

SPEAKER 1: On the question of how a clinician might proceed in evaluation and management of a patient with mycobacterial respiratory disease, specifically nontuberculous mycobacterial disease, it's worth keeping in mind the ideas of what we might do for the patient.

So there are two important backdrop circumstances. One is they likely have bronchiectasis, and have had bronchiectasis for a while, and have potentially progressive bronchiectasis. And that is one area for treatment. And the second is the question around whether they have a nontuberculous mycobacterial infection, and the NTM most likely is the mycobacterium avium complex pathogens.

And we know that there are now concrete data showing utility in treatment of those patients with NTM disease. And not just that, but there are concrete data showing, and recommendations including consensus guidelines, demonstrating an appropriate approach to the diagnosis and the management.

And as the clinician hopefully would know, a reasonable diagnosis of NTM disease should include the recovery of pathogens, as a cardinal feature, but additionally, demonstration of symptoms that would be consistent with a disease state. And demonstration of evidence of organ, specifically in this case lung, injury that would be consistent with that sort of infection. So we can keep those features in mind as the clinician might meet a patient and then proceed with evaluation.

The predominant feature that we use for specific evaluation of disease from radiographic standpoint is now CT scanning. That a lot of the features that are part of the pulmonary manifestations of NTM infection are subtle features that we simply can't adequately evaluate on plain radiographs. And CT scanning has now become the predominant and appropriate approach.

And with high resolution CT scanning-- and I should add, low dose CT scan protocols are completely adequate and should be the mainstay approach. There is no reason to get contrast scanning. There is no reason to undertake high dose protocol CT scanning. Low dose protocol CT scanning is perfectly adequate to reveal the features, which can do a few important things.

Number one, identify and confirm that there is bronchiectasis. Number two, make assessments about the degree to which there might be mucus plugging in those bronchiectatic segments in the lung. Number three, corroborate the suspicion of NTM infection with some fairly unique features that we find associated on CT scan.

One of which is the pattern of what we call, tree-in-bud or nodular changes in peripheral airways. So these are small, at or less than one millimeter dimension airways. Small enough so that when we encounter, or when the patient has, a state of mucus plugging and inflammation in those airways, we see those as small indistinct nodules appended off the ends of airways, and it looks like a tree in springtime bud. And those features are quite unique for NTM infection and not discerned by plain radiographs, so that a CT has incredible utility in that regard.

An added feature about CT scanning, which is hugely important, is that it does allow us to, much more substantively than we can on plain radiographs, assess for the presence of either severe structural disease of advanced bronchiectasis, or the presence of frank cavitory disease associated with NTM disease. That's incredibly important because of the now well-founded observations that cavitory disease, in the face of NTM infection, carries a much worse prognosis.

And without CT scanning to make that distinction between on one hand a nodular bronchiectasis pattern or the presence of cavitory disease with or without nodular bronchiectasis, we would be unable to make that distinction without CT scan. And as I've mentioned, there are substantial clinical management decisions that would be included in that consideration. So that is the piece of evaluation that clinicians need to keep in mind regarding radiograph.

Then the symptomatic features are again, of indolent circumstance, but typically in cases of more active and substantive disease, would include cough and sputum production, would include some sense of malaise, though variably, and may or may not include weight loss. So we have two important arms of the features of clinical diagnosis. And then the third would be whether the patient has microbiologic evidence of disease by the accepted International Consensus Guidelines published in 2007 by the ATS/IDSA.

The requirement is that there be at least two recovered sputum samples that yield the same organism. Or alternatively, a separate source. And while biopsy is possible, the usual separate additional source would be bronchoscopy. So either two sputum samples revealing pathogen, or a bronchoscopic single BAL sample revealing the pathogen. So those would be the necessary microbiologic features that then we can add as our three-legged stool, if you will, to be the basis for making a conclusion about disease presence-- the infectious aspects, the symptomatic aspects, and the CT radiographic aspects.