

# Our biological clock plays crucial role in healing from surgery

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If you have just had knee, shoulder or hip surgery, you may want to take anti-inflammatories in the morning or at noon, but not at night. A McGill-led study shows, for the first time, that circadian clock genes are

involved in healing from surgery. Indeed, the researchers demonstrated that anti-inflammatory medications are most effective in promoting post-operative healing and recovery when taken during the active periods of our biological clocks.

The study, recently published in *Scientific Reports*, also suggests that if anti-inflammatories are taken either in the afternoon or at night, during the resting phases of the circadian [rhythm](#), they can severely deter healing and [bone repair](#) following surgery. That's because these are the periods when cells known as osteoblasts are rebuilding bone.

## **Circadian clock genes involved in healing from surgery**

Although prior research has shown that [circadian clock genes](#) play a role in diseases such as cancer, Alzheimer's, arthritis and Parkinson's, this is the first study to see the effect of the circadian rhythm in any type of surgery or injury. [Faleh Tamimi Marino](#), the Canada Research Chair for Translational Cranofacial Research is the senior co-author on the article, along with Belinda Nicolau and Laura Stone. All are McGill's Faculty of Dentistry.

Inflammation, following surgery, is crucial to healing since part of the process involves both destroying any bacteria that may be in the area, and signaling to attract the cells that will rebuild the tissues. But the process is not a constant.

"There are periods of inflammation that are actually very destructive, and there are periods that are constructive and important for healing," said Faleh Tamimi. "So many [pharmaceutical companies](#) have been trying to develop drugs that will inhibit the destructive processes during inflammation but not interfere with the helpful ones."

He adds, "The idea that I came up with in the shower one [morning](#) is that we could perhaps use the circadian variations in inflammation to our advantage. The destructive component of the circadian rhythm as it relates to bone healing occurs during the day, when cells known as osteoclasts break down bones. The constructive cells, known as osteoblasts that rebuild bones are active at night. By limiting the use of anti-inflammatories to the mornings and giving analgesics at night for the pain, I thought we might get better results in terms of bone healing than if anti-inflammatories are given throughout the day."

## **Significant differences in rates of healing and in genes**

The researchers compared pain and bone healing in two different groups of mice with fractured tibia. One group was given constant doses of anti-inflammatories over a twenty-four hour period, while the others were given anti-inflammatories only in the morning—during the active phases of the circadian rhythm—and analgesics at night. The researchers found that the second group recovered from the pain of the injury, and regained bone strength more quickly and more fully. Surprisingly, they also noticed differences between the groups in the expression of over 500 genes specifically related to [bone](#) healing processes. "Its almost as if morning anti-inflammatories and evening anti inflammatories were two different drugs" adds Faleh Tamimi.

## **The rhythm of the body's own healing**

"When I was a child, and I cut myself, my mother would say to me, don't worry, go to sleep and tomorrow you will be better," said Haider El-Waeli, the first author on the study, who wrote the paper while working on his Ph.D. at McGill and is now a clinical resident at Dalhousie University. "It turns out she was right because most of the healing

happens at night."

"The body has a rhythm," adds Tamimi. "And if you give anti-inflammatories in the morning you are working with the rhythm of the body and when you give them at night, you are working against it so you disrupt the healing."

As a next step, the researchers are collecting preliminary data from a clinical trial monitoring pain and [healing](#) related to extraction of wisdom teeth, using two different drug treatments—one involving exclusive use of anti-inflammatories, and the other administering [anti-inflammatory medications](#) only in the morning and at noon, and analgesics in the afternoon and evening. The preliminary results are promising.

**More information:** H. Al-Waeli et al, Chronotherapy of Non-Steroidal Anti-Inflammatory Drugs May Enhance Postoperative Recovery, *Scientific Reports* (2020). [DOI: 10.1038/s41598-019-57215-y](https://doi.org/10.1038/s41598-019-57215-y)

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