

By Bruce Stutz

PUMPH HEAD

In what has become almost routine,
the heart-lung machine

“breathes” for patients during
coronary-bypass operations.

But could this lifesaving device
have a dark side?

The last thing I remembered was the cold room with

a stainless-steel ceiling. I was about to undergo open-heart surgery, an experience shared by about 500,000 people in the U.S. every year. After the anesthesia took effect, surgeons made an incision in my groin to reach my femoral vein and artery. Through the vein they threaded a tube called a cannula into the right atrium,

an upper chamber inside my heart. This tube, and another attached to the artery, was connected to a cardiopulmonary-bypass pump, also known as a pump oxygenator or a heart-lung machine. A dose of heparin kept my blood from clotting as it traversed the machine's innards. As the venous blood passed through the oxygenator, it was cooled to prevent tissue damage. My body temperature lowered to 25 degrees Celsius (77 degrees

no-man's-land, I felt my moods range from querulous to despondent. I couldn't muster the concentration to deal with the problem. I just wanted to be able to think. Think anything.

I didn't know it at the time, but I was suffering from what surgeons among themselves call "pumphead," an all-too-apt appellation that refers to the dimwitted state in which patients seem to linger after being hooked up to a heart-lung

surgery at Harvard Medical School. After years of animal trials, and with engineering advice and financing from IBM chairman Thomas J. Watson and others, Gibbon solved what was then the major impediment to heart surgery—giving doctors enough time to operate.

Before Gibbon's pump came into use, induction of, or cooling, the patient's body to slow metabolism and blood circulation gave surgeons a 15-minute win-

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Fahrenheit)—deep hypothermia. Surgeons inserted an inflatable clamp into my aorta to seal it off. Two liters of cold potassium solution stopped my heart, and for the next two hours the machine took over. An eight-inch incision below my right breast allowed the doctors to pass cameras and instruments between my ribs and then to repair my congenitally defective heart valve.

I left the hospital a week later. The incision healed quickly and painlessly. In a couple weeks I was out and about on slow but successively longer walks. Within a month I was back in the gym. Mentally, however, I felt a bit hazy, a little disconnected and sometimes even lost. I soon learned that the physician's warning, "You may be a little depressed for a time afterward," would not do justice to the long, dumbfounding struggle against what seemed to be the sudden onset, at 51 years of age, of attention-deficit disorder or incipient senility. Adrift in a clueless

machine for open-heart or, in my case, valve surgery. Other symptoms include patchy recall, social difficulties and personality changes. Pumphead was long suspected from anecdotal and journal reports of patients tested soon after their operations. But only recently did a five-year study of bypass patients indicate that after an initial recovery of mental capabilities in the first few months, the condition often worsens later and persists for years. Could the familiar heart-lung machine—which annually provides life-giving oxygen to blood during 900,000 coronary-bypass operations around the world—be at fault?

Making of the Machine

FIFTY YEARS AGO John Heysham Gibbon, Jr., of Jefferson Medical College in Philadelphia performed the first successful human surgery using a heart-lung machine. He had begun developing the device in the 1930s, as a research fellow in

dow to complete their work. Any longer and the body and brain suffered from a lack of oxygen. Gibbon's machine took blood that would normally go to the heart and lungs, oxygenated it and pumped it back to the arterial system through the aorta. Today the pump's use has become commonplace. Surgeons perform so many coronary-artery-bypass graftings, or CABGs, that they commonly refer to them as "cabbages." But for decades the long-term effects of those operations received little serious study.

That has changed in recent years. In 2001 a *New England Journal of Medicine* article by Mark F. Newman, chair of Duke University Medical Center's department of anesthesiology, and his colleagues revealed that even after five years many coronary-bypass patients still struggled with severe mental impairments. Previous studies had followed subjects for only up to six months. "Adjectives such as 'subtle,' 'transient,' and 'subclinical' have been used to describe the cognitive decline that occurs after CABG, but such descriptions minimize the importance of these changes to clinicians, patients, and their families," the article concludes. Adds Newman: "The month after the study came out, we received 4,000 e-mails from bypass patients. A lot of people were happy just to know they weren't crazy."

In the study, Newman and his group administered five cognitive tests—short-story recall, repetition of number series,

Overview/Cognitive Decline

- The heart-lung machine, first used on humans in 1953, revolutionized coronary surgery by giving doctors an hour or more to operate on a still heart. Previous techniques allowed only 15 minutes.
- Since the inception of the machine, medicine has recorded cognitive decline in patients hooked up to it. The condition, later nicknamed "pumphead," was thought to be short-lived and was often attributed to the general trauma of surgery.
- Recently, long-term studies of patients have shown that pumphead may worsen over time and persist for years. Many factors could be involved, but microscopic cell debris and bubbles generated by the machine are under suspicion.

MECHANICAL HEART AND LUNGS

HEART-LUNG MACHINE circulates oxygenated blood during heart or valve surgery, typically using roller-type pumps. Blood from veins travels to a reservoir and then on to an oxygenator, where it takes up oxygen and releases carbon dioxide; a filter removes debris and bubbles. Initially a heat exchanger cools blood to protect tissue from damage. Doctors then cross-clamp the aorta and stop the heart with a cold potassium solution; the machine performs the functions of the heart and lungs during the procedure. After completion, the heat exchanger rewarms the blood, and surgeons remove the clamps and restart the heart.



HEART-LUNG MACHINE (foreground) is seen in action.

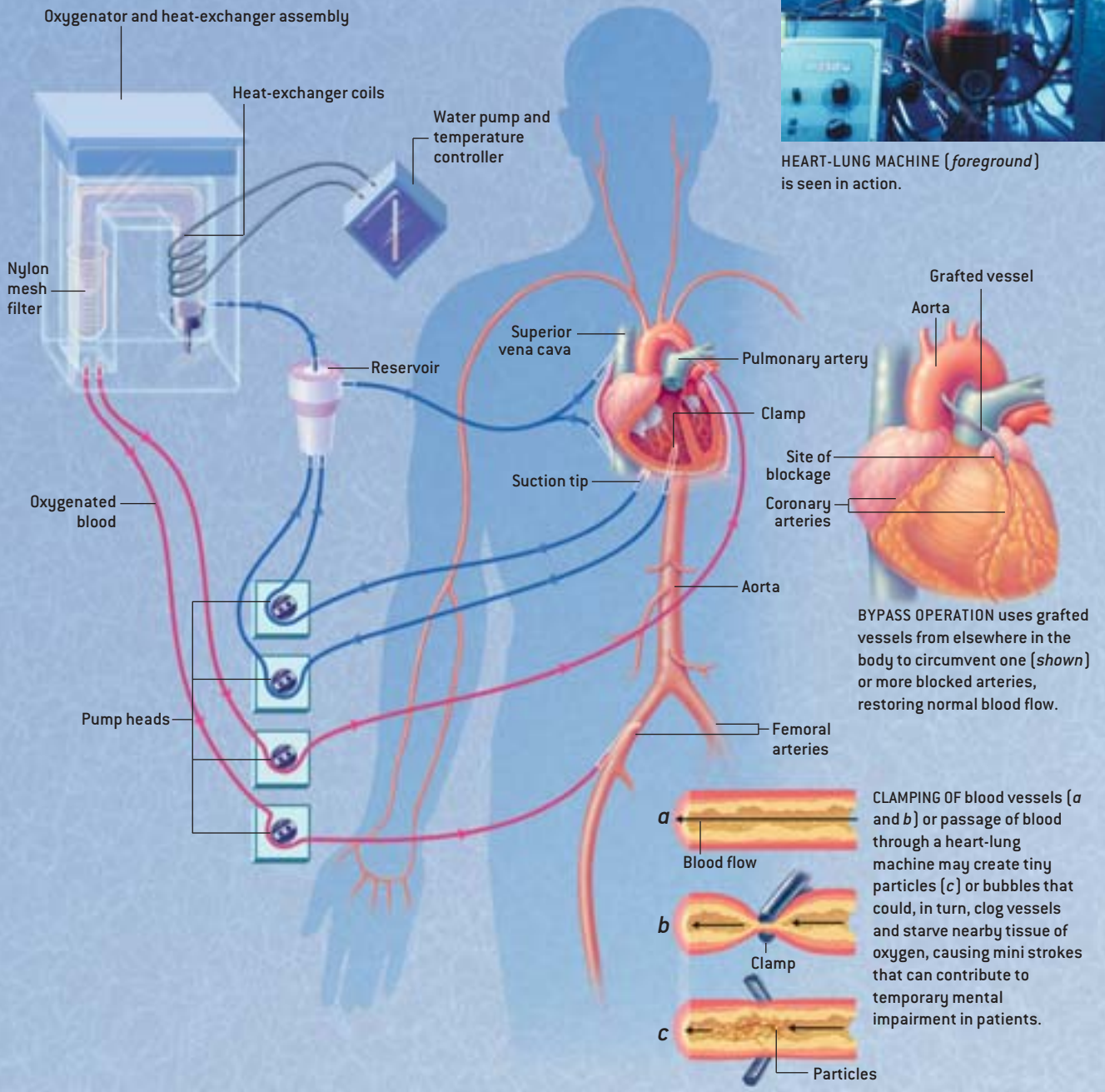


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visual retention, pairing digits with symbols, and connecting a series of numbers and letters—to 261 heart-bypass patients the week before hospitalization, during the week after the operation, after six weeks and again six months later. After surgery, 53 percent of the subjects were unable to match their earlier cognitive performance. Six weeks later, 36 percent continued to be affected, and that number dropped to 24 percent after six months.

Those results surprised no one. Short-term declines in mental function after operations involving the heart-lung machine had been reported in the literature since the beginning, and they were frequently chalked up to the general trauma of surgery. Five years after the first round of tests, however, Newman's team checked in with their subjects once more. Some of them performed about the same as they did originally, but 42 percent fared so poorly that they were again declared cognitively impaired—even after controlling for increased age.

What's to Blame?

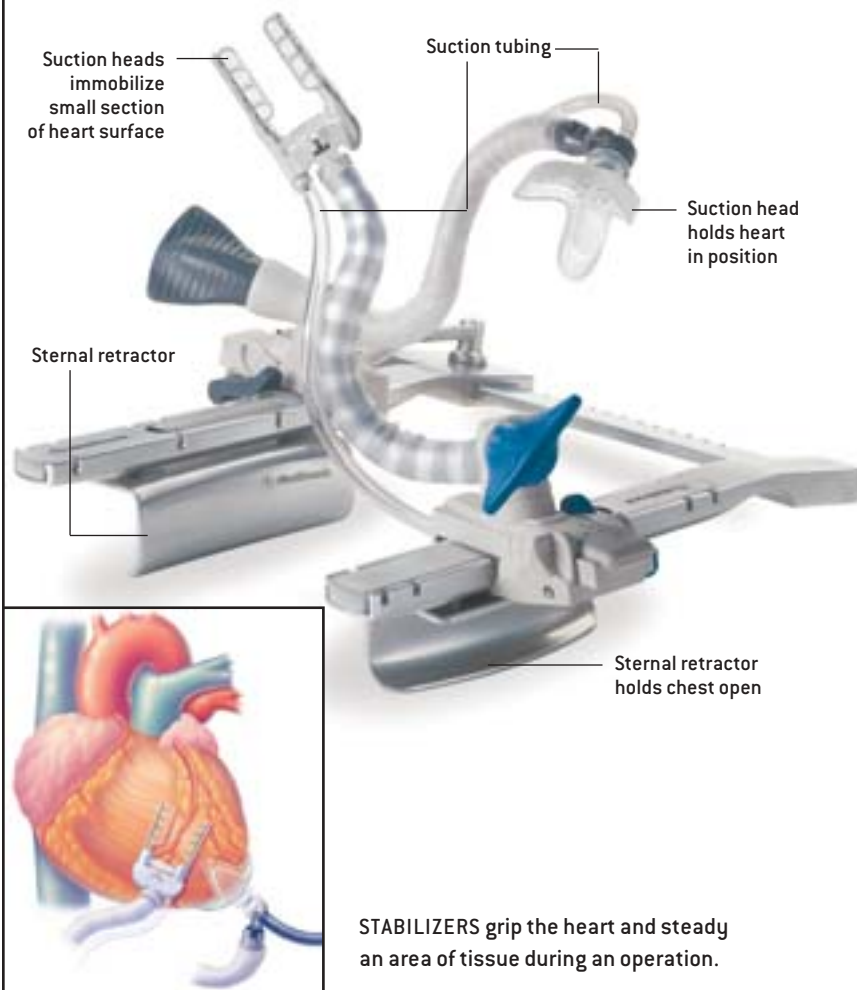
ALTHOUGH THE IDEA is not proved, the heart-lung machine is a suspect in cognitive decline for several reasons. Physicians speculate that the pump may cause damage by altering blood flow or by releasing minute debris—fat particles, blood clots, bubbles—into the patient's bloodstream. Or perhaps red blood cells can be damaged as they journey through the machine, losing their capacity to carry sufficient oxygen to the brain and the rest of the body. In Gibbon's original design—which, with refinements, is often still used—the machine pumped blood through tubing that curved around rollers attached to rotating arms. As the arms turned in eggbeater fashion, the rollers pushed the blood through the tubing. Even in today's machines, contact with tubing can damage cells, or they may be sheared or crushed by the roller pumps.

THE AUTHOR

BRUCE STUTZ is the former editor in chief of *Natural History* magazine and writes most often on science, nature and travel. Stutz is the author of *Natural Lives*, *Modern Times*, a natural and cultural history of the Delaware River Valley.

SURGEON'S HELPING "HAND"

OFF-PUMP SURGERY avoids the use of the heart-lung machine. Using suction, a local-tissue stabilizer (*inset*) immobilizes a section of the heart surface, permitting surgeons to work on the beating organ. Whether this procedure prevents pumphead symptoms is still unclear.



In Gibbon's models, blood dripped over a wire mesh to expose it to oxygen. But this direct contact often led to too much oxygen being absorbed and resulted in oxygen toxicity. Air bubbles were also common, and they could course through the machine and cause blockages in arteries. To minimize both problems, researchers eventually developed a closer approximation of the lung: a gas-permeable synthetic membrane.

Despite these and other improvements—such as polyvinyl tubing that prevents blood cells from adhering to it, centrifugal pumps that handle cells more gen-

tly, gas exchangers that reduce bubble size, and better temperature controls—an intractable problem remains. The entire system, and the surgery itself, can still generate a variety of debris. In addition to bubbles, clotted shards of blood cells, particles of corroded tubing and arterial plaque—all collectively called emboli—can make their way through the pump and cannulae and back into the body. The workings of the pump may loosen debris; some of these materials may also be released when surgeons clamp the aorta to connect the tubing. If the resulting emboli become trapped in small vessels, they can

block blood flow in a manner akin to a mini stroke, starving or even killing nearby tissue.

Technology has all but eliminated the largest of these emboli. Screens of woven polymer thread placed in the machine filter out particles of 0.2 to 5.0 microns in size from the blood. Sutureless connectors reduce manipulation of the aorta, curtailing specks that might otherwise enter the bloodstream. Doppler ultrasound detec-

case), it may be an option for some patients who cannot tolerate the stress of the heart-lung machine. Off-pump surgery now accounts for anywhere from 20 to 80 percent of heart surgeries, depending on the surgeon and the hospital. [For more information about this alternative procedure, see “Operating on a Beating Heart,” by Cornelius Borst; SCIENTIFIC AMERICAN, October 2000.]

Off-pump surgery appears to reduce

is cheaper and that patients may be ready for discharge faster, is it time to retire the heart-lung machine? No one is ready to say that. Too many other factors that occur during and immediately after heart surgery could also be participants in cognitive decline: inflammation, hypoxia (insufficient oxygen delivery to tissues), lowered blood pressure, irregular heart rhythms, or body temperature that is too warm or too cold. Hilary P. Grocott, as-

The overarching question is, What part of what we do is significant with regard to perioperative effects?

tors search for errant microbubbles. If they do appear, the specialist who controls the machine, called the perfusionist, can adjust the flow of blood through the gas exchanger. But microemboli—one tenth the size of the detectable ones and numbering 200 to 300 an hour—may still escape discovery and potentially damage body or brain tissue.

Newman and others believe that these types of anomalies during surgery could cause cognitive problems in patients, but some researchers remain skeptical. For instance, a five-year study of 52 bypass patients at the University of Würzburg in Germany led by Wolfgang Müllges, published last fall in *Neurology*, found essentially no “global decline” in cognitive abilities compared with the baseline (pre-surgery) test performances of subjects. Nevertheless, a growing concern among surgeons about the machine has led to a demand for improvements in its technology and operation as well as a search for an alternative.

The Off-Pump Option

A “BEATING HEART,” or “off pump,” coronary-artery bypass may seem, as one surgeon puts it, “like cutting a gemstone on horseback,” but new instruments can steady the steed while the rider works [see box on opposite page]. The stabilizers are akin to spidery legs with padded feet that grip the heart with vacuum suction. Although off-pump surgery may not be suitable for every situation (it was not in my

the number of larger emboli. In a 2001 study of 40 patients by B. Jason Bowles and his colleagues at St. Francis Hospital in Honolulu, Doppler ultrasound detected an average of only 27 emboli, compared with an average of 1,766 during on-pump operations. Any cognitive benefits, however, were unclear. Other studies have also produced less than definite—or even conflicting—results.

Experts say that all previous attempts to decide which operation is better have been hindered by studies with too few participants, differing designs or goals or with lingering complexities in assessing the quality of cognition—factors that make valid conclusions problematic. In 2007 the U.S. Department of Veterans Affairs will conclude an extensive \$10-million investigation comparing on-pump surgery with off-pump procedures. Led by Frederick L. Grover, chair of the department of surgery at the University of Colorado Health Sciences Center in Denver, the study is monitoring the cognitive outcomes of 2,200 heart patients in 17 V.A. hospitals.

Bearing in mind that off-pump surgery

sociate professor of anesthesiology at Duke, has discovered that patients in whom fever developed within the first 24 hours following coronary-bypass surgery tended to suffer an increased probability of cognitive decline after six weeks; no one is certain whether the fever causes the dysfunction or is a symptom of it.

The overarching question, Newman says, is “What part of what we do is significant with regard to perioperative effects? If different interventions and improvements can change the early results, we think we can [positively] change the slope of [cognitive] decline.” Clearly, medicine will continue to search for better answers.

In the meantime, I have found ways to cope. I’ve planned shorter work periods. I’ve walked frequently and gotten off at a subway station many blocks from my destination in order to navigate the long way back. I’ve played the piano to focus my mind. More than a year and a half after my valve repair, I seem to be returning to life and intelligence as I knew it. Pumpheads, take heart: I wrote this article, didn’t I? SA

MORE TO EXPLORE

Longitudinal Assessment of Neurocognitive Function after Coronary-Artery Bypass Surgery.

Mark F. Newman et al. in *New England Journal of Medicine*, Vol. 344, No. 6, pages 395–402; February 8, 2001.

Cognitive Outcome after Off-Pump and On-Pump Coronary Artery Bypass Graft Surgery:

A Randomized Trial. Diederik Van Dijk, Erik W. L. Jansen, Ron Hijman et al. in *Journal of the American Medical Association*, Vol. 287, No. 11, pages 1405–1412; March 20, 2002.

Protecting the Brain in Coronary Artery Bypass Graft Surgery. Daniel B. Mark and Mark F. Newman in *Journal of the American Medical Association*, Vol. 287, No. 11, pages 1448–1450; March 20, 2002.