Breathing easier: Nature-inspired treatments could relieve acute respiratory distress

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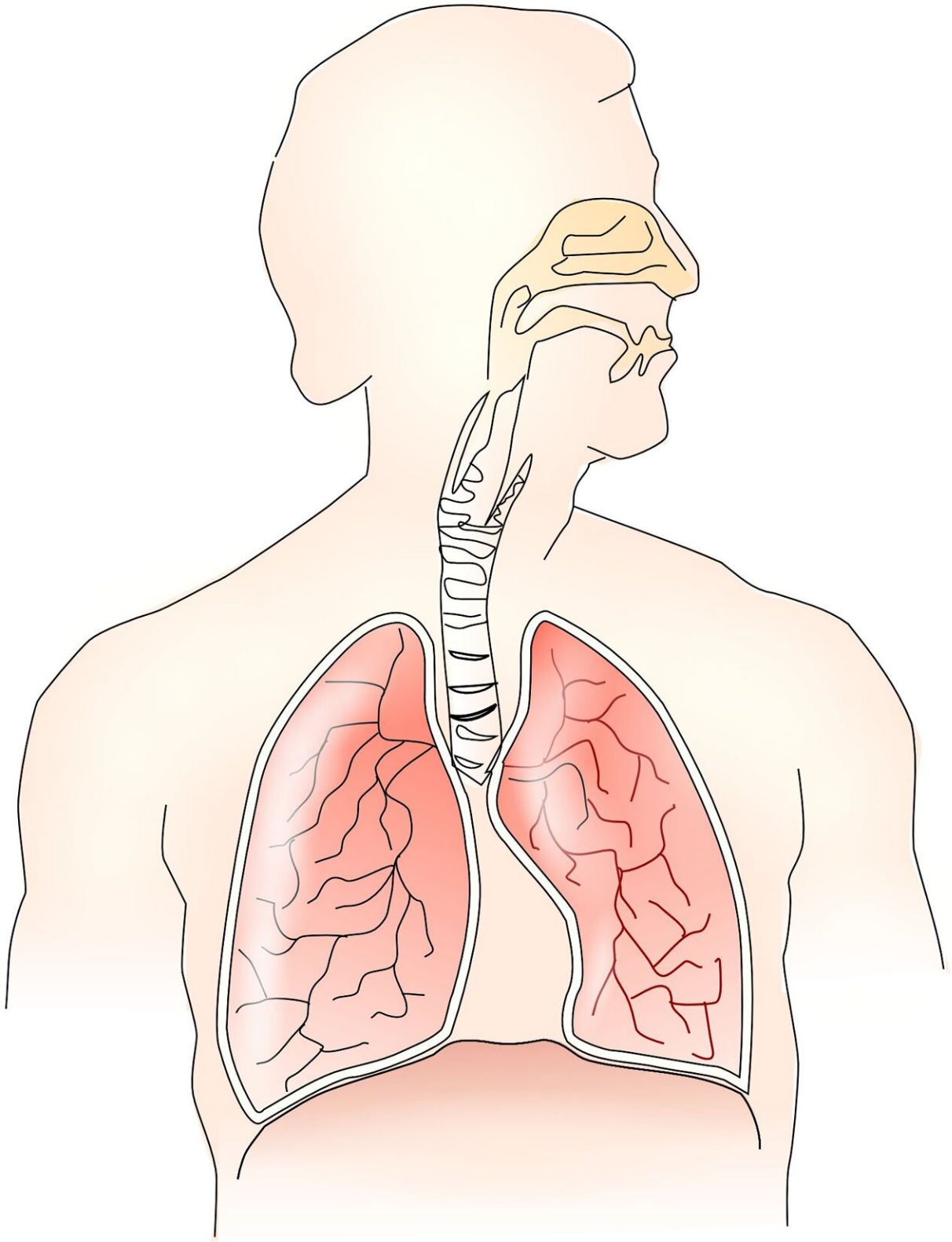

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Researchers are looking to nature for inspiration on how to treat acute respiratory distress syndrome, a life-threatening condition affecting thousands every year.

In 2014, Professor Kai Zacharowski, Director of the Clinic for Anesthesiology, Intensive Care Medicine and Pain Therapy at the Goethe University Hospital of Frankfurt, Germany, was treating a particularly complicated case of Ebola in a patient with acute respiratory distress.

As the man's condition worsened, Zacharowski reached for a new experimental drug—a molecule naturally occurring in the human body (FX06)—that he hoped could stabilize the patient. The intervention worked. An outcome that was both professionally inspiring and personally fulfilling.

"We were able to save the life of a human, a father and a colleague," said Zacharowski.

Pandemic connection

This experience came to Zacharowski's mind several years later when the COVID-19 pandemic broke out. His department at the hospital was responsible for treating the largest number of COVID-19 patients in the Hesse region of Germany.

A large-scale multi-country research effort was formed to try to understand how this treatment could be used to prevent COVID infection progressing to its severest and most life-threatening form: acute respiratory distress syndrome (ARDS).

The COVend project, led by Zacharowski, began in the midst of the pandemic in November 2021. Researchers set out to harness the power of artificial intelligence (AI) and systems biology to better understand how FX06 works in individual patients and determine its therapeutic value as an effective drug, with no known side-effects, for use in the fight against COVID-19.

"We are optimistic that our research will provide unprecedented insights into ARDS," said Zacharowski.

Wider reach

The research team's mission didn't stop there, however. Although COVID-19 drew attention to this very frightening condition, it can be triggered by a variety of factors, including bacterial or viral infection, sepsis, trauma, surgery or blood transfusions. It can also be caused by inhalation of toxic fumes or liquid.

Currently, no effective therapy exists for ARDS and it is a difficult condition for intensive care wards to manage. The COVend researchers estimate that there are between 30,000 and 120,000 cases of ARDS in the EU every year, and that it accounts for around 10% of all intensive care admissions. It also has a very high in-hospital mortality rate of up to 45%.

Acute respiratory distress occurs when fluid builds up in the air sacs (alveoli) of a patient's lungs, preventing them from filling properly with air and stopping oxygen getting into the body, often with fatal consequences. Patients who survive often suffer permanent scarring to their lungs.

"ARDS is a devastating condition that not only has a high mortality rate, but also results in a long recovery for many survivors," said

Zacharowski.

Natural protection

FX06 is a protein fragment naturally present in the human body which binds to the cells lining the blood vessels, helping to protect them. The drug can potentially reduce the mechanical cause of ARDS—when fluid from very small blood vessels leaks into surrounding tissue, including the alveoli.

The COVend research team have successfully put together the first clinical trial for the use of FX06 in mild and moderate ARDS cases. They are currently recruiting around 260 patients in France, Germany, Lithuania, Romania and Spain. Results are expected sometime in early to mid-2026.

The aim is to identify which patients will benefit most from being treated with FX06. To do this, the COVend team are profiling hundreds of molecules in patients' blood and using AI to study their role in disease progression.

"This is a fascinating molecule because it can be used in so many ways," says Dr. Petra Wülfroth, COVend innovation officer and chief scientific officer at F4 Pharma, an Austrian biopharmaceutical company that is a partner in the project.

The research carried out could also prove useful for possible future pandemics as the treatment is directed at a condition that could be set off by a range of different pathogens.

"My dream would be to see this molecule used in intensive care whenever the permeability of small blood vessels is increased—a potentially life-threatening situation."

Breathing like a bird—or fish

Currently, in the absence of an effective pharmaceutical intervention, ARDS patients are often given oxygen or placed on a ventilator to assist their breathing. In severe cases, their blood can be oxygenated outside their body using a technique known as extracorporeal membrane oxygenation (ECMO).

These treatments can, however, have severe side-effects on the patient. With ECMO there is a risk of infection or clotting, while prolonged use of a ventilator can damage lung tissue.

Professor Margit Gföhler, who teaches biomechanics and rehabilitation engineering at the Vienna University of Technology (TU Wien) in Austria, is leading a project called BioMembrOS that will run for three and a half years until mid-2027.

Together with her colleague at TU Wien, Michael Harasek, a specialist in chemical engineering and membrane science, they are coordinating an international research effort to develop an alternative respiratory assistance device inspired by the natural, and highly efficient, breathing mechanisms of fish and birds.

"We need completely different approaches if we want to develop new devices for respiratory support that don't have the problems we see with current options," she said.

When we breathe, oxygen moves from the lungs to the bloodstream through the alveoli and a network of tiny blood vessels called capillaries. At the same time, carbon dioxide passes from the blood to the lungs so that it can be expelled from the body when air is exhaled.

This process is known as gas exchange—and it is severely compromised

in ARDS when the alveoli are flooded. Gas exchange allows the body to replenish oxygen and eliminate carbon dioxide, both of which are necessary for survival.

Novel membrane

The BioMebrOS team, which brings together researchers from Austria, Germany, Italy, Portugal and South Africa, are working on developing a novel membrane structure based on the structural design of birds' lungs, which exchange gas more efficiently than those of mammals. They will also incorporate certain aspects of fish gill respiration, namely their surface contact with fluids.

The idea is to create a device with a membrane that both removes carbon dioxide from the patient's blood as it passes through and infuses it with oxygen.

"Nature has bioengineered the most efficient solutions to life's challenges," said Gföhler. "By adopting the structural and functional characteristics of the most evolved gas exchangers, we will create a radically improved technology."

The first goal of the BioMembrOS researchers is to develop a small, testable prototype of this membrane structure and test its efficiency in in-vitro blood tests.

"The overall goal for the future would be to make it so efficient and small that we could implant it in the patient," said Gföhler, who hopes that devices incorporating their membranes will be available for patients within the next decade.

COVID-19 may have helped to draw public attention to the significant suffering caused by ARDS, but the challenge is far wider. ARDS is seen

in huge numbers of patients worldwide—and respiratory diseases are the third largest cause of death in the EU.

Whether through research into new molecular drugs or improving the way we build medical ventilators, more research is needed to reduce the distress caused to patients around the world. Nature may prove to be an important ally.

More information:

- COVend
- BioMembrOS
- EU health research and innovation

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