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Pulmonary Fibrosis

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The purpose of this poster is to discuss the pathophysiology of pulmonary fibrosis. More specifically, the roles of the inflammatory and immune agents thought to be responsible for stimulating fibrosis in the lungs will be discussed. Pulmonary fibrosis (PF) is a chronic disease of the lungs involving an altered inflammatory response to injury or infection which results in scarring of lung tissue. The lungs are then unable to ventilate or oxygenate effectively due to the scar tissue. PF has not been thoroughly studied compared with many of the more prevalent diseases today. PF affects men more often than women but has seen an increase in both genders since 2000. According to Ley and Collard (2013) the lack of research in PF is partly due to the existence of similar comorbidities such as COPD, other interstitial lung diseases, viral infections, etc. and the unclear definition of PF in the past.

Signs & Symptoms

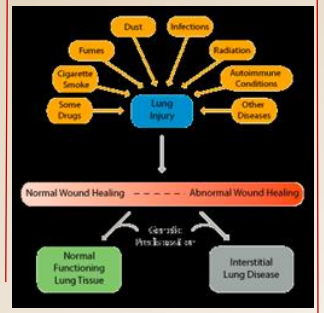
The signs and symptoms of PF are due to the over production of inflammatory mediators and proliferation of scar tissue. These signs and symptoms include, shortness of breath, dry cough, fatigue, fever, chest pain, weight loss, and aching in muscles and joints (Wilson & Wynn, 2009).

Underlying Pathophysiology

Normal lung healing takes place in phases, following the initial injury is a period of healing that begins during the acute inflammation and can take some time to complete. Depending on the injury and how much damage is present, the tissue can regenerate with complete return to normal function. If the damage was more severe, resolution is an acceptable outcome, this is a return to almost normal. During repair, scar tissue replaces destroyed tissue. This type of healing happens with extensive damage and results in tissue that is much less viable than it was before the injury. This replacement of lung tissue with less viable tissue causes lung stiffness and ventilation difficulty. This, in turn, results in decreased gas exchange and hypoxemia.

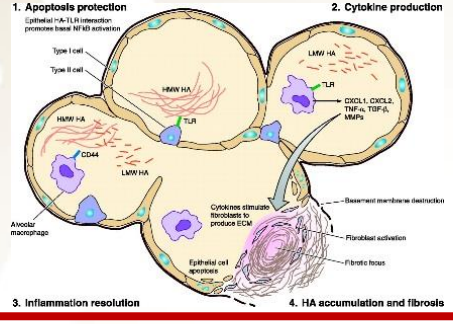
Causes of PF

The injurious agents leading to the chronic inflammation that precedes PF may be an environmental, chemical, or biologic irritant. Sometimes the cause is unknown such as in idiopathic pulmonary fibrosis (IPF). IPF is the most common type of PF.



Pathophysiology of Fibrosis

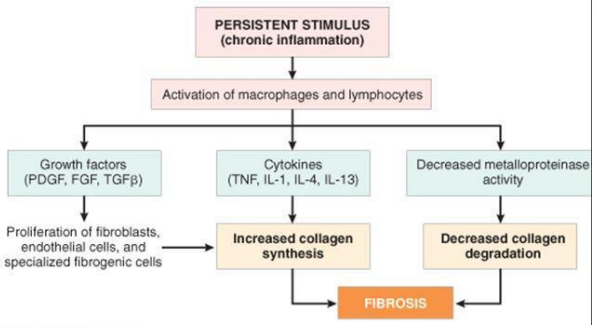
According to current research, it is clear that there is not just one factor that determines the likelihood of developing an altered healing pathway leading to fibrosis of the lung. Altered responses during the reconstructive phase of healing lead to increased recruitment of inflammatory and fibrotic mediators such as cytokines, chemokines, and growth factors. Much of the literature confirms that these mediators are increased in patients with pulmonary fibrosis (PF). Following injury, lung epithelial cells are turned on to signal TGFbeta1 induced expression of connective tissue growth factor (CTGF). CTGF is a pro-fibrotic cytokine that is indicated in fibroblast activation which "express/contribute to the fibrotic matrix proteins and induce further expression of pro-fibrotic cytokines, resulting in progressive fibrosis and establishment of ECM (extra-cellular matrix)." (Wilson & Wynn, 2009). Chronic inflammation exposes one to develop fibrosis and to turn on pro-fibrotic mediators more readily. The proliferation and recruitment of platelets, degranulation, clots, and leukocytes along with the ECM, contribute to the blocking of the damaged endothelium from resolution.



Current Research

According to Wilson & Wynn (2009) PFers lack MMP-2 and MMP-9, peptidases which are required for successful clearance of inflammatory cells. MMP's help determine the amount of collagen deposited during healing. Some research has suggested that the timing of inflammation may be very important in the causation of lung fibrosis as well. On one hand, research has suggested that inflammation may not be a factor in PF as anti-inflammatory agents show no improvement. What's more, late-stage inflammation may actually improve the risk of scarring by clearing cell debris and controlling excessive proliferation. This evidence just goes to show how little is known about PF. (Wilson & Wynn, 2009) On the other hand, more evidence shows that fibrosis is initiated by the inflammatory response at first but requires activation of specific pathways to continue collagen production and contribution to the extracellular matrix, (Wynn & Ramalingam, 2012). This view is more widely accepted due to the fact that inflammatory mediators are found in higher concentrations in PF patients; also, a known risk factor of PF is chronic infections which stimulate inflammation.

Not only do PF patients have excessive inflammatory responses but certain cells in PF patients have actually shown a heightened sensitivity to some very potent pro fibrotic cytokines such as IL-13 and TGFbeta1. According to a study on the responsiveness of fibroblasts, these pro-fibrotic cytokines were shown to interact with each other to stimulate a fibrotic response more so than one stimulator by itself, (Murray, Argentieri, Farrell, Bracht, Sheng, Whitaker, Beck, Tsui, Cochlin, Evanoff, Hogaboam, & Das, 2008)



Significance of Pathophysiology

Differing research findings suggest that there is still much more to be discovered of the pathophysiology of PF. Current understanding of the pathophysiology is important for healthcare providers to know in order to determine diagnostic criteria. Early and accurate diagnosis greatly influences implementation of an effective treatment plan. Knowing the specific pathophysiology is especially important when determining the treatment plan for patients with PF. Healthcare providers must know specifics in disease stages, inflammatory mediator presence, and what these mediators indicate regarding the unique sequence of that patient's condition. Knowing the pathophysiology aids critical thinking and clarifies understanding of when and why therapies and medications work.

Nursing Implications

- Nurses must know the pathophysiology in order to educate PF patients regarding their treatments, medications, and changes in lifestyle.
- A more thorough understanding of the possible contributing factors can allow the bedside nurse to act as an extra filter when checking for treatment and medication contraindications.
- There is evidence that certain biologic agents that are used as treatments and therapies can contribute to PF. One example exists with a study of anti-tumor necrosis factor given as a treatment for rheumatoid arthritis. Of the cases studied, 16% of patients developed lung fibrosis, (Perez-Alvarez, Perez-de-Lis, Diaz-Lagares, Pego-Reigosa, Retamozo, & Bove, 2014).
- Nurses must know the efficacy of the treatments they are administering for PF patients.
- Nurse Practitioners (NP's), specifically, must know diagnostic criteria and variables in disease presentation.
- Healthcare providers must keep up on new research. For example, molecular biomarkers show some promise in evaluating a patient based on their stage of PF and their specific responses and activated pathways regarding inflammation and fibrosis. This research, however, is underpowered and is lacking in validation at this time, (Hambly, Shimbori, & Kolb, 2015).
- It is important for NP's, as leaders in healthcare, to be aware of current research to aid in accurate diagnoses and development the most effective treatment plans.

Conclusion

- Pulmonary fibrosis is a lung disorder characterized by development of a fibrotic pathway following injury and inflammation.
- Initial injury can be caused by environmental, biologic, or chemical irritants. Many times the cause is unknown.
- Lung fibrosis leads to difficult ventilation and perfusion and subsequent hypoxemia.
- Current research shows an increase in inflammatory mediators which stimulate ECM deposition.
- Much research is incomplete or conflicting; this indicates a need for further investigation.
- Knowledge of pathophysiology and current research is crucial for healthcare providers in order to guide their treatment.

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