Clubbing and More-- Your Questions ANSWERED!

Key Points:
• The most reliable indicators of clubbing on physical exam are a profile angle of > 180° or a phalangeal depth ratio of > 1.0.
• Most of the diseases associated with clubbing either involve shunts or neoplasms of the thoracic cavity or GI tract
• Clubbing is not found in pure emphysema but may be found in chronic bronchitis
• An isolated decrease in DLCO can be caused by profound anemia, high levels of carboxyhemoglobin in heavy smokers, early ILD, or vasooclusive disease
• There is no evidence for using Flolan in non-PPH pulmonary HTN

1. What is the pathophysiology of clubbing, and what causes it? Clubbing may occur in isolation or may be the earliest manifestation of hypertrophic osteoarthropathy (HOA), which in its later stages is characterized by periosteal new bone formation and synovitis. HOA occurs with intrathoracic malignancies and cystic fibrosis but is rarely found in other diseases that cause clubbing. A recent “Rational Clinical Examination” article in JAMA found that the two most reliable objective indicators of clubbing were a profile angle > 180° and a phalangeal depth ratio of > 1.0 (see diagram).

The clubbing itself is caused by the proliferation of connective tissue in the nail bed and volar pad of the digits. Why does this happen? Unknown—multiple mediators have been proposed including prostaglandins, ferritin, bradykinin, estrogen, and platelet derived growth factor. The most popular theory of late is that megakaryocytes or large fragments of megakaryocytes bypass pulmonary capillaries (via shunts, or abnormal circulation within a neoplasm) in which they normally break up into platelets; in the systemic circulation, these platelet precursors preferentially lodge in the tips of the digits because of the prevailing patterns of blood flow. Once stuck there, the cells release platelet-derived growth factor and other substances that increase endothelial permeability and activate fibroblasts and other connective tissue cells. This theory does not, however, explain all the reported causes of clubbing.

Clubbing may be familial and/or primary (a.k.a. pachydermoperiostitis); more commonly, it is associated with other diseases listed below. In cases of intrathoracic malignancies, the clubbing reverses if the underlying disease is resected or cured.

- **Pulmonary**: bronchogenic and pleural neoplasms, lung abscess, empyema, bronchiectasis, interstitial pneumonitis (chronic), CF, sarcoidosis, pulmonary AVMs including hepatopulmonary syndrome, benign asbestos-related pleural lesions
- **GI**: IBD, sprue; cancer of the esophagus, liver or bowel; cirrhosis; amebic dysentery
- **Cardiovascular**: Cyanotic congenital heart disease, SBE, AV fistula*, aortic aneurysm**, PDA**
- **Thyroid**: hyperthyroidism ("thyroid acropachy")
- **Other**: HIV? * unilateral
  ** lower extremities only

* unilateral

** lower extremities only
2. **Does clubbing occur in COPD?** Clubbing may occur in COPD if associated with an intrathoracic malignancy, bronchiectasis, or chronic bronchitis but should not occur in pure emphysema.

3. **What causes a decreased DLCO with otherwise normal PFT’s?**
   - Anemia (although many PFT’s will report a corrected DLCO for Hgb)
   - Heavy smokers may have elevated levels of CO Hgb which can decrease the DLCO artificially
   - Early ILD
   - Widespread vasoocclusive disease of the pulmonary microcirculation, either due to an inflammatory process or multiple PE’s

4. **Is there evidence for using Flolan in non-primary pulmonary HTN?** Anecdotal evidence and case reports support using Flolan (epoprostenol) in cases of portopulmonary hypertension; in addition, there are anecdotal reports of utility in chronic, non-primary pulmonary hypertension, but no clinical trials have addressed these questions.

**References:**