Chronic pain affects at least one in three adults in the U.S., which is more than the sum total of those with heart disease, cancer and diabetes combined. For many of these 116 million Americans, their pain is severe and eludes available treatments. In addition to the human suffering, the monetary cost of medical treatment and lost productivity has reached $635 billion a year.

The U.S. needs "a cultural transformation" in the way we view pain, treat it and conduct research on its causes and treatments, says a new report released June 29 by the Institute of Medicine (IOM).

Pain can be protective. Acute pain tells us to pull a finger back from a hot stove, stop walking on a blistered foot or allow a fevered body to rest. It is a warning that bodily injury needs attention and time to heal. But when the pain signal continues for an extended period, "it can become a disease in its own right," Philip Pizzo, dean of the Stanford University School of Medicine and chair of the committee that wrote the IOM report said at the news conference where the report was released.

Pain can actually rewire nerve and brain pathways. In much the same way that memories are created, it can become a self-perpetuating loop that continues to feed back on itself long after the original cause for the pain has resolved.

Chronic pain can shrink the volume of the brain's gray matter, the portion of the brain devoted to thought. Researchers speculate that this decrease results in part from a limited pattern of stimulation of circuits that are preoccupied with a continuous pain loop that crowds out other activity. In addition to that, continuously stimulating the pathway releases more of the neurotransmitter glutamate, an excess of which can be toxic.

The IOM's new report describes chronic pain as a major public health challenge and one that requires aggressive action and a more comprehensive strategy.

The U.S. Department of Health and Human Services should develop "a public population-based approach to dealing with pain as the singularly important integrating factor," Pizzo said. That includes boosting education for doctors and patients, improving research efforts to discover the various roots of chronic pain, and helping government agencies work together better to ensure that people can get access to medications that they need—as well as improve the odds that new ones will be available in the future.

A variable condition

One major challenge of understanding and treating pain is its huge variability. In working with mice, researcher Jeffrey Mogil, at McGill University's Pain Genetics Lab, has found that the response to pain can vary tremendously by breed and by gender. Some of those differences also have been observed in humans. Caucasians appear to be more tolerant of pain than those of African descent. And it is now well established that women on average are more sensitive to pain than are men, although they also have better coping mechanisms for acute pain such as the estrogen receptor–based response that kicks in during childbirth.

Individual differences also are reflected in wide range of responses to painkilling medicines. The treatment of pain has turned out to be one of the most variable and idiosyncratic of all of the fields of medicine, with perhaps hundreds of genes influencing a person's pain reaction and response to therapy.
These factors reinforce the fact that "care for pain begins with the individual and recognizes that it is broadly undefined and that there is no single prescription for dealing with pain," Pizzo said, adding that because of these vast differences, it is also largely self-managed. And as the report committee found, there is a distinct shortage of data about how people in different demographic groups might experience pain, access treatment and respond to it.

**Treatment**

Pain often has taken a backseat to more observable and quantifiable physical ailments in medical practice and training. "In medical education pain generally has received little attention, which has contributed to the problem of undertreatment," the authors of the new report noted. "The need for improved education about pain is especially acute for primary care providers, the front-line clinicians for most people's acute or chronic pain problems." The report says only five of the nation's 133 medical schools have required courses on pain, and just 17 offer such courses as an elective.

Opioids carry a risk for addiction and abuse, which has drawn the attention of law enforcement and led to investigations and prosecutions that some physicians and patients say has inhibited access to effective pain relief.

The committee received an unusually large number of public comments—more than 2,000—in conducting its study. "It is extraordinary how many patients describe themselves as collateral in the war against drugs," where law enforcement concerns for potential abuse take precedent over the medical imperative to treat suffering, said author–journalist Melanie Thernstrom, who participated on the committee as a patient advocate.

Physicians must obtain a license from the U.S. Drug Enforcement Administration (DEA), a federal policing agency, in order to write a prescription for controlled substances such as opioids. The DEA has pulled that license from physicians when it disagrees with their prescribing practices, and has prosecuted some, sending them to jail.

Many patients might have been on low-dose opioids for years, "and suddenly their primary care physician would no longer be willing to prescribe it," Thernstrom said. Some have had to take off from work and drive long distances to a pain specialist "simply to get a prescription every single month." Often those additional costs of travel, missed work and getting specialist treatment are not covered by their health insurance.

Committee member Robert Kerns, a professor of psychiatry at Yale University and director of pain management with the Veterans Health Administration, is encouraged by the White House Office of National Drug Control Policy's recent acknowledgement of these concerns and the importance of striking a balance between legitimate medical needs and law enforcement, he noted at a press briefing on the report.

**Research**

Despite the limitations of current treatment options, innovations to treating chronic pain have been scarce and limited to tinkering with the delivery of existing classes of drugs. Opioids and nonsteroidal anti-inflammatory drugs, such as aspirin and ibuprofen, "have been used in one form or another for hundreds of years and still we have not come up with new and novel agents," explains Sean Mackey, a neurologist and pain specialist at Stanford. "What we desperately need are new classes of medications to really attack pain at every point along where the injury and signals are processed." (Mackey discussed some of these ideas with *Scientific American* in a podcast.)

And to develop new types of drugs, scientists will likely have to gain a better understanding of how the body generates these pain signals in the first place. "We need research that will identify new mechanisms and be able to quickly translate that new basic science knowledge into novel treatments," Mackey said. He believes that translational process requires breaking down compartments of expertise and working together among government agencies, academia and industry as well as across disciplines.

Scientists recently have identified and synthesized a natural pain relief compound with what appears to be a different biological mechanism of action than opioids. But this potential treatment has only been studied in a small number of mice. For those suffering from chronic pain a clearer path to treatment likely cannot come soon enough.

The IOM report recommends, in the short-term, that doctors and patients should be better informed about pain and currently available treatments; barriers to accessing pharmaceuticals should be removed; and alternative treatments that have demonstrated some efficacy, such as physical therapy, should be made more available and covered by insurance. But for the long-term it says a substantial
investment in research is needed to achieve a deeper understanding of the science of chronic pain—and new ways to alleviate it.