IN THE NAME OF GOD

Presenter;foroozan delavarian

presentation

- A 28-year-old man with dyspnea and swelling of the neck

presentation

- The patient is an 18-year-old boy
- Known case of diabetes
- Referred with chest pain, sore throat, sputum, hoarseness, cough and uncontrol BS.

- PMH: DM(From4years,Ins) +
- Covid –
- AWD –
- C/S –
- O/A –

- BP:130/70
- PR:120
- O2Sat:97%(with out o2)
- T:37.1

PHYSICAL EXAMINATION

- H/N:Swelling of the neck with tender ,mobile Post and ant cervical LAP
- Lung:bilateral wheezing
- Heart:NL
- Abdoman:NL
- EXT:NL

PARACLINIC

- VBG=PH:7.45 CO2:24   HCO3:41
- U/A :KETONE +
- ESR:110 CRP:2+ Procalcitonin:0.087
- CBC= W:19.5 Hb:13.1 plt:564
- B/C= - U/C= -

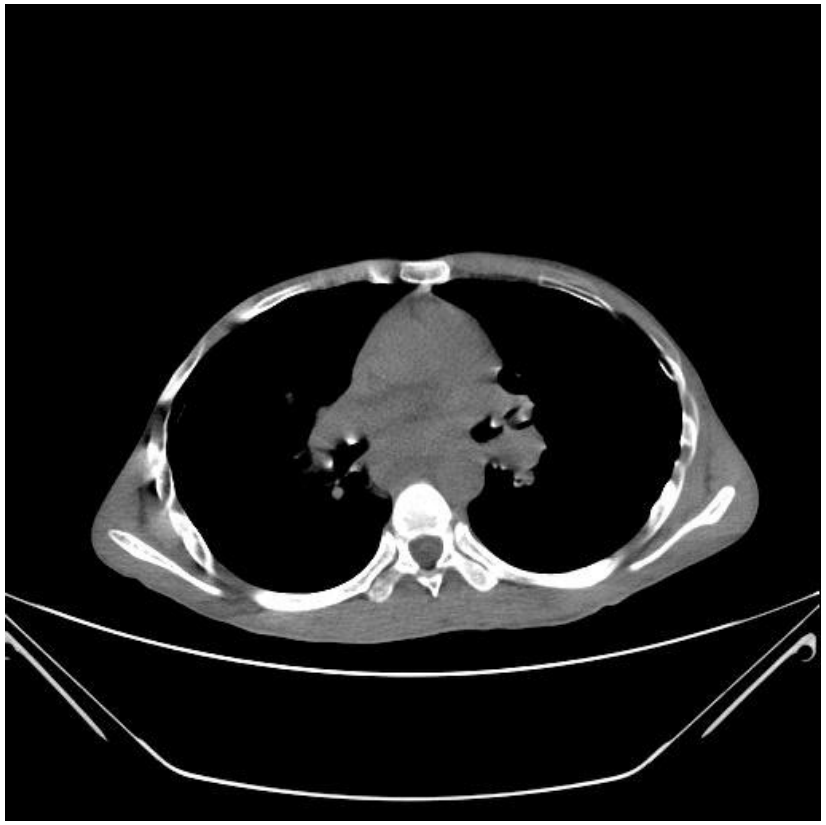
CHEST CT /NECK CT/PNS CT

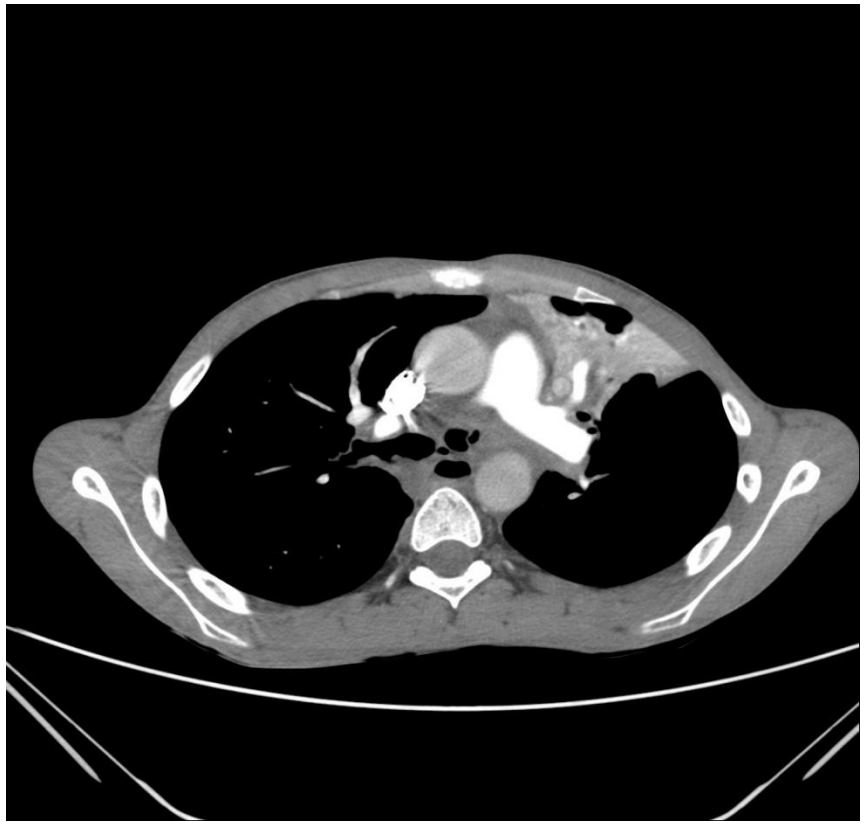
- Large collase consalidtion in left lung
- Mild left side PE
- Distention and fliud are seen in esophagus
- Ant and post cervical LAP (in neck CT)
- PNS CT= NL



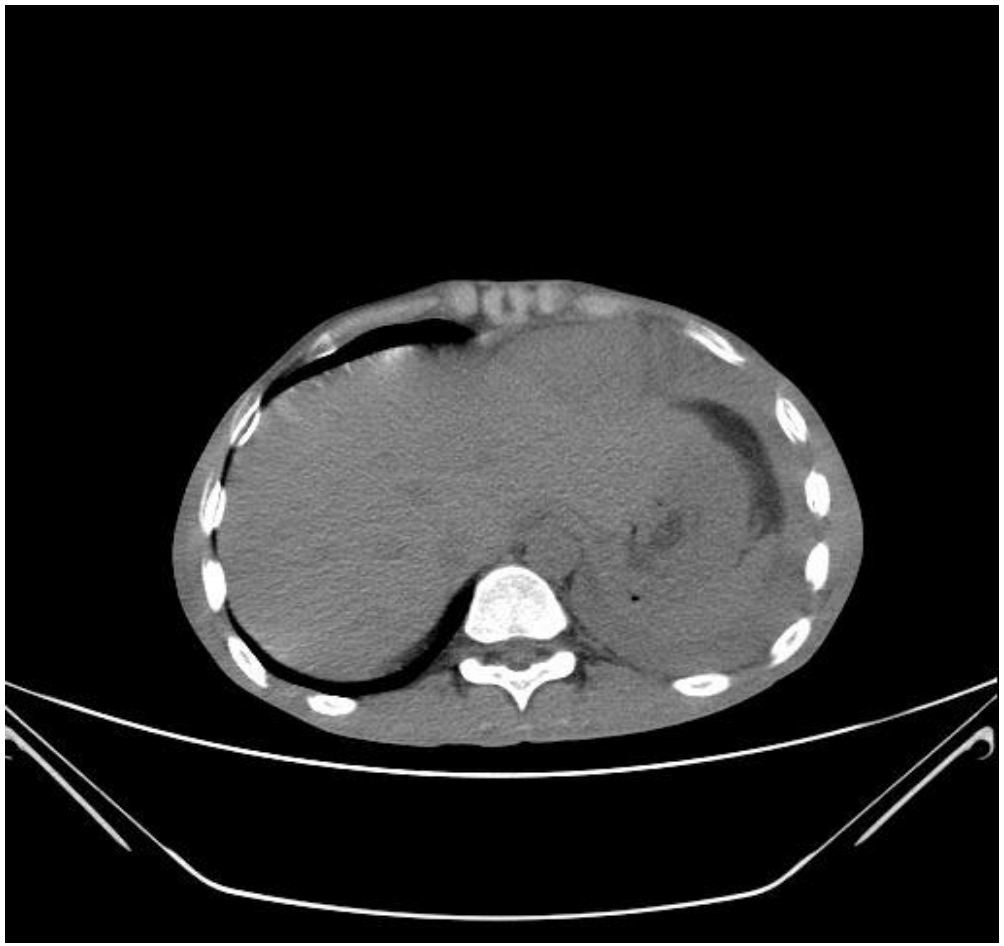


Large collase consalidtion in left lung





Distention and fliud are seen in esophagus/mediastinal LAP



Mild left side PE



Normal PNS CT

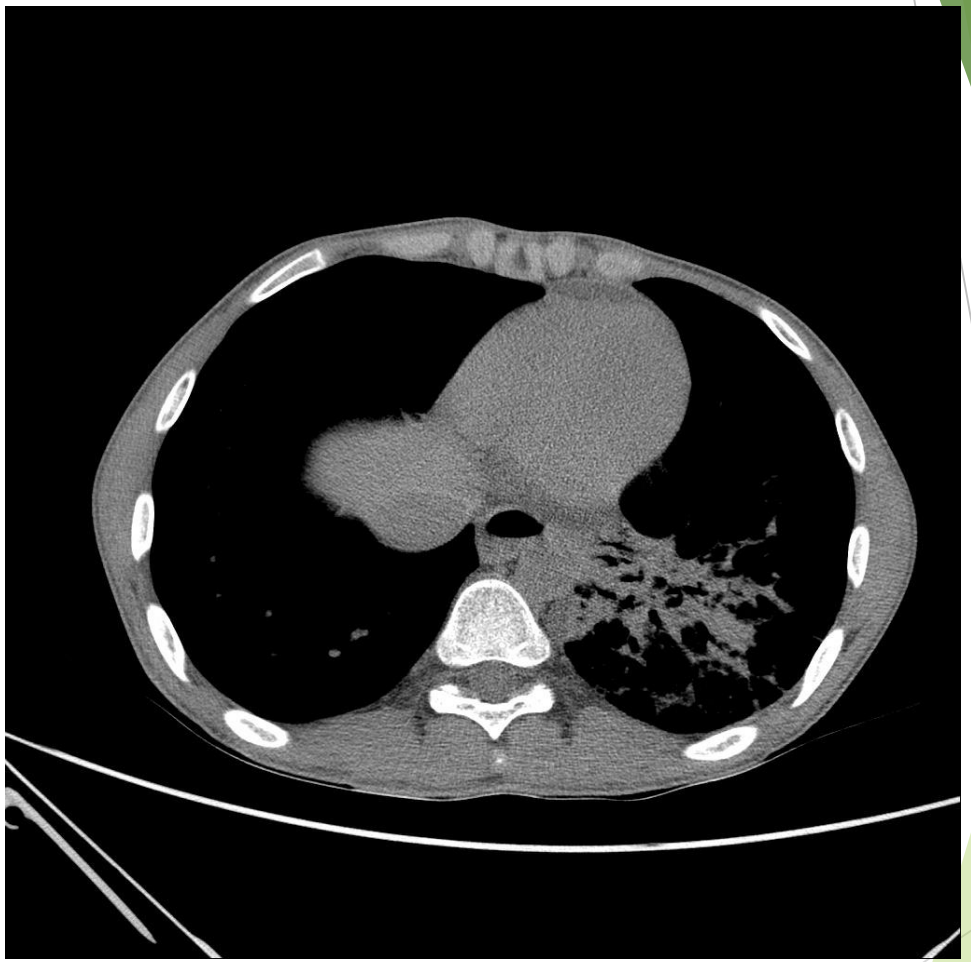
BRONCHSCOPY/Ebus

- RT: creamy tumoral lision(send BAL and cytology)
- Broncoscopy; Enobronchial lymphnode biopsy and bronchial mass biopsy= fungul(mucormycosis)
- BAL:yeast(candida)



Improvement after treatment with amphotricin





Improvement after treatment with amphotricin

Pulmonary Infectious Diseases in Association with Diabetes Mellitus;

- Approximately, 38 % of adults admitted acutely to the general hospital wards are identified to have hyperglycemia.
- Various associated adverse outcomes in hyperglycemic patients include severe hospital-acquired pneumonia, severe pulmonary infections with antimicrobial resistance, particularly *Staphylococcus aureusand Pseudomonas aeruginosa* acute myocardial infarction, trauma, diabetic nephropathy, and diabetic retinopathy.
- Airway-surface-liquid glucose concentration play a major role in protecting the lungs
  against microbial infections

- It is postulated that hyperglycemia affects the lungs by the non-enzymatic **glycosylation of collagen** and by **damaging capillaries**.
- Approximately, 50% of patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) have a blood glucose concentration of equal to or above 7.0 mmol/ liter and *Staphylococcus aureus*, particularly Methicillin-resistant *Staphylococcus aureus* (MRSA) (relative risk 2.1 (95% Confidential Interval (CI) 1.2, 3.8)) is more frequently isolated from sputum .
- Glucose containing in the airway secretions of intubated patients is associated with ICU acquisition of respiratory infections.

- In ICU-admitted patients, glucose in airway secretions are associated with subsequent MRSA acquisition of MRSA (relative risk 1.8 (95 % CI 1.1, 3.6)), indicating that glucose precedes infection. Bacterial organisms utilize saccharides both as substrates for catabolic reactions to provide energy for growth and as carbon for the biosynthesis of new cellular materia.
- Both *Staphylococcus aureus* and *Pseudomonas aeruginosa* possess transporters that allow cellular uptake of D-glucose and are able to metabolize D-glucose.

- A previous *in vitro* study demonstrated that glucose concentration of approximately 50mmol/liter can induce algD transcription and increase the production of alginate, a viscous exopolysaccharide that causes lung deterioration in cystic fibrosis.
- One example of a number of nonimmune mechanisms that have evolved to prevent bacterial infection is controlling airway glucose concentration.

- ASL chemistry has an effect on the secretion and action of antibacterial molecules, in addition to directly affecting bacterial growth and survival.
- Glucose can also inhibit the function of surfactant protein D.

Diabetic lung disease: fact or fiction?

Pathophysiology of lung dysfunction in patients with DM;

The currently known underlying mechanisms for lung dysfunction in patients with DM include hyperglycemia.
hyperinsulinemia

1-autonomic neuropathy

2- oxidative stress

3- micro/macroangiopathy of alveolar capillaries and pulmonary arterioles

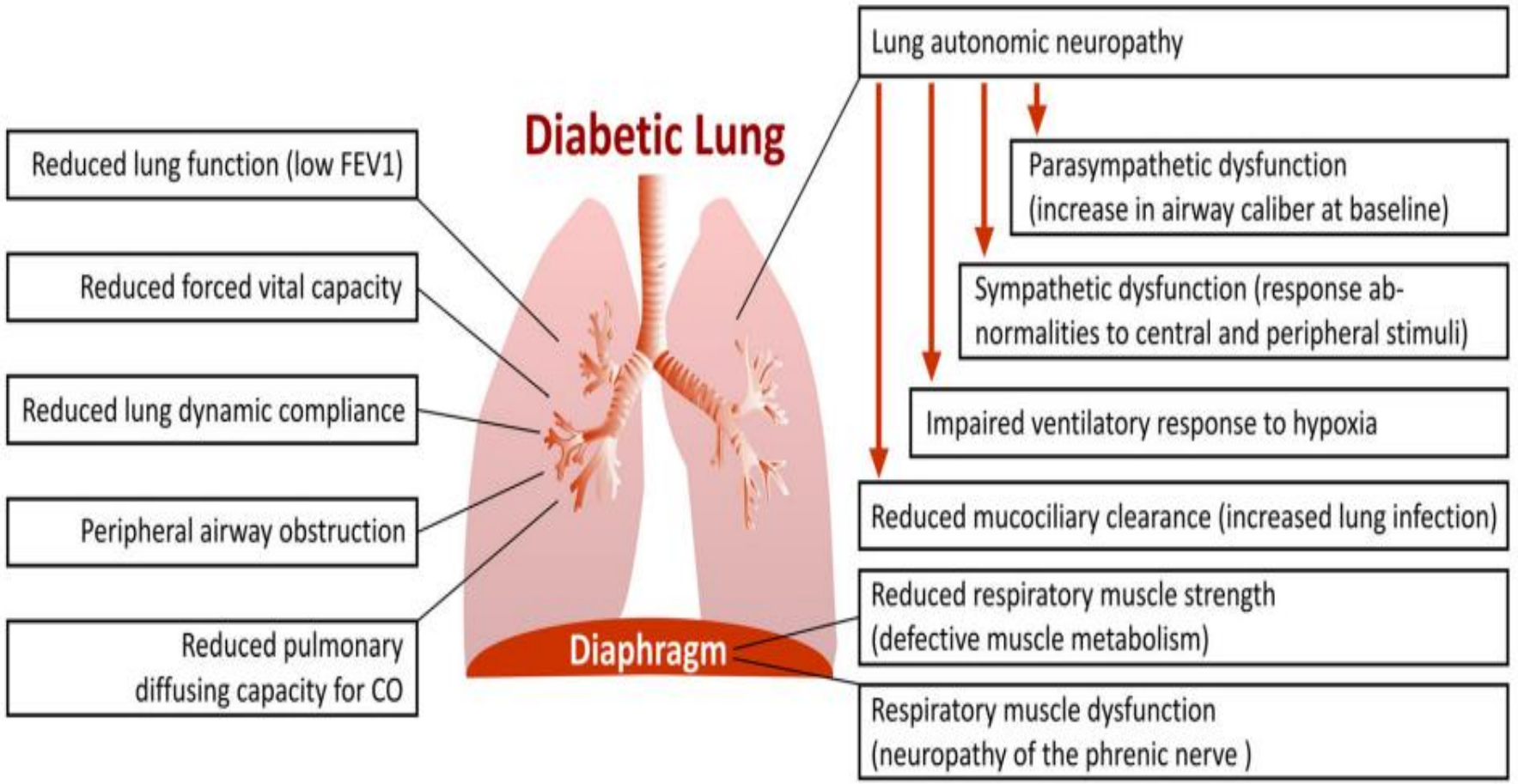
4-glycosylation of tissue proteins

5- collagen and elastin changes

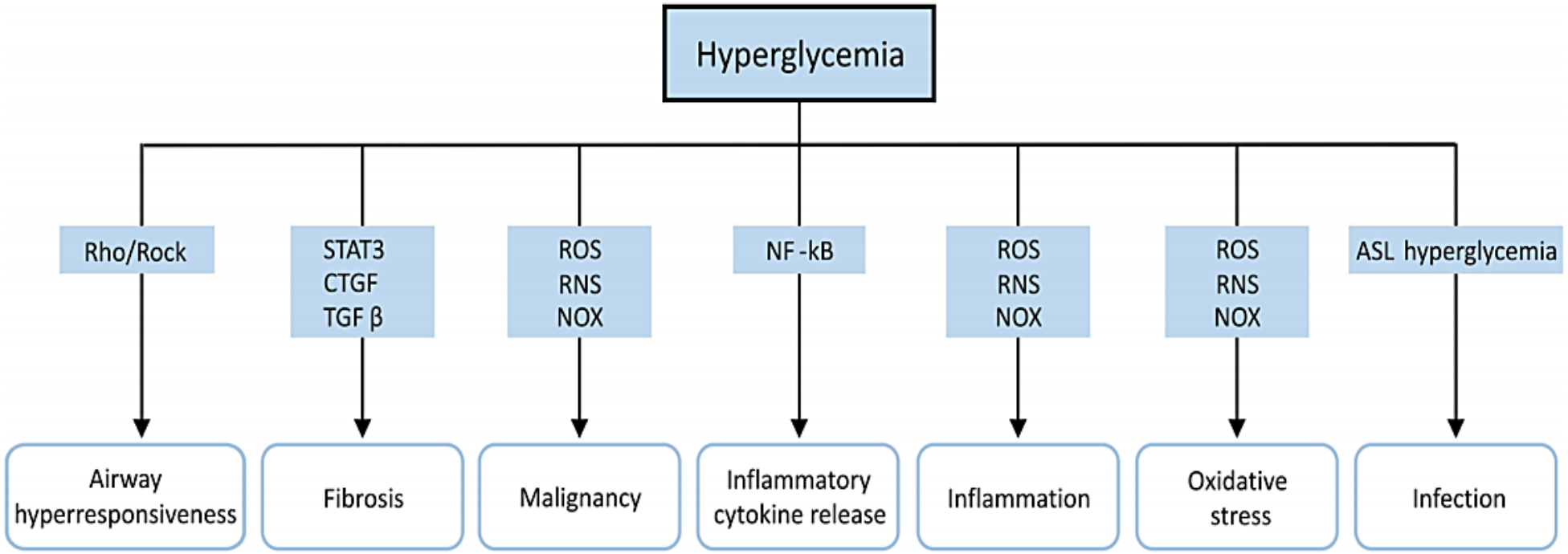
6-alteration of connective tissue

7-Surfactant dysfunction

8- malfunction of respiratory muscles


Diabetic Lung
Reduced lung function (low FEV1)
Reduced forced vital capacity
Reduced lung dynamic compliance
Peripheral airway obstruction
Reduced pulmonary diffusing capacity for CO
Diaphragm
Lung autonomic neuropathy
Parasympathetic dysfunction (increase in airway caliber at baseline)
Sympathetic dysfunction (response ab-normalities to central and peripheral stimuli)
Impaired ventilatory response to hypoxia
Reduced mucociliary clearance (increased lung infection)
Reduced respiratory muscle strength (defective muscle metabolism)
Respiratory muscle dysfunction (neuropathy of the phrenic nerve)

- reduction in the lung function of diabetic patients characterized by low forced expiratory volume in one second is two to three times faster than that of normal nonsmoking subjects.


Hyperglycemia
Rho/Rock
STAT3
CTGF
TGF β
ROS
RNS
NOX
NF -kB
ROS
RNS
NOX
ROS
RNS
NOX
ASL hyperglycemia
Airway hyperresponsiveness
Fibrosis
Malignancy
Inflammatory cytokine release
Inflammation
Oxidative stress
Infection

DM and lung cancer

- Previous studies have shown a positive correlation between DM and colorectal, breast, endometrial, kidney and pancreatic cancer.(controversy)

DM and lung infection

- A wide range of neutrophil and macrophage functions, including chemotaxis, adherence, phagocytosis, ability to kill phagocytosed microorganisms with free radicals and respiratory burst are impaired in DM.
- A reduced complement system C4 and humoral immunity associated with a reduced number and response of T cells increase the susceptibility of diabetic patients to infection.

- Loose junctions between airway epithelial cells, which increase the transepithelial glucose gradient along with an increase in the glucose concentration of the airway surface liquid due to hyperglycemia, may dampen the airway defense against infection, resulting in lung acterial overgrowth in DM.
- staphylococcus aureus and Streptococcus pneumoniae; influenza virus; opportunistic pathogens such as Klebsiella pneumoniae, Pseudomonas aeruginosa; and fungal infections with Mucorales and Aspergillus species, are frequent causes of lung infection in DM.

- It has been reported that pneumonia has the greatest , incidence and severity among diabetic patients with elevated HbA_{1c} levels.
- DM is associated with a poor prognosis, increasing the rate of pleural effusion and mortality in community-acquired pneumonia.
- Initial administration of the first antibiotic given not later than 8 h of triage is associated with fewer complications and lower mortality in diabetic patients with pneumonia.

DM and pulmonary tuberculosis

- DM may increase the risk of developing active tuberculosis by approximately three-fold Diabetic patients are.
- also prone to develop drug-resistant tuberculosis resulting in antituberculosis treatment failure, disease relapse after the completion of treatment and increased mortality.
- Alveolar residential cells (monocytes and macrophages) play an important role in the pathogenesis of tuberculosis.

DM and asthma

- Overall, there is increasing evidence for a positive correlation between the occurrence of T1DM and symptoms of asthma at the population level.
- It has been suggested that autoimmune diseases such as T1DM and allergic diseases such as asthma may have some common immunopathogenetic mechanisms, influenced by environmental factors such as lifestyle and living conditions.

- T2DM and obesity may increase the risk of asthma to two and three times greater than that in normal subjects, respectively
- Obesity decreases the effectiveness of asthma therapy and increases the rate of hospitalizations due to asthma exacerbations to levels nearly five times greater than those of asthmatic subjects without obesity

- It is concluded that not only type 1 and type 2 diabetic patients but also offsprings of diabetic mothers are at increased risk of developing asthma

DM and chronic obstructive pulmonary disease (COPD);

- Chronic inflammation and systemic oxidative stress— associated with increased levels of CRP, TNF-α, IL-1, IL-6, and fibrinogen—are shared features in COPD and DM.
- random blood glucose ≥7 mmol/l is associated with poor outcomes and increased COPD-related morbidity and mortality in hospitalized patients in the intensive care unit .
- Hyperglycemia (i.e., random blood glucose ≥7 mmol/l) upon presentation to the intensive care unit was found to be a useful predictor of poor outcomes and to confer the greatest risk of treatment failure with nonin- vasive ventilation in patients with severe COPD.

- It has been shown that inhaled corticosteroids in patients with COPD are not associated with an increased risk of new onset DM, hyperglycemia or a significant change in HbA1c levels .
- On the other hand, metformin treatment over a 2– year follow-up period in patients with coexisting DM and COPD reduced emergency room visits and hospitalization, especially in low-complexity COPD.

DM and cystic fibrosis

- DM is the most common and life-threatening complication of cystic fibrosis due to pancreatic insufficiency and the abnormal timing and delayed and blunted secretion of insulin.
- CFRD adversely affects lung function (average forced expiratory volume in one second of 52% in cystic fibrosis patients with diabetes compared with 72% in nondiabetic patients)

- The severity of pulmonary dysfunction is positively correlated with the degree of insulin deficiency (causing glucose intolerance and protein catabo- lism) in patients with CFRD .
- Some studies have found that insulin treatment improves lung function and increases forced expiratory volume in one second in patients with CFRD.

DM and acute lung injury (ALI) / acute respiratory distress syndrome (ARDS)

- The reports on the association of DM and ALI or ARDS reveal inconsistent findings .
- It has been shown that T2DM does not affect the lung physiopathology in patients with ARDS
- The preventive mechanism of DM against ARDS development is not completely understood. Studies on experimentally induced DM show that the preventive effect may be attributed to decreased neutrophil numbers and function, impaired nuclear factor κ-light-chain-enhancer' of activated B- cells activation, reduced superoxide generation, insulin growth factor and its receptor deficiency, leptin resistance and lower concentrations of inflammatory cytokines such as tumor necrosis factor-α, IL-1β, IL-6, and prostaglandin E2.

- In clinical studies intensive insulin therapy shortened the time of mechanical ventilation and decreased mortality and/or morbidity rates among hyperglycemic patients with prolonged intensive care unit stays, regardless of whether they had a history of diabetes or not.

DM and pulmonary hypertension

- . Epidemiological studies have revealed that diabetic patients are at higher risk for developing pulmonary hypertension associated with markedly worse survival .

- More detailed human and animal studies are recommended to elucidate the exact underlying mechanism that may spare the pulmonary vasculature from (or make it prone to) toxic effects of DM, such as hyperglycemia, hyperinsulinemia, oxidative stress and chronic inflammation. The incidence of pulmonary hypertension in different types of DM should be defined in more robust epidemiological studies.