JEM: Neutrophils are less aggressive at night, explaining why nighttime heart attacks cause less damage than daytime events

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A CNIC study reveals that neutrophils—a type of immune cell—are less aggressive at night, explaining why nighttime heart attacks are less severe than those occurring during the day

Heart attacks that occur at night are less severe than those that strike during the day. A new study from the Centro Nacional de Investigaciones Cardiovasculares (CNIC) explains why. Published in the Journal of Experimental Medicine, the study led by Dr. Andrés Hidalgo's group at the CNIC shows that neutrophils—a type of white blood cell—have an internal clock that regulates their aggressiveness throughout the day and determines the extent of damage they cause to the heart after a heart attack.

The researchers also developed a pharmacological strategy in experimental models to block the molecular clock in neutrophils, keeping them in a "nighttime" state and thereby reducing their harmful potential during a heart attack.

The immune system protects the body against microorganisms that cause infection. Because humans are diurnal—active during the day and asleep at night—the likelihood of exposure to pathogens is higher during the day. The immune system therefore adjusts its activity peaks to this circadian rhythm.

However, this same defensive response can become harmful. It is well known that in stressful situations such as myocardial infarction, the immune system can cause severe collateral damage to tissues.

Decades of research have shown that almost half of the cardiac damage after a heart attack is caused by neutrophils. Interestingly, this type of inflammatory damage fluctuates naturally throughout the day, suggesting the existence of circadian mechanisms that limit neutrophil activity and protect the body.

In collaboration with the Multidisciplinary Translational Cardiovascular Research Group at the CNIC, led by **Dr. Héctor Bueno**, the researchers examined data from thousands of patients at *Hospital 12 de Octubre*. The analysis confirmed that lower neutrophil activity at night results in less severe heart attacks during this period. The team then developed a pharmacological strategy in experimental models to block the molecular clock in neutrophils, reducing their harmful potential during infarction.

“The compound mimics a factor that the body produces mainly at night,” explains Dr. Hidalgo. “In a way, this factor ‘tricks’ neutrophils into thinking it’s nighttime, reducing their toxic activity.”

Study first author Dr. Alejandra Aroca-Crevillén highlights that the observed protection stems from a change in cellular behavior: “At night, neutrophils migrate to the damaged area while sparing healthy tissue. During the day, they lose this directionality and cause more damage to surrounding tissue.”

This study is one of the first to harness the circadian rhythms of the immune system to modulate inflammation without compromising infection defense. “We were surprised to find,” adds **Dr. Aroca-Crevillén**, “that blocking the neutrophil circadian clock not only protects the heart, but also improves responses to certain microbes and even reduces embolisms associated with sickle cell anemia.”

The findings reveal a neutrophil circadian ‘checkpoint’ that protects against excessive inflammation and can be therapeutically activated to protect the body.

The authors conclude that the results open the door to new therapies based on chronobiology (the branch of biology that studies how living organisms structure their physiological processes in time), with the potential to protect the heart and other organs from inflammatory damage without weakening the body’s natural defenses.

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