ON THE BRAIN

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Injuries on the Field—and in the Brain

How many times have we heard television announcers exclaim, "Wow, he really got his bell rung," as the play shows a football player taking a hit to the head? Not only does this reaction trivialize what has happened to the athlete, it also points to a lack of understanding throughout the sports world on the issue of head injuries. Concussions, in truth, are not the stuff of high-color commentary. They are troubling, severe, and sometimes fatal injuries to the brain.

A concussion, also known as a traumatic brain injury, is a blow to the head that causes the brain to move rapidly inside the skull. "In a concussion, the brain actually gets rotated," says William P. Meehan III, MD, a clinical instructor in orthopedic surgery at Harvard Medical School and a member of the Brain Injury Program at Children's Hospital Boston. "The brain doesn't bang against the skull, nor does it develop a bruise or contusion from such a collision. Rather, a concussion damages the brain because it causes the organ to rapidly rotate inside the skull."

This rapid rotation causes nerve cells in the brain to stop functioning properly. To work well, nerve cells require external and internal environments that contain certain concentrations of particular electrolytes, specifically, sodium ions on the outside and potassium ions on the inside. When the neurons fire, these ions trade places; sodium ions move into the cell through the cellular membrane, while potassium ions travel from the cell into the surrounding environment.

continued on page 2

CONTENTS

A Tribute To Daniel C. Tosteson

Photo courtesy of Magdelena Tosteson

Daniel C. Tosteson, a founder and an active supporter of the Harvard Mahoney Neuroscience Institute (HMNI), died on May 27, 2009 at home in Boston from complications of Parkinson's disease. While dean of the Harvard Medical School, Tosteson worked closely with philanthropists Hildegarde and David Mahoney to establish the Institute at HMS in 1990. He remained a council member, and an advocate as well as a mentor to HMNI for nearly two decades.

A powerful force for change in medical education, Tosteson served as the administrative leader of HMS from 1977 to 1997. During his tenure, he worked to reshape how medicine was taught and transformed the School's curriculum to emphasize case-based learning within a team environment, an approach that influenced curricular reform at medical schools throughout the nation. In his efforts to forge innovative collaborations with forward-thinking organizations and individuals, he helped develop the idea for HMNI. The Institute has brought together talented scientists whose work advances our knowledge of neurological function and psychiatric disorders such as addiction. In addition, HMNI aims to promote communication between researchers and the public, foster scientific exchange, and recognize national leaders in public education in neuroscience.

HMNI joins the Tosteson family in mourning their loss. His wisdom, leadership, and support will be missed by all who knew him.

continued from page 1

When the head is dealt a blow, these ion concentrations are disrupted and the nerve cells fail to fire properly, according to research published in the *Journal of Neurosurgery*.

The Centers for Disease Control and Prevention (CDC) estimates that 1.6 million to 3.8 million sports- and recreation-related head injuries occur each year; 75 percent of these injuries are classified as concussions. Football players suffer this form of injury more often than athletes in other competitive sports do. According to the CDC, football-related concussions account for more than 60 percent of all traumatic brain injuries.

Subtle Signals

Following a concussion, a range of symptoms may manifest in a matter of minutes or even seconds. These symptoms can include a blank, vacant, or unfocused stare; delayed verbal or motor responses; confusion; disorientation; slurred speech; and gross coordination abnormalities. Different symptoms can manifest hours or days later and can include persistent headache, poor attention and concentration, memory dysfunction, nausea or vomiting, irritability, fatigue, disturbed sleep, and anxiety. And contrary to popular belief, one can suffer a concussion yet not be rendered unconscious.

"Loss of consciousness is a symptom, but in most cases, the symptoms are subtle," says Pierre A. d'Hemecourt, MD, a lecturer on orthopedic surgery at HMS and a physician in the sports medicine and brain injury programs at Children's. "To diagnose a concussion, we use a twenty-one-point system that assesses difficulty in concentrating and in remembering, mood changes, headache, dizziness, and fogginess—a significant complaint. Not all of these symptoms are always present." Diagnosis can be difficult, though, because concussion symptoms overlap those of dehydration, depression, and headaches from other causes.

The Centers for Disease Control and Prevention (CDC) estimates that 1.6 million to 3.8 million sports- and recreation-related head injuries occur each year; 75 percent of these injuries are classified as concussions.

According to Meehan and d'Hemecourt, the on-field diagnosis of concussion for an injured athlete includes a symptom check, simple tests for cognition and balance, and a neurological examination. The cognitive testing for this diagnostic process, they add, is more effective if the athlete has undergone a preseason baseline concussion test; doctors and trainers then have a reference against which to measure the injured player's responses.

No-Play Zone

Diagnosing this type of injury is one thing, judging when it is safe for an athlete to again play is quite another. Guidelines regarding the immediate return of injured athletes to the playing field are somewhat controversial. Young athletes who experience a head injury—participants in high-school sports or in youth sports like Pop Warner football—should not return to play on the day of the injury; athletes at the college and professional levels, however, can do so after being cleared by proper testing.

"Once injured athletes are without symptoms for a day or two, they can begin to increase their activity level," says d'Hemecourt. "But the general rule for return-to-play is for the athlete to be completely symptom-free."

Guidelines published in the *British Journal of Sports Medicine*, which have no direct influence on rules governing sports in the United States, created

some controversy because many physicians felt their strictness might deter athletes from reporting head injuries. In fact, the number-one reason high school athletes cite for not reporting a concussion, says Meehan, is that they did not recognize it as a serious injury.

Diminishing Returns

Although concussion symptoms typically resolve on their own—and most athletes recover from their injuries—some individuals may experience chronic cognitive and neurobehavioral difficulties.

In addition, research also shows that a person's susceptibility to future concussions increases with each such injury. Multiple traumas to the brain also lengthen subsequent recovery times—and cause increasingly significant brain dysfunction.

Impatience with the recovery process can also impede healing. Athletes whose symptoms from one concussion have not cleared before they receive another head injury can suffer from Second Impact Syndrome (SIS), marked by brain swelling as a result of the loss of regulation of the brain's blood supply. If untreated, the condition can lead to massive swelling of the brain and, ultimately, respiratory failure.

"Second Impact Syndrome is the primary reason cited for not sending someone back to play without their having fully recovered from their concussion symptoms," says Meehan.

Multiple concussions can also lead to what is known as chronic traumatic encephalopathy (CTE), a condition that, in boxers, is commonly referred to as punch drunk. CTE, a progressive disorder that results from repeated blows to the head, can lead to dementia in people as young as 40 or 50 years old. Although the mechanisms of CTE are not well understood, scientists speculate that a loss of neurons, scarring of brain tissue, development of senile plaques and neurofibrillary tangles, hydrocephalus, and damage to the cerebellum may all play a part.

There is, however, little evidence that repeat concussions necessarily lead to cumulative brain damage; some physicians argue that athletes who develop CTE are genetically predisposed to the condition.

No Silver Bullet

While helmets and other protective equipment are essential to reducing sports injuries, both Meehan and d'Hemecourt are skeptical about claims that football helmets can prevent concussions. The demand for greater safety, however, continues to spur innovation in the sporting goods industry.

A 2006 University of Pittsburgh Medical Center study of players using the Riddell Revolution football helmet showed a 31-percent decrease in their risk of concussion when compared with players wearing traditional helmets. For athletes who had never suffered a concussion, the relative risk fell by 41 percent.

Another entry into the field of protective sports equipment has come from a Massachusetts company, Xenith, which has developed a football helmet that it says absorbs energy and disperses impact, deflecting much of it from the head. The company's helmet is lined with a thermoplastic material that can adapt to the force of impact.

Meehan and d'Hemecourt say concussion prevention starts with education—for athletes, coaches, trainers, and parents. Proper tackling and checking techniques should be taught at all levels of sports. … "Parents need to be vigilant and to have a low threshold for these types of injuries."

"Don't get me wrong," says d'Hemecourt, "Football helmets are a good idea. But they're designed to prevent catastrophic brain injuries, not concussions. Helmets stop significant trauma, but they have not yet been reliably shown to reduce concussions. They help against direct impact, but not the acceleration and deceleration injuries that cause the shearing forces in the brain that produce concussions."

Mouth guards are also an important piece of equipment for athletes playing contact sports, although Meehan says there is no clinical evidence showing this equipment reduces concussion risk. Such guards may be more effective for boxers, who get hit in the jaw more often than football or hockey players do.

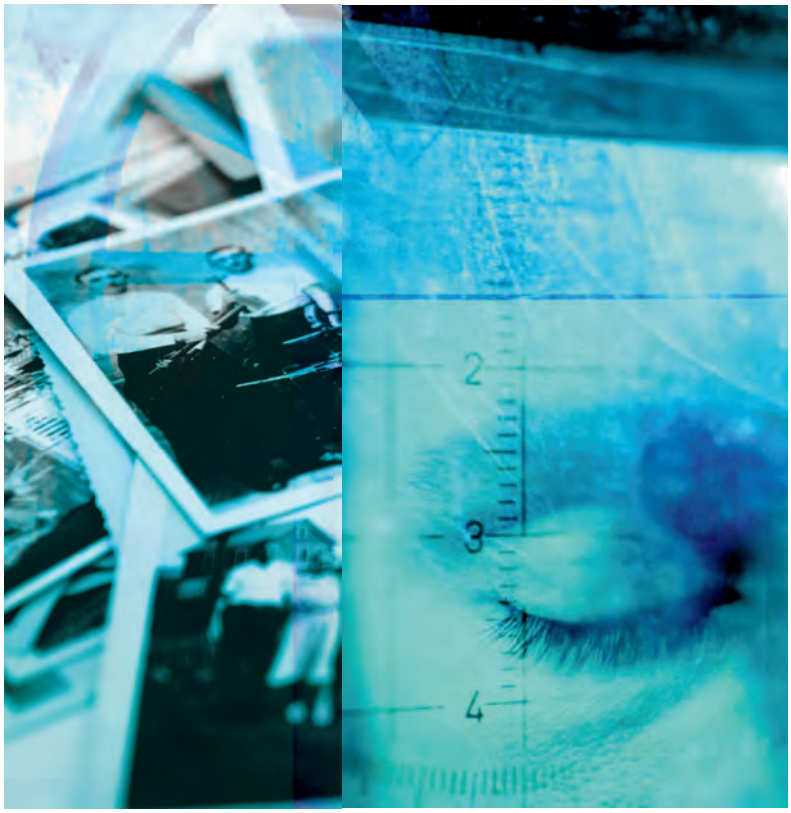
Meehan and d'Hemecourt say concussion prevention starts with education—for athletes, coaches, trainers, and parents. Proper tackling and checking techniques should be taught at all levels of sports. Guidelines for returning to play need to be strictly enforced. Padded goalposts, pylons, and other on-field protections can also help reduce the risk of head injury.

"Education has to filter from top to bottom," says d'Hemecourt. "There are still coaches out there who frown on athletes coming off the field for an injury. Parents need to be vigilant and to have a low threshold for these types of injuries."

Dream a Little Dream

"There is nothing like a dream to create the future," wrote Victor Hugo, the 19th-century French author.

Robert Stickgold, PhD, would agree. Stickgold, an associate professor of psychiatry at Harvard Medical School and the director of the Center for Sleep and Cognition at Beth Israel Deaconess Medical Center, has long studied the role of sleep in memory and emotional processing. And dreams, he has found, are indeed about the future.



The brain knits experiences into a narrative that, during sleep, forms a dream.

According to Stickgold, dreams are recent autobiographical episodes—memories of times, places, and emotions, for example—that become woven with memories of the past to create a memory that can be referenced later.

Stickgold says how we dream may be a function of what could be considered the brain's default network. This network of interconnected brain regions, which includes the thalamus, medial prefrontal cortex, and posterior cingulate cortex, remains active during comparatively quiet periods.

An example of one such quiet period is REM slumber, a stage of sleep characterized by rapid eye movement (REM), irregular heart beat, and increased rates of respiration. REM sleep is discontinuous, chunked into four or five periods that together make up about 20 percent of our slumber. It is during these REM episodes that brain structures in the default network exert influence, and it is during REM sleep that vividly recalled dreams mostly occur. Some research suggests it is during these periods that memories are integrated and consolidated.

Personal Tales

Any time we access autobiographical information, interpret the behavior of others, or figure out how we will do something, we create a narrative, Stickgold says. During sleep, that narrative takes the form of a dream.

"This whole process creates a story," says Stickgold. "That's a seminal feature of dreams: You don't see a snapshot or a static picture. You experience stories unfolding in what appears to be real time."

Stickgold says that when people lie down and start to fall asleep, certain events, such as tasks they failed to begin or finish before they slept, are tagged as incomplete by the brain.

"The brain lines these items up for subsequent processing during dreaming," he says. "But the brain works to figure out what's important and what's not. It's determining what information to keep, what information to throw away, and what actions we will need to take in the future."

If our dreams are composed of mundane events from the previous day, why are so many of them fantastical? One theory is that perception and reality are not aligned, so things go off-kilter, rendering our dreams strange, even meaningless. Stickgold says it's more likely that when we dream, the brain juxtaposes newly processed information with input already stored. Our brains then pull these bizarre juxtapositions together to create a fantastic scene.

Stickgold believes dreams allow us to make associations that we wouldn't make when we're awake and our brains are more actively engaged. Sometimes such associations are valuable. But sometimes they are useless, more fiction than fact. And far from being slices of future reality, they are merely "the stuff of dreams."

Bullying and the Brain

This is the third in a series of articles on how internal and external forces affect the brain.

Bullying has long been a painful part of schoolyard interactions. But in recent years, reported incidents in which children are the victims of verbal, physical, psychological, or social abuse have escalated. In the United States today, bullying plays a significant role in school shootings, suicides, and other tragic events.

Research provides another lens on the magnitude of this violence. Studies report that nearly 77 percent of teachers and 47 percent of parents say their students or children have been the victims of bullying. When both victims and perpetrators are considered, the phenomenon touches one U.S. schoolchild in three.

According to the American Psychological Association, bullying is an aggressive act intended to cause harm, happens repeatedly over time, and occurs in relationships where there is an imbalance of power or strength. It can take many forms: name-calling, malicious teasing, social exclusion, and physical acts such as hitting, kicking, pushing, and choking. And today's wired world has produced a new variant of this abuse—cyberbullying. The National Crime Prevention Council describes cyberbullying as any act in which the Internet, interactive and digital technologies, or cellular phones are used to torment, threaten, harass, or humiliate a person.

Brain Drain

Despite its growth as a social problem, the phenomenon of bullying has not received much study. But one researcher who is tackling the issue empirically is Martin H. Teicher, MD, PhD, an associate professor of psychiatry at Harvard Medical School and the director of the Developmental Biopsychiatry Research Program at McLean Hospital. In recent work, Teicher has looked at peer verbal abuse and its effects on the brain. Preliminary indications are that the brains of children who are verbally abused may indeed suffer damage, particularly in a region known as the corpus callosum.

The corpus callosum, the largest bundle of nerve fibers in the brain, connects the brain's right and left hemispheres. Damage to this nerve bundle during the development of a child's brain can lead to long-term problems, such as trouble imagining the consequences of one's behavior, or difficulties processing social problems and mental challenges. In short, throughout their lives verbally bullied children may find themselves ill-equipped to handle social interactions.

Teicher's current study builds on earlier research by him and his McLean colleagues that found that parental verbal abuse can injure certain brain pathways and potentially lead to depression, anxiety, and language difficulties. The researchers found that specific tracts of nerve fibers had been disturbed in the brains of young adults, ages 18 to 25, who had histories of parental verbal abuse but no other form of maltreatment. The affected tracts—the arcuate fasciculus, cingulate bundle, and fornix—are involved with the processing of language and emotion, and with memory and learning.

"We know that early exposure to adverse childhood experiences such as physical, sexual, or emotional abuse increases the risk of depression, suicide, and alcohol abuse later in life," says Teicher. "Our data from more than 1,600 young adults suggests that exposure to bullying may be another prominent risk factor for these destructive behaviors."

Teicher also has been looking into the effects that insults such as sexual-abuse bullying can have on brain structures as they develop. He has found that the hippocampus, which plays a role in inhibition, memory, and spatial orientation, seems most affected by exposure to childhood sexual abuse during the ages of 3 to 5 and 11 to 13; the corpus callosum is vulnerable to damage between ages 9 and 10; and the prefrontal cortex is fragile to insult from ages 14 to 16. So a child's brain is affected differently, Teicher says, if that child is exposed to sexual abuse in elementary school, middle school, or high school.

The timing of exposure to bullying creates other problems down the road. Those tormented in elementary school are more likely to suffer from psychosomatic problems as adults, while those who are severely abused during the middle school years can, as they mature, experience a disruption in the integration of consciousness, memory, identity, and perception—a disorder known as dissociation. High school students who are bullied are more likely to exhibit aggression as adults.

Bundles of Anxiety

While the stereotypical schoolyard bully is a boy, boys and girls are equally prone to becoming bullies. Boys often engage in physical bullying, while girls tend to use verbal or social tactics, such

continued on page 7

This is Your Brain on Steroids

In the 1970s and 1980s, East Germany, a country of 17 million people, became a sporting powerhouse, successfully competing in Olympic and international contests against countries like the United States and the Soviet Union, each of which had populations of more than 200 million. As part of this push for sports achievement, thousands of amateur East German athletes were given performance-enhancing drugs. The effort worked. At the 1968 Summer Olympics, East Germany won 9 gold medals; at the summer games four years later, it garnered 20. But when the Berlin Wall fell in 1989, so too did the East German façade. Thousands of athletes came forward to tell how they had been required to ingest or be injected with drugs—all in an effort to have them excel on the playing field.

Those drugs, they later learned, were natural and synthetic forms of anabolic-androgenic steroids (AAS), a class of steroid hormones related to testosterone, a male hormone responsible for secondary sex characteristics. AAS boost protein synthesis within cells, a metabolic process that builds tissue, especially muscle. In addition to fostering this anabolic growth, steroids trigger androgenic, or masculinizing, changes such as a thickening of the vocal cords and an increase in body hair.

"All of the drugs in the anabolic-androgenic steroid family are both anabolic and androgenic," says Harrison G. Pope Jr., MD, a professor of psychiatry at Harvard Medical School and the director of the Biological Psychiatry Laboratory at McLean Hospital. "You can't have one property without the other."

New Kids on the Block

The history of steroids is surprisingly short. In 1935, two scientists who were testing the effects of testosterone in dogs found that under certain circumstances the hormone could increase muscle mass. Slightly more than two decades later, methandrostenolone, known as dianabol, became the first synthetic AAS to be available commercially in the United States. Primarily used to treat burn victims and certain conditions in the elderly, the synthetic hormone also found a home in the community of elite competitive weightlifters; its developer, John Zeigler, was one himself and had served as the doctor to the U.S. team competing in the 1954 World Weightlifting Championships in Austria. Word of the performance-enhancing benefits of AAS spread throughout the sports community. Cheating scandals became rampant, resulting in the institution of drug-testing policies and, in the 1990s, to the U.S. government's reclassification of steroids as controlled substances. Organizations such as the International Olympic Committee, the National Basketball Association, the National Football League, and the National Collegiate Athletic Association also banned the use of anabolic-androgenic steroids by their athletes. Today, simple possession of the substances without a prescription can carry a prison sentence of up to one year.

Pump Up the Health Problems

In addition to their muscle-enhancing effects, steroids cause a host of side effects. In men, the hormones can reduce sperm count; shrink testicles; cause infertility, baldness, and the development of breasts; and may even increase risk for prostate cancer. Women users suffer a range of androgenic effects, including an increase in facial hair, male-pattern baldness, and a deepening of the voice, as well as changes in or cessation of their menstrual cycles. In adolescents, AAS can stunt growth; the hormones cause bones to mature prematurely, before they have lengthened naturally. In addition, use of these steroids increases the risk of liver tumors and of high blood pressure and can enlarge and thicken the heart's ventricles, particularly the left ventricle, thereby changing the organ's ability to efficiently pump blood through the body.

Although the effects of these steroids on the brain are incompletely understood, scientists do know that the substances bind to androgen and estrogen receptors on a cell's membrane. Steroids then turn this bond into a portal to a cell's nucleus, where they influence gene expression and ultimately stimulate anabolic growth.

"In ordinary doses," says Pope, "anabolic steroids have few psychiatric effects. Even those who take them in fairly large doses often have no psychiatric effects."

In the long term, however, AAS use can alter some of the same pathways and chemicals in the brain that are affected by other abused drugs. These chemicals include neurotransmitters, such as dopamine, serotonin, and the opioid system. Dopamine plays a role in cognition, voluntary movement, mood, attention, and learning, while serotonin helps in the modulation of mood, anger, and aggression. The opioid system helps to

control pain, reward, and addictive behavior. These mechanisms operate similarly in adolescent and adult brains, says Pope.

Perhaps the most damaging effects of AAS are psychological. Abusers who stop taking the drugs can experience withdrawal, including mood swings, restlessness, loss of appetite, insomnia, and reduced sex drive. Studies of AAS abusers also have found an increase in irritability and aggression and, in certain instances, acts of violent crime.

In the late 1980s, the popular press began reporting cases of what is known colloquially as "'roid rage," behavior characterized by uncontrolled outbursts of anger, frustration, and combativeness. A substantial majority of steroid users, however, show no behavioral abnormalities, says Pope.

"Occasionally, some will show behavioral abnormalities that are out of character," he adds. "We haven't proved indisputably that steroids cause these reactions in any individual, but I've seen enough cases to suggest they do create such effects in certain people."

Uncharted Terrain

Although anabolic steroid use can lead to dependence, Pope says that unlike other addictive drugs, steroids do not produce a feeling of euphoria. People who become dependent on steroids, however, are at a heightened risk of becoming dependent on other drugs, opiates in particular.

"The thing that is remarkable about steroid dependence is that it afflicts hundreds of thousands of people, yet it remains the only major form of substance dependence that is almost completely unexplored," says Pope.

In a recent study, Pope and some of his McLean colleagues examined the biological and psychological characteristics of steroid-dependent individuals. They found that men who had used steroids but had not become dependent on them were almost indistinguishable from never-users in terms of childhood family structure, antisocial behavior, education, psychological history, and

continued on page 8

Bullying and the Brain *continued from page 5*

as ostracism. As some studies have shown, many bullies have authoritarian personalities as well as the strong need to control or dominate others. Other studies suggest that although bullies do not often suffer specifically from self-esteem problems, they may use bullying as a tool to conceal shame or anxiety.

"The curious thing that I've seen in clinical practice," says Teicher, "is that bullies are often riddled with anxiety. They not only tend to be bigger and stronger than other kids, but they are also more anxious. This anxiety comes out in the form of aggressive behavior."

Some studies say that children bully because they have been isolated and have a deep need for belonging yet do not have the social skills needed to develop and keep lasting friendships. In a study published in 2008, University of Chicago researchers found that bullies appear to enjoy inflicting pain on others. Aggressive youths who participated in the study were shown films of people inflicting physical pain on others. The scientists found that the structures that form part of the brain's reward and pleasure circuitry, particularly the amygdala and ventral striatum, became active while the youths watched the videos. The researchers speculate that in bullies the brain's natural impulse for empathy may be disrupted.

The effects of bullying are enduring and noticeable until about age 25, research shows. But studies beyond this age are few, so the full long-term effects have yet to be uncovered.

In 2008, researchers at Yale University School of Medicine conducted a meta-analysis of 37 studies that examined bullying and suicide among children and adolescents. They found that bullying victims are up to nine times more likely to report suicidal thoughts than children who have not been bullied—and that bullies themselves have a heightened risk for suicidal behavior.

Stress Test

U.S. schools are paying more attention to bullying behavior among students, says Teicher. Many are implementing anti-bullying programs that focus on fostering better peer relations, reducing antisocial behavior, and improving the social climate in the classroom. Because bullying during adolescence often occurs off school grounds, however, he thinks school-based programs may have less of an effect than their advocates anticipate—or hope.

Teicher says the effects of bullying can be mitigated in children who build strong relationships with their parents and solid friendships with peers. The key is to help children manage the stresses they face when young—even when those stresses are delivered by troubled children who feel compelled to hurt.

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This is Your Brain on Steroids *continued from page 7*

drug and alcohol use. Those who became steroid-dependent, however, were more likely to have had a first-degree relative with an alcohol- or substance-abuse problem, to have grown up in a single-parent home, and to have exhibited behavioral problems, such as running away from home, stealing, or breaking and entering.

Pope says further studies are needed to determine if, based on current knowledge of who is at risk, interventions can be developed to treat or prevent dependence.

"Unfortunately," he adds, "science doesn't fully have the answers about steroids. The first large wave of illicit steroid users is only now reaching middle age, so the long-term effects of abuse are just starting to declare themselves. We expect definitive data to appear over the next decade."

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