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Life

Why the line between life and death is now more blurred than ever

Brains resurrected after death, communications with people in comas and advances in cryogenics all suggest that life's end is less final than we thought

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FOR the Egyptians, death was simple. You stopped breathing and your friends and family bid you farewell. Then they poked a hook up your nose and scraped out your brain, safe in the knowledge that they would see you again in the afterlife.

These days, figuring out the difference between life and death has got more problematic. For starters, there is no globally agreed definition of death, which means you can be pronounced dead in one country yet wouldn't be in another. Then there is the recent discovery that death doesn't happen in an instant, but over weeks. Add to that the inevitable storm generated by experiments revealing that brains can be resuscitated hours after death. No wonder scientists, philosophers and even the Vatican are asking how we should decide when dead really is dead.

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Until the mid-20th century, our definition of death was unambiguous: you were dead when you stopped breathing and had no pulse. Things got complicated with the invention of the ventilator, a machine that could maintain breathing for a person who would otherwise be declared dead. At about this time, doctors began transplanting organs from the dead into the living and found that they could increase the success rate by using a ventilator to provide the donor heart with oxygen. These "beating-heart cadavers" were legally alive even though their brains had ceased to function.

The resulting quandary of how to remove an organ without committing murder eventually led to the 1980s Uniform Determination of Death Act in the US, which introduced the concept of brain death. Now you could be pronounced dead either when your heart had stopped or when all areas of your brain had irreversibly ceased to function.

Despite this, the criteria doctors use to declare death still vary from person to person, hospital to hospital, state to state and country to country, says Ariane Lewis 🔗 https://nyulangone.org/doctors/1700046075/ariane-k-lewis, director of neuro-critical care at NYU Langone Health in New York. There are differences in the assessments that are carried out, for instance.

Fortunately, we have progressed from the 19th-century practices of sticking leeches up a person's anus or pinching their nipples. These days, doctors are more likely to observe whether the eyes are responsive to light – a sign of activity in the brainstem – whether pricking the nail beds elicits any sign of pain, and whether breathing occurs once a ventilator is switched off. A doctor might also do an EEG, which identifies electrical activity in the brain, to rule out the possibility that something else might be

masquerading as death. Drugs, alcohol and hypothermia can all slow breathing to undetectable levels.

According to the American Academy of Neurology, there have been no reports of anyone recovering 🔗 https://www.who.int/servicedeliverysafety/ddcr78.pdf full brain function after a determination of brain death using recognised tests. But here is where things have become sticky. Not everyone's brain completely stops working when they experience brain damage or when their heart stops beating. And we don't know the minimal level of brain activity necessary to be considered alive, which means mistakes are possible.

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Recently, Brian Edlow at Massachusetts General Hospital discovered that half of the people in his emergency room who had been diagnosed as being in a coma or minimally conscious state with severe brain damage and no apparent awareness could respond to questions 🔗 /article/mg24232360-800-shocking-evidence-shows-people-in-vegetative-states-may-be-conscious/#ixzz60RUe0sJq/ when placed in an MRI scanner. Four out of eight of them could follow instructions such as "imagine squeezing your right hand", as revealed by brain activity in response to his questions. It was an uncomfortable finding, given that tests like these aren't routine, and these patients can become candidates for having their life support switched off.

Another complication is that death isn't an event but a process. Sit beside someone who has just been declared dead and you may see spontaneous finger movements 🔗 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(05)72081-X/fulltext or even witness their entire upper body jerking as their arms fly up to their chin – a phenomenon resulting from reflexes that occur via the spine, bypassing the brain. In fact, muscle and skin cells can go on living without any instructions from the brain for weeks after death. What's more, hundreds of genes, including those involved in inflammation and heart contraction, actually "wake up" within the first 24 hours 🔗 http://newscientist.com/article/2094644-hundreds-of-genes-seen-sparking-to-life-two-days-after-death/ after death, which is probably a reaction to the cellular processes that occur from lack of oxygen. The body doesn't know it is dead, and fights to stay alive, long after our arbitrary sentence has been passed.

"Hundreds of genes actually 'wake up' in the first 24 hours of death"

But if the brain has stopped working, that's irreversible, right? Perhaps not. Historically, it was thought that minutes after the oxygen supply is cut off, cells begin to break down and die, becoming irretrievably damaged unless oxygen is quickly replenished. Earlier this year, however, a team led by Zvonimir Vrselja at Yale School of Medicine managed to revive pig brains 🔗 https://www.nature.com/articles/s41586-019-1099-1 hours after death. Four hours after the animals were decapitated, their brains were removed from their skulls and connected to an artificial perfusion system, which pumped a blood substitute around them. Incredibly, after 6 hours, the brains began to function again. Blood vessels responded to drugs designed to make them dilate and contract. Cells began to regain their metabolism. Changes to the structure of the brain thought to lead to irretrievable damage reverted to normal. And, astonishingly, when stimulated by an electrode, neurons responded by creating action potentials, the electrical activity by which brain cells communicate.

Although the team didn't see any signs of consciousness or pain, these kinds of technologies have serious implications for our definition of death. If the procedures could be done in humans, people who are declared brain dead by our current standards might be resuscitated. At the very least, this would exacerbate the tension between doctors trying to save the life of an individual, and those wanting to use their organs to save others.

"Earlier this year, a team managed to revive pig brains hours after death"

The notion of brain resuscitation is being explored elsewhere too. Accidents involving people falling into freezing lakes reveal that the brain can withstand a lack of oxygen much more readily at low temperatures. At UPMC Presbyterian hospital in Pennsylvania, doctors aim to replicate this phenomenon, putting people with severe wounds into a state of suspended animation 🔗 /article/mg22129623-000-gunshot-victims-to-be-suspended-between-life-and-death/, providing more time to save their lives. The trial

will replace patients' blood with cold saline, flushing it through the heart and into the brain. With no blood circulating and no brain activity, they will be clinically dead for 2 hours during which surgeons will try to fix their injuries before slowly warming them again with fresh blood. "The brain isn't like the heart," says Greg Fahy at 21st Century Medicine, a biotech company in California. "It doesn't need a jump-start. If you restore normal conditions, that gives it the opportunity to start again."

Cryogenics could make death reversible
Murray Ballard

As if that wasn't eerie enough, consider this. Hundreds of people across the world are stored in giant metal tubes full of liquid nitrogen, being cryogenically frozen. "Frozen" is actually a misnomer – most have had all the liquid in their bodies replaced with a kind of de-icer, which is then cooled rapidly to a crystal-like state. In theory, this process, called vitrification, maintains cells in the state they were in at the moment before cooling, while also stopping ice crystals forming, which can puncture tissues and destroy delicate brain cells. Whether these people are alive or dead comes down to our interpretation of one important word in the definition of death: irreversible. If you believe that one day we will be able to resuscitate a brain, and if it has been preserved intact, and if the injuries that caused the original death could be repaired – then these people aren't truly dead.

Where does this end?

That is a stretch of the imagination, although progress is being made. Fahy has been working on vitrification for decades – ultimately to allow transplant organs to be stored indefinitely. Using rabbits and pigs, his team has already cracked the challenge of preserving the delicate structures /article/2077140-mammal-brain-frozen-and-thawed-out-perfectly-for-first-time/ of the brain almost perfectly using vitrification. He has also shown that a vitrified rabbit kidney can be warmed up and function perfectly well back in the body.

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"It's very possible that trials like the one in Pennsylvania, and our own, are going to change our definition of death," says Fahy. "No doubt we will ultimately conclude that death depends on circumstance." Before we developed the defibrillator, you were dead minutes after your heart stopped beating, he notes. Then we realised that by reducing the temperature we might bring someone back to life hours after their brain has stopped working. "Where does this end?" he asks. "Is there a limit somewhere that you cannot overcome? Are there opportunities to help people who we'd otherwise assume are dead? It certainly gives you pause for thought."

Such questions have even reached the top echelons of the Catholic church. Recently, the Vatican asked to talk to Stephen Valentine, the architect behind Timeship, a project aiming to build a facility in Texas that could cryogenically store hundreds of human organs, brains and bodies indefinitely. "I didn't hold back," he says. "They were fascinated by the concept of storing people and organs, and of suspended animation. There was a genuine interest about life extension and what it meant for the soul and for definitions of life and death."

In performing this kind of research, we are confronting issues that challenge all our beliefs about what it is to die, says Valentine. Admittedly, no cryopreserved person has yet been brought back to life. "But the chance of it happening is increasing every year," he says.