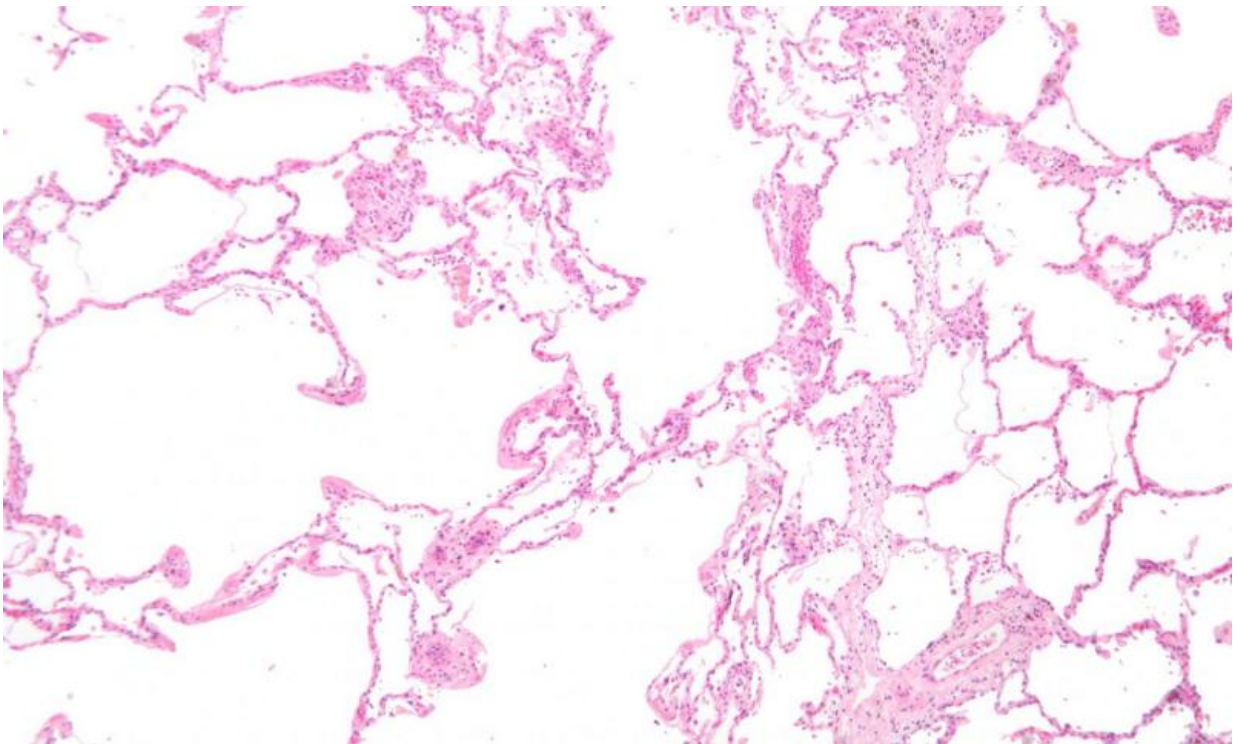


Nanoparticles wiggling through mucus may predict severe COPD

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Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

In a proof-of-concept experiment, researchers from Johns Hopkins Medicine say they have successfully used microscopic man-made particles to predict the severity of patients' chronic obstructive pulmonary disease (COPD) by measuring how quickly the particles

move through mucus samples. The technique, say the researchers, could eventually help doctors deliver more effective treatments sooner.

"If further studies verify our findings, nanoparticles could establish early which patients with COPD are more likely to need more intensive interventions to avoid adverse outcomes," says Enid Neptune, M.D., associate professor of medicine at the Johns Hopkins University School of Medicine, who partnered with Justin Hanes, Ph.D., and Jung Soo Suk, Ph.D., from the Center for Nanomedicine at the Wilmer Eye Institute at Johns Hopkins.

A report on the research was published Aug. 1 in the *European Respiratory Journal*.

According to the *World Health Organization*, 65 million people have moderate to severe COPD, making it the fifth leading cause of death worldwide. Linked to smoking and pollution, COPD describes a group of incurable, chronic inflammatory, lung-damaging processes marked by coughing, breathlessness and excessive production of spit and [mucus](#). Currently, the best diagnostic tool for COPD is spirometry, which measures how deeply a person can move air out through their lungs after taking a deep breath.

"Spirometry gives us a good picture of a person's current lung function, but tells us very little about how their disease will progress," says Neptune, which is why finding a predictive biomarker is so important.

In search of one, the research team focused on mucus, the slimy lubricant secreted by tissues that line airways, intestines and other body passages, forming protective barriers and—in the lungs—sweeping away potentially harmful particles inhaled with the air we breathe. Mucus has a structure similar to a water-filled sponge, with many tiny interconnected pores.

Hanes and Suk had previously engineered nanoparticles that don't stick to the mucus and discovered that these "muco-inert" particles were capable of navigating through the maze of mucus pores covering the airways. "The diffusion of muco-inert particles in airway mucus is primarily hindered by mucus' structure, and thus the mucus pore size can be estimated based on how fast the particles travel within the mucus samples collected from patients," says Suk.

"That suggested to us that the structure of the mucus in people with COPD might be distinct and affect the way foreign particles or even pathogens move," says Neptune.

To test this, the researchers next collected mucus samples from 33 patients who were active or former [smokers](#): Seven of the smokers had no history of COPD, 18 had mild to moderate COPD, and eight had severe COPD as determined by lung function.

The team then added nanoparticles labeled with a fluorescent marker that could be traced by an ultrasensitive camera into the mucus and observed their movement, watching for the speed at which the nanoparticles diffused through the sample.

The researchers found that in mucus collected from patients with COPD, the nanoparticles moved significantly slower compared with patients without COPD, indicating that their mucus had a more restricted structure, which is harder for the [nanoparticles](#) to navigate. The effect was even more pronounced when observing the nanoparticle behavior in mucus samples from patients with severe COPD, indicating that the pore size within the mucus shrinks as COPD progresses.

"If this restricted structure impacts the ability of immune cells to engage infectious pathogens in the lungs, it could potentially serve as a predictor for COPD flares, a critical risk factor in COPD progression," says

Neptune.

The researchers state that if future, larger studies validate their findings, the structure of mucus could provide new insight into how COPD progresses, as well as improve therapy.

More information: Jane F. Chisholm et al. Nanoparticle diffusion in spontaneously expectorated sputum as a biophysical tool to probe disease severity in COPD, *European Respiratory Journal* (2019). [DOI: 10.1183/13993003.00088-2019](https://doi.org/10.1183/13993003.00088-2019)

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