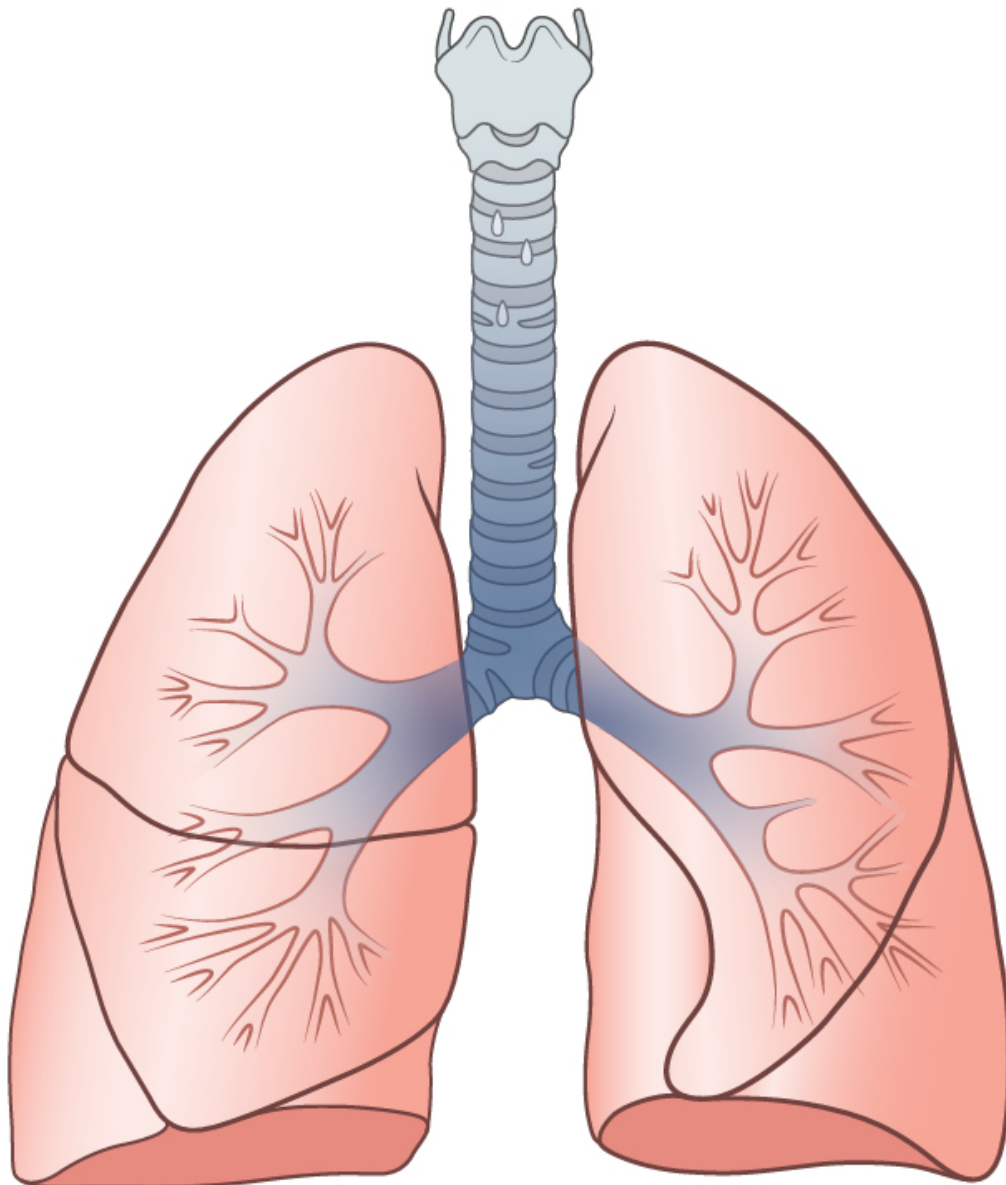


Immigrants in your lungs? Study showing how bacteria get there could help disease research

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The researchers conclude that most bacteria in the lungs arrive there through microaspirations -- tiny droplets of saliva from the mouth that evade the barrier that usually keeps them out. Credit: University of Michigan

They traveled a huge distance, evaded a protective barrier, and found themselves in a strange and unwelcoming land.

They're looked at suspiciously for possible links to dangerous diseases, and are under constant threat of being expelled from their adopted home. Their contribution to the greater community is only beginning to be understood. And every day, more of them arrive.

"They" are immigrants - of the microscopic kind. Specifically, they're bacteria living in human lungs. And new research pinpoints just how they get there, and opens the door to more research on what happens to them - and our bodies - as a result.

Writing in the journal *mBio*, researchers from the University of Michigan Medical School and VA Ann Arbor Healthcare System offer microbiome-based evidence that most of the bacteria in the lungs of healthy people got there by way of "microaspiration."

In other words, they rode in on tiny droplets of saliva that made it from the microbe-filled mouth to the lungs. That means they avoided the movable "wall" of tissue called the epiglottis that keeps most saliva from getting into the lower respiratory tract.

By studying the DNA of these bacteria throughout the lungs of healthy volunteers, the researchers confirmed that the population of microbes in

the lungs closely resembles the population found in the mouth. And by studying their distribution within the airways, the researchers could determine their most likely route of entry.

They found that many of the immigrant microbes make their home near the main carina, the spot at the end of the trachea where the airway branches off to the left and right lungs. This spot in the lungs is a "landing pad" where aspirated saliva - because of gravity and our upright posture - is likely to collide with the airway. But some bacteria manage to make it all the way to the deepest reaches of the pulmonary system, and reside in the tiny air sacs called alveoli.

Wherever the bacteria land, the researchers found, they join a community made up of mostly other recent immigrants. Few microbes are thought to be long-term residents of healthy lungs. Unlike the gut, healthy lungs are an inhospitable environment for bacteria, with little nutrition, and constant surveillance by the lung's immune system.

"This is the most comprehensive topographic survey of the healthy [lung microbiome](#) to date. It adds to the evidence that healthy lungs are like an island whose population is determined by the balance of immigration and elimination of species: who moves in and who moves out," says Robert P. Dickson, M.D., the first author of the new study. "The microbiome of the lung plays by a different ecologic rulebook than the gut microbiome, and this study helps clarify what those rules are."

He and his colleagues, inspired by classic models of ecology, have proposed an "adapted island model" of the lung microbiome, in which the lung's ecosystem is determined by the competing pressures of microbial immigration and elimination.

▲ 1 Bronchoscope contamination control

● 2 Proximal trachea

● 3 Mid-trachea

● 4 Main carina

● 5 Proximal bronchus intermedius

● 6 Distal bronchus intermedius

● 7 Right middle lobe orifice

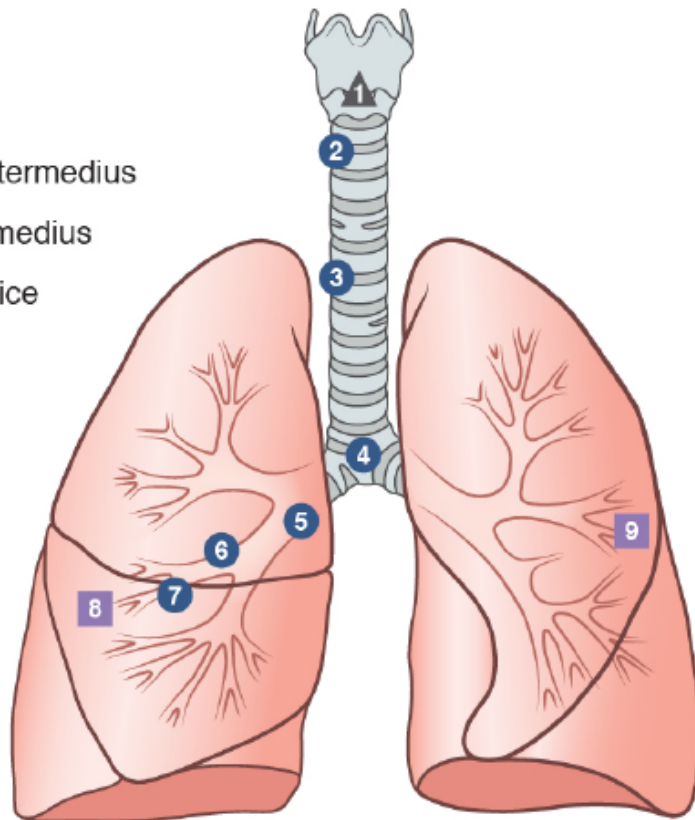
■ 8 Right middle lobe

■ 9 Lingula

▲ Bronchoscope contamination control

● Protected specimen brush

■ Bronchoalveolar lavage



The researchers sampled the microbiome in the lungs of healthy volunteers at many points, using a bronchoscope -- a tool commonly used by doctors to study lung disease. They show the technique could be used in future lung microbiome research. Credit: University of Michigan

Careful exploration

The new paper doesn't just describe the lung microbiome ecosystem - it also shows that scientists who want to study it in the future can feel confident using standard techniques that doctors already use to look for signs of [lung disease](#).

Dickson and his colleagues did their study in eight healthy volunteers who underwent bronchoscopy at VAAHS - allowing the researchers to pass a scope down their throat and into their lungs while they were under conscious sedation.

The team got samples of lung bacteria using two different techniques to sample nine separate sites in the lungs of each volunteer. One technique, called protected specimen brushing, used a special catheter that keeps bacteria from the mouth and throat from contaminating the samples taken in the airways.

Suspicion of such contamination has kept some researchers from fully accepting the results of previous lung microbiome research. So, to test for this contamination, the researchers took one sample on a brush held in the middle of the airway, and the rest using brushes that they gently touched to the airway wall.

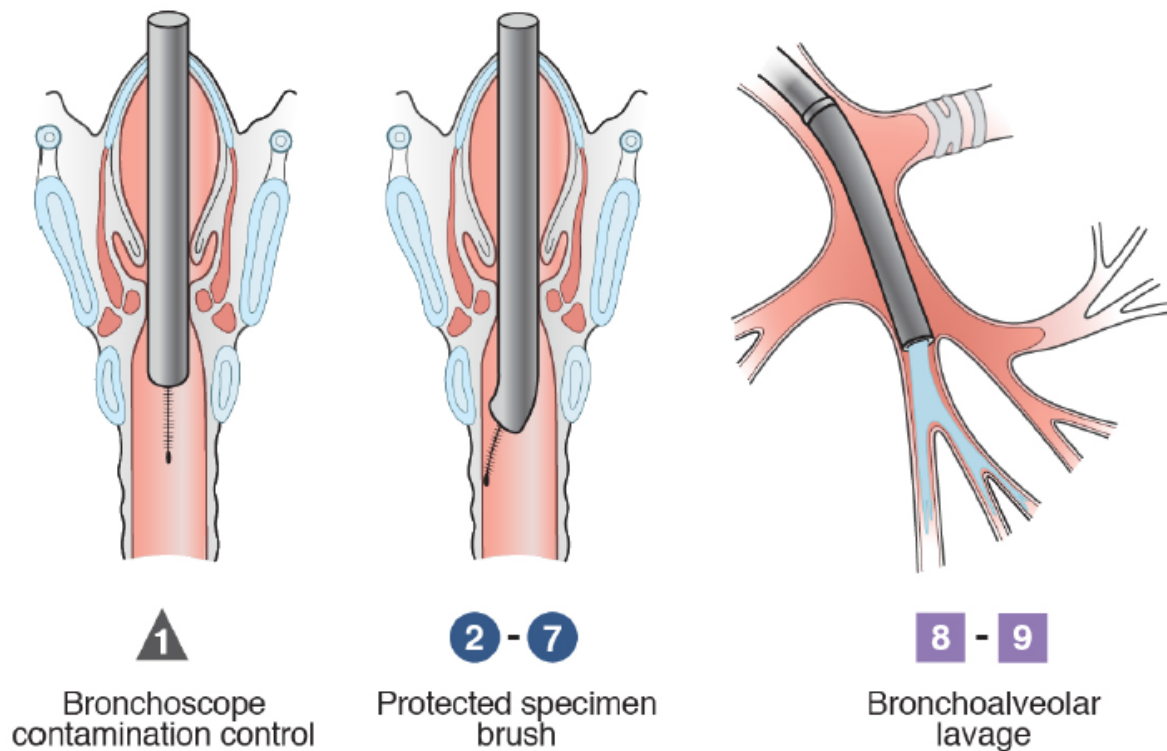
The researchers got other samples through bronchoalveolar lavage, in which they squirt a small amount of fluid into the deepest part of the lung and then suction it back into the bronchoscope, bringing microbes along with it.

They then analyzed the bacterial DNA that they found in all these samples.

"We found no evidence of [upper respiratory tract](#) bacteria in these contamination control specimens," says Dickson. "This reassured us that the rest of our samples truly reflected lung bacteria, and not just contamination from the procedure," brought in by the bronchoscope as it passed through the throat

Taken together, the results suggest bronchoscope-based techniques can be used to study the lung microbiome—in sickness and in health.

"The lungs are our largest interface with the outside environment, with 70 square meters of surface area," says Dickson. "That's 30 times the size of the skin, and twice the size of the gastrointestinal tract. And this study confirms that they're under constant bombardment by diverse communities of bacteria."



The researchers used a tiny brush and squirted liquid into the deepest reaches of the lungs to gather samples of the bacteria that live throughout the pulmonary system Credit: University of Michigan

The researchers emphasize that these volunteers were healthy, and had no symptoms that suggested pneumonia or other respiratory disease. "These volunteers were as healthy as you or me," Dickson says. "We are

probably all aspirating small amounts of bacteria constantly, and so long as our immune system is intact they rarely make us sick."

Dickson notes that microaspiration in healthy people has been observed for nearly a century in studies using medical imaging techniques. "We've known about the existence of microaspiration for decades," says Dickson. "But this is the first time we've been able to find its ecologic fingerprint."

Taking the research forward

Now that they understand more about the immigration question, Dickson and his colleagues aim to focus future research on what happens in people who have problems with the elimination part of the "adapted island" equation.

Inability to cough irritants out of the lung, or carry them out through the sweeping action of hair-like cilia on lung cell surfaces, could lead to more microbes staying longer in the lungs than normal. And that could lead to a higher risk of lung infection.

Such research could lead to better understanding of the lung microbiome's importance in conditions such as chronic obstructive pulmonary disorder, cystic fibrosis or the types of lung failure seen in intensive care units like the one where Dickson works at Michigan Medicine, the U-M academic medical center.

"If healthy lungs are like Antarctica - where conditions aren't good for microbe reproduction - then diseased lungs are more like a tropical island, where lower rates of elimination and altered environmental conditions permit the persistence and reproduction of certain bacteria," he says.

As the father of two young children, he also thinks it would be interesting to study how the lung microbiome changes when a person has a viral infection that causes the upper respiratory tract to produce much more nasal secretions. "I certainly look at my kids with their constantly runny noses and wonder if their lung microbiome look more 'nasal' than 'oral.'"

And, as researchers begin to uncover the impact of common medications such as antibiotics and proton pump inhibitors on the microbiome in the digestive system, he notes that it's not unreasonable to think that these drugs also affect the [lung](#) microbiome. He and colleagues have in critically ill patients.

More information: Robert P. Dickson et al, Bacterial Topography of the Healthy Human Lower Respiratory Tract, *mBio* (2017). [DOI: 10.1128/mBio.02287-16](https://doi.org/10.1128/mBio.02287-16)

Provided by University of Michigan

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