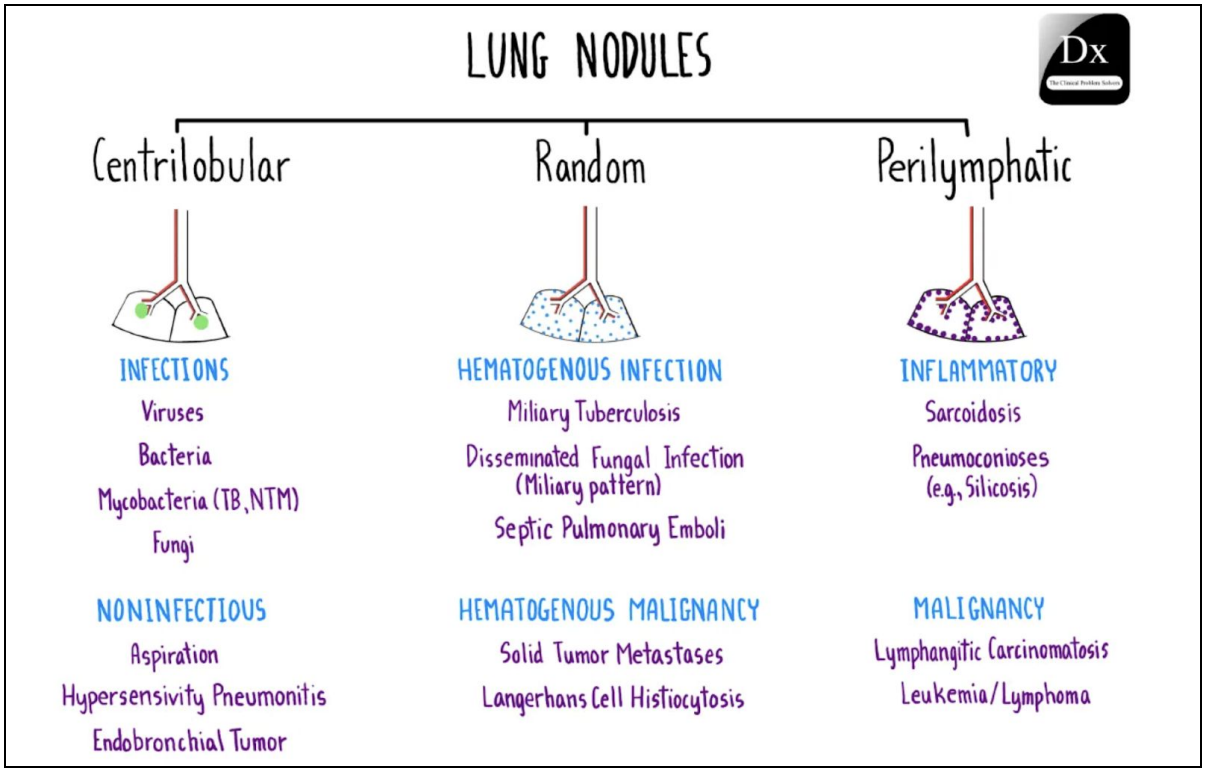
An Approach to Lung Nodules: Video Schema Script



INTRO

Welcome back, Clinical Problem Solvers! This is Nikita Deshpande. I am a medical student at Georgetown and today, we're going to walk through how to approach lung nodules.

Let's start with a case to frame our discussion.

A 56-year old gentleman comes to clinic with three weeks of low-grade fever, fatigue, and a non-productive cough. He denies night sweats, chest pain, and dyspnea. The patient also complains of left eye pain. On review of systems, he acknowledges 10 pounds of unintentional weight loss over the past month. His physical exam is notable for conjunctival erythema, and painful skin lesions over the lower extremities.

A subsequent chest x-ray shows an enlarged mediastinum. To better characterize this finding, you order CT imaging. The CT scan shows **perilymphatic pulmonary nodules** and **mediastinal lymphadenopathy**.

Wait - Perilymphatic nodules - what could this mean?

Before we continue with our patient and delve into the schema, let's zoom out for some overall context.

On CT imaging, we observe **four main radiographic patterns.** These include reticular patterns, high attenuation patterns, low attenuation patterns, and nodular patterns - today's let's focus on nodular patterns.

A nodule is a white spot or shadow seen on CT imaging, and it represents a mass of lung tissue. We can further characterize lung nodules based on **WHERE nodules localize** within the **secondary pulmonary lobule.**

The secondary pulmonary lobule is the smallest unit of the lung. **Airways** are centrally located within the lobule**, blood vessels** are diffusely located throughout the lobule, and **lymphatic vessels** are peripherally located along the lobule.

We can use this **anatomical knowledge** of the **secondary pulmonary lobule** to understand what types of diseases lead to specific nodules. **Let's unpack this further!**

As you can see from this image, there are **three main nodular patterns we see on CT imaging**.

Disease processes can be clustered…

- around the center of a lobule - known as centrilobular nodules,
- randomly within the lobule - know as randomly distributed nodules,
- or along the lymphatics of a lobule - known as perilymphatic nodules.

What causes these specific localization patterns to occur?

Here are a few principles to guide your thinking.

First - because the airways sit at the center of the secondary pulmonary lobule, most diseases that track the **airways** will lead to **centrilobular nodules**

Second - While the pulmonary artery is initially oriented towards the center of the lobule, blood feeds nearly **all areas** of the lung parenchyma. So, most diseases that travel through the **bloodstream** will result in a diffuse pattern, and cause **random nodules.**

Third - Since the lymphatic vessels track along the peripheral borders of the lobule, diseases that either involve the lymphatics, or spread through the lymphatics, will result in **perilymphatic nodules.**

With this framework in mind, let's dive in!

Processes that reach the lung parenchyma **via inhalation** often track the airways and result in **centrilobular nodules**. The two buckets we consider here, are infectious and non-infectious etiologies.

Infections from **inhaled pathogens** result in central nodules because as pathogens move through the respiratory tract, our airways introduce these pathogens into the central region of secondary pulmonary lobules.

So - what should your **infectious differential** include?

Keep a **broad differential** because **viral, bacterial, mycobacterial, or fungal agents** can be at play.

And beyond infectious agents, our airways can also introduce other substances to the lungs. **Three NON-INFECTIOUS etiologies** to think about are aspiration, hypersensitivity pneumonitis, and endobronchial tumors.

For instance, think about a **patient with GERD, who has a high baseline risk of aspiration**. Similar to the inhalation of pathogens, any reflux of gastric contents from the esophagus into the airways could introduce (aspirated material) into the centrilobular region.

Another example is **Hypersensitivity pneumonitis.**

In this disease, our airways bring various **irritating environmental antigens in contact with our lungs**. Because these antigens reach lung tissue through the airways, they also result in a centrilobular pattern.

Finally, **endobronchial tumors can also produce central nodules.**

Endobronchial tumors are cancers that arise in the airways. And again, since our airways connect to the center of lobules, these tumors result in central nodules.

Examples include squamous cell carcinoma, adenocarcinoma, and small cell carcinoma, among others.

That **covers the centrilobular branch.**

Now, let's walk through the randomly distributed nodules.

Randomly dispersed nodules do not localize to any particular region of the lung lobule. Instead, these nodules have **widespread distribution** because they spread through the **bloodstream**.

Blood vessels nourish every part of a secondary pulmonary lobule, which is why hematogenously-spread etiologies result in a **random and diffuse pattern.**

Two buckets to keep in mind are **hematogenously-spread *infection*, and hematogenously-spread *malignancy*.**

When it comes to **infection**, think of **pulmonary-tropic pathogens which have the potential to systemically disseminate throughout the bloodstream.** Examples include mycobacterium tuberculosis, non-tuberculous mycobacteria, and disseminated fungal infections like coccidiomycosis.

Another **infectious etiology** that can produce random nodules are **septic pulmonary emboli.**

This happens when some endovascular nidus of infection mobilizes through the right side of the heart, and enters the pulmonary vasculature, resulting in septic pulmonary emboli. Potential sources include **tricuspid valve vegetations, septic venous thrombophlebitis, or infected venous catheters.**

Beyond infection, various cancers also **spread hematogenously -** these include **solid tumors such as sarcomas or carcinomas,** and **Langerhans cell histiocytosis**.

Alright, so we have officially covered **the infectious and malignant** causes of random pulmonary nodules.

Before we move on, I want to quickly highlight **TB and fungal** infections - if you recall, we've mentioned them in **two sections** – **centrilobular and random.**

This is because **TB and fungal infections** can reach the lungs in **two ways**. Either they can **track the airways** and result in **centrilobular nodules**, OR they can **disseminate systemically** through the bloodstream and result in **random nodules**.

Phew! Now that we've gone through random nodules, let's move on to the final branch of the schema.

Perilymphatic nodules are nodules that track along the **lymphatic vessels of a pulmonary lobule.** Diseases that result in perilymphatic nodules either **involve** the pulmonary lymphatics, or, **spread through** the pulmonary lymphatics.

The **two buckets** we consider here are **inflammatory causes, and malignant causes.**

When it comes to **inflammatory** causes, think of **sarcoid and the pneumoconioses.**

Why does an inflammatory process like sarcoid result in perilymphatic nodules?

Sarcoid involves an exaggerated T-cell response. As T-cells travel through the lymphatics, activated T-cells can reach the pulmonary lymphatics.

Another disease process that results in perilymphatic nodules are the pneumoconioses.

The pneumoconioses result from **occupational exposure** to inhaled particles like **silica.** Chronic particulate exposure **irritates the alveolar macrophages** - once activated, these macrophages travel through the **pulmonary lymphatics** for antigen presentation, and can produce nodules along the way.

In particular, **silicosis and coal workers' pneumoconiosis** are known for producing pulmonary perilymphatic nodules.

That covers the **inflammatory causes** - let's review the **malignant causes**.

Remember - **malignant etiologies can result in perilymphatic nodules** when they spread through the lymphatic system.

The two groups to consider here are **lymphangitic carcinomatosis**, and **leukemia/lymphoma.**

Lymphangitic carcinomatosis refers to **metastatic cancers** that have spread to the **lungs via the lymphatics.**

Leukemias and lymphomas can also cause perilymphatic nodules. Leukemias can **spread through the lymphatics through leukemic infiltration**. And since **lymphomas are cancers**

of lymph node tissue, by definition they **spread** through the lymphatics and can result in perilymphatic nodules.

Great job, team - that is **all you need to know** for lung nodules!

Just to step back and connect the schema with our case - **remember our patient**, the 56-year old man who was found to have **perilymphatic nodules on CT scan**? Now we're armed with the information we need to make sense of his imaging.

Based on our patient's chief complaint of **subacute fever and weight loss,** initially our differential might include states associated with inflammation - think of the CPSolvers' **IMADE mnemonic here**, which includes states like insidious infection, malignancy, or autoimmune disease.

When we layer on the patient's **perilymphatic nodules**, this radiographic finding suggests that **a pulmonary process** might localize the patient's source of inflammation.

From our schema, we know that **perilymphatic nodules** suggest two possibilities: either a **chronic inflammatory process**, or a **malignant process**.

Although **definitive diagnosis** would require confirmational testing like biopsy of a mediastinal lymph node, when we consider our patient's **perilymphatic nodules** along with

-his **left eye pain and conjunctival erythema**,
-his **painful lower extremity skin nodules**,
-and his **inflammatory symptoms like fever**,

these collective findings prioritize an **inflammatory process** like sarcoid over a malignant process.

Thus, sarcoidosis is a leading potential diagnosis for the patient's perilymphatic nodules.

That's all, Clinical Problem Solvers! Thanks for hanging in till the end! If you'd like to hear more case-based examples of how to think about Lung Nodules, listen to the CPSolvers Podcast, **Episode #49 or Episode #66**.

To recap, today we discussed **three main buckets** for **evaluating pulmonary nodules on chest CT**.

For **centrilobular nodules**, we think about any etiology associated with the **airways**. For **random nodules**, we consider **blood-borne infection and cancers**. And when analyzing **perilymphatic nodules**, we think about processes that **involve pulmonary lymphatics, or are spread through pulmonary lymphatics.**

This concludes the Clinical Problem Solvers' approach to lung nodules. **Thank you for watching!**
