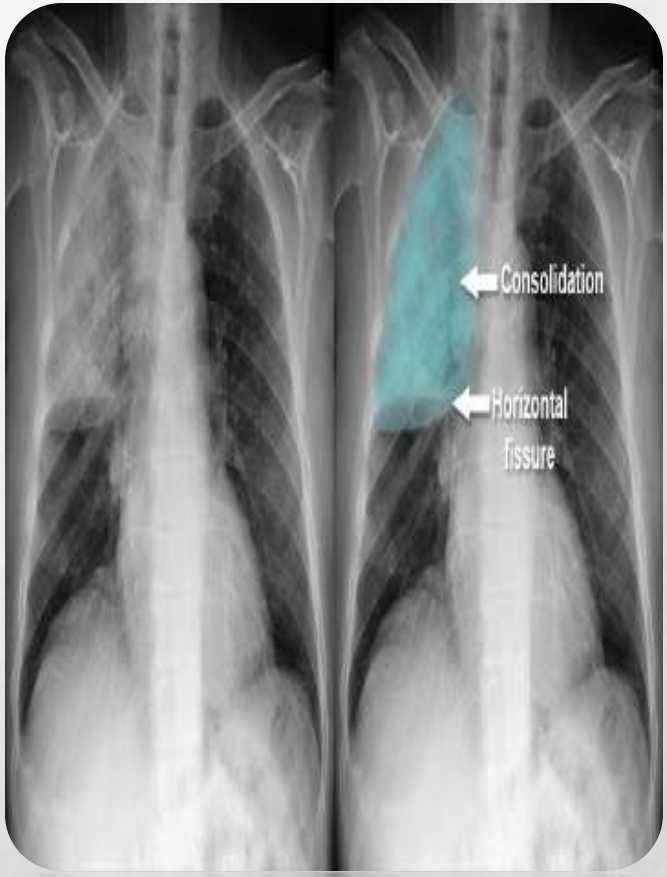
- ✓ Acutely spiking hs-cTnI with raised NT proBNP reflects **acute CHF presentation** due to **acute coronary syndrome .**

RENAL FUNCTION MARKERS (CREATININE AND ELECTROLYTES)

Test	Interpretation	Clinical Significance
Elevated Creatinine and low eGFR	impaired kidney clearance.	**Cardio-Renal Syndrome**, poor cardiac output leads to kidney failure. .
Hyponatremia	Low sodium concentration.	A hallmark of **advanced HF** severity.
Hypokalemia	Low potassium concentration.	due to the use of **Loop Diuretics** (like Furosemide). Can ↑risk of arrhythmias.

BIOCHEMICAL INVESTIGATION

Test	Result	Reference range
C-Reactive Protein (CRP)	150 mg/L	< 10 mg/L
Random blood Glucose	180 mg/dL	70 - 100 mg/dL
WBC Count	18,500 /mm^3	4,500 - 11,000/mm^3



DIAGNOSIS

Pneumonia

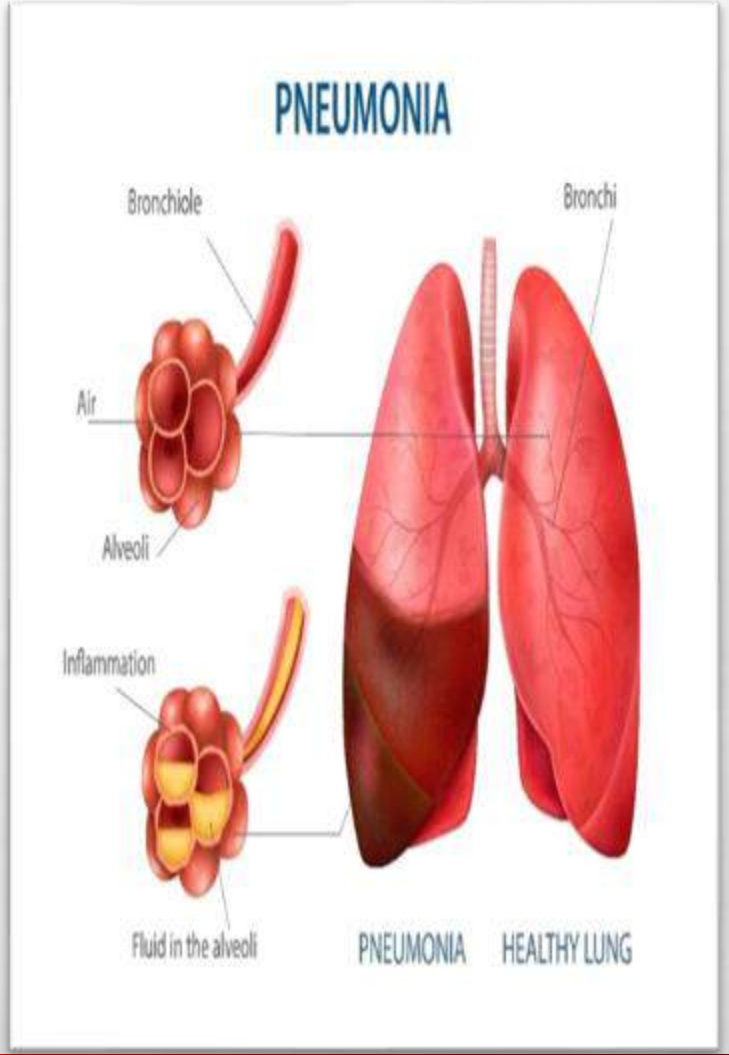
PULMONARY CAUSES

Pneumonia:

An acute inflammatory infection of the lung parenchyma (alveoli and bronchioles).

Biochemical investigations are done for

- ✓ Diagnosis,
- ✓ Determining etiology (bacterial vs. viral),
- ✓ Predicting severity, and
- ✓ Monitoring treatment response.



PNEUMONIA: ARTERIAL BLOOD GAS ANALYSIS

Test	Typical Findings	Interpretation & Clinical Significance
Partial Pressure of O_2 (PaO_2)	**Hypoxemia** **Decreased** (mostly <80 mm Hg)	Defining feature. a ventilation/perfusion mismatch leads to **hypoxemia**.
Oxygen Saturation (SaO_2)	**Decreased.** (often <92%).	Directly reflects the **hypoxemia**. Indicates ↓↓oxygen carrying capacity.
P^H	**Increased** pH > 7.45	**Respiratory Alkalosis.** Rapid breathing causes "blows off" CO_2, making the blood more alkaline.

PNEUMONIA: KEY INFLAMMATORY MARKERS

Test	Typical Finding Pneumonia	Interpretation & Clinical Significance
C-Reactive Protein (CRP)	**Markedly Elevated**	Correlate with disease severity **monitoring treatment response**
Procalcitonin (PCT)	**Elevated** (Especially in severe illness.	A specific marker: Often **high:** bacterial infections **low**: viral infections. whether to **start** or **stop** or **de-escalation of antibiotics.**

PNEUMONIA: OTHER INVESTIGATIONS

Test	Typical Finding Pneumonia	Interpretation & Clinical Significance
Electrolytes, Blood sugar, and kidney function.	Imbalances	particularly if the infection leads to complications or severe illness.

PNEUMONIA: BIOCHEMICAL MARKER

Procalcitonin (PCT):

- ✓ A peptide precursor to the hormone calcitonin synthesized in response to inflammation. It is significantly and specifically elevated during bacterial infections.
- ✓ Pattern rises rapidly during bacterial infection and falls with successful treatment.

Clinical Significance:

- ✓ Helpful in distinguishing a bacterial cause of dyspnea (e.g., pneumonia) from a viral or non-infectious cause.
- ✓ Can guide antibiotic therapy decisions on whether to start or stop antibiotic therapy and can help differentiate bacterial from viral pneumonia.

Limitations:

- ✓ less sensitive in localized infections.

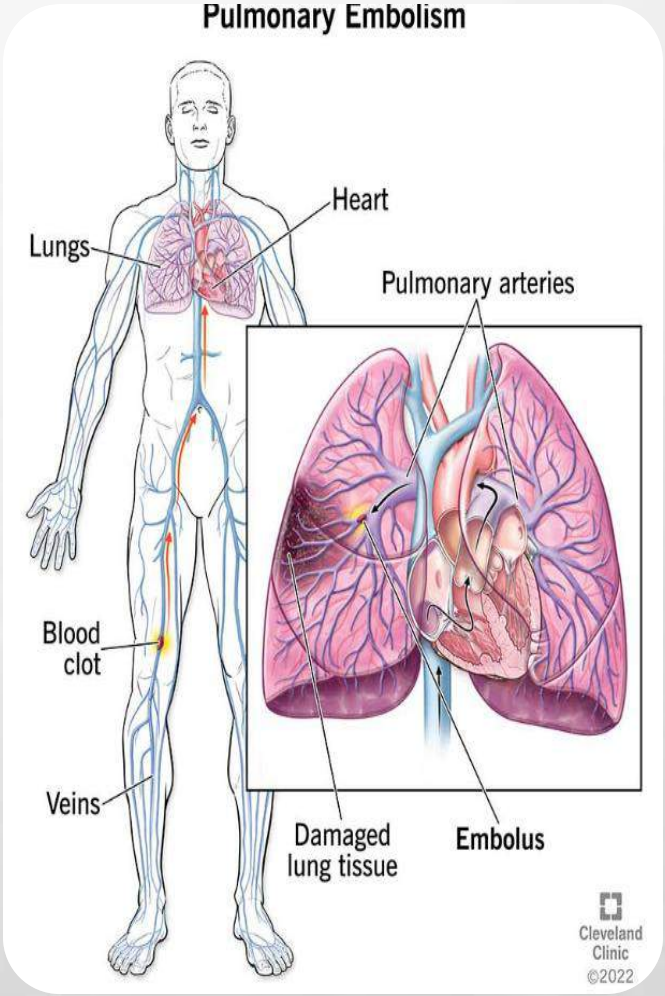
PULMONARY CAUSE: PULMONARY EMBOLISM (PE)

Pulmonary embolism (PE):

Blockage of an artery in the lungs, typically by a blood clot.

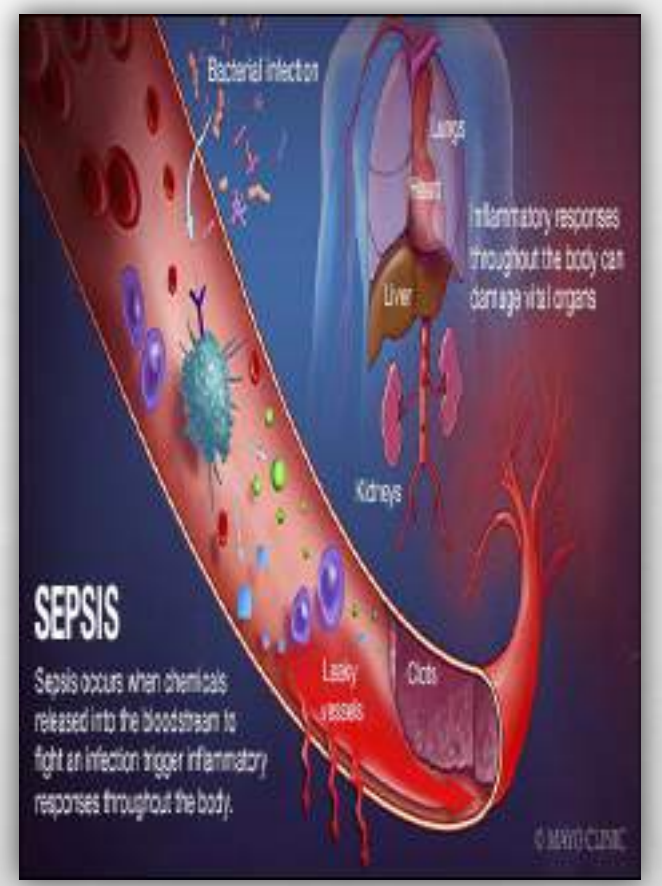
Dyspnea is the most common presenting feature of pulmonary embolus (PE)

- ✓ Biochemical marker: D-dimer.
- ✓ Interpretation: a normal (negative) d-dimer in a low-risk patient can help rule out PE.
- ✓ An elevated d-dimer requires further investigation.



DYSPNEA IN SEPSIS: SEVERE SYSTEMIC INFECTION

- ✓ Multifactorial
- ✓ Biochemical investigation: **lactate and procalcitonin.**
- ✓ Tissue hypoperfusion leads to anaerobic respiration and lactic acid build-up.
- ✓ Acute Respiratory Distress Syndrome due to capillary leak.
- ✓ Interpretation: Elevated serum lactate is a marker of tissue hypoperfusion.



HEMATOLOGIC CAUSE: SEVERE ANEMIA

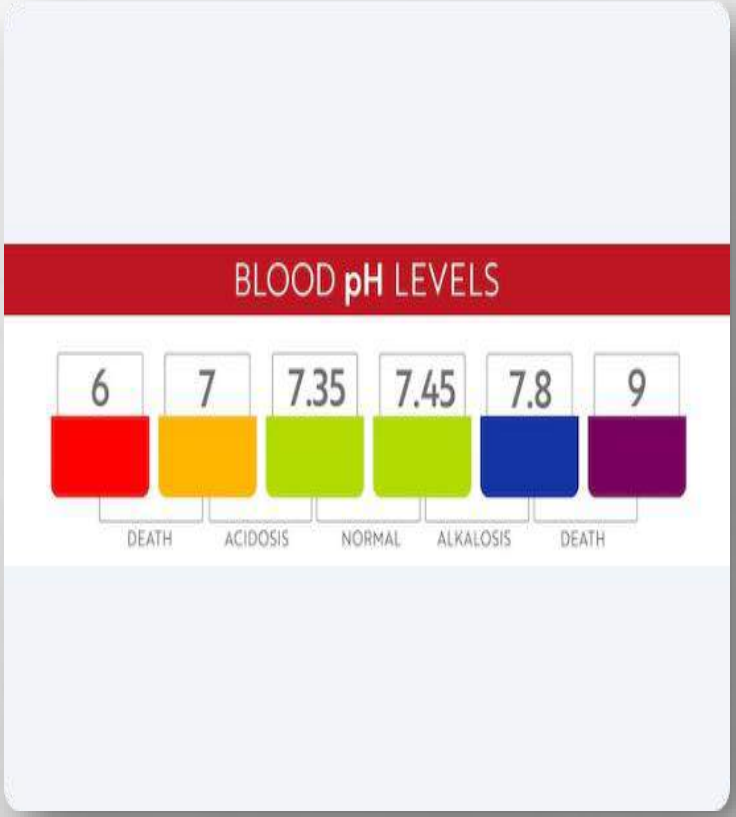
Severe Anemia

- ✓ Investigation: Hemoglobin %.
- ✓ Reduced oxygen-carrying capacity of the blood leads to shortness of breath, especially on exertion.

METABOLIC CAUSE: METABOLIC ACIDOSIS

Metabolic acidosis such as in diabetic ketoacidosis (DKA) or kidney failure.

- ✓ Biochemical investigation: ABG and serum electrolytes.
- ✓ The body compensates for acidosis by increasing the respiratory rate (Kussmaul breathing) to blow off CO_2.
- ✓ ABG will show a low p^H and low HCO_3.



RENAL AND OTHER SYSTEMIC DISEASE (RENAL FAILURE)

- ✓ **Advanced renal failure** can lead to fluid overload and metabolic acidosis.
- ✓ Fluid retention can cause pulmonary edema, and uremic acidosis can drive rapid breathing.
- ✓ **Interpretation**: elevated BUN and creatinine levels indicate impaired kidney function.

DIFFERENTIAL MATRIX: CARDIOPULMONARY

Condition	Pathophysiology	Primary Biomarker	Confirmatory Test
ACS	Myocardial Ischemia	hs Troponin I ↑	Angiography
Heart Failure	Volume Overload	BNP (High)	Echocardiography
Pneumonia	Infection	Procalcitonin (High)	CXR / CT Chest
Pulmonary Embolism	Vascular Obstruction	D-Dimer (High)	CT Angiography (CTPA)

DIFFERENTIAL MATRIX: SYSTEMIC/METABOLIC

Condition	Pathophysiology	Primary Biomarker	Confirmatory Test
Metabolic Acidosis	Acidemia Compensation	pH / HCO3 (Low)	Arterial Blood Gas
Severe Anemia	Low O2 Capacity	**Hemoglobin (Low)**	Complete blood count
Acute Renal Failure	Vol Overload / Acidosis	**Creatinine (High), BUN**	
Sepsis	Inflammation / ARDS	**Lactate / PCT**	

PREANALYTICAL ERROR

PREANALYTICAL ERROR

The most common source of mistakes in laboratory diagnostics.

To minimize pre-analytical error, the sample must be collected with

- ✓ Proper fill up of requisition form,
- ✓ Providing patients' information (Name, age, sex, full history, clinical signs and symptoms, time of collection).
- ✓ Supervising during drawing of blood using the correct anticoagulant tube,
- ✓ Transporting quickly, and
- ✓ Processing/storing according to laboratory protocol.

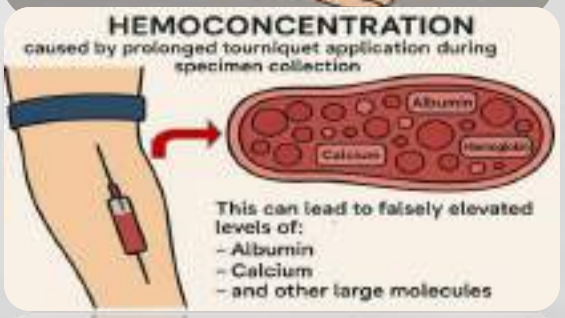
SAMPLE COLLECTION ERRORS

Patient misidentification/mislabeling:

- ✓Collecting from the wrong patient or mislabeling
- ✓Unlabeled or improperly labeled specimens

Improper phlebotomy technique:

- ✓Prolonged tourniquet application
- ✓Traumatic venipuncture: cause hemolysis.
- ✓Drawing from an I/V line site or above an I/V: results in dilution or contamination of the sample with iv fluids.



SAMPLE COLLECTION ERRORS

Sample quality/quantity issues:

- ✓ Icteric serum/plasma
- ✓ Hemolyzed blood
- ✓ Lipemic serum/plasma
- ✓ Septicemic serum/plasma

Might causes faulty results as the light pass-through sample are interrupted during colorimetric measurement.

SAMPLE COLLECTION ERRORS

Sample quality/quantity issues:

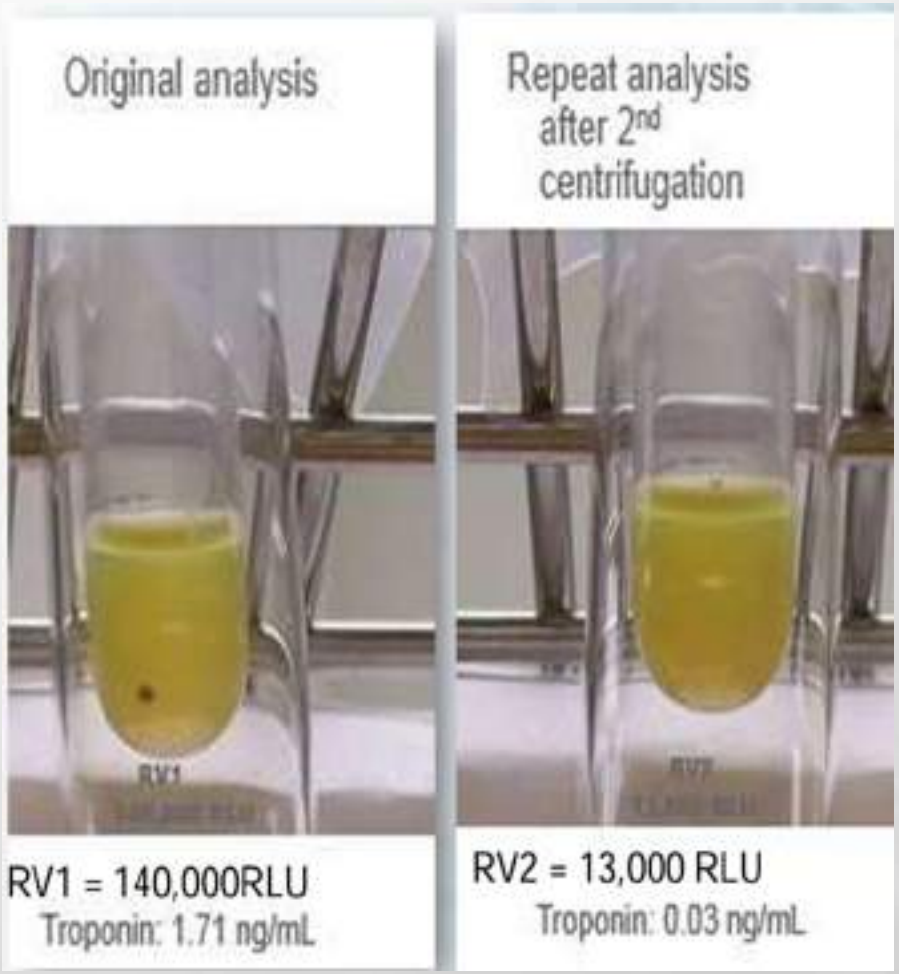
Hemolysis:

- ✓ Release of intracellular components (potassium, LDH, and magnesium) into the plasma/serum.
- ✓ Also interferes with spectrophotometric measurements.
- ✓ **Insufficient sample volume ("short draw")**:
- ✓ Incorrect ratio of blood to anticoagulant
- ✓ Errors in coagulation test results like prolong PT and APTT.

SAMPLE HANDLING ERRORS

Improper mixing of blood with the additive :

- ✓ Insufficient mixing leads to clotting (clotted blood in an anticoagulated tube),
- ✓ Vigorous shaking causes hemolysis



ANTI COAGULANT AND TUBE USE ERRORS

Incorrect Order of Draw:

- ✓ Drawing tubes in the wrong sequence leads to cross-contamination.
- ✓ Drawing an EDTA tube before a tube used for potassium measurement interferes result.
- ✓ Na-F should be used foe blood glucose estimation

TRANSPORT AND HANDLING ERRORS

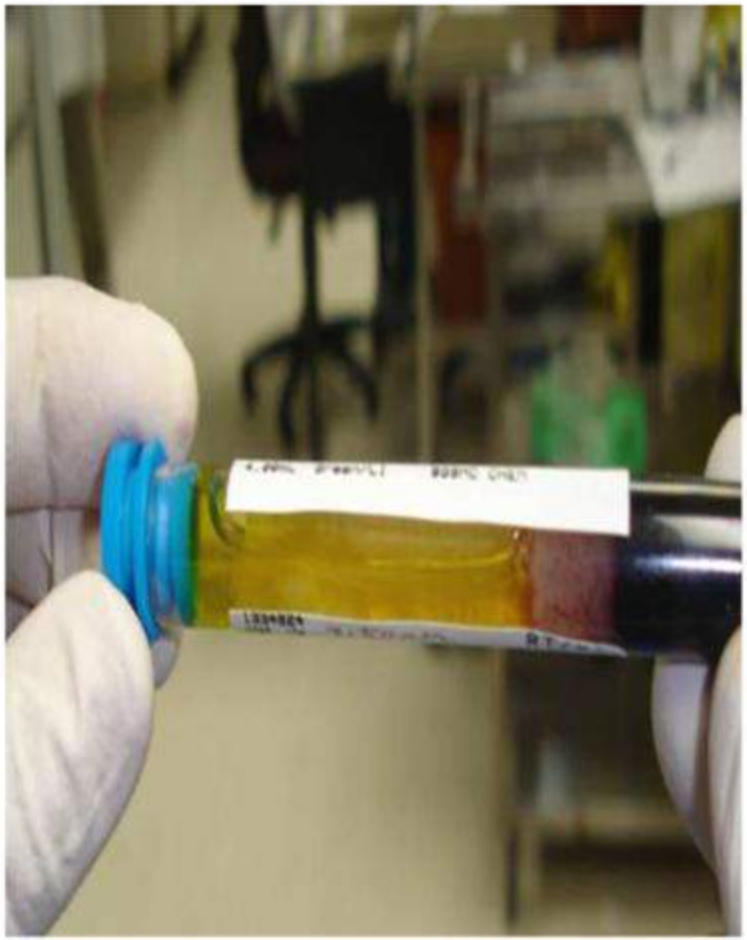
Delayed or inappropriate transport/processing:

- ✓ **Delay in separation (centrifugation):**

causing analytes to change

G**lucose levels decrease** over time due to anaerobic glycolysis.

- ✓ **Delay in centrifugation of coagulation tubes (citrate):** can lead to shortened clotting times.



📦 TRANSPORT AND HANDLING ERRORS

Improper storage/transport temperature:

- ✓ **Exposure to extreme heat or cold:**

freezing causes hemolysis.

Exposing to excessive heat can degrade temperature-sensitive analytes.

- ✓ **Failure to use a coolant:**

Without immediate cooling **blood gases**, **lactic acid** and **ammonia** can be falsely elevated.

For ABG, sample should be transported as early as possible for getting accurate result.

TAKE HOME MESSAGE

- ✓ "Biochemical evaluation is not a replacement for clinical judgment, but a powerful lens to clarify the physiological reality behind the symptom of breathlessness.

- ✓ The biochemical approach of breathlessness relies on a targeted, multi-marker panel.

TAKE HOME MESSAGE

- ✓ By rapidly identifying key biomarkers along with other investigation, clinicians can quickly narrow down the broad differential diagnosis and initiate life-saving treatment for cardiac, thromboembolic, or severe respiratory failure.

- ✓ Pre analytical error has profound impact on overall outcome of laboratory reports and diagnosis of disease. We should adopt appropriate technologies, guidelines to minimize the occurrence of errors.

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Q & A
QUESTIONS
AND
ANSWERS

THANK YOU