Cough, Dyspnea, And Lung Nodules

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This chapter covers four main points designed to help you order the correct first test when evaluating patients with cough and dyspnea and to understand imaging of pulmonary nodules:

1. The main decision about imaging of the pulmonary symptoms of cough and dyspnea is when to order a chest computed tomography (CT) study.
2. For patients with cough, a chest x-ray (CXR) is done first, usually followed by evaluation and treatment of common causes of cough, with a chest CT ordered only after eliminating common causes or if there are red flags in the clinical history.
3. For patients with dyspnea, a CXR is done first, followed by an urgent CT if there are red flags for a pulmonary embolism.
4. Pulmonary nodules typically will undergo CXR and CT, along with biopsy/excision, sequential CT, or positron emission tomography (PET) depending on the circumstances of the patient and size of the lesion.

CXR AND CT

The primary care provider has few options when ordering studies for evaluation of such cardiopulmonary complaints as cough and dyspnea. For the most part, the main decision will be whether to order a plain film or not, and when to proceed to CT. With regard to plain films of the chest, most texts emphasize that chest plain films are not always necessary to work up common cardiopulmonary complaints. While this is certainly true in an academic sense, most patients with chest symptoms, in fact, seem to undergo plain film examination relatively early in the diagnostic work-up, and it is difficult to fault this practice since the downside is minimal, the patient expects that the study will be ordered, and the safety of having excluded a large chest malignancy is reassuring. CT exams, on the other hand, are ordered much less frequently and usually later in the course of evaluation: they cost more, generally require the injection of IV contrast material, subject the patient to higher doses of radiation, and also reveal asymptomatic incidental pulmonary nodules requiring additional work-up.
Figure 1. Pneumothorax in a 53 year old man with chest pain and dyspnea following trauma. A. PA inspiration chest x-ray shows a subtle pleural line (arrow) on the right side. B. PA expiration chest crowds the pulmonary vessels. C. On the CT study, the pneumothorax is much more conspicuous (arrow). D. Chest x-ray shows resolution of the pneumothorax following chest tube placement (arrow).

The standard two view chest plain film examination consists of a frontal exam taken with the anterior aspect of the chest closer to the film\textsuperscript{1}.
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(“PA” or posterior-to-anterior with respect to the path of the x-rays through the patient) and the x-ray source approximately 6 feet (72 inches) away from the film. The patient typically stands for the examination if possible, with the arms brought forward so the scapulae project to the side (or along the lateral margins) of the lungs. The exam is taken in full inspiration. The lateral study is done with the left side closest to the film/recording device. Note that variation in any of several technical aspects (distance, portion of the patient closest to the film/detector, degree of inspiration) may produce large changes in the appearance of the radiograph.

Alternatives to the “standard” upright PA and lateral view, like changes in the technical factors of the study, will alter the result. Typical variations include obtaining the study in a portable fashion, usually done in an AP manner so that the patient’s back is to the film, which magnifies the heart. Non-portable supine exams also universally use the AP technique, again magnifying the heart. These studies are also performed at less than 72 inches from the x-ray tube to the film/recording device, another factor that magnifies the heart. Note also that when the patient is supine rather than upright, pleural fluid will flow to a dependent position along the dependent posterior chest wall so that, instead of demonstrating a dense (and easily recognized) band across the lower chest, the fluid will cause the entire associated lung to look slightly denser than it otherwise would. A similar phenomenon occurs with air in the pleural space: it moves to the anterior aspect of the chest and the entire lung looks slightly more lucent than it otherwise would. A crescent of air along the superior chest is typically easy to identify on an upright chest radiograph, but generalized lucency of the hemithorax much less so.

Decubitus films may solve the problem of identifying fluid or air in the pleural space. In these exams, the patient is placed with one side down (the side of the suspected effusion, or opposite the suspected pneumothorax) and a film is taken (usually AP). Layering of the fluid along the dependent aspect of the patient or air along the non-dependent aspect facilitates diagnosis.

Chest CT may be performed as a more accurate alternative to decubitus views (Figure 1), and is also almost always the study of choice as the next imaging study in the workup for any significant, worrisome, or confusing finding on a chest radiograph. Chest CT has undergone the same, relatively rapid, evolution with the advent of helical/multidetector scanners as has CT of other body parts. Twenty years ago, most deployed CT scanners were so slow that it was only practical to scan most patients at 8 or 10 mm slice thickness, and a contrast bolus would only result in vascular enhancement of a handful of slices. Nowadays most facilities have machines capable of (and use protocols calling for) 2 mm slices with excellent contrast of the vascular tree throughout the study. This has blurred or eliminated the distinction between “standard” and “high resolution” CT of the lungs, since routine CT scans are now performed with a technique that would once have been considered “high resolution”. In addition, many radiologists routinely use workstations for image interpretation which allow image manipulation with, for example, construction of what are called “maximum intensity projection” maps or “MIPs” which allow easier and better detection of pulmonary nodules (Figure 2).

1 I will use the term “film” throughout the chapter, but a recording device has replaced film in modern radiography equipment.
The two main decisions facing the ordering physician when it comes to CT are: 1) “When do I order the CT?” and 2) “Do I order it without, or with, IV contrast material?” The first question is the subject of most of the rest of this chapter. The second question is best answered: “With contrast, if at all possible”. Contrast allows visualization of the vascular tree, which is essential for diagnosis of pulmonary embolism and pulmonary arteriovenous malformations, and which is helpful to distinguish mediastinal vessels from lymph nodes and masses. The main reasons not to use contrast are if the patient is in renal failure (see pages 251-254 for further discussion of rules for contrast injection in renal failure), or if the scan is being done only to follow up a pulmonary nodule (or pulmonary nodules), (see later section in this chapter on “Pulmonary Nodules”).

Figure 2. Chest CT exam showing the value of “Maximum Intensity Projections” or “MIPs”. A. Routine chest CT filmed at lung windows shows a similar appearance for both the nodules and the vessels (imaged “on end”). B. MIP CT image demonstrates that these 10 mm thick slices (which record only the densest pixels from the slab) show the nodule as an oval density (as before), but the vessels as tubular, branching structures. These images make evaluation of the lung parenchyma for small nodules much easier.

Figure 3. Pneumonia in a 34 year old woman with cough, fever, and shortness of breath. A. PA chest obtained prior to illness shows clear lungs. B. PA chest obtained during illness (right) shows extensive right lung opacity.
COUGH

One may divide patients with cough into those with acute cough (generally less than 3 weeks duration) and chronic cough (more than 3 weeks duration). Patients with acute cough, particularly when accompanied by a febrile illness or productive cough, will typically have a chest x-ray to identify consolidation indicating pneumonia (Figure 3). In rare cases, the radiograph may demonstrate an unpleasant surprise in the form of a pulmonary mass (Figure 4), in which case the patient may still have pneumonia which has developed secondary to an obstruction “upstream” from the mass. These patients typically require CT for further characterization of the mass and associated hilar and mediastinal nodes and the remainder of the pulmonary parenchyma for synchronous independent tumors and metastases.

Figure 4. Lung cancer in a 68 year old man with hemoptysis. A. PA chest shows consolidation of the left upper lobe (white arrow) and left hilar fullness (black arrow). B. Lateral exam confirms abnormal opacity in the so-called “anterior clear space”, anterior to the trachea. C. Coronal reformatted CT shows the area of consolidation in the left upper lobe corresponding to the plain film findings. D. Axial CT shows lymphadenopathy along the left pulmonary artery (white arrow) as well as lung consolidation. Lung cancer was subsequently diagnosed.
Patients with pneumonia occasionally have normal chest radiographs early in the course of the disease, or when dehydrated or immunocompromised (Figure 5). CT will usually demonstrate abnormal opacity of the lung parenchyma in such cases and can be performed if there is a quandary about whether or not to treat the patient or if the diagnosis of pneumonia needs imaging documentation.

In patients with acute cough, several “red flags” should provoke earlier ordering of both the chest x-ray and the subsequent CT. Red flags include symptoms such as fever, sweats or chills, unintentional weight loss, hemoptysis, and dyspnea, which suggest underlying infection, tumor, and/or pulmonary embolism. Note that while many smokers do not seek medical attention for their cough, if a smoker does come in for evaluation of cough the most important feature is whether there has been any change in the character of the cough: chronic, unchanged cough likely represents chronic bronchitis whereas a changed cough is worrisome for the development of a malignancy.

In patients with chronic cough, a chest x-ray will typically be obtained although it will usually be normal. This follows because most cases of chronic cough are secondary to post-nasal drip, gastroesophageal reflux disease, and asthma (especially variant asthma), and these diseases either produce no chest x-ray findings or subtle nonspecific findings. Diagnostic algorithms typically call for a careful review of systems in patients with chronic cough to elicit any subtle history of these diseases, with further diagnostic testing in those cases where there are suggestive symptoms. Suspected post-nasal drip may be further evaluated with sinus films, suspected GERD with pH monitoring of the esophagus (not endoscopy or a barium esophagram), and suspected asthma with spirometry and metacholine challenge.

In those patients with no features to suggest one of these three diseases, the patients still probably has

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2 More recent texts often use “upper airway cough syndrome” rather than the term “post-nasal drip”.

Figure 5. Radiographically occult pneumonia in a 78 year old woman with cough, syncope, and weakness. A. PA chest obtained at the time of the illness shows no obvious consolidation. B. Chest CT performed to exclude pulmonary embolism shows obvious opacity in the left lung base (arrows). There were no pulmonary emboli, and the patient’s symptoms resolved and her elevated white blood cell count returned to normal with antibiotic treatment.
one of the three diseases but simply are not clinically manifesting any symptoms other than cough. In this case, the options include either testing for the three diseases as noted above, or treating the patient as if they had one of the diseases and noting the response, with the assumption that eradication of the cough with treatment for the disease (nasal glucocorticoids and/or antihistamine-decongestant combination for post-nasal drip, H2 blockers for GERD, bronchodilators for asthma) proves that the patient has the disease.

At some point in this evaluation process – usually after all else has failed, although perhaps earlier if there is an abnormal chest x-ray – a CT may be obtained. Unfortunately, such CT studies provide clinically meaningful information in a minority of cases. Helpful findings which may be seen include bronchiectasis, unsuspected tumor, and interstitial lung disease. Regarding interstitial lung disease, volumes have been written regarding the radiographic appearances of the literally dozens of diseases that fit into this category, and from a radiologist’s viewpoint the best summary I can offer is that the CT findings are almost always nonspecific. While combinations of imaging features and clinical findings allow formulation of a reasonable differential diagnosis, lung biopsy is nearly always required to secure a specific diagnosis.

In some 10 to 25 percent of patients, despite all diagnostic testing listed here, the cause of cough may remain unclear.

**DYSPNEA**

The term “dyspnea” indicates unpleasant or uncomfortable breathing and for the purposes of discussion here will be assumed to include patients with shortness of breath. Dyspnea, like cough, is a nonspecific symptom associated with many diseases, and the usual decisions to make in imaging are when to order a chest x-ray and when to proceed to a chest CT. “Red flags” prompt earlier ordering of chest CT exams. As with cough, red flags include symptoms such as fever, sweats or chills, unintentional weight loss, and hemoptysis, which suggest underlying infection, tumor, and pulmonary

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Figure 6. Pneumonia in a 33 year old woman with dyspnea. A. PA chest obtained at the time of the illness shows extensive consolidation of the right lung. B. PA chest obtained following the illness shows clearing of the pneumonia.
embolism. Many patients with pneumonia present with dyspnea rather than cough (Figure 6).

Severe, acute onset dyspnea, particularly when associated with chest pain, may herald one of two critical diagnoses: pneumothorax and pulmonary embolism. Chest x-rays should be obtained immediately in any patient with severe acute onset dyspnea, and while a plain film will demonstrate pneumothorax (Figure 1), contrast-enhanced CT is necessary to diagnose pulmonary embolism (Figure 7). In cases of suspected pulmonary embolism, measurement of D-dimer may be helpful as an elevated level suggests pulmonary embolism and should prompt urgent CT examination.

Dyspnea caused by congestive heart failure (Figure 8) may be further evaluated with echocardiography. Typically, these patients do not need to undergo CT scanning.

Imaging results in patients with dyspnea are less likely to be normal than imaging results in patients with chronic cough. The imaging studies will often demonstrate at least some cause of the symptoms, even if the exact diagnosis is elusive and requires further testing. Nonetheless, many diseases that produce dyspnea demonstrate either few CT findings (asthma) or nonspecific findings (chronic obstructive pulmonary disease or COPD).

Figure 7. CT examination demonstrating pulmonary embolism in a 74 year old woman with acute onset of shortness of breath. A. Portable chest plain film examination was normal, as is often the case with pulmonary embolism. B. Chest CT examination demonstrates multiple filling defects within the pulmonary arteries, diagnostic of pulmonary embolism.
PULMONARY NODULES

Pulmonary nodules and masses may be symptomatic, discovered as part of a search for metastatic deposit, or discovered as an incidental finding. Symptomatic lesions, for example a chest mass that has involved the chest wall or which has undergone necrosis causing chest pain, requires prompt work-up (Figure 9). CT with possible CT-guided biopsy may be appropriate, with likely early referral to a chest surgeon, oncologist, or both for treatment.

In patients with known malignancy undergoing screening for metastatic deposit, new chest masses are usually malignant. Note that in this regard, oncologists frequently monitor cancer patients with CT (rather than simply plain films) because of CT’s increased sensitivity (Figure 10). Lesions incidentally discovered on chest x-ray typically undergo CT as the next step in evaluation, unless there is an old chest x-ray establishing stability for at least two years (see below). The CT may demonstrate that an apparent pulmonary nodule on the chest x-ray represents a benign abnormality (as noted below).

With incidentally discovered lesions found at CT scanning, the work-up depends upon the size of the lesion and risk status of the patient (Table) in a way that is difficult to memorize. In general, the goal is to identify and remove malignancies as early as possible, while not routinely removing benign lesions. This is very difficult to accomplish. One way to think about the process is to attempt to establish whether the lesion has any features which unequivocally demonstrate that it is benign and therefore may be ignored. These include:

1. Typical benign pattern of calcification. While not all calcification within a pulmonary nodule indicates a benign lesion, most does, especially if the calcification is uniform (Figure 11) or “popcorn” like in appearance.
2. The lesion contains fat. Fat, though far less frequently encountered than calcification, indicates a benign lesion. A uniformly fatty lesion is a lipoma, whereas one with a small amount of fat distributed among other tissue is a hamartoma (Figure 12).
3. The lesion represents a typical arteriovenous malformation. These lesions demonstrate conspicuous feeding and draining vessels and obvious enhancement with contrast. If
large and symptomatic, these lesions may be embolized (Figure 9).

4. The lesion shows stability on sequential scans. The typical cut-off for assuming that stability equates with a benign lesion is two years, although this is somewhat arbitrary and controversial. There are, of course, two ways to establish stability: to look backward at old exams, and to sequentially follow the patient forward. As for looking backward, questioning the patient for possible prior studies of any kind may be helpful—for example, nodules at the lung base may be visible on prior CT scans of the abdomen (Figure 13). If no old films are available, then one must decide whether to:

A. Do nothing. This is an option if the lesion measures less than 5 mm and the patient has no risk factors. This follows from the fact that such small pulmonary nodules are common (seen in up to 50% of patients) but almost always benign (less than 1% malignant).

B. Follow the lesion with sequential CT studies (Figure 14). This is usually done with lesions of intermediate size particularly absent patient risk factors (see Table).

C. Proceed to PET imaging. This is a good choice for lesions at least 8 – 10 mm in size. Lesions that are hypermetabolic (Figure 15) are nearly always malignant and require removal, whereas those that are not hypermetabolic can be followed with sequential CT studies. Nonhypermetabolic lesions should not be ignored unless they have been proven stable for at least two years, as there are a few cancers (especially bronchioalveolar carcinoma) which are not hypermetabolic. So called “ground glass” lesions (named because they have a density which is greater than normal lung tissue, but are not so dense that they obscure vessels, on CT study) are more worrisome and biopsy or prolonged (3-5 year) follow-up of these lesions should be performed.

D. Any increase in lesion size is a cause for concern and unless there is some overwhelming reason not to do so, lesions showing an increased size on sequential studies should probably be removed.

<table>
<thead>
<tr>
<th>Size</th>
<th>Further Evaluation</th>
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<tbody>
<tr>
<td>&lt; 4 mm</td>
<td>No smoking, asbestos exposure, or known malignancy</td>
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<tr>
<td>&gt; 4 to 6 mm</td>
<td>CT @ 12 months; if no change, stop</td>
</tr>
<tr>
<td>&gt; 6 to 8 mm</td>
<td>CT @ 6 months; if no change repeat at 24 months</td>
</tr>
<tr>
<td>&gt; 8 mm</td>
<td>CT @ 3, 9, and 24 months or PET or biopsy</td>
</tr>
</tbody>
</table>

Table: Recommended follow-up for incidentally discovered nodules discovered at non-screening CT for patients 35 years or older. Adapted from MacMahon H et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society, Radiology 2005;237:395-400.
Figure 9. Arteriovenous malformation in a 34 year old woman with chest pain. A. Chest radiograph shows a mass in the left upper lobe. B. Axial contrast-enhanced CT shows an intensely enhancing lesion. C. Coronal reformatted contrast enhanced CT shows a feeding vessel characteristic of an arteriovenous malformation. The patient underwent embolization therapy. D. Follow-up coronal CT filmed at bone windows shows embolic material within the lesion. The patient’s pain remitted following treatment.
Figure 10. Metastatic disease in a 74 year old man with both breast and prostate cancer (!), with CT demonstrating lesions not seen on plain film examination. A. PA upright chest shows subtle, easily missed opacity in the medial right upper lung. B. Coronal reconstruction CT clearly shows a spiculated mass in the right upper lobe (arrow) along with an additional, more inferior lesion. Axial localizing line is at the plane of the axial slice in C. C. Axial CT also shows a spiculated mass. D. More inferior image shows bulky lymphadenopathy from metastatic deposit posterior to the right pulmonary artery (arrow).
Figure 11. Benign granuloma in a 67 year old woman.  
A. Baseline PA plain film examination shows a right upper lobe pulmonary nodule.  
B. Later PA plain film obtained for pain shows an apparent increase in size of the lesion.  
C. Coronal reconstruction shows a densely calcified lesion (arrow) at the location of the nodule on the chest radiograph. The horizontal localizing line is at the plane of the axial slice.  
D. Axial CT also shows a densely calcified lesion. No further work-up was required, as the lesion has a completely benign appearance.
Figure 12. Hamartoma in a 74 year old woman with an incidentally discovered chest lesion. A. Chest radiograph obtained for shortness of breath demonstrates a lesion in the right middle lobe (arrow). B. Axial CT study filmed on pulmonary windows shows a mass (arrow). C. Magnified CT shows fat within the lesion with negative Hounsfield units indicating fat. D. Subsequent CT of the abdomen performed two years later for another reason shows that the lesion is stable.
Figure 13. Chronic granulomatous disease in a 72 year old woman with an incidentally discovered pulmonary nodule. A. Chest radiograph of a 72 year old woman with leukocytosis following a total knee replacement shows a right pulmonary nodule (arrow). B. The patient had no old chest radiographs, but the scout film from a prior abdominal CT showed the nodule unchanged from three years earlier (arrow).

Figure 14. Chronic granulomatous disease in a 61 year old woman with incidentally discovered pulmonary nodules. Sequential studies show a small, stable nodule in the right lung base (black arrow). Note that on non-MIP studies, the nodules resemble vessels (white arrow). This is the same study as Figure 2, above, demonstrating the value of MIPs.
Figure 15. Adenocarcinoma in a 63 year old woman with pneumonia. A. Chest radiograph shows right upper lobe pneumonia (white arrow) and a contralateral left upper lobe pulmonary nodule (black arrow). B. CT study shows the pneumonia (white arrow) and the pulmonary nodule (black arrow). C. PET scan shows hypermetabolism at the location of the nodule (white arrow). D. A CT directed biopsy with the needle in the lesion (arrow). Adenocarcinoma was found at pathology.
SUMMARY

Most patients with cough and dyspnea will get a chest x-ray, and the main decision is whether and when to order a CT study. Common causes of cough are often treated empirically prior to proceeding to a chest CT. For patients with dyspnea, an urgent CT is performed if there are red flags for pulmonary embolism. Pulmonary nodule work-up is often performed with chest x-ray followed by CT (if no old films are available to demonstrate nodule stability), with biopsy/excision, sequential CT, or PET-CT depending on the circumstances of the patient and the size of the lesion.
REFERENCES

1 Goroll AH and Mulley AG. “Evaluation of subacute and chronic cough” Chapter 41 in Primary Care Medicine: Office Evaluation and Management of the Adult Patient, 6th edition, Lippincott William & Wilkins. They write: “Chest radiography is essential when historical or physical evidence raises the question of carcinoma, pneumonitis, tuberculosis, heart failure, or bronchiectasis. However, the test is overused and not necessary in the nonsmoker who presents with a persistent cough after a recent upper respiratory infection and whose physical examination findings are normal.

2 Seller RH. Cough. Chapter 9 in Differential Diagnosis of Common Complaints. Saunders, 2000, Philadelphia. The authors note: “Most people who complain of cough do not have bronchogenic carcinoma. However, 70% to 90% of patients with bronchogenic carcinoma develop a cough at some time during the course of their disease.”


7 Weinberger SE, Silvestri RC. Treatment of subacute and chronic cough in adults. UpToDate, accessed 9/14/09.

8 Weinberger SE. Diagnostic evaluation and initial management of the solitary pulmonary nodule. UpToDate, accessed 9/15/09.