

NIH News in Health

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Fixing Flawed Body Parts Engineering New Tissues and Organs

How can you mend a broken heart? Or repair a damaged liver, kidney, or knee? NIH-funded scientists are exploring innovative ways to fix faulty organs and tissues or even grow new ones. This type of research is called tissue engineering. Exciting advances continue to emerge in this fast-moving field.

Tissue engineering could allow doctors to repair or replace worn-out tissues and organs with living, working parts. Most important, tissue engineering might help some of the 120,000 people on the waitlist to receive donated kidneys, livers, or other organs.

Doctors have long used tissue-engineered skin to heal severe burns or other injuries. But most tissue engineering methods are still experimental. They've been tested only in laboratory dishes and sometimes in animals, but only a few new approaches have been tested in people. Several clinical studies (involving human volunteers) are in the early stages of testing newly developed tissues.

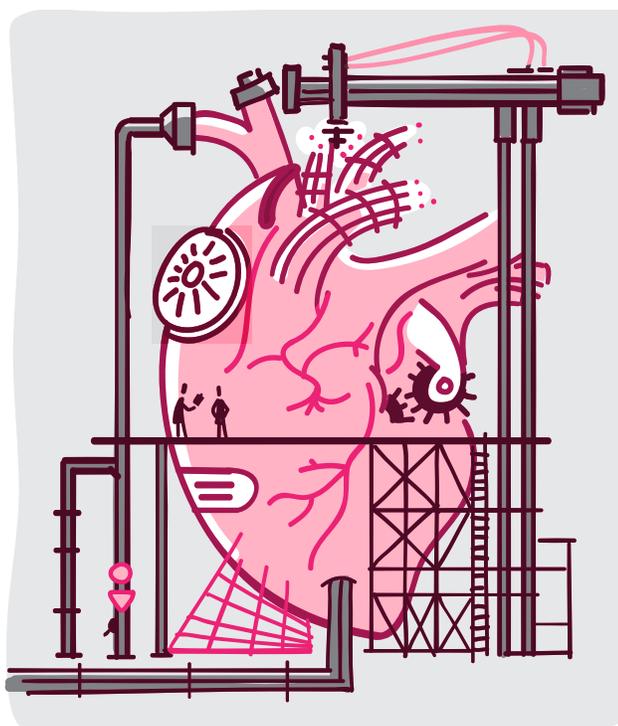
"With this approach, scientists are combining engineering and biology to restore a damaged organ or tissue, whether it's been damaged by disease or injury or something else," says Dr. Martha Lundberg, an NIH expert in heart-related tissue engineering.



Definitions

Stem Cells

Immature cells that have the potential to develop into many different cell types in the body.



Some scientists are creating special net-like structures, or scaffolds, in desired shapes and then coaxing cells to grow within them. Some use a mixture of natural substances called growth factors, which direct cells to grow and develop in certain ways.

"Other scientists are using different 3-D bioprinting technologies—some are like fancy inkjet printers—to create new tissues or organs," Lundberg says. They've printed 3-D kidneys and other organs that look like the real thing. But while most of these printed body parts have the right shape, they're not fully functional.

"Scientists haven't yet figured out how to print an organ that includes the correct blood vessel patterns, nerve connections, and other components that come together in a

mature organ," Lundberg says. "When creating a new organ, if it can perform the right job and functions, it may not need to look like the real thing."

Many tissue engineering methods use **stem cells**, which can be nudged to turn into different cell types. One research team guided human stem cells to become a 3-D structure that can respond to light. The method might one day lead to new therapies for eye disorders. Other stem cell approaches may lead to improved treatment for spinal cord injuries, diabetes, and more.

Another approach, called decellularization, involves removing all the cells from an organ. What's left behind is a thin, pale framework that contains the organ's natural structural proteins, including the pathways for tiny blood vessels and nerves. By infusing new cells into this mesh-like matrix, some researchers have successfully created working animal kidneys, livers, hearts, lungs, and other organs.

The decellularization technique was used by Dr. Martin Yarmush and his colleagues to create a functional

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rat liver that included a network of working blood vessels. Yarmush is a biomedical engineer at Rutgers University and the Massachusetts General Hospital. The engineered livers his team created were kept alive in the laboratory for days and functioned for several hours after transplantation into rats. The researchers are now working to help those transplanted livers survive even longer. They're also scaling up the methods to create a decellularized human liver that can be repopulated with functional cells.

"A parallel effort we are pursuing involves taking a donated organ that is not considered transplantable for a particular reason, and then using a reconditioning solution and perhaps



Wise Choices For Healthy Organs and Tissues

The kidney is the most transplanted organ in the U.S., followed by the liver, heart, and lungs. You can protect all of your body's organs through healthy behaviors:

- Eat a balanced diet.
- Stay physically active.
- Maintain a healthy weight.
- Limit alcohol.
- If you smoke, take steps to quit.
- Take medications only as directed.

Consider signing up as an organ and tissue donor. For information, visit www.organdonor.gov/stateMap.asp.

even stem cells to revitalize the organ so it becomes transplantable," Yarmush says.

Other researchers are working to repair damaged body parts that are still in the body. At the University of Washington in Seattle, Dr. Charles Murry and colleagues are searching for ways to fix injured hearts. One of their latest studies used human stem cells to repair damaged hearts in monkeys. The stem cells were coaxed to become early-stage heart cells, which were then infused near the heart injury.

The new cells made their way into the damaged heart muscle and organized into muscle fibers in all of the treated monkeys. The infused stem cells replaced nearly half of the damaged heart tissue and began beating in sync with the heart. Still, the scientists note they need years of research before this type of therapy might be tried in people.

Some methods are already being tested in humans. Dr. Martha Murray, a surgeon at Boston Children's Hospital, is exploring new ways to heal a common knee injury known as a torn ACL (anterior cruciate **ligament**). Athletes who do a lot of twisting and turning, as in basketball or soccer, are at risk for damaging the ACL.

"Typical treatment today, called ACL reconstruction, works well, and



Definitions

Ligament

Tough, flexible tissue that connects bones to each other.



Web Links

For more about advances in tissue engineering, click the "Links" tab at: <http://newsinhealth.nih.gov/issue/Feb2015/Feature1>

it gets patients back to the playing field at a relatively high rate," Murray says. But the surgery involves removing a piece of tendon from elsewhere in the body and using that to replace the ACL. "So it involves making 2 injuries that the body has to heal from. And even with this treatment, patients still develop arthritis in the knee 15 to 20 years later," Murray adds. "We wanted to find a better therapy—something less invasive."

After testing several biomaterials, Murray's team found that stitching a bioengineered sponge between the torn ends of an injured ACL allows blood to clot and collect around the damaged ligament. Because blood naturally contains stem cells and growth factors, the blood-soaked sponge acts as a "bridge" that encourages ACL healing. The sponge is made of some of the same proteins normally found in ligaments, and it dissolves after a few weeks.

Studies in large animals showed that the bioengineered sponge was much less likely to lead to arthritis, and it healed ACL injuries as well as standard reconstruction surgery. The U.S. Food and Drug Administration recently approved human safety testing of the sponge in 10 people with ACL injuries.

Metal, plastic, and other non-biological devices can also replace or enhance malfunctioning body parts. One promising possibility still in development is an artificial kidney that could be implanted in the body and used in place of dialysis to treat end-stage kidney disease. Scientists are also studying a synthetic glue modeled after a natural adhesive that

might help to repair tissues in the body. You can learn more about these and other cutting-edge studies at www.nibib.nih.gov/science-education/bionic-man. ■

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Galled by the Gallbladder?

Your Tiny, Hard-Working Digestive Organ

Most of us give little thought to the gallbladder, a pear-sized organ that sits just under the liver and next to the pancreas. The gallbladder may not seem to do all that much. But if this small organ malfunctions, it can cause serious problems. Gallbladder disorders rank among the most common and costly of all digestive system diseases. By some estimates, up to 20 million Americans may have gallstones, the most common type of gallbladder disorder.

The gallbladder stores bile, a thick liquid that's produced by the liver to help us digest fat. When we eat, the gallbladder's thin, muscular lining squeezes bile into the small intestine through the main bile duct. The more fat we eat, the more bile the gallbladder injects into the digestive tract.

Bile has a delicate chemical balance. It's full of soluble cholesterol

produced by the liver. This is a different type of cholesterol than the kind related to cardiovascular disease. If the chemical balance of bile gets slightly off, the cholesterol can crystallize and stick to the wall of the gallbladder. Over time, these crystals can combine and form gallstones.

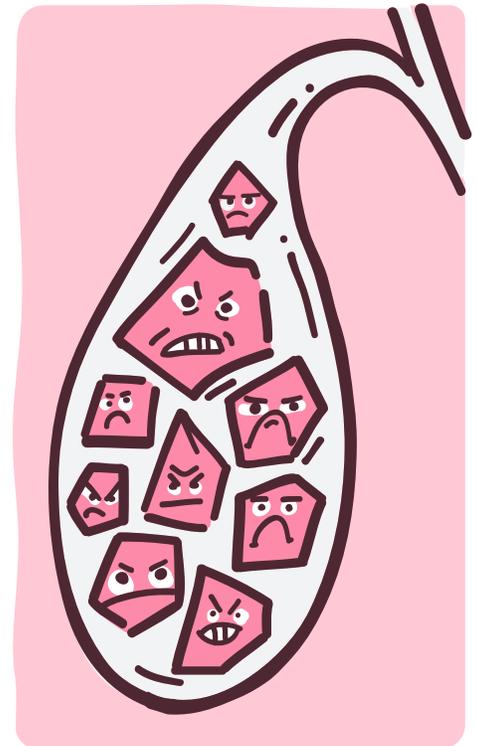
Gallstones can range from the size of a grain of sand to that of a golf ball. When the gallbladder injects bile into the small intestine, the main bile duct can become blocked by these crystalline stones. That may cause pressure, pain, and nausea, especially after meals. Gallstones can cause sudden pain in the upper right abdomen, called a gallbladder attack (or biliary colic). In most cases, though, people with gallstones don't realize they have them.

The causes of gallstones are unclear, but you're more likely to have gallstone problems if you have too much body fat, especially around your waist, or if you're losing weight very quickly. Women, people over age 40, people with a family history of gallstones, American Indians, and Mexican Americans are also at increased risk for gallstones.

"For the average person with an average case, the simplest way to diagnose a gallstone is by an ultrasound," says Dr. Dana Andersen, an NIH expert in digestive diseases.

If left untreated, a blocked main bile duct and gallbladder can become infected and lead to a life-threatening situation. Gallbladder removal, called a cholecystectomy, is the most common way to treat gallstones. The gallbladder isn't an essential organ, which means you can live normally without it.

Gallbladder removal can be done with a laparoscope, a thin, lighted tube that shows what's inside your abdomen. The surgeon makes small cuts in your abdomen to insert the surgical tools and take out the gall-



bladder. The surgery is done while you are under general anesthesia, asleep and pain-free. Most people go home on the same day or the next.

Researchers have long investigated medications that can prevent gallstones from forming, but these therapies are currently used only in special situations.

It's uncommon for the gallbladder to cause problems other than gallstones. Gallbladder cancer is often difficult to treat, as it's usually diagnosed at an advanced stage. But such cancers are relatively rare.

While the gallbladder may not be the star of the digestive system, it still plays an important role. Treat it well by maintaining a healthy diet and getting regular exercise, and the little bag of bile should do its job. Don't ignore pain or symptoms, and see your doctor if you're in discomfort, especially after eating. ■



Wise Choices

Symptoms of a Gallstone Attack

Talk with your doctor if you have:

- severe pain in the upper-right side of the abdomen that starts suddenly and lasts from 30 minutes to many hours.
- pain under the right shoulder or in the right shoulder blade.
- indigestion after eating foods high in fat or protein, including desserts and fried foods.

Seek help right away if you have these signs of a serious attack:

- abdominal pain that lasts more than 5 hours.
- nausea and vomiting.
- fever or chills.
- yellowish color of the skin or the whites of the eyes.
- dark urine or light-colored stools.



Web Links

For more about the gallbladder, click the "Links" tab at: <http://newsinhealth.nih.gov/issue/Feb2015/Feature2>



Health Capsules

For links to more information, see these stories online:
<http://newsinhealth.nih.gov/issue/Feb2015/Capsule1>

Many Older People Take Anti-Anxiety Meds Despite Risks

Despite known risks, older people often take benzodiazepines, a class of drugs that helps treat anxiety and sleep problems. New research raises questions about why benzodiazepines are prescribed so often when safer alternatives may be available.

Benzodiazepines include the medications alprazolam (Xanax), diazepam (Valium), and lorazepam (Ativan). Although effective for short-term use, they can have serious risks. Benzodiazepines can impair thinking, movement, and driving skills in older people and increase the risk of falls. Long-term use can lead to dependence, and stopping the drug may lead to withdrawal symptoms.

NIH-funded researchers studied benzodiazepine use over a 1-year period. They found that about 1 in 20 U.S. adults, ages 18 to 80, received a benzodiazepine prescription. This fraction rose with age, from about 3% among those 18 to 35, to 9% in those 65 to 80. Long-term use (over 4 months) also rose with age.

Women were about twice as likely as men to take benzodiazepines. Among women 65 to 80 years old, 1 in 10 was prescribed this class of drug, with almost a third of those receiving long-term prescriptions.

Most prescriptions for benzodiazepines were written by non-psychiatrists. "These medications can pose

real risks, and there are often safer alternatives available," says study co-author Dr. Michael Schoenbaum of NIH. Practice guidelines recommend psychotherapy approaches and antidepressants as the initial treatment for anxiety. For sleep problems, guidelines recommend behavioral changes as the first approach.

"Our findings strongly suggest that we need strategies to reduce benzodiazepine use, particularly for older women," Schoenbaum says. ■

Treatment for Alcohol Problems

An estimated 17 million Americans have an alcohol use disorder. But research suggests that only a fraction of them seek professional help. No matter how severe the problems may seem, most people can benefit from some form of therapy.

A new easy-to-read publication from NIH can help individuals and families understand the available treatment options. The 16-page booklet, *Treatment for Alcohol Problems: Finding and Getting Help*, covers the latest research-based therapies and things to consider when choosing among them.

Two types of treatments provided by health care professionals have been shown to benefit people with

alcohol use disorders. These are behavioral treatments (which focus on changing drinking behaviors) and medications (which are often paired with behavioral treatment).

The booklet also includes information about mutual-support groups such as Alcoholics Anonymous. And it provides tips for recognizing alcohol problems and advice for friends and family.

The publication is available online at <http://pubs.niaaa.nih.gov/publications/treatment/treatment.htm>. You can also order free print copies by calling 1-888-MY-NIAAA (888-696-4222) or visiting <http://pubs.niaaa.nih.gov/publications/english-order.htm>. ■



Featured Website Find a Cancer Center

www.cancer.gov/find-a-cancer-center

NIH's National Cancer Institute (NCI) supports specialized cancer research centers that deliver cutting-edge cancer treatments to people in communities across the country. This interactive map can help you find an NCI-designated center near you and learn about its patient services and research.

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