

Drugs used to treat lung disease work with the body clock

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Scientists from The University of Manchester have discovered why medication to treat asthma and pneumonia can become ineffective.

The findings, published in *Nature Medicine*, show that drugs widely used to treat lung diseases work with the body clock.

In the UK pneumonia, which is caused by an infection, affects around 1 in 1000 adults each year and is more serious for babies, young children, the elderly, smokers and those with an underlying health condition.

More than 5 million people in the UK are affected by asthma and the NHS spends around £1 billion a year treating and caring for people with the disease.

The research, led by Professors David Ray and Andrew Loudon from The University of Manchester, found out that cells lining the lung airways have their own body clock which is the time-keeper for [lung inflammation](#) - both conditions cause swelling (inflammation) in the lungs.

And the team discovered that more severe lung inflammation happens as a result of the loss of the body clock working in these cells.

Professor Loudon said: "We found a key molecule known as CXCL5 that facilitates lung inflammation which is a key regulator of how [immune cells](#) get into tissues. The loss of CXCL5 completely prevents

the time of day regulation of lung inflammation which opens up new ways to treat lung diseases."

During the research, the team uncovered how glucocorticoid hormones from the adrenal gland are vital in controlling the level of inflammation in the cells lining the airway.

Professor Ray said: "This hormone works through the glucocorticoid receptor, a major regulator of gene expression. We wanted to find out therefore if glucocorticoid medicines, like prednisolone or dexamethasone would also show a time of day effect, and our research shows they do."

The team concluded that the rhythm of the clock in the lining of the [cells](#) in the lungs is important for lung diseases like asthma, and chronic [obstructive pulmonary disease](#).

Professor Loudon said: "In this work we define a major circadian control on lung inflammation which affects responses to bacterial infection, or pneumonia. We know that many lung diseases indeed show a strong time of day effect, including asthma, and deaths from pneumonia."

Our bodies anticipate the change from day to night by having an internal, or circadian clock. This explains why it is hard to adjust to shift work. The body clock regulates sleep, but now has been discovered to also regulate our immune system.

"We live in a world that is divided into day and night. As a result our behaviour varies by time of day; we sleep at night, and are active, and eat during the day. Increasingly our lives are disconnected from this ancient rhythm, with artificial light, shift work, and jet lag," concluded Professor Ray.

More information: An epithelial circadian clock controls pulmonary inflammation and glucocorticoid action. *Nature Medicine* DOI: [10.1038/nm.3599](https://doi.org/10.1038/nm.3599)

Provided by University of Manchester

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