

Cigarette smoking impairs ligament healing, researchers find

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The list of reasons you shouldn't smoke has gotten longer. Researchers at Washington University School of Medicine in St. Louis are reporting that smoking interferes with ligament healing.

Studying mice with knee ligament injuries, the team discovered cigarette smoking impairs the recruitment of cells to the injury site and delays healing following ligament-repair surgery. They reported their findings in the *Journal of Orthopaedic Research*.

The researchers looked at the mouse medial collateral ligament (MCL), a ligament that supports the knee joint in both mice and people. Each year in the United States there are more than 20 million reported ligament injuries, and MCL injuries are the most common. They also are the most common injuries seen in competitive and recreational sports. It's not clear exactly how many MCL injuries occur annually because many go unreported.

"A lot of MCL injuries never make it to an emergency room because patients will have a sore knee but don't seek treatment," says Rick W. Wright, M.D., associate professor of orthopaedic surgery and a senior investigator on the MCL study.

Previous studies have demonstrated that the mouse provides a good paradigm for what happens in injured human knees.

"This is a good model for knee ligament injury, but it could be a model

for ligament injuries anywhere in the body," says co-investigator Linda J. Sandell, Ph.D., professor of orthopaedic surgery. "It's likely the biology is transferable to other knee ligaments, elbow ligaments, shoulder ligaments, you name it."

To look at the effects of smoking, Sandell, Wright and their colleagues used a system developed at the School of Medicine in which mice are placed inside smoking chambers six days per week. The mice don't actually have cigarettes in their mouths, but they get enough passive fumes to "smoke" two cigarettes daily, the equivalent of a person smoking about four packs per day. Mice were placed in the smoking chambers for two months prior to MCL surgery and then again after surgery to mimic the behavior of humans who continue to smoke following an injury.

The researchers say athletes who smoke should keep these findings in mind before driving for a lay-up, sliding into second base or lacing up a pair of ice skates.

The soft tissue healing that occurs following ligament injuries occurs in stages. There is an immediate pooling of blood near the injury, the sort of hemorrhaging that will cause swelling right away. This initial response is followed by several days of inflammation, in which cells called macrophages flock to the injury site and secrete substances called cytokines and chemokines. Those, in turn, recruit more cells to assist in healing. That process of cellular proliferation and synthesis lasts for several days to several weeks. The final stage of healing involves remodeling of the tissue and can continue for months and even years.

An earlier study found an increase in cell density and in gene activity to produce type I collagen in the first week following MCL injury, so in this study the researchers paid close attention to cell density, biomechanical function and gene expression during the first week after

MCL repair. In mice exposed to cigarette smoke, cell density was lower and type I collagen gene expression was reduced.

"Our studies also have shown a decreased macrophage response that may help explain why we see this delayed or decreased healing response," Wright says.

Between 20 and 25 percent of the U.S. population smokes. Wright and Sandell say that although the prevalence of smoking among athletes is slightly lower, a significant percentage of recreational and even professional athletes continue to smoke. Many others use chewing tobacco, which may cause some of the same effects. But that's not yet clear since the mice in this study were exposed to smoke rather than to nicotine only.

"There are two ways to do smoking studies in animal models," Sandell explains. "One looks only at a single component, like nicotine. The other way is to use a method like the one we employed that includes all of the toxins found in smoke. We think exposing the mice to cigarette smoke itself is most relevant because when people smoke, they don't get individual components. They get everything."

Sandell and Wright say their findings point to yet another reason smokers would do well to quit.

"Many patients don't want to hear it, but these results suggest that smoking affects anyone who needs ligament-repair surgery." Wright says. "I counsel surgery patients to at least try to decrease smoking because, if nothing else, that will improve the healing of their surgical incisions. Quitting smoking is good health management regardless, but in patients having this kind of surgery, there are extra advantages."

Wright and Sandell are conducting more studies. Currently they are

comparing mice exposed to smoke before MCL surgery to those exposed both before and after surgery to see whether ending smoking might assist ligament healing.

"Because ligament injuries usually occur suddenly, it's unlikely people will stop smoking until after their injury," Sandell says. "So we want to learn whether smoking cessation near the time of surgery might help reverse the healing delays we saw in this study."

Source: Washington University

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