Melanie: Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole. And today, we're discussing diagnostic delay and misdiagnosis in interstitial lung disease and the consequences can be grave.

Joining me is Dr. Namrata Patel. She's the Clinical Director of the Interstitial Lung Disease Program at Penn Medicine.

Dr. Patel, it's such a pleasure to have you join us today. Tell us a little bit about why interstitial lung diseases are so difficult to diagnose. What are some of the barriers to timely diagnosis?

Dr Namrata Patel: First of all, early symptoms are oftentimes really mild and can be attributed to more common diagnoses, such as allergies, asthma, chronic bronchitis, or even heart disease, so maybe months before a patient gets a CT scan that shows that the symptoms are in fact due to an initiative of lung disease process.

Even after that CT scan, given that the disease is relatively rare and can be nuanced in terms of their diagnoses, patients oftentimes require additional testing, subspecialty referral, and in some cases, even a biopsy to obtain the final diagnosis. In fact, we actually now know that more than half of patients surveyed by the Pulmonary Fibrosis Foundation reported having at least one misdiagnosis before getting the final diagnosis. And it took a median of seven months from the onset of symptoms to diagnosis. And even then, about 29% of responders said that they didn't get their final diagnosis until about two years after their initial symptoms.

Melanie: Is there an association, Dr. Patel, between delayed access and survival? How does this difficulty you just described affect patient outcomes?

Dr Namrata Patel: In order to answer your question thoroughly, I think the first thing is just because to kind of talk about the impact of getting the right diagnosis and how tricky and critical it is to help them guide the right treatment, that then can impact the patient outcomes in terms of survival, quality of life, and try to really prevent that time that patients are disabled from their diseases.

So I'm just going to step a little back a little bit in terms of prior to just talking about where we first try to intervene and get the patient the help they need by diagnosing them accurately. This can actually be tricky because we don't have a lot of guidance from societies. We actually have two documents that help us guide the diagnosis within the most common interstitial lung diseases, idiopathic pulmonary fibrosis. These are recently published. And although they do have a lot of overlapping consensus, there's actually important and meaningful differences in the guidelines that then make it tricky to diagnose this disease. In many cases, we rely upon the clinical expertise and judgment together with patient preferences to determine how best to proceed.

I'll give you an example that, in patients oftentimes that have fibrotic lung diseases, that are

disease of scarring from the lungs, they're oftentimes diagnosed with idiopathic pulmonary fibrosis. In fact, some of the clues that these aren't actually idiopathic and due to reversible causes such as hypersensitive pneumonitis or auto-immune lung diseases can be at least initially quite subtle and requires an astute clinician to look at closely their history and their clinical findings to be able to diagnose the patients with this disease.

The reason this is important is that it's important to manage the patients for these other less common diseases, because these less common diseases sometimes can be managed differently with different medications and can even be more amenable to treatment.

And then that means that, you know, if we find these patients have these other lung diseases that can oftentimes respond to anti-inflammatory therapy or immunosuppressive therapy, in these particular diseases, we can actually improve patient's symptoms and their lung disease. And so it's important for those patients to diagnose them early, to get them on the path to the directed treatment for their lung disease to help them gain lung function.

Oftentimes though the patients have these fibrotic lung diseases that may not be responsive to immunosuppressive therapy. And this is idiopathic pulmonary fibrosis. And in these set of patients, we actually do have two FDA approved anti-fibrotic therapies, pirfenidone and nintedanib, that can actually reduce the rate of decline in the forced vital capacity to about less than half of that with patients on placebo. This means so the sooner the patients get diagnosed, the sooner that the patients can start on the right therapy and the sooner we can change their rate of decline in lung function and thus delay the time when the patient has a meaningful exercise limitation or need for oxygen or really disability. And we really want to prevent the death in these patients. And in this particular case, time is alveoli and alveoli is lung function.

Melanie: Do patients need a biopsy generally? Tell us a little bit about diagnosis?

Dr Namrata Patel: Diagnosis with certain advances in our ability to know signs and symptoms of disease just by talking to patients. And especially with the advances in high-resolution CT scans of the chest, as well as availability of blood work to test for triggers of lung disease, we can oftentimes make diagnoses without a biopsy.

However, in certain cases, a biopsy should and is considered. The biopsy can be done through a procedure called a bronchoscopy, which is a minimally invasive procedure, but yields small tissue sample. It's about one to two millimeters big. And sometimes those samples aren't enough to make a confident diagnosis. In those cases, we sometimes request a surgical lung biopsy, which is a little bit more complicated and invasive. Given in either one of these biopsy procedures that there's a risk of bleeding, lung collapse, or even exacerbations of their initial lung disease, these should be performed only when necessary to help inform the diagnosis and treatment plan.

Even after the biopsy, it's oftentimes important, just as important as getting the biopsy and the tissue, is how it's interpreted by an expert pathologist as well as rediscussion of the case

with the radiologist and the pulmonologist together with the helpful information from the biopsy to arrive at that accurate diagnosis.

Melanie: Now, speak a little bit briefly about what's going on in treatment.

Dr Namrata Patel: I would say that the treatments really need to be specific to the diagnosis. Recently, we've been able to use anti-fibrotic therapies in patients who have scarring as a result of other inciting events. For instance, in patients with scleroderma-related initial lung disease, we can use anti-fibrotic therapy to help delay progression in their pulmonary dysfunction, as well as patients with broad range of lung diseases that in the end result in progressive fibrosis, we can also use these anti-fibrotic therapies, both nintedanib and pirfenidone to help in these certain situations. They have side effects that make it difficult for certain patients to tolerate them. So it's very important to work with the patient to assess their tolerance, to help them tolerate that, so they can get the benefits of the medication. It's also important to track for toxicities as these medications can cause abnormalities in liver function and has other side effects that need to be tracked.

The other group of therapies, I would say, are anti-inflammatory therapies in lung diseases. And that can range anywhere from corticosteroids like prednisone. We do understand in this field that although prednisone can help inflammation, it has a whole host of side effects. And so one of the things that we strive to do is to control the inflammation or the immune system from attacking the lungs with other medicines that do the trick without the same set of side effects.

Now, these medicines are also complicated and have their own set of side effects that we as clinicians need to be making sure that we are aware of. So we can advise our patients on how to best take them and how to best monitor for side effects and ensure their safety while they're trying to use these medications to improve their lung function.

We oftentimes follow these patients closely, not only to make sure they're tolerating the medications and watching their lung function, but also to make sure that they are getting better and these medications are actually helping our patients.

Melanie: Well, thank you so much, Dr. Patel. So as we wrap up, tell us about the interstitial lung disease program at Penn Medicine. You briefly mentioned a multidisciplinary approach and how important that is and how you can help patients have a more accurate and earlier diagnosis for interstitial lung disease. Give us a summary, if you would.

Dr Namrata Patel: I'm fortunate to work with a program that has several interstitial lung disease doctors whose clinical expertise and the majority of their patient care is with patients with interstitial lung disease. So given that the diseases are rare, I feel like that experience allows the clinician to understand these more rare diseases.

The other thing that we are privileged to have is a group of pulmonologists and specialized thoracic radiologists and lung pathologists, who meet weekly at a multidisciplinary diagnosis

meeting so that we can offer this resource.

When patients come, we generally see them, have a full exam, review all the testing and then present patients at the multidisciplinary conference to get that diagnosis and then help treat them with some of these medicines. I'm also fortunate to have a team of nurse practitioners and nurses and a specialty pharmacist, who is able to help prescribe the medications and help guide patients to limit the toxicity and modify the regimen if necessary to increase patient's tolerance. And then we follow the patients.

This is something that patients will oftentimes have for many years, lifelong. These medicines oftentimes don't work very quickly. So it requires a lot of management over time. One of the things that I did want to add is that as much as we can help many patients with the disease, some we can help improve and then some we can help delay the progression, many of those diseases do progress. And in the event of that progression, I think we can still help patients, both at our center and at many other centers by giving them help with their symptoms with oxygen, with guidance on how they live their daily lives to make the most of what they can from the lungs that they have. And then there's also a time to consider whether or not lung transplantation would be a helpful solution to help them prevent further disability from their disease, particularly in those diseases that we can't really cure with our medications.

Melanie: Thank you so much, Dr. Patel, for joining us today. To refer your patient to Dr. Patel or other members of our team, please visit our website at pennmedicine.org/refer or you can call (877) 937-PENN. That concludes this episode from the specialists at Penn Medicine. Please remember to subscribe, rate and review this podcast and all the other Penn Medicine podcasts. I'm Melanie Cole.