

PHYSIOLOGY

THE LIMITS OF

An underwater photograph with a blue color palette. The scene is filled with numerous bubbles of various sizes, rising from the bottom right towards the top. In the lower right corner, there is a blurry, out-of-focus object that appears to be a diver's mask or a piece of equipment. The overall atmosphere is serene and mysterious.

An underwater photograph with a blue color palette. On the left side, a vertical column of white bubbles rises from the bottom. In the bottom left corner, a jellyfish with a brownish, umbrella-like top and long, thin, translucent tentacles is visible. The background shows the rippling surface of the water.

BREATH HOLDING

It's logical to think that the brain's need for oxygen is what limits how long people can hold their breath. Logical, but not the whole story

By Michael J. Parkes

Michael J. Parkes is senior lecturer in applied physiology at the School of Sport and Exercise Sciences at the University of Birmingham in England. He also works at the Wellcome Trust Clinical Research Facility at the University Hospitals Birmingham NHS Foundation Trust.



TAKE A DEEP BREATH

and hold it. You are now engaging in a surprisingly mysterious activity. On average, we humans breathe automatically about 12 times per minute, and this respiratory cycle, along with the beating of our heart, is one of our two vital biological rhythms. The brain adjusts the cadence of breathing to our body's needs without our conscious effort. Nevertheless, all of us also have the voluntary ability to deliberately hold our breath for short periods. This skill is advantageous when preventing water or dust from entering our lungs, when stabilizing our chests before muscular exertion and when extending how long we can speak without pause. We hold our breath so naturally and casually that it may come as a surprise to learn that fundamental understanding of this ability still eludes science.

(Feel free to exhale now, if you haven't already.)

Consider one seemingly straightforward question: What determines how long we can hold our breath? Investigating the problem turns out to be quite difficult. Although all mammals can do it, nobody has found a way to persuade laboratory animals to hold their breath voluntarily for more than a few seconds. Consequently, voluntary breath holding can be studied only in humans. If the brain runs out of oxygen during a lengthy session, then unconsciousness, brain damage and death could quickly follow—dangers that would render many potentially informative experiments unethical. Indeed, some landmark studies from past decades are unrepeatable today because they would violate the safety guidelines for human subjects.

Nevertheless, researchers have found ways to begin answering the questions surrounding breath holding. Beyond illuminating human physiology, their discoveries might eventually help save lives both in medicine and in law enforcement.

DETERMINING THE BREAK POINT

IN 1959 physiologist Hermann Rahn of the University at Buffalo School of Medicine used a combination of unusual methods—slowing his metabolism, hyperventilating, filling his lungs with pure ox-

xygen, and more—to hold his breath for almost 14 minutes. Similarly, Edward Schneider, a pioneer of breath-holding research at the Army Technical School of Aviation Medicine at Mitchel Field, N.Y., and, later, Wesleyan University, described a subject lasting for 15 minutes and 13 seconds under comparable conditions in the 1930s.

Still, studies and daily experience suggest that most of us, after inflating our lungs maximally with room air, cannot hold that breath for more than about one minute. Why not longer? The lungs alone should contain enough oxygen to sustain us for about four minutes, yet few people can hold their breath for even close to that long without practice. In the same vein, carbon dioxide (the exhaled waste product made by cells as they consume food and oxygen) does not accumulate to toxic levels in the blood quickly enough to explain the one-minute limit.

When immersed in water, people can hold their breath even longer. This extension may stem in part from increased motivation to avoid flooding the lungs with water (it is unclear whether humans possess the classical diving reflex of aquatic mammals and birds that lowers their metabolic rate during breath holding while submerged). But the principle remains true: breath-holding divers feel compelled to draw a breath well before they actually run out of oxygen.

IN BRIEF

What determines how long someone can hold a breath? People usually need to gasp for air long before their brain or body runs out of oxygen (the obvious limitation).

Investigating what limits our control over breath

holding has been difficult, but decades of research suggest that the diaphragm, which contracts to inflate the lungs, plays a key role.

The best hypothesis is that the diaphragm sends signals to the brain about how long it has been con-

tracted and how it is biochemically reacting to depleted levels of oxygen or rising levels of carbon dioxide. Initially those signals cause mere discomfort, but eventually the brain finds them intolerable and forces breathing to start again.

As Schneider observed, “it is practically impossible for a man at sea level to voluntarily hold his breath until he becomes unconscious.” Unconsciousness might occasionally occur under unusual circumstances, such as in extreme diving competitions, and some anecdotes suggest rare cases in which children can hold their breath long enough to pass out, but laboratory studies confirm that normally we adult humans cannot do it. Long before too little oxygen or too much carbon dioxide can hurt the brain, something apparently brings us to the break point (as researchers call it) past which we cannot resist gasping for air.

One logical, hypothetical explanation for the break point is that specialized sensors in the body observe physiological changes associated with breath holding and trigger a breath before the brain shuts down. Obvious candidates for such sensors would be ones that watched for lengthy expansions of the lungs and chest or that detected reduced levels of oxygen or elevated levels of carbon dioxide in the blood or the brain. Neither of those ideas appears to hold up, however. The involvement of volume sensors in the lungs appears to have been ruled out by various experiments conducted between the 1960s and the 1990s by Helen R. Harty and John H. Eisele, working independently in Abe Guz’s laboratory at Charing Cross Hospital in London, and by Patrick A. Flume, then at the University of North Carolina at Chapel Hill. Their experiments showed that neither lung-transplant patients, whose nerve connections between lungs and brain were severed, nor patients receiving complete spinal anesthesia, whose chest-muscle sensory receptors were blocked, could hold their breath for abnormally long periods. (It is significant that those anesthesia experiments did not affect the diaphragm muscle, however, for reasons that will become apparent.)

Research also seems to exclude the involvement of all the known chemical sensors (chemoreceptors) for oxygen and carbon dioxide. In humans, the only known sensors detecting low blood oxygen levels are in the carotid arteries just underneath the angle of the jaw, which supply blood to the brain. The chemoreceptors detecting raised carbon dioxide levels are in the carotid arteries and in the brain stem, which controls regular breathing and the other autonomic (involuntary) functions.

If the oxygen chemoreceptors caused the urgent sensation of break point, then without their feedback, people ought to be able to hold their breath until rendered unconscious. Experiments in Karlman Wasserman’s laboratory at the University of California, Los Angeles, have shown, however, that patients still cannot do so if the nerve connections between chemoreceptors in their carotid arteries and the brain stem are severed.

What Triggers Break Point?

Break point is the moment during a held breath when it becomes impossible for the breath holder to resist gasping for air. Training in breath holding can extend it, as can meditation, flooding the body with oxygen and purging it of carbon dioxide (CO₂). Finding what truly determines break point has nonetheless been frustratingly difficult. Research has ruled out some possibilities, however, and the beginnings of an explanation might be in sight.

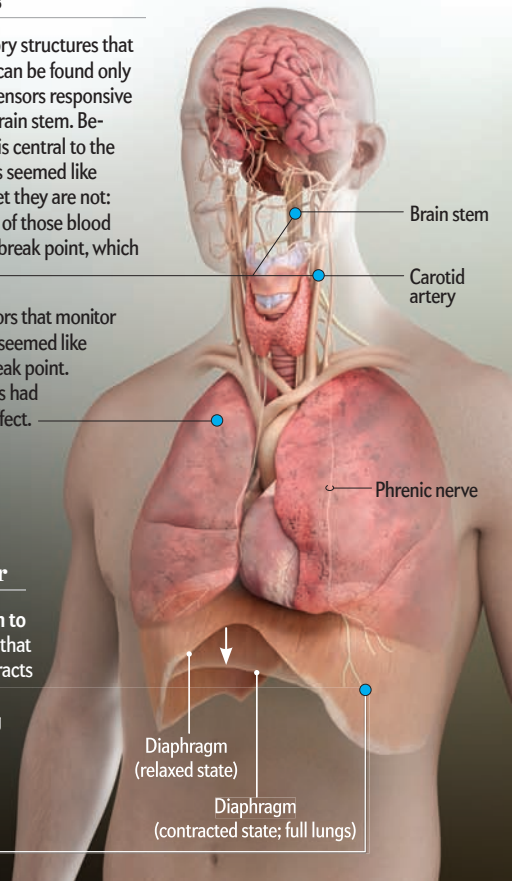
Ruled-Out Hypotheses

Blood gas chemoreceptors: Sensory structures that react to oxygen levels in the blood can be found only in the carotid arteries in humans; sensors responsive to CO₂ are in the carotids and the brain stem. Because the exchange of those gases is central to the purpose of breathing, these sensors seemed like logical controllers of break point. Yet they are not: if they were, critical concentrations of those blood gases would absolutely determine break point, which experiments show is not the case.

Volume sensors in the lungs: Sensors that monitor the expansion of the chest or lungs seemed like another possible determinant of break point. Yet experiments where those nerves had been cut or paralyzed showed no effect.

Best Hypothesis So Far

Nerve signals from the diaphragm to the brain: Most evidence suggests that the diaphragm muscle, which contracts to fill the lungs, sends discomfort signals to the brain about how long it has been holding a breath. The brain then subconsciously weighs this information against other considerations to determine how much discomfort is endurable.



Moreover, if reduced oxygen or elevated carbon dioxide levels alone dictated the break point, then beyond some threshold levels, breath holding should be impossible. Yet numerous studies have shown this not to be the case. It would also be true that after the gas levels triggered a break point, breath holding would remain impossible until the arterial oxygen and carbon dioxide levels returned to normal. But that prediction is not borne out, either, as researchers have casually observed since the early 1900s. In 1954 Ward S. Fowler of the Mayo Clinic described formally how after maximum breath holding, subjects could immediately do it a second time if they inhaled only an asphyxiating gas—and even a third time, despite their blood gas levels becoming progressively worse.

Further work has verified that this remarkable repeated breath-holding capability is independent of the number or vol-

ume of inhalations of the asphyxiating gas. Indeed, in 1974 John R. Rigg and Moran Campbell, both at McMaster University in Ontario, demonstrated that it persists even when the subjects merely attempt to exhale and inhale with their airway closed.

Taken together, all these experiments involving repeated breath-holding maneuvers suggest that the need to draw a breath somehow relates to the muscular act itself and not directly to its gas-exchange functions. When the chest is greatly inflated, its natural tendency is to recoil unless the inspiratory muscles of breathing hold it in the inflated state. So researchers of the break point began to look for answers in the body's neurological and mechanical controls over these inspiratory breathing muscles. As part of that work, they also wanted to learn whether breath holding involves a voluntary halt of the automatic breath-

ing rhythm that drives these muscles or the prevention of the breathing muscles from expressing this automatic rhythm.

UNREPEATABLE EXPERIMENTS

THE NORMAL RHYTHM of our breathing can be said to begin when the brain stem sends impulses down our two phrenic nerves to the bowl-shaped diaphragm muscle underneath the lungs, telling it to contract and inflate the lungs. When the impulses stop, the diaphragm relaxes and the lungs deflate. In other words, some rhythmic pattern of neural activity—a central respiratory rhythm—mirrors the cycle of our breaths. In humans it is still technically and ethically impossible to measure this central rhythm directly from the phrenic nerves or from the brain stem. Investigators have devised ways to record the central respiratory rhythm indirectly, however: by monitoring instead the electrical activity in the diaphragm muscle, the pressure in the airway or other changes in the autonomic nervous system, such as the heartbeat rhythm (known as respiratory sinus arrhythmia).

Working from such indirect measurements, Emilio Agostoni of the University of Milan in Italy showed in 1963 that he could detect a central respiratory rhythm in human subjects holding their breath well before they reached break point. In related experiments at the University of Birmingham in England in 2003 and 2004, graduate student Hannah E. Cooper, anesthetist Thomas H. Clutton-Brock and I used respiratory sinus arrhythmia to show that the central respiratory rhythm never stops: it persists throughout breath holding. Breath holding must therefore involve suppressing the diaphragm's expression of this rhythm, possibly through a voluntary, continuous contraction of that muscle. (Various experiments seem to have ruled out the involvement of other muscles and structures involved in normal breathing.) Break point may similarly depend on sensory feedback to the brain from the diaphragm—reflecting, for example, how stretched or unusually overworked it may be.

If so, then paralyzing the diaphragm to eliminate its sensory feedback to the brain ought to allow subjects to prolong their breath holding greatly if not indefinitely. Such was the expectation in one of the most alarming breath-holding experiments ever, which Campbell performed at Hammersmith Hospital in London in the late 1960s. Two healthy, conscious volunteers consented to have all their skeletal muscles temporarily paralyzed with intravenous curare—except for one forearm, with which they could signal their wishes. The subjects were kept alive with a mechanical ventilator; breath holding was simulated by switching it off, and the subjects indicated their break point by signaling when they wanted the ventilator restarted.

The result was astonishing. Both volunteers were happy to leave the ventilator switched off for at least four minutes, at which point the supervising anesthetist intervened because their blood carbon dioxide levels had risen perilously. After the effects of the curare had worn off, both subjects reported feeling no distressing symptoms of suffocation or discomfort.

For obvious reasons, such a daring experiment has rarely been repeated. Some others have tried and failed to replicate Campbell's findings, but their courageous volunteers reached break point after such a short duration that their carbon dioxide levels barely rose above normal. Those observations suggest that the subjects might have chosen to end the tests early, possibly because of discomfort from the air tubes holding open the

A REALM OF THEIR OWN

Secrets of Champions

People who excel at breath holding often rely on four key principles. Extended breath holding poses serious risks for unconsciousness, brain injury and death, however. Medical assistance should always be standing by.

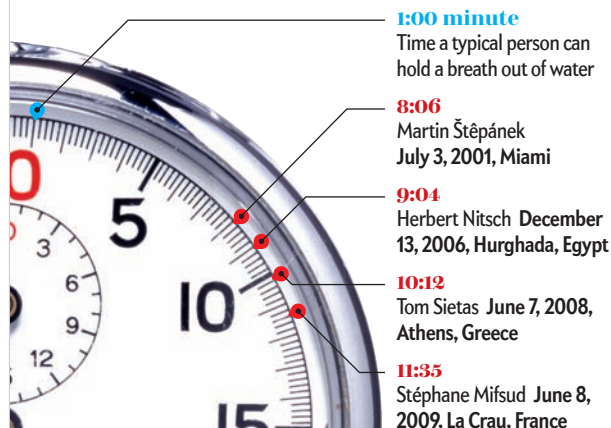
REALLY FILL THE LUNGS: Some athletes hyperinflate the lungs beyond their normal maximum through a technique known as buccal pumping, rhythmically moving the floor of the mouth to draw in extra air. The elevated pressures inside the lungs that result, however, pose a risk of arterial gas embolism—gas bubbles in the blood that can damage the brain or coronary capillaries.

RELAX TO SLOW METABOLISM: At rest, human metabolism consumes about 0.36 liter of oxygen per minute. By fasting for 12 hours and lying quietly awake, one can lower oxygen consumption to just 0.27 liter per minute, which makes the air in the lungs last about 33 percent longer.

INHALE PURE OXYGEN: Fresh air is usually only about 21 percent oxygen. Studies show that inhaling 100 percent oxygen can double the duration of breath holding. Yet doing so also raises the possible danger that regions of the lungs may collapse once all the oxygen they contain is extracted.

HYPERVENTILATE: Hyperventilation before breath holding can lower the levels of carbon dioxide in the blood, which in studies has sometimes doubled the time until break point. Yet it can also be counterproductive: hyperventilation tends to speed up how quickly the body consumes oxygen and produces carbon dioxide. Moreover, it restricts the supply of blood reaching the brain and disarms reflexes that protect the brain from inadequate oxygen. —*The Editors*

Notable Records*



*Achieved while motionless and facedown in water, without first inhaling pure oxygen

glottis (a modern safety requirement not present in Campbell's experiment) and because of their greater awareness of the life-threatening risk. Nevertheless, some equally remarkable experiments by Mark I. M. Noble, working in Guz's laboratory at Charing Cross Hospital in the 1970s, seem to confirm that diaphragm paralysis prolongs breath-holding duration. Instead of total body paralysis, Noble and his colleagues used the much less life-threatening maneuver of paralyzing the diaphragm alone by anesthetizing only the two phrenic nerves. Doing so doubled subjects' average breath-holding duration and reduced the usual uncomfortable sensations that accompany breath holding.

CURRENT BEST EXPLANATION

THE BALANCE OF EVIDENCE thus favors the speculation that a voluntary, lengthy contraction of the diaphragm holds the breath by keeping the chest inflated. The break point may depend very much on stimuli that reach the brain from the diaphragm in this unusual contracted state. During such a lengthy contraction, the brain might subconsciously perceive the unusual signals from the diaphragm as vaguely uncomfortable at first but eventually as intolerable, causing the break point. The automatic rhythm then regains control.

This hypothesis is not fully fleshed out, but it fits nicely both with Fowler's observations (that any release of breath holding, necessarily by relaxing the diaphragm, enabled another one) and with the effects of lung inflation and blood-gas manipulation on breath-holding duration. Relaxing the diaphragm even a bit and exhaling slightly would delay break point by relieving the signals from the stretch sensors in the diaphragm. Raising the oxygen level and lowering the carbon dioxide level in the blood would also extend breath-holding capability by reducing biochemical indicators of fatigue in the diaphragm. Anything that prevents the brain from monitoring such information—for example, by blocking the nerves between the diaphragm and the brain—will extend duration. The tolerance of the brain to such unpleasant signals will also depend on your mood, motivation and ability to be distracted by, say, mental arithmetic.

This hypothesis is only the simplest unifying explanation for the experimental observations. Some of these experiments used too few subjects to be the basis for reliable generalizations, and ethical permission to repeat them may never be granted. Key pieces of the jigsaw puzzle may still be missing.

Moreover, a puzzle piece that does not yet quite fit comes from another of Noble and Guz's dramatic (and now ethically unrepeatable) breath-holding experiments. They tripled the duration of breath holding in three healthy subjects by anesthetizing their two sets of cranial nerves (the vagus nerves, which go from the brain to organs in the chest and abdomen, and the glossopharyngeal nerves, which go to the glottis, larynx and other parts of the throat). This result would appear to have been achieved without affecting the diaphragm, except that it is also possible that the vagus nerves, too, carry some signals from the diaphragm. It seems less likely that the larynx itself contains a muscle involved in breath holding: in 1993 when surgeon Martyn Mendelsohn of Sydney, Australia, viewed the glottis (via a camera inserted through a nostril), the glottis often remained open throughout breath holding. This observation, too, seems to support the conjecture that the diaphragm's role is key.

SAVING LIVES

BETTER UNDERSTANDING of what limits people's ability to hold their breath has practical uses in medicine. As part of the treatment for breast cancer, for instance, patients receive radiation therapy, during which the goal is to lethally dose the entire tumor without damaging the healthy tissues all around it. Doing so requires minutes of radiation exposure, during which a patient must try to keep her breast motionless. Because breath holding for so long is impractical, current practice uses short bursts of radiation timed to fall between a patient's breaths, when her chest is moving least. Yet with each breath, the breast moves and may not necessarily return to exactly the same position. Medical physicist Stuart Green, clinical oncologist Andrea Stevens, anesthetist Clutton-Brock and I are now starting experiments funded by University Hospital Birmingham Charities to test whether it would be feasible to prolong breath holding sufficiently to aid radiotherapy treatment.

A practical understanding of breath holding might also be of value to law-enforcement personnel when they are forcibly restraining suspects. Every year around the world some people under restraint may die accidentally. Raising the metabolic rate, compressing the chest, lowering the blood oxygen level and raising the blood carbon dioxide level all shorten the duration of a person's breath holding. So someone who is angry, has been fighting or is being forcibly held down may well need to draw a breath earlier than someone who is relaxed.

In 2000 Andrew R. Cummin and his team at Charing Cross Hospital studied what happened after eight healthy subjects breathed out maximally and held their breath after cycling moderately for one minute: the duration of their maximum breath holding plummeted to 15 seconds, the average amount of oxygen in their blood fell dramatically and two of them developed irregular heartbeats. Consequently, the researchers concluded that the "cessation of breathing for short periods during vigorous restraint ... may account for unexplained deaths in these circumstances." Law-enforcement authorities have carefully compiled guidelines for the use of forcible restraint; they should be observed scrupulously.

Such investigations of breath holding open windows into vital aspects of human physiology. Clearly, more groundbreaking discoveries, particularly about the diaphragm itself, remain ahead—which leaves some of us breathless in anticipation. ■

MORE TO EXPLORE

Diaphragm Activity during Breath Holding: Factors Related to Its Onset. E. Agostoni in *Journal of Applied Physiology*, Vol. 18, No. 1, pages 30–36; 1963.

Behavioural and Arousal-Related Influences on Breathing in Humans. S.A. Shea in *Experimental Physiology*, Vol. 81, No. 1, pages 1–26; 1996.

CO₂-Dependent Components of Sinus Arrhythmia from the Start of Breath Holding in Humans. H. E. Cooper, M. J. Parkes and T. H. Clutton-Brock in *American Journal of Physiology—Heart and Circulatory Physiology*, Vol. 285, No. 2, pages H841–H848; 2003.

Contribution of the Respiratory Rhythm to Sinus Arrhythmia in Normal Unanesthetized Subjects during Positive-Pressure Mechanical Hyperventilation. H. E. Cooper, T. H. Clutton-Brock and M. J. Parkes in *American Journal of Physiology—Heart and Circulatory Physiology*, Vol. 286, No. 1, pages H402–H411; 2004.

Breath-Holding and Its Breakpoint. Michael J. Parkes in *Experimental Physiology*, Vol. 91, No. 1, pages 1–15; 2006.

SCIENTIFIC AMERICAN ONLINE

Learn how the diving reflex may extend breath holding underwater at ScientificAmerican.com/apr2012/breath-holding