The flesh and bones of Dr. John Collins Warren

Dr. John Collins Warren (1778-1856), renowned surgeon and co-founder of the MGH, is buried at tranquil Forest Hills Cemetery in Jamaica Plain, but he also is sequestered in a closed, coffin-like box in storage at Harvard’s Warren Museum. How can that be possible? The disposition of his body was unclear for many years, but recent research has unearthed the facts.

Warren left precise instructions in a letter to his son about what should be done with his “mortal remains after the spirit has quitted them.” He wanted his body taken to Harvard Medical School (where he taught for 38 years) to be “examined or dissected [and] any morbid parts … carefully preserved.” He further instructed that his bones were to be “whitened, articulated, and placed in the lecture room of the Medical College, near [his] bust” as “a lesson useful … to morality and science.” Warren’s skeleton is indeed at Harvard in the anatomical museum that he founded, but his descendants allow the box to be opened only for family members. Dominic Hall, curator of the Warren Anatomical Museum, explains that the historical files have no records of how this came to be, but it is a tradition the museum still honors.

A marker in the Warren family plot at Forest Hills bears the name “Johannes Collins Warren,” but it was incorrectly assumed by most observers (aware that his skeleton was at Harvard) that the name was merely there as a token of remembrance. My own high school Latin was not equal to the task of translating the inscription on the Warren stone (Animae vestis carnea hoc tumulo conditur), but I now know (with the help of a classicist) that it means: “The fleshy clothing of the soul is buried in this grave.”

Warren bought the plot in 1852 and pre-arranged for several long-deceased (Continued on page 4)

Using science to scare for a good cause

The Victorian Home on Washington Park in Newton might look ordinary from the outside, but tonight (Oct. 28) it will be transformed into a world filled with vampires, ghouls, skeletons, witches, spiders and eyeballs.

That house is the home of Lisa Feldman Barrett, PhD, a research scientist in the MGH Department of Psychiatry who runs the Interdisciplinary Affective Science Laboratory. Barrett’s lab studies emotion and how different emotions – fear, anger, sadness – are formed in the brain.

Every Halloween Barrett hosts Sophia’s Annual Haunted House in her stone basement. Going on its 12th year, 100 percent of proceeds from ticket sales are donated to the Greater Boston Food Bank. The original idea for the haunted house came from Barrett’s daughter, Sophia, now 17 years old.

Although the haunted house can be scary, blood and gore are left at the door. (Continued on page 2)
Creating organs – one cell at a time

ON ANY GIVEN DAY in the Ott Lab at the MGH a number of studies are underway. Bioreactors, each with an organ inside, are hooked to complicated networks of tubes carrying special solutions into the organ’s cellular scaffolding. This is the world of Harald Ott, MD, a thoracic surgeon who leads the lab’s activities. Ott’s hope is that one day the discovery of how to create organs for a multitude of medical benefits will emerge.

Ott’s clinical practice brought him to the field of organ regeneration. “As a physician, it can be heartbreaking to work with patients in organ failure because you realize at some point there is nothing else left for options,” says Ott. “After starting my training, I began to realize our tools to treat patients suffering from heart failure, end stage lung disease, and kidney failure are extremely limited. As we get better at treating acute diseases and injuries, more patients will develop end-stage organ failure and require innovative solutions.”

Ott and his research team are working to generate replacement tissues and organs on demand. For example, patients diagnosed with kidney or heart failure could have some of their cells harvested to engineer replacement kidneys. The impact would be two-fold: patients would not have to wait years for an organ transplant and also would not require immunosuppressants to prevent rejection.

The secret lies in the organ’s extracellular matrix. “You can think of this as scaffolding in each organ, which can be likened to a construction blueprint,” says Ott. “Cells, as the smallest living units, live in the scaffolding like people live in a building, and together they make our tissues and organs work. We base our regenerative efforts on native matrix, the original blueprint on which organs were built. We then move the old and damaged cells out, and bring the new ones in, creating a healthy organ.”

Recently, the Ott Lab has brought scaffolds to human scale, so researchers now can generate blueprints of human hearts, lungs, kidneys and extremities. The team now is working on driving human stem cells to form functional tissue on these scaffolds, and to develop transplant protocols, to prepare for clinical application. “While we are still years away, we have moved from small-scale research in animal cells to human-scale research across cells in several organ systems,” says Ott.

A CLOSER LOOK:
Ott examines one of the decellularized organs in his lab.
Having a horrible time – and loving it

“DON’T OPEN THAT DOOR!”

“Run AWAY from that ominous sound, not toward it!”

“Why are you walking and not running?!”

For people who enjoy horror movies, chances are they – or someone they’re watching with – has called out these things. So why do so many people love being scared?

The strength of a horror film is its depiction of regular people undergoing extraordinary ordeals, something we can all identify with psychologically, says MGH’s resident horror expert Steve Schlozman, MD, associate director of the Clay Center for Young Healthy Minds, who also teaches an undergraduate seminar focusing on horror films and stories at Harvard College.

“The data on why certain types of people like horror is limited but pretty interesting,” says Schlozman. “Horror is popular among people who enjoy the experience of being scared – who literally get revved up in terms of heart rate and breathing rate during the film – but who also like to solve the puzzle of why they’re scared in the first place.”

Brains, Schlozman says, love puzzles, which are an adaptive mechanism our brains undertake so we can stay out of danger. “When you’re scared, such as when watching a horror movie or sitting on a roller coaster, you can trigger two types of responses. The first is the fight-or-flight response, which sits in the lower crevices of the brain – primarily the amygdala. This area is evolutionarily primitive and creates a surge of adrenaline. Your heart rate increases. Your breathing increases. In other words, your brain is preparing you for survival mode and everything else can wait.”

The second type of response is more complex, he adds. “It still has that fight-or-flight response, but then it kicks that response north to the more sophisticated regions of the brain in order to reasonably assess the threat.”

So how does a horror expert pick his favorite horror movie? “There are so many! How much time do you have!” says Schlozman.

The brain on fear

HAUNTED HOUSES, hayrides and mazes are all designed to induce fear – a fear most people willingly accept when they enter one of these scary situations. During these episodes one may experience an adrenaline rush, cold sweat and flushed cheeks – but what does a person’s brain look like when it is fearful?

“Our brains detect fearful events or stimuli and react quickly to either help us run away from the fearful thing we encounter or fight it if we can’t run,” says Mohammed Milad, PhD, MGH Department of Psychiatry researcher. “Since childhood, we learn to fear certain situations, actions or behaviors. We learn that bears are dangerous and to either run away or remain at high alert when walking in the woods where bears may be around.”

Brains can distinguish and not induce a fearful response if the context is appropriate. If a person sees a bear in the zoo, and it is far away from them with no chance of it attacking, then the person may simply enjoy its majestic size and power. The same applies for Halloween. “Seeing someone wearing a scary clown mask on Halloween is fun, and while you may be scared, you can still control it and enjoy,” Milad says. “But if you were to see someone with the same mask on a Tuesday evening in March with no context, your response would be completely different.”

Milad’s research seeks to answer if people can learn not to fear. The ventral medial prefrontal cortex works to regulate and control fear, and in patients with anxiety disorders, this brain region appears not to be as active as it should. Milad’s team is working to find new ways to improve the activation of this brain area to help advance treatments for anxiety.

“Fear is adaptive and important for survival,” Milad says. “Without it, we would become extinguished through risky behaviors such as not being afraid of a bear when you walk in the woods. That said, fear becomes unhealthy when it becomes excessive and an impediment to our daily lives. This excessive fear comes from your brain and is no different from other illnesses we experience.”

Zombies, more than scary?

ZOMBIES – fictional beings appearing as reanimated human corpses – have been around since the early 1800s in literary works and have appeared in film since the 1930s. Schlozman, who also authored the book The Zombie Autopsies, explains what can be learned about the brain through zombie culture.

WHY DO PEOPLE LOVE ZOMBIES SO MUCH?

They’re empty shells, and as such we can project onto them all of our unbridled feelings. They remind us that most of what makes us angry isn’t about us. The guy you’re stuck behind in the DMV isn’t fumbling to find his old license to make you mad. You just happen to be behind him. That’s a lot like a zombie’s desire for flesh. It doesn’t care whose flesh. There’s nothing special about your flesh if a zombie eats you. It’s just that you happen to be there. None of us is special or unique to a zombie.

WHAT PARTS OF THE BRAIN WOULD BE MOST SUSCEPTIBLE TO INFECTION IN A ZOMBIE APOCALYPSE?

If you’re hungry, the ventro-medial part of the hypothalamus is involved. If you can’t think, the frontal cortex takes a hit. If you shamble, the cerebellum and the basal ganglia are off. Finally, if you are in attack mode, that amygdala has got to be revved up, which provides us with our primal instincts.
--- A good scare
(Continued from page 1)

Barrett and her nearly 20 postdoctoral fellows and graduate students, whom she recruits as actors to play monsters and vampires, use an interesting method to scare their guests: They use what they know from scientific research.

“We use it as a team building exercise,” Barrett says. “The whole thing is choreographed without gore and we don’t rely on those cheap, gory decorations. It’s so easy to startle people with blood and guts, and we find that to be like cheating. We try to use the science of emotion to scare.”

For example, researchers have found that feeling uncertain about whether something is alive is extremely arousing. Heightened arousal – when experienced in a haunted house or on a roller coaster – is experienced as fear. Though it is not responsible for triggering fear, the amygdala is a structure in the brain that controls arousal and uncertainty, and is also very sensitive to sclera (the whites of the eyes). Therefore, Barrett and her monsters cut out the eyes of their Halloween masks so the human eyes of the wearer are seen clearly.

“We pose monsters and ghouls so it is uncertain whether or not they are alive,” Barrett says. “And, using timing to maximize surprise, the monsters and ghouls grab a visitor’s attention by flashing the whites of their eyes. All this enhances arousal in the visitor, setting the stage for fear.”

To cater to all ages who attend the haunted house, there are three levels of scary: “No scares” mean actors stand still, act friendly and will unmask if asked; “medium scary” is when actors move in creepy ways; and “super scary” is when anything goes and actors can jump out and surprise attendees.

The charity haunted house typically raises between $2,000 and $3,000 and garners a crowd of about 450 people each year. In previous years the event has included a witch’s coven and dead Snow White coming to life. This year, patrons can look forward to a haunted dinner and a bat cave with vampires. Attendees need not worry: No ghouls will go hungry at this haunted house.

“Neighborhood restaurants donate money to feed the monsters so they don’t eat the patrons,” Barrett says. “It’s really a community event.”

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Historical oddities:
Strange medical tools

LONG BEFORE the days of Cal-Stat, medical lasers and microscopes, before any high-tech monitors, scanners and machines, medical professionals used simple devices in the care and treatment of patients. Looking back throughout history, doctors and scientists experimented with some pretty strange and eerie — by today’s standards — tools. The Paul S. Russell, MD, Museum of Medical History and Innovation has an archive of some creepy — yet fascinating — surgical artifacts. Eight are presented here. For those interested in learning more about MGH’s history, the museum is open Monday – Friday from 9 am – 5 pm.

Museum mysteries: Murder bottles

BEHIND THE SCENES at the Paul S. Russell, MD Museum of Medical History and Innovation at the MGH, there sits a box labeled “Collection of nursing bottles, breast pumps and nipple shields.” These baby nursing supplies are similar to those of a contemporary hospital nursery except these artifacts date to the late 19th century, when bottle feeding was a brand-new concept. The little glass bottles were meant to ease the burden of child care that Victorian mothers faced. Often sporting such whimsical names as “Feed The Baby” and “Mummie’s Darling,” the bottles were patented and introduced in the late 1800s. Although many women continued to breastfeed, bottle feeding became a way to help those mothers who were unable to breastfeed, could not afford a wet nurse, or who wanted the freedom of not having to be accessible for feeding 24 hours a day – as well as wrestling multiple times throughout the day with a restrictive corset.

The bottles worked simply. After the banjo-shaped bottle was filled with liquid, often cow or breast milk, a long rubber tube was inserted through a stopper in the bottle’s thin neck. The section of the tube outside the bottle was fitted with a rubber nipple. The shape of the bottle and the length of the tube allowed a child to hold and eat from the bottle without help, giving mothers freedom to take care of other household duties.

With this modern convenience, however, came untold tragedy. Infant mortality rates during the
**Museum mysteries: Murder bottles**

Late Victorian era were high, with fewer than two babies of every 10 surviving until 2 years of age. While providing sustenance, these bottles also delivered poison to many of the babies. Bacteria of all kinds flourished in the difficult-to-clean hoses, and the design of the bottles, unlike those of the more open household bottles and jars, also provided breeding grounds for molds and diseases.

Even the Victorian age Martha Stewart wasn’t helpful. Isabella Beeton was a household management guru and her 1861 book, *Mrs. Beeton's Household Management*, provided counsel on everything that the busy lady of the house needed to know about child rearing, and how to keep her household in tip-top shape. When it came to baby bottles, this domestic expert advised that washing nipples every two to three weeks was sufficient. Unfortunately, the impure environment of the rubber nipple allowed for even more bacteria to grow with abandon, and added to the contaminated bacteria already collecting in the bottles.

By the time Buffalo, New York outlawed the bottles in 1897, they had acquired the moniker “murder bottles.” After widespread condemnation by medical communities in the U.S. and abroad, many other cities and states followed suit. Surprisingly, however, the bottles continued to be available and popular until the 1920s as the promise of independent feeding remained appealing.

— Michelle Marcella, manager of the Russell Museum

**MGH’s rue morgue**

**“THIS ONE’S ready for Allen Street.”**

It is a phrase universally heard and understood throughout the halls of the MGH, though remains a mystery to some, as no “Allen Street” exists around the hospital. In 1874, however, one did.

The Allen Street House, built in 1874, was a brick building north of Bulfinch West that was used not only as the autopsy building but also doubled as a mortuary. For the 60 years that Allen Street existed, according to Webster Bull in *Something In the Ether*, it had a morbid connotation. In 1896, a new pathology building was added alongside it, intensifying the association. Only two openings existed to the building, a small door for workers to pass through and a larger door for hearses.

Although it no longer physically exists – Blossom Street lies where Allen Street was – it remains a common reference when a patient is taken to the morgue.

— By Lewis Thomas in the 1937 edition of the HMS yearbook, the Aesculapiad, taken from *Something in the Ether*

**Ode to Allen Street**

*Canto III*

But let us speak of Allen Street—that strangest, darkest turn, Which squats behind a hospital, mysterious and stern. It lies within a silent place, with open arms it waits For patients who aren’t leaving by the customary gates. It concentrates on end results and caters to the guest Who’s battled long with his disease and come out second best. For in a well-run hospital, there’s no such thing as death. There may be stoppage of the heart, and absence of the breath— But no one dies! No patient tries this disrespectful feat. He simply sighs, rolls up his eyes, and goes to Allen Street. Whatever be his ailment—what’s the sickness be, From “Too, too, too much insulin” to “What’s this in his pees?” From “Gastric growth,” “One lung (or both),” or “Question of Cirrhosis” To “Exitus undiagnosed,” or “Generalized Necrosis”— He hides his head and leaves his bed, and covered with a sheet, He rolls through doors, down corridors, and goes to Allen Street. And there he’ll find a refuge kind, a quiet sanctuary, For Allen Street’s that final treat—the local mortuary.

— By Lewis Thomas in the 1937 edition of the HMS yearbook, the Aesculapiad, taken from *Something in the Ether*

**BENJAMIN BELL TREPHINE C. 1801**

Trepanning involves cutting holes in the skull, which many felt helped release diseases and “bad spirits” from the body. Trephines, used to the drill the holes, came in all forms. This T-shaped drill replaced an earlier version that resembled a carpenter’s brace and bit. The center pin on the stem enabled the pin within the circular saw (see teeth) to be adjusted during sawing to prevent damage to the brain tissue.

**BIGELOW IMPROVED LITHOTRITE C. 1890**

Lithotrites were used for crushing stones in the bladder. The long female blade is inserted into the bladder through the urethra. A mechanism in the handle provides a way for the heavily notched male blade to clamp onto the stone to extract it from the bladder as the instrument was removed from the body.

**BLOOD TRANSFUSION APPARATUS C. 1880**

This early blood transfusion apparatus collected the blood of the donor into an attached metal cup (not shown) that was then pumped directly into the recipient.
The mummy at the MGH

ON MAY 21, 1823, an advertisement was printed in a Boston newspaper, inviting the public to take a close-up look at “The Egyptian Mummy.” *This curious relic of antiquity, together with the sarcophagi in which it was contained when taken from the catacombs of ancient Thebes, is to be seen at Doggett’s Repository of Arts, No. 16, Market Street. The proceeds of the exhibition, after deducting two hundred dollars for the Boston Dispensary, will be appropriated to the Massachusetts General Hospital. Price of admission 25 cents.*

Earlier in the month, the MGH received from the city of Boston the mummy, complete with painted wooden inner and outer coffins. The ensemble had been given to the city by Jacob Van Lennep, a Dutch merchant living in the Greek city of Smyrna in the early 19th century. It is thought that Van Lennep, who was also the counsel general of the Netherlands, bought the mummy as a gift to Boston as a way to impress his native New England in-laws. The mummy had arrived in Boston on April 26, 1823, on the British ship the *Sally Ann*. He was placed under the care of the ship’s captain, Robert B. Edes, along with Bryant P. Tilden, Esq., who ultimately made the decision to give the mummy to MGH.

Padihershef – as he would later be identified – spent the next year traveling in a multi-city tour of the East Coast, raising an estimated $1,200 for patients of the MGH. Upon his return to the hospital, he was displayed in the historic Ether Dome, where he has remained for nearly 200 years. For more than a century, little was known about the MGH’s most popular resident; however, examination of hieroglyphics on his coffin suggested Padi was a 40-year-old stonecutter from the Necropolis in Thebes who lived some 2,500 years ago. More recent medical information now estimates Padi was between 20 and 30 years old and was instead a “tomb finder” or prospector – someone who looked for spaces in the Theban necropolis that could serve as burial spaces.

Padi has been studied throughout his time at the MGH – first by John Collins Warren, MD, cofounder of the MGH and its first surgeon (read more about Warren on page 1) – and later through X-ray examinations conducted in 1931 and 1977. He underwent extensive restoration by experts in 1984. In 2013, Padi received an additional restoration and a full-scale medical investigation, including full body CT scanning, which produced many details about Padi’s life that were previously unknown.

Padihershef is on display in the Ether Dome and can be viewed by the public weekdays from 8 am to 5 pm.

Flesh and bones

(Continued from page 1)

family members buried elsewhere to be exhumed and re-interred in a newly constructed underground vault beside his own morbid parts. The shuffle occurred in August 1856. All of the remains now in the vault are contained in urns – the older ones because they were “repackaged” after decades of moldering in the ground; and Warren’s because the dissection and subdivision of his body made the parts destined for Forest Hills amorphous and compact.

Medical historians and other admirers of the famous surgeon can now locate his “mortal remains” to pay their respects, but one mystery remains: Who determined that his skeleton should remain out of public view?

—Jeff Mifflin, MGH archivist