

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



آشنایی با عوامل شیمیایی جنگی یا تروریستی

دکتر مصطفی قانع

متخصص داخلی – فوق تخصص بیماری های ریه
استاد دانشگاه علوم پزشکی بقیه الله (عج)

Chemical Agents

- Pulmonary agents: chlorine, phosgene, cyanide
- Blister agents: Lewisite and the nitrogen mustard agents
- Nerve Agents: Tabun, sarin and VX
- Lachrymators: CN (Mace), CS
- Insecticides: Malathion, parathion and sevin

شناسایی با شکایات و علائم

- Pulmonary Agents: asphyxia, mucosal edema and bronchorhea.
- Blister Agents: Burn-like phenomenon affecting eyes, bronchi and skin
- Nerve agents: nausea, fasciculations, rhinorrhea, bronchorrhea, sweating, drooling, diarrhea, loss of consciousness, flaccid paralysis, apnea

تشخيص باليني غاز اعصاب

- **Eyes:** Miosis, tearing, conjunctival injection (pain, dim vision, blurred vision)
- **Nose:** Rhinorrhea
- **Airway:** Bronchoconstriction, bronchorrhea, dyspnea, cough
- **GI:** Hypermotility, nausea, vomiting, diarrhea, cramps
- **Skeletal muscles:** Fasciculations, twitching, paralysis, muscle weakness
- **CNS:** High dose Loss of Consciousness, seizures, apnea; Low dose cognitive difficulties
- **Other:** Salivation and diaphoresis

تشخيص باليني غاز اعصاب

- Mild: Miosis, rhinorrhea, dyspnea, weakness, blurred vision
- Severe: *as above with* – Loss of consciousness, seizures and apnea – death
- Onset: Within seconds to minutes of exposure
- Treatment: Atropine and pralidoxime auto-injectable.

تشخيص باليني غاز اعصاب

- Mild: Local sweating and fasciculations
- Moderate: Nausea, vomiting, diarrhea, weakness
- Severe (as above plus): Loss of consciousness, seizures, apnea – death
- Onset: 5 min to 18 hrs
- Treatment: Atropine, diazepam and 2-PAM (2 pyridine-aldoxime-methiodide), ventilatory and cardiovascular support.

عوامل تاؤلزا

- Mustard gas vapor causes no pain on contact.
- Onset: 4 to 8 hrs (range 2 to 24 hrs)
- Initial/Mild: Erythema, periorbital edema, blurring, oro-nasal edema, hoarseness, non-productive cough
- Late/Severe: Corneal damage, leukocytopenia, decreased RBC & platelets, sepsis, airway obstruction, atelectasis, sepsis, DIC, death
- TX: Early skin decontamination, anti-lewisite, support care similar to burn management.

عوامل خفه کننده

- Severe: Brief period of hyperpnea, seizures, decreased breathing rate, arrhythmias, apnea – death
- Mild: Nausea, vertigo, weakness, shortness of breath.
- TX: Amyl nitrite by inhalation; sodium nitrite and sodium thiosulfate IV; assisted ventilation and oxygen

درمان و مراقبت

- *Early* and GENTLE Skin decontamination
- Pulmonary Agents: OXYGEN, amyl nitrate inhalation, IV sodium nitrate or sodium thiosulfate
- Blister agents: *Early* and *Gentle* skin surface decontamination to include the eyes, anti-Lewsite for internal injury, & burn wound care
- Nerve agents: Atropine sulfate, 2-Pam (2 pyridine-aldoxime-methiodide) and Valium (diazepam)

مدیریت و مراقبت کادر درمان

- Military hospitals treating Iranian casualties of the Iran-Iraq War had casualties in hospital personnel
- The Tokyo Experience: 10% of EMT, firefighters and police became casualties – none seriously; 110 hospital staff became casualties, 1 nurse required hospitalization.

پیام اصلی

1. آموزش
2. آمادگی
3. ارتباط



Etiology

Burden of Injury

Pathology

Pathophysiology

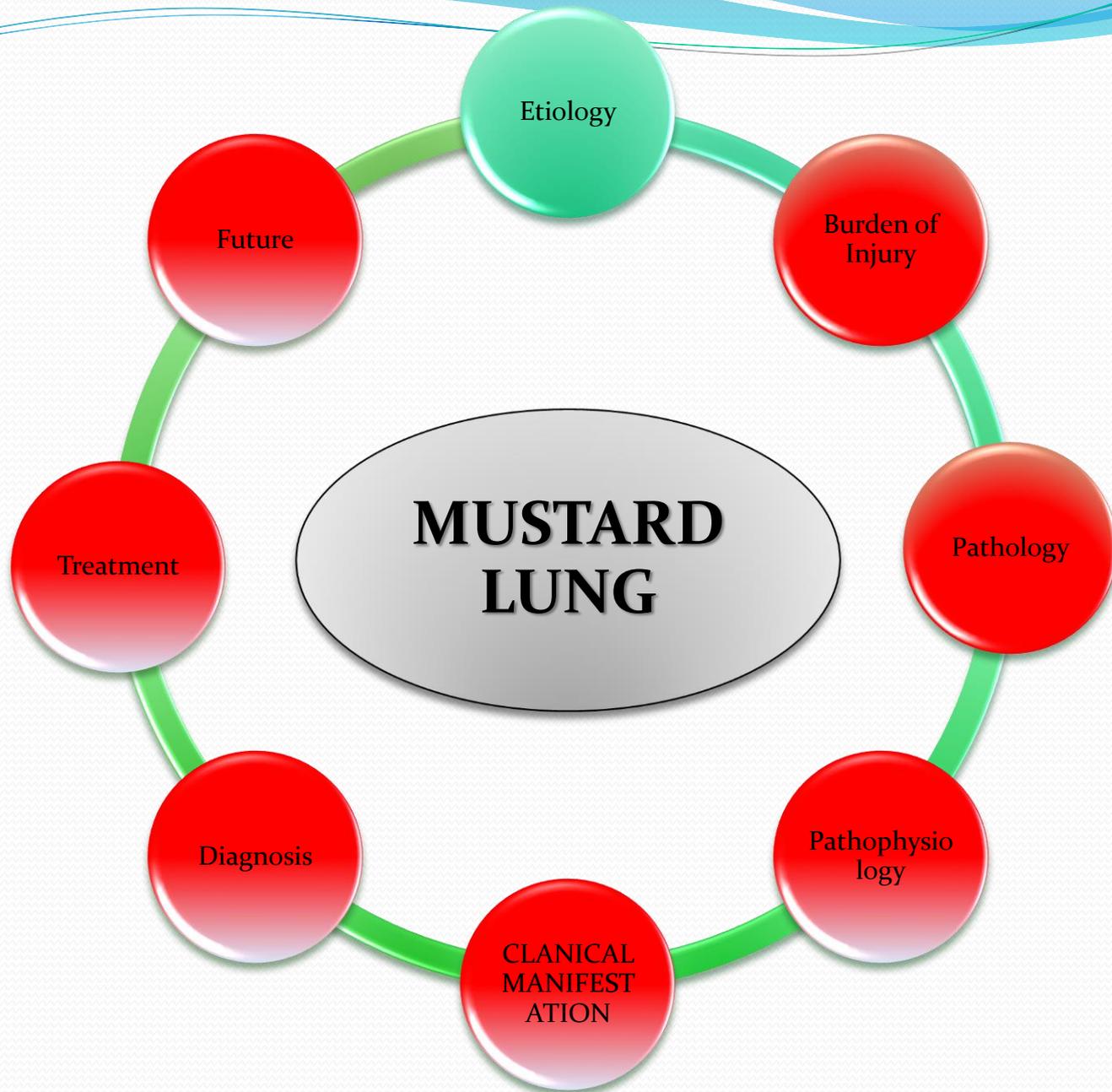
CLINICAL MANIFESTATION

Diagnosis

Treatment

Future

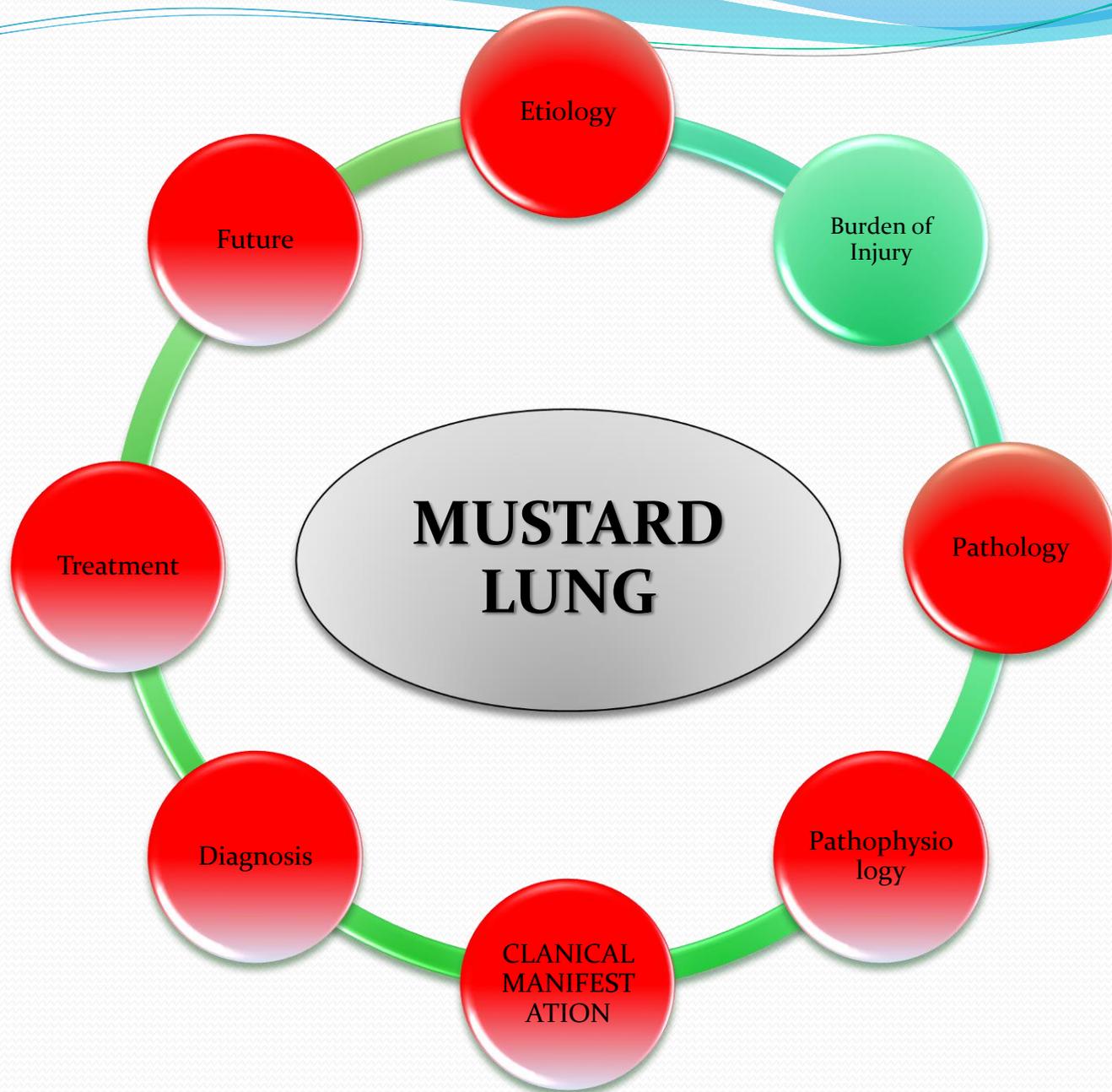
MUSTARD LUNG



Etiology and burden of disease:

- Mustard gas is a chemical alkylating agent that can be frequently absorbed through skin, respiratory system ,genital tract ,and ocular system.
- Khateri S, **Ghanei M**, Keshavarz S, Soroush M, Haines D. J Occup Environ Med. 2003 Nov;45(11):1136-43. Reviewb(Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent.)





Etiology

Burden of Injury

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CLANICAL
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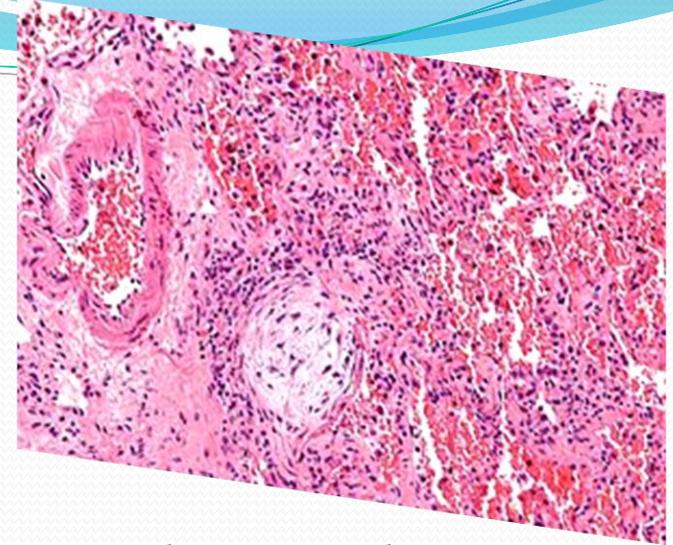
**MUSTARD
LUNG**

Burden of disease:

- approximately 34000 Iranian known to have sustained Mustard lung exposure during the IRAN , IRAQ war of 1980-1988 and survived over decades afterward were screened for distribution of the most commonly occurring medical problems.
- Khateri S, **Ghanei M**, Keshavarz S, Soroush M, Haines D. J Occup Environ Med. 2003 Nov;45(11):1136-43. Reviewb(Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent.)

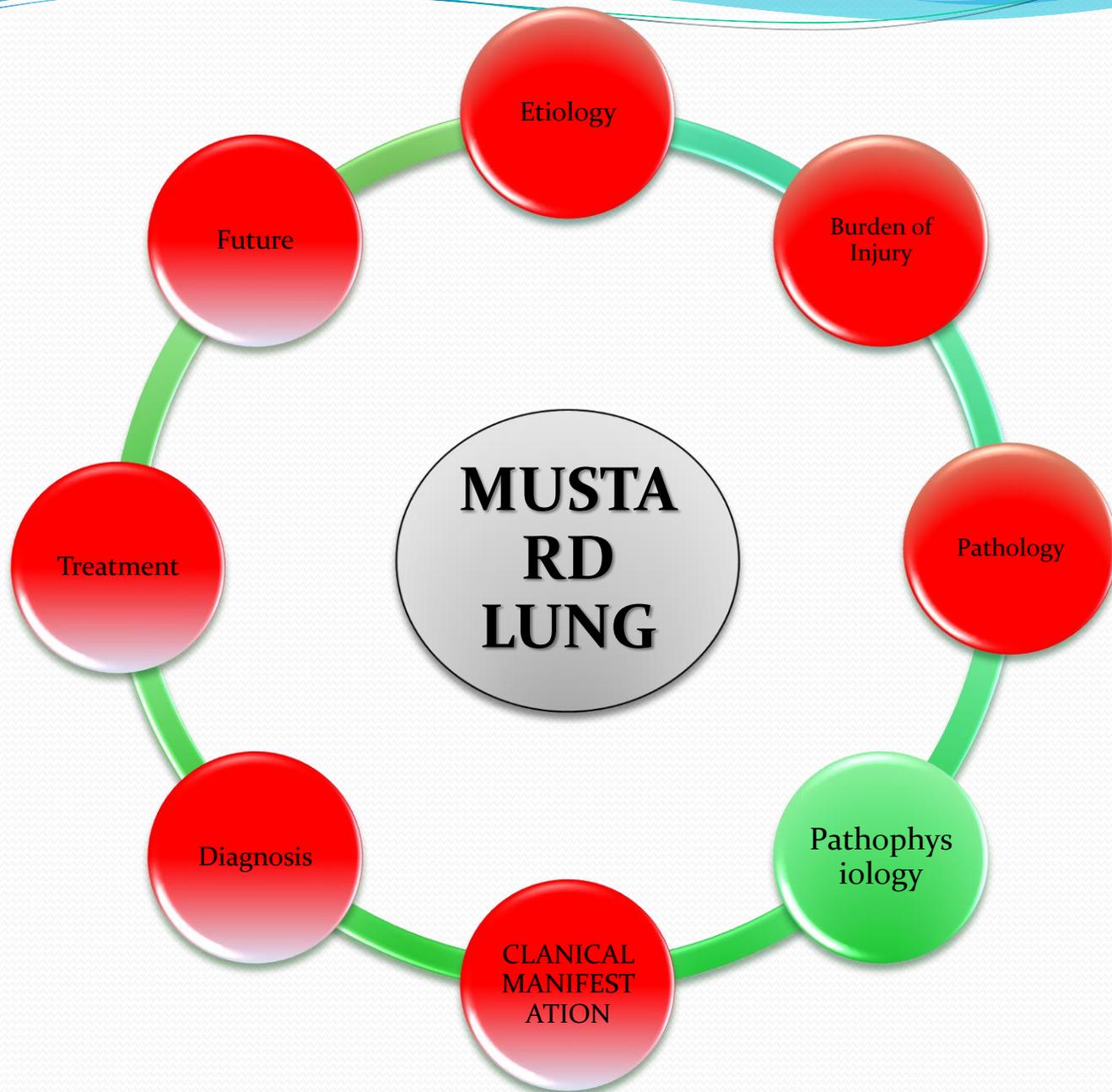


Pathologic changes:



- A direct type of bronchiolitis is seen in mustard exposed patients.
- submucosal fibrosis of bronchioles leading to partial or complete occlusion of small airways.
- Inflammatory cell infiltrates may or may not be present.
- Organizing pneumonia may be present.
- Lung fibroblasts play a major role in pathologic changes.

- Saber H, Saburi A, Ghanei M. *Inhal Toxicol.* 2012 Nov;24(13):900-6. doi: 10.3109/08958378.2012.725783. Review. (Clinical and paraclinical guidelines for management of sulfur mustard induced bronchiolitis obliterans; from bench to bedside.)



PATHOPHYSIOLOGY:

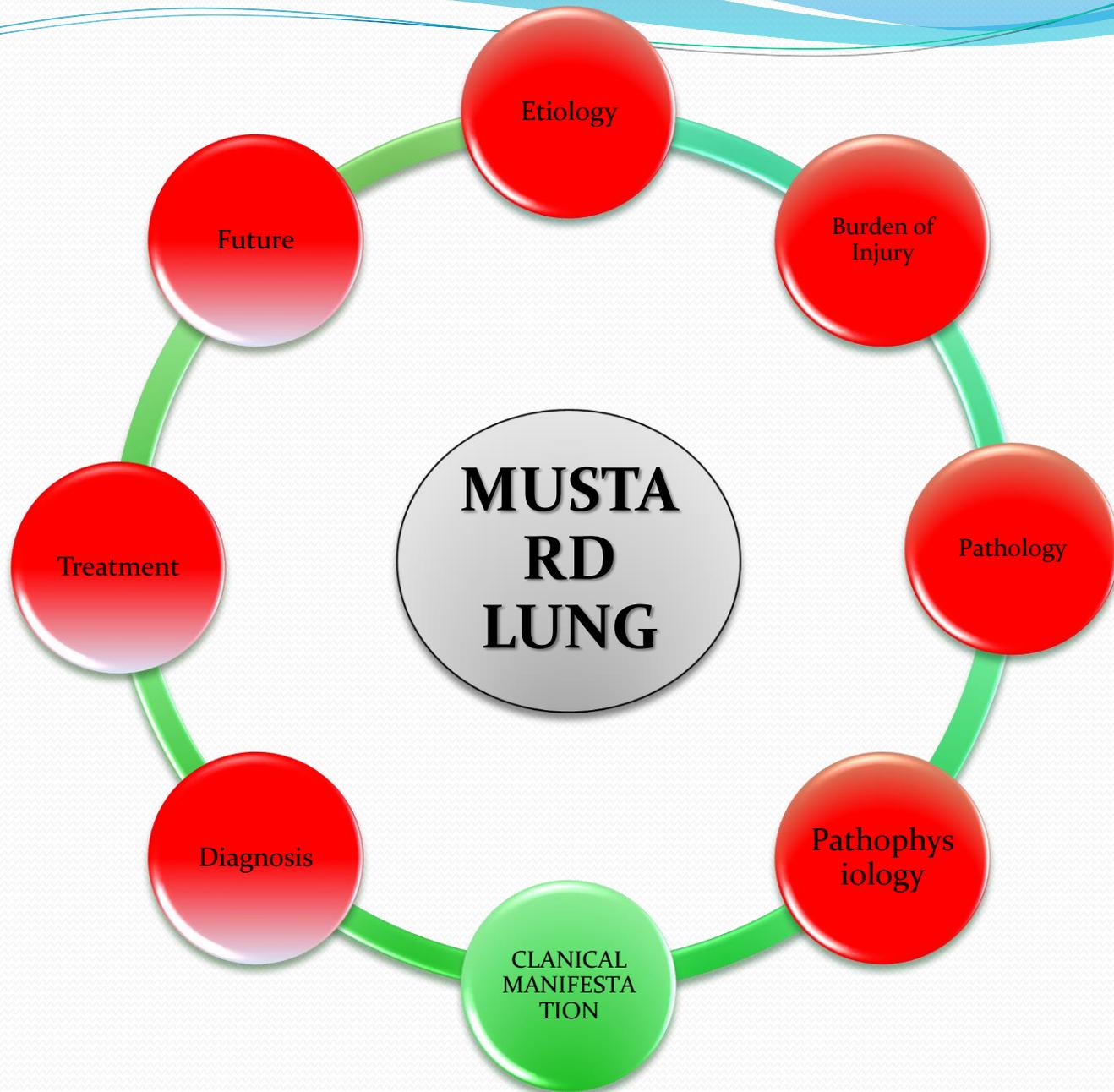
Oxidative stress
—

apoptosis
—

pathophysiology

inflammation
—

Protease and
antiprotease
—



Clinical manifestations:

- General early symptom after SM exposure include: dyspnea ,tachypnea and respiratory distress (severe flu like symptoms)
- General late symptom include:chronic cough ,haemoptysis ,dyspnea ,sleep disorders and
- Incidence of respiratory events and nocturnal hypoxemia during sleep in Mustard exposed patients were high.
- Mustard gas can impair different parameters of speech aerodynamics
- Vahedi E, Fazeli Varzaneh AR, Ghanei M, Afsharpaiman S, Poursaleh Z. Sleep Breath. 2014 Dec;18(4):741-8(The effect of nightly nasal CPAP treatment on nocturnal hypoxemia and sleep disorders in mustard gas-injured patients)
- Heydari F, **Ghanei M.** J Commun Disord. 2011 May-Jun;44(3):331-5(Effects of exposure to sulfur mustard on speech aerodynamics.)

Clinical manifestation:

- Respiratory problems are the greatest cause of long term disability among these patients that are manifested as
 - bronchiectasis,
 - large airway narrowing and
 - airway remodeling.
 - Chronic laryngitis was seen in considerable number of exposed victims, nearly 20 years after high exposure to Mustard gas.
-
- Akhavan A, Ajalloueyan M, **Ghanei M**, Moharamzad Y. Clin Toxicol (Phila). 2009 Feb;47(2):142-4(Late laryngeal findings in sulfur mustard poisoning.)

Clinical manifestation:

- Moderate to severe exposure to sulfur Mustard has equal risk of late pulmonary complications, while mild exposure has lesser risk.
- Hemoptysis per se in exposed SM patients could not be considered as a valuable evidence of lung malignancy, and it is more likely due to other pathogenesis of respiratory system in SM patients.
- **Ghanei M**, Adibi I, Farhat F, Aslani J. Chron Respir Dis. 2008;5(2):95-100(Late respiratory effects of sulfur mustard: how is the early symptoms severity involved?)
- **Ghanei M**, Eshraghi M, Jalali AR, Aslani J. Environ Toxicol Pharmacol. 2006 Sep;22(2):128-3(Evaluation of latent hemoptysis in Sulfur Mustard injured patients.)

Clinical manifestation:

- Since a high majority of patients had more than a single cause of chronic cough, multiplicity of cause of chronic cough in patients is indicative of evaluation for possible exposure for chemical fumes, especially SM.
- Direct toxic effect of SM can lead to tracheobronchial stenosis with different degrees of involvement ranging from diffuse tracheal stenosis to stenosis of the isolated left main bronchus or glottic and subglottic stenosis.
- **Ghanei M**, Hosseini AR, Arabbaferani Z, Shahkarami E. Environ Toxicol Pharmacol. 2005 Jul;20(1):6-10(Evaluation of chronic cough in chemical chronic bronchitis patients.)
- **Ghanei M**, Hosseini AR, Arabbaferani Z, Shahkarami E. Environ Toxicol Pharmacol. 2005 Jul;20(1):6-10(Tracheobronchial stenosis following sulfur mustard inhalation.o

Clinical manifestation:

- Many civilian and military people who have been presented in contaminated area without sign and symptom at the time of exposure, are suffering from respiratory problems later.
- Major GERD symptoms(include heartburn and acid regurgitation once or more per week)among the individuals with the past history of exposure to SM toxic gas, is substantially higher than normal populations.
- **Ghanei M**, Fathi H, Mohammad MM, Aslani J, Nematizadeh F. Inhal Toxicol. 2004 Jul;16(8):491-5(Long-term respiratory disorders of claimers with subclinical exposure to chemical warfare agents.)
- Karbasi A, Aliannejad R, **Ghanei M**, Sanamy MN, Alaeddini F, Harandi AA. J Res Med Sci. 2015 Jul;20(7):636-9(Frequency distribution of gastro esophageal reflux disease in inhalation injury: A historical cohort study.)

Clinical manifestation:

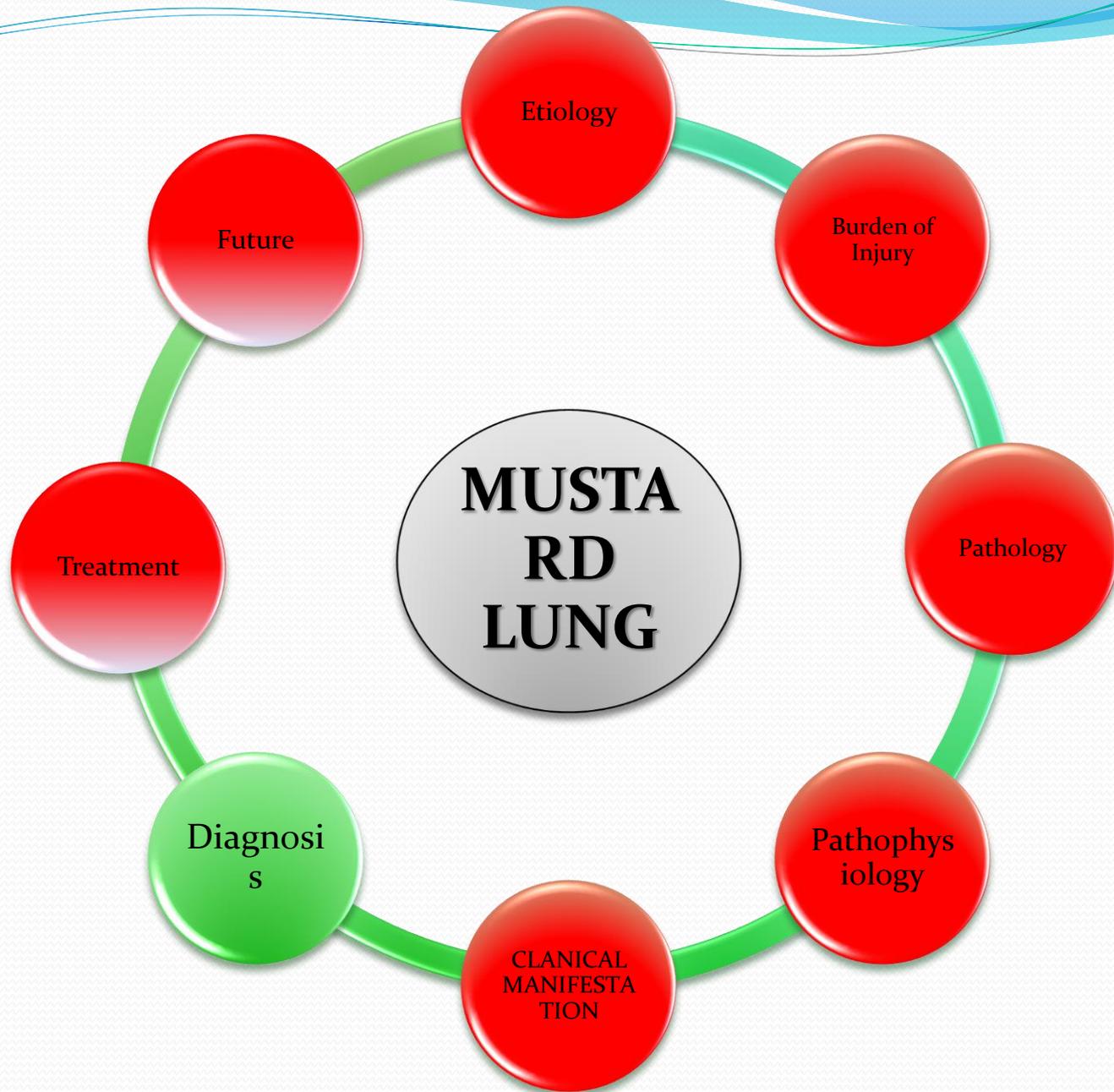
- The presence of esophagitis due to GERD would increase the AHR and treatment with pantoprazole would decrease AHR in patients with proved esophagitis and no previous history of asthma after 6 month.
- Most of BO patients after exposure to SM suffer from GERD (90%).
- GERD could be considered as an aggregative factor for exacerbation in this patients.
- Karbasi A, Ardestani ME, **Ghanei M**, Harandi AA. J Res Med Sci. 2013 Jun;18(6):473-6(The association between reflux esophagitis and airway hyper-reactivity in patients with gastro-esophageal reflux.)
- Aliannejad R, Hashemi-Bajgani SM, Karbasi A, Jafari M, Aslani J, Salehi M, **Ghanei M**. J Res Med Sci. 2012 Aug;17(8):777-81(GERD related micro-aspiration in chronic mustard-induced pulmonary disorder.)

Clinical manifestation:

- Bronchiolitis obliterans ,along with other lung disorders ,can be considered as contributors in pathogenesis of esophagitis in MG exposed patients.

- Arefnasab Z, **Ghanei M**, Noorbala AA, Alipour A, Babamahmoodi F, Babamahmoodi A, Salehi M. Iran J Public Health. 2013 Sep;42(9):1026-33(Distal esophagitis in patients with mustard-gas induced chronic cough.)





Diagnosis:

- CXR: non specific
- HRCT (expiratory): significant air trapping
- PFT: 85% is near normal or mild obstruction ,and 15% show moderate to severe obstruction.
- Bronchoscopy: secretion,inflammation and sometimes airway narrowing.
- CBC: leukocytosis and elevated inflammatory markers(ESR and CRP).

Diagnosis: Heart Failure

- Echocardiography: diastolic dysfunction and RV septum abnormality.
- Our result present base line Right Ventricle value for MG exposed patients and show mild but significant changes after 3 decades.further cellular and molecular studies are needed to evaluate underlying mechanisms of MG cardiotoxicity
- Khosravi A, Motamedi MA, Kazemi-Saleh D, Aslani J, Ghanei M. J Clin Ultrasound. 2018 Feb;46(2):160-164(Long-term right ventricular changes in mustard-exposed patients: A historical cohort.)

Imaging :Chest HRCT

- HRCT can be a very useful method for differentiating between Mustard lung, resistant asthma and lung injuries due to cigarette smoking.
 - HRCT is neither pathognomonic of the disease nor a good predictor of disease severity but it might be suggestive of Mustard lung injuries.
 - The result show that air trapping and TBM are correlated, both as long term sequel in Mustard gas exposed cases. Because air trapping is highly suggestive of bronchiolitis obliterans, we conclude that both bronchiolitis obliterans and TBM are caused by single underlying process affecting small and large airways, respectively, in this group of patients.
 - Chest HRCT finding of bronchiectasis, air trapping, MPA, SWT, BWT were seen in SM patients < after exposure to SM. This finding suggest the diagnosis of BO.
-
- **Ghanei M**, Ghayumi M, Ahakzani N, Rezvani O, Jafari M, Ani A, Aslani J. Radiol Med. 2010 Apr;115(3):413-20(Noninvasive diagnosis of bronchiolitis obliterans due to sulfur mustard exposure: could high-resolution computed tomography give us a clue?)
 - Heydari F, **Ghanei M**. J Commun Disord. 2011 May-Jun;44(3):331-5(Noninvasive diagnosis of bronchiolitis obliterans due to sulfur mustard exposure: could high-resolution computed tomography give us a clue?)
 - **Ghanei M**, Akbari Moqadam F, Mohammad MM, Aslani J. Am J Respir Crit Care Med. 2006 Feb 1;173(3):304-9. Epub 2005 Oct 27(Tracheobronchomalacia and air trapping after mustard gas exposure.)
 - **Ghanei M**, Mokhtari M, Mohammad MM, Aslani J. Eur J Radiol. 2004 Nov;52(2):164-9(Bronchiolitis obliterans following exposure to sulfur mustard: chest high resolution computed tomography.)

Cardio Pulmonary Exercise Test

- Abnormal gas exchange may be present in sulfur Mustard patients. They have low VO_2 in CPET. Impaired cell O_2 consumption could be hypothesis for low VO_2 in this cases.
- Aliannejad R, Saburi A, **Ghanei M**. *Pulm Circ*. 2013 Apr;3(2):414-8. doi: 10.4103/2045-8932.113174(Cardiopulmonary exercise test findings in symptomatic mustard gas exposed cases with normal HRCT.)
- Saber H, Saburi A, **Ghanei M**. *Inhal Toxicol*. 2012 Nov;24(13):900-6(Clinical and paraclinical guidelines for management of sulfur mustard induced bronchiolitis obliterans; from bench to bedside.)

Differential Diagnosis

- Asthma
- COPD(due to cigarette smoking)
- Infection
- Interstitial lung disease





**MUSTA
RD
LUNG**

Etiology

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Pathology

Pathophys
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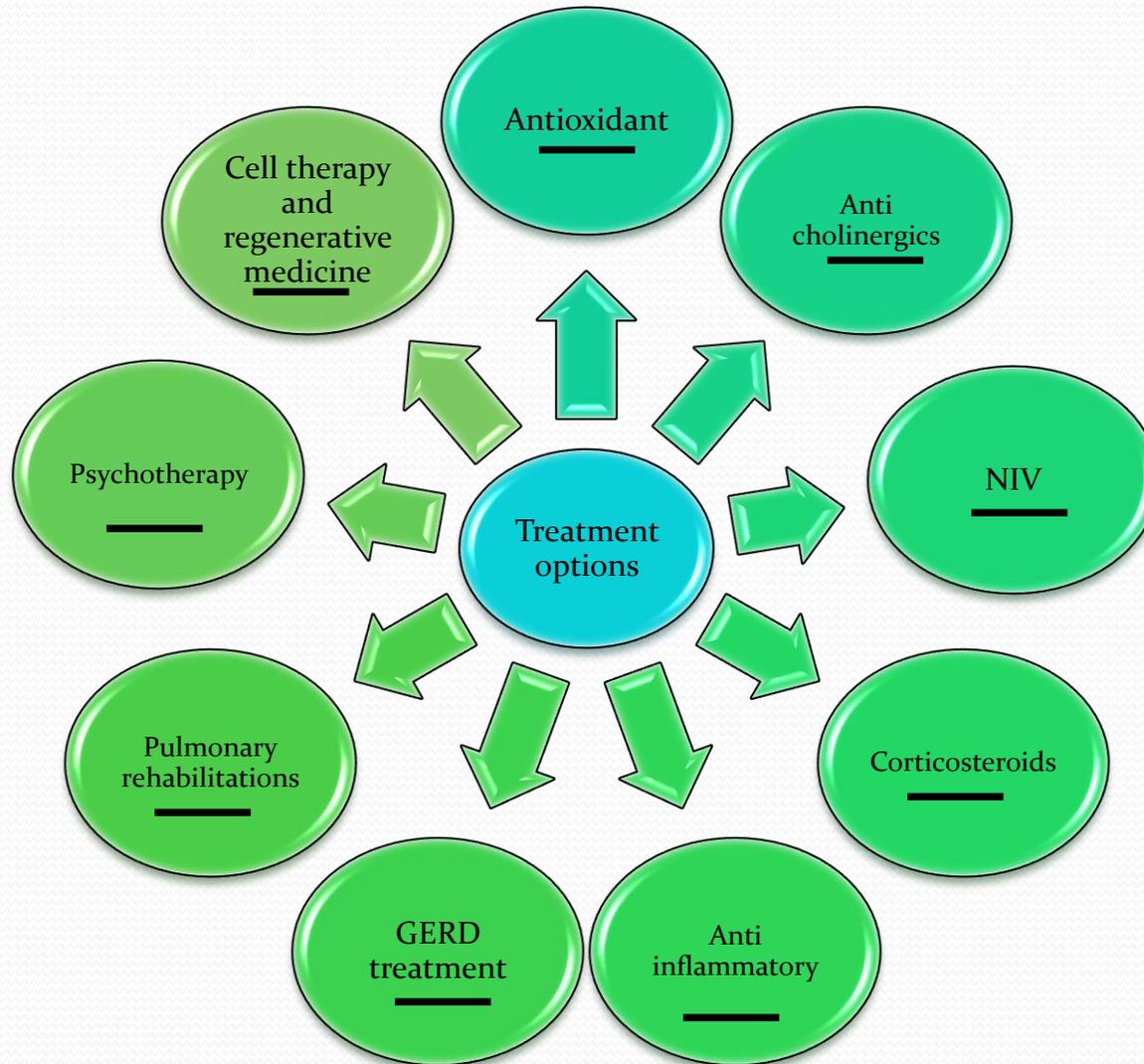
CLANICAL
MANIFESTA
TION

Diagnosis

Treatment

Future

Treatment:



Anti oxidant:

- antioxidant therapy with potent antioxidants such as N-acetylcysteine and curcumin may be helpful to mitigate SM-induced OS damages.
- Regarding the promising effect of curcuminoids on the measures of systemic oxidative stress, clinical symptoms and HRQOL. These phytochemicals may be used as safe adjuvants in patients suffering from chronic SM-induced pulmonary complications who are receiving standard treatments.
- Panahi Y, **Ghanei M**, Bashiri S, Hajhashemi A, Sahebkar A. Drug Res (Stuttg). 2015 Nov;65(11):567-73 (Effects of Curcuminoids-Piperine Combination on Systemic Oxidative Stress, Clinical Symptoms and Quality of Life in Subjects with Chronic Pulmonary Complications Due to Sulfur Mustard: A Randomized Controlled Trial.)
- Panahi Y, **Ghanei M**, Hajhashemi A, Sahebkar A. J Diet Suppl. 2016;13(1):93-105. doi: 10.3109/19390211.2014.952865. Epub 2014 Aug 29 (Short-term Curcuminoid Supplementation for Chronic Pulmonary Complications due to Sulfur Mustard Intoxication: Positive Results of a Randomized Double-blind Placebo-controlled Trial.)
- Panahi Y, **Ghanei M**, Hashjin MM, Rezaee R, Sahebkar A. Crit Rev Eukaryot Gene Expr. 2017;27(3):247-266 (Perspective in future pharmacological approach to sulfur mustard lung injuries.)



- Curcuminoids were safe and well tolerated throughout the trials. Short term adjunctive therapy with curcuminoids can suppress systemic inflammation in patients suffering from SM induced chronic pulmonary complications.
- NAC increases the main antioxidant product of lung named Glutathione (GSH) in these patients. Every therapeutic that can enhance cellular antioxidant supply may be effective on both mentioned pathways.

New antioxidant treatment

- *Z. multiflora* reduces inflammatory cells and oxidant biomarkers, while increase antioxidant biomarkers and improved PFT tests in SM exposed patients in a two moth treatment period.

Anti cholinergics:

- Inhalation of tiotropium bromide in combination with pulmonary rehabilitation could improve some plethysmographic lung volumes and clinical outcomes in patient with chronic pulmonary diseases due to SM.

- Shohrati M, Jalili M, Afshar H, Najafian B, Qazvini A, Zaeri M, Amini Harandi A, **Ghanei M**. Iran Red Crescent Med J. 2015 Dec 5;17(12):e20026(Efficacy of Tiotropium Bromide and Rehabilitation Treatment on Pulmonary Function of Patients With Sulfur Mustard Lung Injury.)



NIV:

- NIV can be used as an effective new palliative method in the treatment of Mustard lung and Mustard airway disorders. Subjects with very severe disease benefitted differently from NIV.

- Aliannejad R, Peyman M, **Ghanei M**. Respir Care. 2015 Sep;60(9):1324-9. doi: 10.4187/respcare.02900. Epub 2015 May 19(Noninvasive Ventilation in Mustard Airway Diseases.)



Corticosteroids:

- inhaled corticosteroids and long acting beta2 agonists are effective in treatment of patients with chronic bronchiolitis following exposure to sulfur mustard. A medium dose of fluticasone salmeterol has the same effect on the airway reversibility, rather than a very high dose beclomethasone with only short term acting beta agonist.
- Short term corticosteroid therapy has a significant effect on lung function of 50% with Mustard gas induced bronchitis in exacerbation occasions. We suggest a short term bolus steroid treatment to triage the patients into responder for subsequent treatment.
- **Ghanei M**, Shohrati M, Harandi AA, Eshraghi M, Aslani J, Alaeddini F, Manzoori H. *Inhal Toxicol.* 2007 Aug;19(10):889-94. (Inhaled corticosteroids and long-acting beta 2-agonists in treatment of patients with chronic bronchiolitis following exposure to sulfur mustard.)
- **Ghanei M**, Khalili AR, Arab MJ, Mojtahedzadeh M, Aslani J, Lessan-Pezeshki M, Panahi Y, Alaeddini F. *Basic Clin Pharmacol Toxicol.* 2005 Nov;97(5):302-5 (Diagnostic and therapeutic value of short-term corticosteroid therapy in exacerbation of mustard gas-induced chronic bronchitis.)



Anti inflammatory:

- Administration of clarithromycin and NAC for the treatment of BO in SM exposed patients improve symptom and pulmonary function. This result may have been related to therapeutic effects of a macrolide antibiotic on chronic bronchitis and BO in this patients.
- Azithromycin has also been effective in improving clinical conditions, pulmonary function tests, inflammatory indexes, and life quality of the veterans.
- **Ghanei M, Abolmaali K, Aslani J.** *Curr Ther Res Clin Exp.* 2004 Nov;65(6):495-504. (Efficacy of concomitant administration of clarithromycin and acetylcysteine in bronchiolitis obliterans in seventeen sulfur mustard-exposed patients: An open-label study.)



GERD Treatment

- Long term treatment with high dose omeprazole improve GERD as well as cough, and quality of life ,but not changed respiratory function indices in sulfur Mustard cases with respiratory symptoms.
- Emami MH, Talaei M, Panahi Y, Saburi A, **Ghanei M**. J Res Med Sci. 2014 Nov;19(11):1027-33.(Efficacy of omeprazole on cough, pulmonary function and quality of life of patients with sulfur mustard lung injury: A placebo-control, cross-over clinical trial study.)



Treatment of eye complications

- As indicated clinically, patients who suffer from delayed ocular complications of sulfur mustard (DOCS) benefit from:
 - treatments for dry eyes
 - therapeutic contact lenses
 - amniotic membrane transplantation
 - blepharorrhaphy
 - tarsorrhaphy
 - limbal stem cell transplantation
 - corneal transplantation,
 - topical steroids
 - immunosuppressive

- 
- In spite of penetrating keratoplasty, lamellar keratoplasty and keratolimbal allograft had a good long-term survival.

Treatment of skin complications

- Some of the delayed cutaneous complications (DCCS) such as itching affects the quality of life of victims:
 - Regular but not frequent showering and bathing
 - applying sunscreen compounds
 - topical corticosteroids
 - systemic antihistamines
 - Several compounds such as capsaicin cream, pimecrolimus, IFN- γ , phenol-menthol; Aloe vera/olive oil cream, cetirizine, doxepine, and hydroxyzine were evaluated in DCCS patients with some benefits

Pulmonary rehabilitations:

STUDY PROTOCOL

Open Access



Pulmonary rehabilitation in patients with mustard gas lung disease: a study protocol for a randomized controlled trial

Mohamad Reza Sedighi Moghadam¹, Mostafa Ghanei^{2*}, Klaus Kenn³ and Nicholas S. Hopkinson⁴

Abstract

Background: More than 60,000 people have health problems due to chemical weapons exposure during the Iran–Iraq war. Respiratory consequences of mustard gas exposure are common and disabling; medical interventions have limited effect. Patients complain of cough, sputum, breathlessness and exercise limitation. We hypothesized that patients with this condition would benefit from pulmonary rehabilitation.

Methods: We outline the protocol for an assessor-blind, two-armed, parallel-design randomized controlled clinical trial (IRCT2016051127848N1). Sixty patients with respiratory disease due to documented sulfur mustard gas exposure will be randomized to either take part in a 6-week pulmonary rehabilitation programme or receive usual care. Inclusion criteria include forced expiratory volume in 1 second < 80% predicted and Medical Research Council dyspnoea score ≥ 3 . The primary endpoint will be the change in cycle endurance time at 70% baseline exercise capacity at 6 weeks. Lung function, physical activity, the strength and endurance of the quadriceps muscle, and quality of life will also be compared. Outcomes will be assessed at 6 weeks and 12 months. Health care utilization will also be assessed.

Discussion: If the study confirms that rehabilitation is effective for patients with mustard gas lung disease this should prompt provision of the intervention to this patient group.

Trial registration: Iranian Registry of Clinical Trials, [IRCT2016051127848N1](https://www.irct.ir/IRCT2016051127848N1). Registered on 24 May 2016.

Keywords: Pulmonary rehabilitation, Chemical warfare, Mustard gas, Randomized controlled trial

Symptom relief:

- Nebulized morphine have clinical benefit on respiratory complaint of patient due to exposure to SM, without significant side effect.
- There are benefit of using helium. Oxygen adjunct with non invasive positive pressure ventilation in patient exposed to SM with acute respiratory decompensation.

- Shohrati M, **Ghanei M**, Harandi AA, Foroghi S, Harandi AA. Pulm Med. 2012;2012:610921(Effect of nebulized morphine on dyspnea of mustard gas-exposed patients: a double-blind randomized clinical trial study.)
- **Ghanei M**, Rajaeinejad M, Motiei-Langroudi R, Alaeddini F, Aslani J. Heart Lung. 2011 May-Jun;40(3):e84-9(Helium:oxygen versus air:oxygen noninvasive positive-pressure ventilation in patients exposed to sulfur mustard.)

Psychotherapy:

- Spirituality is key factor among a participants in accepting and coping with their chronic illness complications.
 - MBSR(Mindfulness based stress reduction) can improve individuals quality of life but not lung function in chemically pulmonary injured veterans.
 - freedom technique (EFT) may be a new therapeutic approach for improving psychological and immunological factors.
-
- Ebadi A, Ahmadi F, **Ghanei M**, Kazemnejad A. Nurs Health Sci. 2009 Dec;11(4):344-50(Spirituality: a key factor in coping among Iranians chronically affected by mustard gas in the disaster of war.)
 - Arefnasab Z, **Ghanei M**, Noorbala AA, Alipour A, Babamahmoodi F, Babamahmoodi A, Salehi M. Iran J Public Health. 2013 Sep;42(9):1026-33.(Effect of Mindfulness Based Stress Reduction on Quality of Life (SF-36) and Spirometry Parameters, in Chemically Pulmonary Injured Veterans.)
 - Babamahmoodi A, Arefnasab Z, Noorbala AA, **Ghanei M**, Babamahmoodie F, Alipour A, Alimohammadian MH, Riazi Rad F, Khaze V, Darabi H. Iran J Allergy Asthma Immunol. 2015 Feb;14(1):37-47(Emotional Freedom Technique (EFT) Effects on Psychoimmunological Factors of Chemically Pulmonary Injured Veterans.)



- 
- The physicians in charge of veterans emphasize the importance of a healthy lifestyle, appropriate financial/social/cultural supports, and a degree of reassurance and supportive care on the clinical improvement of patients.

Immunotherapy

- Interferon gamma (IFN- γ) and helium: oxygen combination were also used in severe exposure with good results
- IFN gamma has favorable effects on the quality of life and alleviates respiratory symptoms in patients suffering from chronic SM induced pulmonary complications. A modulation of cytokines and oxidative stress appears responsible for the clinical efficacy of IFN gamma.
- Panahi Y, Ghanei M, Vahedi E, Ghazvini A, Parvin S, Madanchi N, Bagheri M, Sahebkar A. J Immunotoxicol. 2014 Jan-Mar;11(1):72-7(Effect of recombinant human IFN γ in the treatment of chronic pulmonary complications due to sulfur mustard intoxication.)

Cell therapy and regenerative medicine:

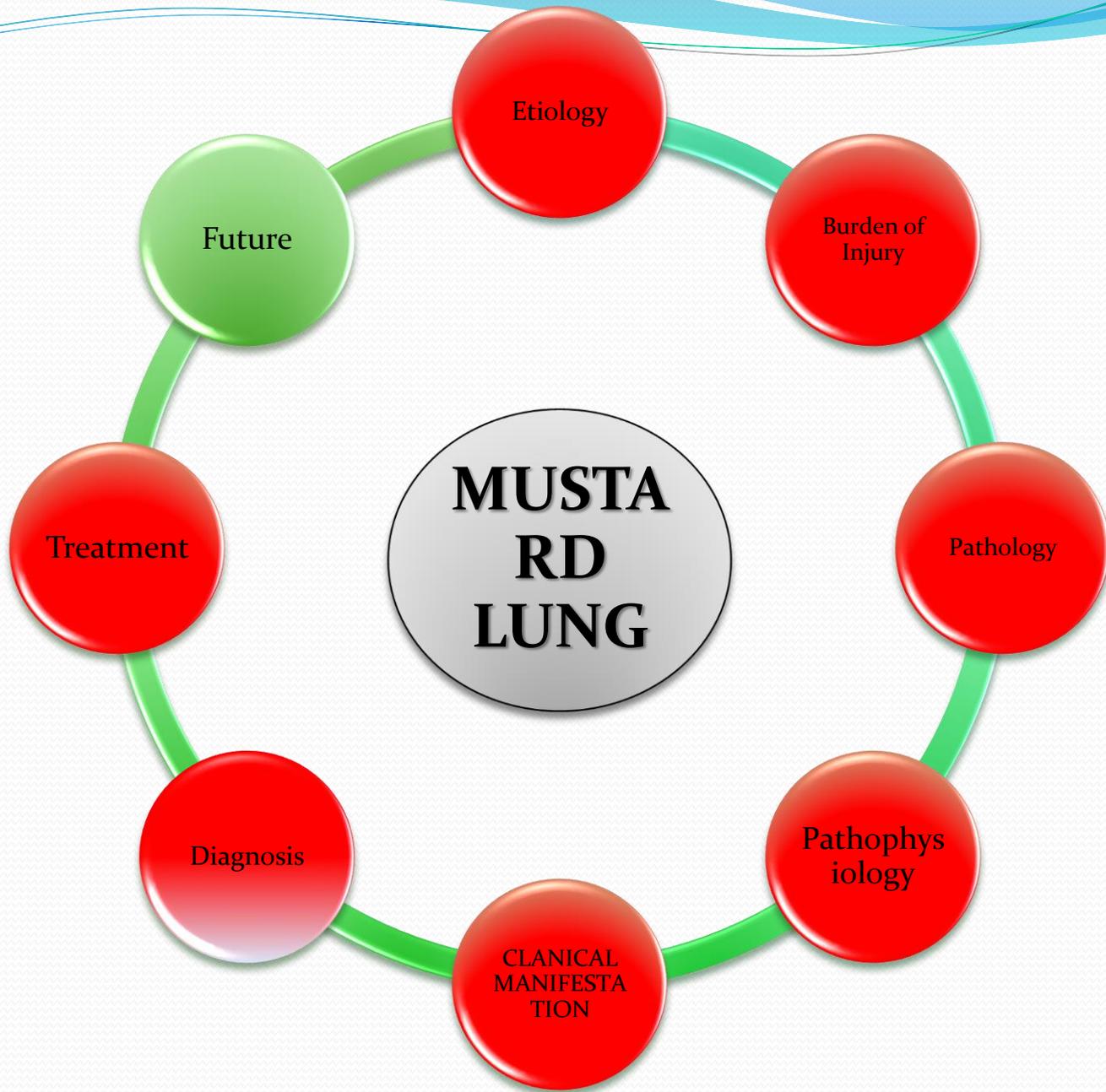
- Systemic mesenchymal stem cell administration appears to be safe in SM exposed patients with moderate to severe injury and provide a basis for subsequent cell therapy investigation in other patients with this disorder.

- Nejad-Moghaddam A, Ajdari S, Tahmasbpour E, Goodarzi H, Panahi Y, **Ghanei M**. Cell J. 2017 Apr-Jun;19(1):117-126. Epub 2016 Dec 21(Adipose-Derived Mesenchymal Stem Cells for Treatment of Airway Injuries in A Patient after Long-Term Exposure to Sulfur Mustard.)



chemotherapy

- studies on the therapeutic effects of available genetic and epigenetic medications were included. Currently, four gene therapeutics, two cancer vaccines with genetic bases, and seven epigenetic medications are available for cancer treatment. Genetic and epigenetic cancer treatments including:
 - Gendicine
 - Imlygic
 - Provenge,
 - Cimavax-EGF
 - Azacitidine
 - Vorinostat
 - Romidepsin
 - Belinostat



Future:

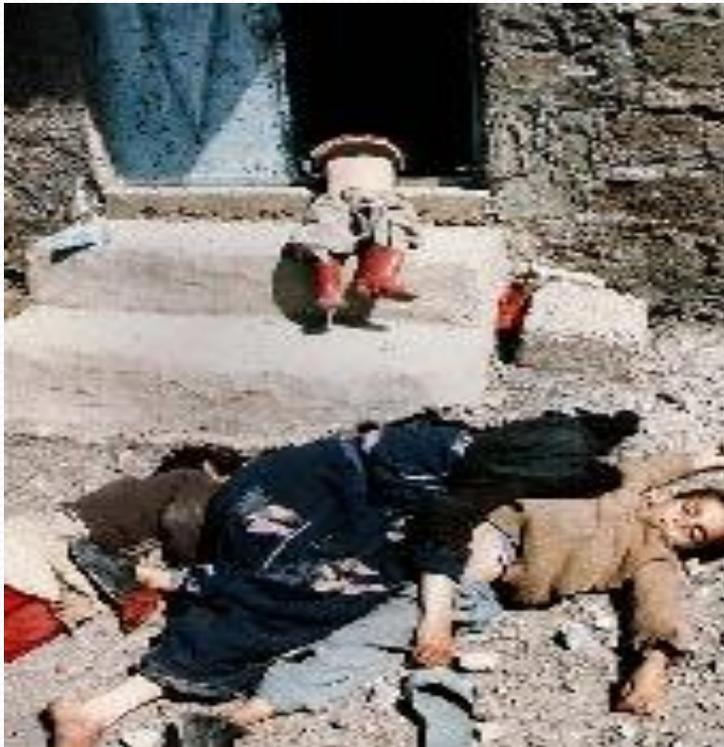
- it is necessary to find the main etiology of the mustard lung (regarding to the role of TGF- β increases and oxidant-antioxidant imbalances) to find the completely effective treatment for these patients.
- The distinguishing characteristics of lung carcinogenesis in these Mustard gas victims, suggest that a single exposure may increase the risk of lung cancer development in some individuals.
- Saburi A, Shohrati M, **Ghanei M**. J Res Med Sci. 2012 Nov;17(11):1092-3. No abstract available.(Perspective in future pharmacological approach to sulfur mustard lung injuries.)
- Hosseini-khalili A, Haines DD, Modirian E, Soroush M, Khateri S, Joshi R, Zendehtdel K, **Ghanei M**, Giardina C. Mutat Res. 2009 Aug;678(1):1-6.(Mustard gas exposure and carcinogenesis of lung.)

Future:

- SM can cause human lung cancer after long term exposure, but there has not been strong and effective evidence for only short term, and acute single high dose exposure until now.
- Saburi A, Shohrati M, **Ghanei M**. J Res Med Sci. 2012 Nov;17(11):1092-3. No abstract available.(Perspective in future pharmacological approach to sulfur mustard lung injuries.)
- **Ghanei M**, Harandi AA. Clin Lung Cancer. 2010 Jan;11(1):13-7(Lung carcinogenicity of sulfur mustard.)



Halabja























Clinical Manifestations

- Patients with unexplained recurrence to antipsychotic therapy, irreversible psychosis or deterioration, and/or with a disturbance of consciousness, autonomic, and/or neurological findings.
- Patients do not readily fit one diagnosis.
- Principally in any cases with overlap of both dissociative features, manifestations should be considered as the "parent" disorder.

Long Term Antipsychotic Drug Exposure in Schizophrenia: A Review of the Literature
Journal of Clinical Psychopharmacology, 2011; 31(1): 1-10

Clinical Manifestations

- Patients with unexplained recurrence to antipsychotic therapy, irreversible psychosis or deterioration, and/or with a disturbance of consciousness, autonomic, and/or neurological findings.
- Patients do not readily fit one diagnosis.
- Principally in any cases with overlap of both dissociative features, manifestations should be considered as the "parent" disorder.

Long Term Antipsychotic Drug Exposure in Schizophrenia: A Review of the Literature
Journal of Clinical Psychopharmacology, 2011; 31(1): 1-10

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