

# HEALTHCARE HORIZON

*The Newsletter of the Minneapolis Medical Research Foundation*

## Researchers Study Vaccine for Drug Addiction

Addiction to opioid drugs like morphine, heroin, codeine, and oxycodone takes an enormous toll on society. These drugs act like a thief. They can steal a person's life, as the craving for drugs overwhelm his or her ability and desire to be involved with family and friends and to be a productive member of society. The spiral of drug addiction leads to economic loss, social rejection, crime, and potentially death.

When people become physically addicted to drugs their brain chemistry changes to the point that they can not function without the drugs. Most opioids overwhelm the brain's reward circuitry, causing intense feelings of pleasure. With regular use, the brain adapts to being exposed to the drugs, leading to dependence, and making it extremely difficult for the addicted person to function without the drug.

Paul Pentel, MD, and fellow researcher Marco Pravetoni, PhD, have begun a bold project to develop a new treatment for addiction to opioids. With a new grant from the National Institutes of Health, they have begun research on a vaccine to help people addicted to opiate-derived drugs.

This opioid vaccine will be what is called a multivalent vaccine - one that stimulates the immune system to produce several kinds of antibodies. Vaccines against drugs work similarly to vaccines against viruses in that

both prime the body's immune system to recognize and attack foreign organisms or substances. However, the end result of a vaccine against opioids is that it reduces the pleasurable effects of the drugs by reducing their entry to the brain.

Drug vaccines are effective because they are able to reduce the amount of active drug molecules reaching the brain. This is a very complicated pharmacological process, but fundamentally what happens is that the immune system creates antibodies that bind to the drug molecules when they enter the bloodstream. When these antibodies are attached to the drug molecules, they are too large to pass from the bloodstream into the brain. If the drug molecules do not make it to the brain cells, they cannot produce the pleasurable effect drug users normally experience.

The vaccine may not entirely mute the effects of drugs. Some of the molecules escape the antibodies and make their way to brain cells. However, as with vaccines for other drugs of abuse, anti-opioid antibodies could have enough of an impact that they may blunt the pleasure-giving power of the drug, helping drug addicts manage their treatment.

Dr. Pentel emphasizes that this vaccine would not be a cure-all for opioid addiction. Rather, it would be another weapon in the arsenal to treat opioid addiction. There is

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*For most of us, the word vaccine triggers memories of getting shots as a child to prevent diseases like measles or influenza. But researchers are also studying the use of vaccines for problems like drug addiction or diseases like cancer.*

*Vaccines work by getting the immune system to identify and attack foreign substances in the body. MMRF researchers are investigating how the body's immune system can be used to mitigate the effects of illicit drugs, which could help to a drug-addicted person overcome his addiction. Some researchers are even looking at ways of taking the needle out of vaccination, instead using patches and inhalants to administer vaccines.*

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a high social stigma for drug treatments like methadone because it needs to be given to patients every day to be effective. The opioid vaccine would probably only need to be administered every few months, as the body builds up antibodies to the opioid drugs. Many people coping with addiction would be more willing to enter a treatment program if it doesn't require them to visit a methadone clinic every day.

His team is taking special care to ensure that the effectiveness of certain opioid-based medicines will not be affected by this vaccine. For example, the vaccine will not target methadone and buprenorphine, in order to preserve their potential use as painkillers or for treatment of opioid addiction.

Dr. Pentel is building off of earlier work developing a similar vaccine for nicotine addiction. He and fellow researchers Dan Keyler, PharmD and Mark LeSage, PhD have spent years developing a nicotine vaccine that is effective at reducing the nicotine's effects in animals. This vaccine has moved into clinical trials and could be an effective treatment option for smokers trying to quit.

The vaccine for opioid-derived drugs will take years to develop, but if it shows efficacy in preclinical studies it has the potential to be a powerful new tool to help people overcome opioid addiction.

## You Can Overcome Addiction

If you or someone you love is struggling with drug or alcohol addiction, it's important to know that help is available to you. Often the first step to recovery is admitting that there is a problem. The Hennepin Faculty Associates (HFA) physician's group at Hennepin has an Addiction Medicine Program that takes a holistic approach to recovery - helping people overcome the

physical addiction to drugs and alcohol, but also working with the emotional and mental problems that can co-exist with addiction.



The program offers specialized services tailored to each

patient's unique circumstances. Newly admitted patients are given a thorough day-long biological, psychological, and social evaluation by a multidisciplinary team to determine which course of treatment will best help him or her manage and overcome the addiction.

If you would like to learn more about the services offered by the HFA Addiction Medicine Program, please contact them by phone at 612 347 7600.

## From Milan to Minneapolis



Marco Pravetoni, PhD, is one of the researchers working on the opioid vaccine. He has had a long journey to get to MMRF as he originally came from Milan, Italy. Marco grew up in Italy and as a university student earned a master's degree in veterinary biosciences at the Università degli Studi di Milano, Milan. His master's level work was focused on in-vitro fertilization and embryology in cattle.

While in Italy, Marco met Dr. Sheldon Sparber from the University of Minnesota, Department of Pharmacology. Dr. Sparber was spending a sabbatical year at the Pharmacology Department at the University in Milan. Dr. Sparber was intrigued by Marco's work on gene expression in embryos and asked Marco if he'd like to work with him in Minnesota. Almost immediately, Marco agreed. He came to Minnesota in April 2001 to work with Dr. Sparber. He spent three years in Sparber's lab and continued his education by taking classes in the Department of Pharmacology.

Marco's move to Minneapolis was not his first time to North America. He had traveled New York City and Boston a few times for vacation and even had a fellowship in Quebec City for several months.

After a few years in Minnesota, Marco decided to pursue a PhD from the Department of Pharmacology. Some of the courses were taught by Paul Pentel, MD, MMRF President, and Professor of Medicine. After many discussions with Dr. Pentel about his research, Marco

# Your Genes & Drug Addiction

## Gavin Bart, MD, Says Both Nature and Nurture Play a Role in the Development of Addiction.

Understanding how drug addiction develops is a crucial part of creating new addiction treatments. Research has shown that environment, the chemical effects of drugs in the brain, and genes play a role in the development of addiction, so each must be addressed for a treatment program to be successful.

In 2005, MMRF and Hennepin welcomed Gavin Bart, MD, to the hospital. Dr. Bart is the Chief of Addiction Medicine. He is researching the role that genetics play in the development of addiction. He argues that efforts to treat addiction need to look beyond the short term detoxification of patients, to providing ongoing addiction treatment to help prevent future relapses.

His research examines the physiological and genetic factors that play into the development of addiction and affect treatment outcomes. An individual's stress response appears to play a significant role in the likelihood that someone will develop or relapse to addiction. People who have a specific, abnormal stress response are more likely to develop an addiction and are more likely to relapse after treatment. For example, the

began post-Doctoral studies with him in 2008.

In July of 2008, Marco came to work at MMRF with Dr. Pentel on the new opioid vaccine research project. His first year at MMRF has been busy. He's been developing the antigens that will be used in the vaccine to stimulate the immune system to produce antibodies when certain drugs enter the bloodstream.

Marco has enjoyed his time in America. When asked what he finds different in the US versus in Europe he says that he really likes that in America you can climb the academic or corporate ladder based on your own merit. You still have to work hard, but it's not like in Europe where sometimes personal or political connections will get you farther in life than your own hard work. Marco has adapted well to our cold winters and says they don't bother him too much. Besides, the long winters give him more time for the winter sports he enjoys, like cross country skiing.

Welcome to MMRF Marco! We wish you success in your research!

nearly 80 percent relapse rate seen in heroin addicts may be related to ongoing effects of an abnormal stress response. Appropriate use of medications such as methadone or buprenorphine can return stress response to normal and patients receiving these medications have a relapse rate of only 30 - 40 percent, similar to disease relapse-rates seen in patients treated for hypertension.

Understanding the biology involved in addiction and relapse is just the first step to create new drug addiction treatment methods. Dr. Bart hopes that his research will be used by others to develop new drugs that correct the biological factors that predispose people to developing addiction and relapsing into drug use.

He is conducting research to tease out which genes influence the formation of drug addiction and impact the effectiveness of addiction treatments. In his clinical work, he treats people from many different ethnic backgrounds. Research has shown that one group in particular, the Hmong, responds particularly well to opiate addiction treatment methods compared to persons from other ethnic groups. While receiving exactly the same treatment, people of Hmong background require a lower dose of methadone and have a lower treatment drop-out rate.

The Hmong remain a relatively uniform and isolated population in America, and only a very small percentage of the population is addicted to opiate-based drugs like smoking opium. Dr. Bart hopes that by studying this population's unique response to treatment that he can discover which genes are contributing to their improved response to opiate addiction treatment. Hopefully then, this information can be used to improve treatment options for the general population or other ethnic groups.

Despite our improved understanding of the role that genes play in drug addiction, Dr. Bart insists that the answer to treating addiction will never be as simple as popping a pill. There are many biological and environmental factors that contribute to the development of drug addiction and the likelihood that one will relapse. The effects of drugs on the mind/body, genetic predispositions, and a person's environment all must be addressed to overcome drug addiction.

# UNDERSTANDING

# DRUG ABUSE & ADDICTION

**M**any people do not understand why individuals become addicted to drugs or how drugs change the brain to foster compulsive drug abuse. They mistakenly view drug abuse and addiction as strictly a social problem and may characterize those who take drugs as morally weak. One very common belief is that drug abusers should be able to just stop taking drugs if they are only willing to change their behavior. What people often underestimate is the complexity of drug addiction - that it is a disease that impacts the brain and because of that, stopping drug abuse is not simply a matter of willpower. Through scientific advances we now know much more about how exactly drugs work in the brain, and we also know that drug addiction can be successfully treated to help people stop abusing drugs and resume their productive lives.

Drug abuse and addiction are a major burden to society. Estimates of the total overall costs of substance abuse in the United States - including health - and crime-related costs as well as losses in productivity - exceed half a trillion dollars annually. This includes approximately \$181 billion for illicit drugs, \$168 billion for tobacco, and \$185 billion for alcohol. Staggering as these numbers are, however, they do not fully describe the breadth of deleterious public health - and safety - implications, which include family disintegration, loss of employment, failure in school, domestic violence, child abuse, and other crimes.

## **What is drug addiction?**

Addiction is a chronic, often relapsing brain disease that causes compulsive drug seeking and use despite harmful consequences to the individual who is addicted and to those around them. Drug addiction is a brain disease because the abuse of drugs leads to changes in the

structure and function of the brain. Although it is true that for most people the initial decision to take drugs is voluntary, over time the changes in the brain caused by repeated drug abuse can affect a person's self control and ability to make sound decisions, and at the same time send intense impulses to take drugs.

It is because of these changes in the brain that it is so challenging for a person who is addicted to stop abusing drugs. Fortunately, there are treatments that help people to counteract addiction's powerful disruptive effects and regain control. Research shows that combining addiction treatment medications, if available, with behavioral therapy is the best way to ensure success for most patients. Treatment approaches that are tailored to each patient's drug abuse patterns and any co-occurring medical, psychiatric, and social problems can lead to sustained recovery and a life without drug abuse.

Similar to other chronic, relapsing diseases, such as diabetes, asthma, or heart disease, drug addiction can be managed successfully. And, as with other chronic diseases, it is not uncommon for a person to relapse and begin abusing drugs again. Relapse, however, does not signal failure - rather, it indicates that treatment should be reinstated, adjusted, or that alternate treatment is needed to help the individual regain control and recover.

## **What happens to your brain when you take drugs?**

Drugs are chemicals that tap into the brain's communication system and disrupt the way nerve cells normally send, receive, and process information. There are at least two ways that drugs are able to do this: (1) by imitating the brain's natural chemical messengers, and/or (2) by overstimulating the "reward circuit" of the brain.

Some drugs, such as marijuana and heroin, have a similar structure to chemical messengers, called neurotransmitters, which are naturally produced by the brain. Because of this similarity, these drugs are able to “fool” the brain’s receptors and activate nerve cells to send abnormal messages.

Other drugs, such as cocaine or methamphetamine, can cause the nerve cells to release abnormally large amounts of natural neurotransmitters, or prevent the normal recycling of these brain chemicals, which is needed to shut off the signal between neurons. This disruption produces a greatly amplified message that ultimately disrupts normal communication patterns.

Nearly all drugs, directly or indirectly, target the brain’s reward system by flooding the circuit with dopamine. Dopamine is a neurotransmitter present in regions of the brain that control movement, emotion, motivation, and feelings of pleasure. The overstimulation of this system, which normally responds to natural behaviors that are linked to survival (eating, spending time with loved ones, etc.), produces euphoric effects in response to the drugs. This reaction sets in motion a pattern that “teaches” people to repeat the behavior of abusing drugs.

As a person continues to abuse drugs, the brain adapts to the overwhelming surges in dopamine by producing less dopamine or by reducing the number of dopamine receptors in the reward circuit. As a result, dopamine’s impact on the reward circuit is lessened, reducing the abuser’s ability to enjoy the drugs and the things that previously brought pleasure. This decrease compels those addicted to drugs to keep abusing drugs in order to attempt to bring their dopamine function back to normal. And, they may now require larger amounts of the drug than they first did to achieve the dopamine high—an effect known as tolerance.

Long-term abuse causes changes in other brain chemical systems and circuits as well. Glutamate is a neurotransmitter that influences the reward circuit and the ability to learn. When the optimal concentration of glutamate is altered by drug abuse, the brain attempts to compensate, which can impair cognitive function. Drugs of abuse facilitate nonconscious (conditioned) learning, which leads the user to experience uncontrollable cravings when they see a place or person they associate with the drug experience, even when the drug itself is not available. Brain imaging studies of drug-addicted individuals show changes in areas of the brain that are critical to judgment, decision making, learning and memory, and behavior control. Together, these

changes can drive an abuser to seek out and take drugs compulsively despite adverse consequences—in other words, to become addicted to drugs.

### **Why do some people become addicted, while others do not?**

No single factor can predict whether or not a person will become addicted to drugs. Risk for addiction is influenced by a person’s biology, social environment, and age or stage of development. The more risk factors an individual has, the greater the chance that taking drugs can lead to addiction. For example:

***Biology.*** The genes that people are born with – in combination with environmental influences – account for about half of their addiction vulnerability. Additionally, gender, ethnicity, and the presence of other mental disorders may influence risk for drug abuse and addiction.

***Environment.*** A person’s environment includes many different influences – from family and friends to socioeconomic status and quality of life in general. Factors such as peer pressure, physical and sexual abuse, stress, and parental involvement can greatly influence the course of drug abuse and addiction in a person’s life.

***Development.*** Genetic and environmental factors interact with critical developmental stages in a person’s life to affect addiction vulnerability, and adolescents experience a double challenge. Although taking drugs at any age can lead to addiction, the earlier that drug use begins, the more likely it is to progress to more serious abuse. And because adolescents’ brains are still developing in the areas that govern decision making, judgment, and self-control, they are especially prone to risk-taking behaviors, including trying drugs of abuse.

### **Prevention is the Key**

Drug addiction is a preventable disease. Results from NIDA-funded research have shown that prevention programs that involve families, schools, communities, and the media are effective in reducing drug abuse. Although many events and cultural factors affect drug abuse trends, when youths perceive drug abuse as harmful, they reduce their drug taking. It is necessary, therefore, to help youth and the general public to understand the risks of drug abuse, and for teachers, parents, and healthcare professionals to keep sending the message that drug addiction can be prevented if a person never abuses drugs.

*This article was originally published by the National Institute on Drug Abuse, a part of the National Institutes of Health.*

# Best of Hennepin, CME and Celebration Event

This May, the partners of the Hennepin medical campus will be hosting The Best of Hennepin Continuing Medical Education & Celebration Event hosted at The Depot, in downtown Minneapolis. The continuing medical education event is for physicians, nurses, health care providers, and Hennepin alumni. Hennepin County Medical Center designates this educational activity for a maximum of 16.0 AMA PRA Category 1 Credits™.

The Best of Hennepin conference includes several social events where attendees and their guests can reconnect with old friends and colleagues and enjoy downtown Minneapolis. There will be a special night at the Guthrie Theater and a dinner dance celebration with musical entertainment as part of this exciting event. To see a schedule of presentations and to register, visit [www.bestofhennepin.org](http://www.bestofhennepin.org).



## Social Event Information

**Thursday evening** there will be a special presentation of the musical *Caroline or Change* at the new Guthrie Theatre on the Mississippi River waterfront in downtown Minneapolis. The play is based on the book by critically acclaimed author **Tony Kushner** (*Angels in America*) with music by **Jeanine Tesori** (*Thoroughly Modern Millie*).

Set in 1960s Lake Charles, Louisiana, the play centers on Caroline Thibodeaux, an African American maid and the Jewish family for whom she works. Social changes and upheavals are transforming the nation, just as the Gellman family attempts to redefine itself after the death of Noah's mother and his father's remarriage. To teach him the value of money, Noah's stepmother tells Caroline to take the change she finds in Noah's pockets at laundry time. When he leaves a twenty-dollar bill, Caroline faces a decision between maintaining her relationship with Noah and using the money to help her own children. Visit the Guthrie website for more information on this play, [www.guthrietheater.org](http://www.guthrietheater.org).

**Friday evening** will be a celebration of the 25th anniversary of Hennepin Faculty Associates. There will be a dinner and dance with live band *Synergy* held at The Depot. The dinner dance will celebrate Hennepin's achievements and milestones, including special recognitions of Hennepin employees and alumni.

**CME conference fee: Physician: \$395, After May 1: \$495**

**Non-physician: \$295, After May 1: \$395; Sponsor a Resident/Retired Physician: \$225**

**Family and friends are encouraged to join you at these special events!**

(Please Indicate how many guests will attend when registering.)

Thursday evening, May 14, Guthrie Theatre ticket price per person: \$46

Friday evening, May 15, dinner dance price per person: \$75

## Contact Information

### For General Questions:

Robin Hoppenrath, Administrative Manager  
Office of the Medical Director, HCMC  
Telephone/Voicemail: 612 873 7128  
E-mail: [robin.hoppenrath@hcmcd.org](mailto:robin.hoppenrath@hcmcd.org)

### For Registration Questions:

Jane Lieberman, Director of Events & Donor Relations  
Minneapolis Medical Research Foundation  
Telephone/Voicemail: 612 347 4582  
E-mail: [jlieberman@mmrf.org](mailto:jlieberman@mmrf.org)

# 6th Annual Downtown Dinner Health Series

Join us and give new meaning to “A Healthy Meal!”

Starting this spring, doctors and medical experts from Hennepin County Medical Center will lead a series of one hour health educational discussions at **Palomino restaurant** in downtown Minneapolis. This is your opportunity to acquire cutting edge information from leading physicians who care for patients, conduct research, and teach tomorrow’s doctors on topics critical to health and well-being.

**Registration/Mixer 5:30pm - 6:15pm**

**Speaker 6:15pm - 7:15pm**

**Network with the Doctor 7:15pm - 7:45pm**

\$25 per session. All sessions include dinner and a drink.



Palomino, 825 Hennepin Ave, Minneapolis, MN 55402

Contact Jane Lieberman for more information: 612 347 4582, [jlieberman@mmerf.org](mailto:jlieberman@mmerf.org). Register now at

[www.MinnesotaMonthly.com/healthseries](http://www.MinnesotaMonthly.com/healthseries)



## Live to be 100 or Die Trying ~ Tuesday, May 19

David R. Hilden, MD, FACP and Meghan M. Walsh, MD, MPH

Take charge of your health! Drs. Meghan Walsh and David Hilden will help you get the most out of your health care. Get insider tips on how to select a doctor that’s right for you, important screening tests, strategies for living a healthy life, and a doctor’s opinion on how to maximize the short time you have with your physician.



## Menopause: The Times They Are A Changin’ ~ Tuesday, September 15

Tara L. Gustilo, MD

Menopause is a natural biological process. Why, then, can it feel like a medical illness to some and not to others? The medical and emotional symptoms can disrupt sleep, zap energy and trigger a roller coaster of emotions. Many treatments, from lifestyle changes to hormone therapies and beyond can help. Dr. Tara Gustilo will discuss traditional and alternative methods to managing menopause today and for a lifetime!



## Addiction: The Number One Preventable Cause of Death ~ Tuesday, October 20

Gavin B. Bart, MD

The use of alcohol, tobacco, and other drugs are the largest contributors to early disability and death in both the developed and developing worlds. Dr. Gavin Bart, director of the Division of Addiction Medicine at Hennepin County Medical Center will discuss what the latest advances in science and medicine teach us about the prevention and treatment of addiction.



## Stroke Prevention and Intervention: Time is Brain ~ Tuesday, November 17

Robert Taylor, MD

Dr. Robert Taylor, Hennepin Stroke Center’s Interventional Neurologist will teach you prevention guidelines to reduce your risk factors for stroke. Learn to recognize stroke signs and symptoms and explore 10 questions and answers about stroke that can save your life. Time is brain.