

ward 4

A Legacy of Discovery



Birth of a Research Center



MALLINCKRODT WARD 4 CIRCA 1940S.

Medical research has been integral to Massachusetts General Hospital (MGH) since its opening in 1821. Traditionally, though, research was a byproduct of treating individual patients rather than its own pursuit.

In the early 1900s, research in the U.S. began to mature with the emergence of clinical research centers: hospital units designed, equipped, and staffed solely to advance medical knowledge.

One of the earliest and most successful was **Ward 4**, opened at MGH on November 4, 1925.

Birth of a Research Center

An expansive mission

Funded largely by private benefactors, Ward 4 by design lacked a specific goal or disease focus. Rather, it was built upon faith that brilliant researchers, given space, resources, and support to follow their curiosity, would produce spectacular results.

A national role model

As post-WWII affluence drove a surge in government-funded medical research, Ward 4 served as a model for new National Institutes of Health (NIH) research centers nationwide. The 500-bed NIH Clinical Center in Bethesda, Maryland, opened in 1953, included at least 15 MGH alumni on its staff.

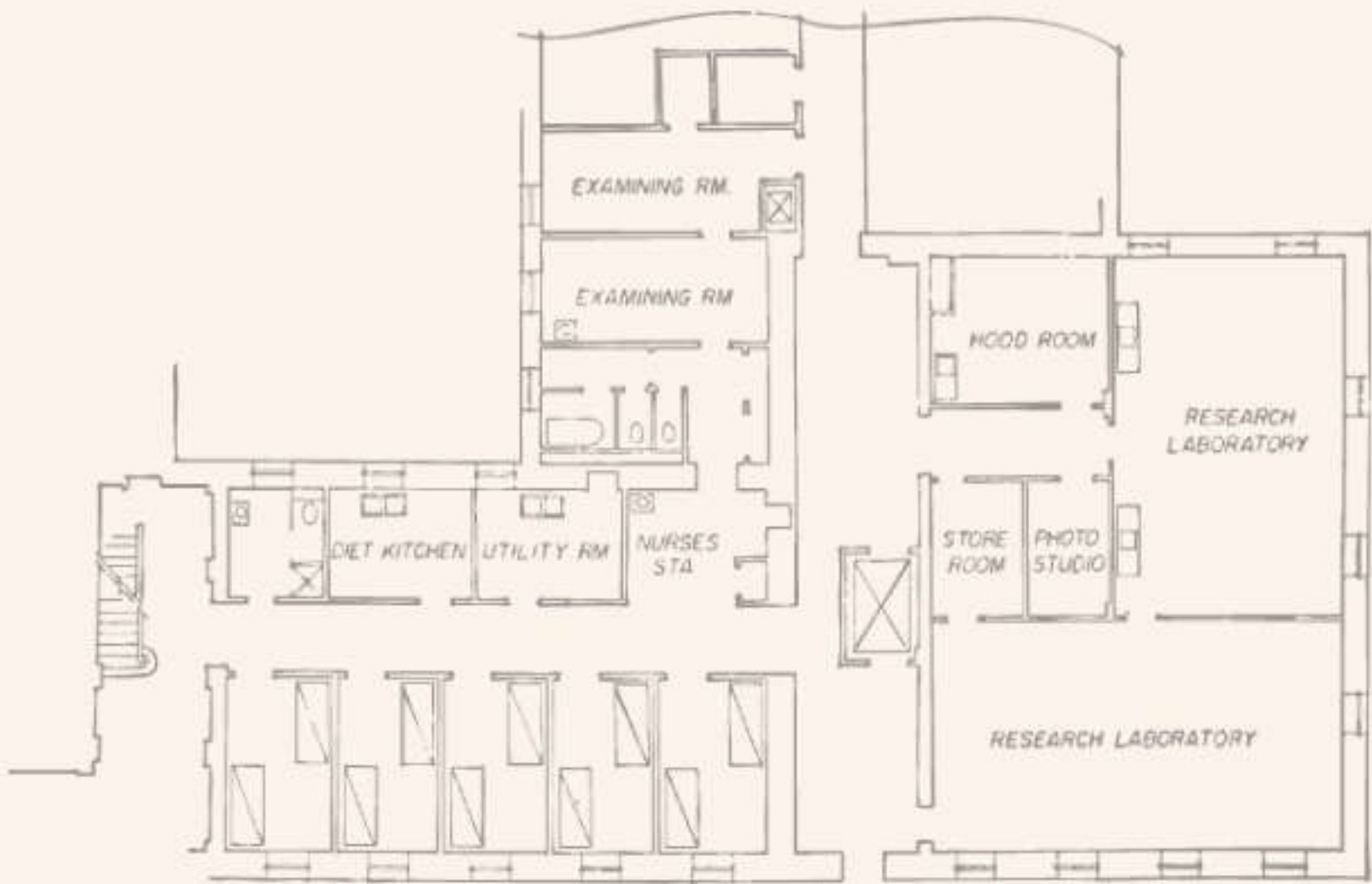
The Space

Located on the first floor of the historic Bulfinch Building, Ward 4 boasted:

- 10 beds
- 2 examining rooms
- 1 kitchen
- 2 laboratories
- 1 photo studio
- 1 hood room (used to vent harmful gases)

The operating budget for 1926, including board, lodging, medicine, and nursing, was

\$15,000



What's in a Name?

For a facility devoted to exacting research, the clinic's naming was delightfully random. When MGH trustees preferred a number to a title, founder James Howard Means, MD, decided "Ward 4" sounded "short and sweet." Other MGH wards went by 7, 16, 30, and 31. The reasons are lost to history.

The Visionary

David Linn Edsall (1869–1945)

The arrival of David Linn Edsall, MD, in 1912 as chief of medicine marked a turning point in the hospital's development as a modern research institution. A specialist in metabolic research, public health and industrial medicine (now known as occupational medicine), Edsall envisioned a "teaching and investigative clinic" and assembled and trained a team of young interns for careers in research.



EDSALL ALSO SERVED AS HARVARD MEDICAL SCHOOL DEAN AND FIRST DEAN OF THE HARVARD SCHOOL OF PUBLIC HEALTH.



Courtesy Pezzotti Estate

The Founder

James Howard Means (1885-1967)

When Edsall left MGH in 1924 to become dean of Harvard Medical School, it fell to protégé and endocrinologist James Howard Means, MD, to carry the mantle for the new clinic. Means used as his prototype the four-bed Metabolism Ward started at New York's Bellevue Hospital in 1913, and where Means had worked in 1916.

MEANS LED WARD 4 UNTIL HIS RETIREMENT IN 1951. IN THIS PORTRAIT BY PIETRO PEZZATI APPEARS A PAINTING OF THE BULFINCH BUILDING, LONGTIME SITE OF THE WARD.

Research Pioneers

Though it was open to any area of medical research, the lion's share of Ward 4 researchers pursued advances in endocrinology, metabolic research and industrial medicine, including:

Lead poisoning

Ward 4 couldn't have come at a better time for its inaugural researcher, endocrinologist **Joseph C. Aub, MD**. By the 1920s, lead was recognized as an industrial poison endangering painters, plumbers, rubber mixers and other workers. Leaded gasoline raised fears of much wider exposure. Ward 4's first patient subjects had absorbed high levels of lead but showed no acute illness. Adjusting the intake of calcium and acid-producing salts made it possible to control "de-leading" in the bloodstream and bones. Aub's research produced breakthroughs in prevention and a fast-acting intravenous treatment for acute lead poisoning.



AUB, A PIONEER IN UNDERSTANDING LEAD POISONING, DURING A TIME WHEN KNOWLEDGE OF ANOTHER HAZARD (TOBACCO) WAS SCANT.

In 1952, **Harriet L. Hardy, MD**, and **William H. Baker, MD**, brought relief to two Ward 4 subjects with chronic lead poisoning, using a therapy called EDTA which draws lead from the body into the bloodstream and renders it harmless. EDTA is still used for chronic lead poisoning.

Hearing loss

In 1928, **Eugene A. Crockett, MD**, administered parathyroid hormone in hopes of relieving deafness due to otosclerosis, bony overgrowth in the inner ear. Though it proved unsuccessful, Means noted, "negative results serve a useful purpose in clarifying a field no less than do positive ones." Surgery later provided answers.

"Negative results serve a useful purpose in clarifying a field no less than do positive ones."

— James Howard Means, MD



FORBES SPENT FOUR DECADES AT MGH.

Center for the History of Medicine, Harvard University

Endocrine disorders

Anne P. Forbes, MD, trained under and collaborated with Fuller Albright, MD (see next section). Most famously, she led the way in identifying Forbes-Albright syndrome: a rare disorder caused by tumors in the pituitary gland.

Bone metabolism and sex hormone disorders

Of all the researchers who passed through Ward 4, the most notable may be **Fuller Albright, MD**, an endocrinologist who significantly advanced the understanding of bone metabolism and sex hormone disorders.

Recruited to Ward 4 as an intern by Joseph Aub, Albright set high standards for thoroughness and precision in patient histories and bedside observation. As a scientist, he quickly embraced emerging technologies, including hormone assays of blood and urine, x-rays and biopsies. Among his achievements:

- **Groundbreaking research** on hyperparathyroidism and its opposite condition, hypoparathyroidism, osteoporosis and Paget's disease.
- **Establishing a kidney stone clinic**, known as "The Quarry," and an Ovarian Dysfunctions Clinic, devoted to research of sex hormone disorders.
- **Co-discovery of diseases** such as McCune-Albright syndrome – a congenital condition that arises in puberty and causes bone dysplasia, hyperpigmentation of the skin and endocrine disorders, and Forbes-Albright syndrome.



MGH PHYSICIAN FRITZ TALBOT PAINTED ALBRIGHT'S PORTRAIT.

➤ The Indispensable Role of Research Nurses

“The year [1925] brought a Research Ward which opened in September. Already 5 student nurses have gone into that ward.”

In this understated fashion, the *Quarterly Record* of the MGH Nurses Alumnae Association marked the onset of an extraordinary era of research nursing on Ward 4.

Unlike the heralded research physicians, Ward 4’s nurses often labored in anonymity. Yet nurses played a unique and indispensable role in advancing research.

In addition to the traditional tasks of overseeing the daily care and wellness of patients, Ward 4 nurses were charged with conforming to strict research protocols.

The early nursing staff consisted of a head nurse supported by four nursing students provided on a rotating basis by the MGH Training School for Nurses. A staff dietitian monitored and recorded patient meals as well as waste with meticulous accuracy.

“A mistake in measurements of any kind or in arithmetic is just as much a sin from the point of view of the success of scientific investigation as is a mistake in the dosage of drugs given to a patient from the point of view of the patient’s welfare.”
— James Howard Means, MD

Marian MacAulay, head nurse

Marian MacAulay defined the role of head nurse on Ward 4 for a full decade, from 1941 to 1951. A scrapbook she created about those years reveals the close bonds that developed on the research ward between clinicians and researchers. In 1948, MacAulay presented a paper before a large nursing audience on “Nursing Management of Patients Receiving Radioactive Medicine.”

A testament to the national reputation of Ward 4 and to her own skills, MacAulay in 1951 was recruited, along with Ward 4 dietitian Shirley Wells, to serve as director of nursing and dietitian, respectively, for the new Oklahoma Research Institute and Hospital in Oklahoma City.

Overdue recognition

In 2016, the American Nurses Association formally recognized clinical research nursing as a specialized practice.

Medical research has changed incalculably

since 1925. But for nurses, the dual mandate of patient care and research precision has not, says Mary E. Larkin, MS, RN, a nurse and historian who has spent much of her 50-year MGH career in research: “The patient is always first. The protocol is a close second. You must follow every detail. It makes a difference in the outcome of the science.”

“Ward 4’s founders had the right idea that without clinical research, science couldn’t advance. And without having a place for people to conduct the research that’s going to be consistent and conducted appropriately, new treatments wouldn’t be possible.”
— Kathryn E. Hall, DNP, MS, ANP-BC, NE-BC, Nurse Director for the Translational and Clinical Research Centers

TOP: DIETITIAN SHIRLEY WELLS, MACAULAY AND FULLER ALBRIGHT; BOTTOM: MACAULAY WITH ALBRIGHT ASSOCIATE FREDERIC BARTTER, MD.



Funded largely by private benefactors, Ward 4 by design lacked a specific goal or disease. Rather, it was built upon faith that brilliant researchers, given space, resources, and support to follow their curiosity, would produce spectacular results.

Patient ID	Visit #	Patient Initials	Visit Start	Visit End	RN	Comments
18A	✓ 1991	WK 1	8:00	11:00	Chen	Lab coverage
18B	✓ 1991	INPATIENT	8:00	11:00	Chen	
20B	✓ 1991	INPATIENT	8:00	11:00	Chen	
22	1991	Int	8:00	11:00	Chen	Discrepancies
24A	1775	MOD/V1	8:00	11:00	Chen	7AM
↓	1758	SCREEN	8:00	11:00	Chen	7AM
24B	✓ 1775	MOD 2	8:00	11:00	Chen	7AM
↓	1775	MOD/V1	8:00	11:00	Chen	7AM
26A	✓ 1752	10	8:00	11:00	Chen	7AM
26B	✓ 1726	1	8:00	11:00	Chen	7AM
↓	1734	3	8:00	11:00	Chen	7AM
28A	1742	6	8:00	11:00	Chen	7AM
28B	✓ 1805	supine	8:00	11:00	Chen	7AM
28A	1805	supine	8:00	11:00	Chen	7AM
28B	1716	Flu	8:00	11:00	Chen	7AM
30A	1670	post-rep	8:00	11:00	Chen	7AM
30B	1670	post-rep	8:00	11:00	Chen	7AM
32A	✓ 1670	OLVH	8:00	11:00	Chen	7AM
32B	✓ 1603	supine	8:00	11:00	Chen	7AM
34A	✓ 1603	supine	8:00	11:00	Chen	7AM
34B	✓ 1603	supine	8:00	11:00	Chen	7AM
40A	1603	supine	8:00	11:00	Chen	7AM
40B	1603	supine	8:00	11:00	Chen	7AM
38A	1580	HF	10:00			

A WHITEBOARD IN THE TCRC INDICATES STUDY VISITS ACROSS A SINGLE DAY.



WARD 4 COMBINED BEDSIDE AND LAB SPACE IN THE BULFINCH BUILDING.



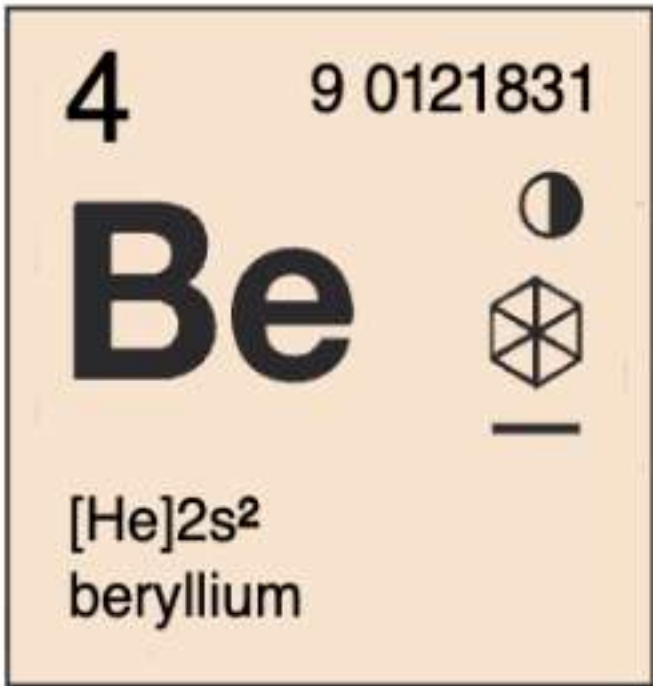
DIET TECHNICIAN ANTOINETTE RILEY-PUREFIED FOLLOWS A PROTOCOL FOR A PATIENT'S DIET.

➤ Extraordinary Patients

As essential components of Ward 4's mission, patients received the highest care and were never charged. For many, contributing to medical progress was a point of pride.

Mrs. A.K. and beryllium

A 24-year-old woman came to Ward 4 in 1950 weak and short of breath. Eight years earlier she had spent just two weeks in a shop using the industrial metal beryllium to manufacture fluorescent lamps. Treatment with adrenocorticotrophic hormone (ACTH) greatly reduced her symptoms and, according to Harriet Hardy, MD, prolonged her life by two years. Mrs. A.K.'s case helped prompt recognition of beryllium as an industrial poison.



The strange case of “Mr. Twaddle”

A man admitted in 1945 with advanced prostate cancer appeared to be near death. After experimental treatment with the synthetic female sex hormone stilbestrol, his condition improved dramatically. He remained in good health for four years until his death in an accident. A postmortem examination showed no trace of cancer. While this treatment did not lead to a cure for prostate cancer, Joseph Aub, MD, noted: “The significance of this case is that a man far along in this disease can turn around and get well.”



ON PLEASANT DAYS, WARD 4 PATIENTS, LIKE THOSE ON OTHER WARDS, WERE TREATED TO REST OUTSIDE.

Life on Ward 4

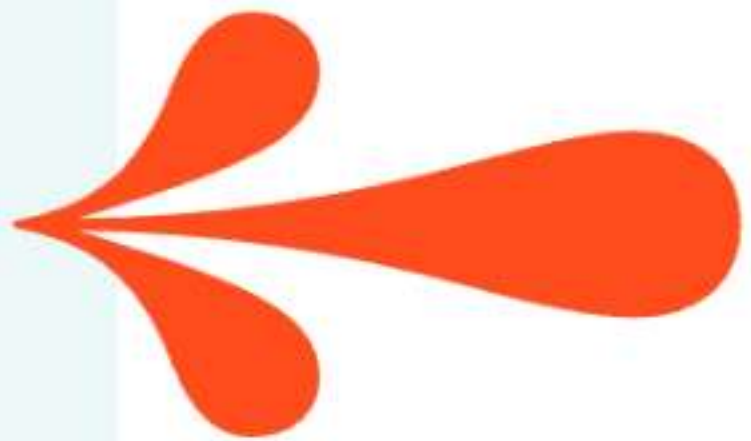
Despite the clinical setting, Ward 4 staff strove to create a “homelike spirit.” Patients wore their own clothes rather than hospital gowns and strolled outside or had their beds taken out to the lawn in nice weather. Though their diets were strictly regulated for health and research purposes, patients socialized over bridge, movie nights, radio and, later, television. A social worker helped them adapt to life on the ward, a librarian kept them supplied with books and a vocational worker taught basket-making, weaving and knitting.

The shrinking sea captain

- Among the earliest and most celebrated cases was that of **Captain Charles Martell**, a strapping, 6'1" World War I mariner who, starting in 1918 at age 22, mysteriously began to lose stature. By the time he arrived on Ward 4 in 1926, Martell stood 5'6", had developed a chest wall deformity and was passing what looked like fine white gravel in his urine.
- **Physicians diagnosed hyperparathyroidism:** overactivity in the parathyroid gland, located in the neck. Based on previous lead poisoning research by Aub, they deduced that excess parathyroid hormone was eroding Martell's bones and that a parathyroid tumor might be to blame. Yet multiple explorations revealed no abnormalities.
- **In 1932, he returned for further exploratory surgery.** Martell, keenly interested in his treatment and eager that his case help others, urged doctors to “keep on operating.” In a seventh procedure, surgeons found and removed a tumor not in his neck but deep in Martell's chest—a possibility that the patient himself had raised.
- **Despite that success, Martell died just weeks later** due to complications from a subsequent kidney stone operation. Yet just as he had hoped, his case helped other patients. Within a year, similar tumors were successfully removed from eight patients at MGH.

The significance of “Mr. Twaddle”'s case, said researcher Aub, was that “a man far along in this disease can turn around and get well.”

IN THIS 1918 PHOTO,
CAPTAIN CHARLES
MARTELL WAS 6'1". BY
HIS ARRIVAL IN WARD
4 HE HAD SHRUNKEN
TO THIS HEIGHT.



➤ The Modern Era

Over the years, Ward 4 would undergo steady changes in its name, location and facilities. Yet the underlying mission of advancing medical research and knowledge has never wavered.



MEI SOUCIE, RN, APPLIES EKG LEADS TO A PATIENT.

The last years as Ward 4

Robert M. Neer, MD, assumed leadership of the ward in 1968 from legendary Harvard Medical School educator and endocrinologist Daniel D. Federman, MD. But it was an earlier Ward 4 luminary—Fuller Albright—who inspired Neer’s own breakthrough research in osteoporosis.

Though high parathyroid hormone levels were known to be associated with bone loss in humans, Albright in 1929 found daily injections of parathyroid hormone increased bone mass in rats. Neer surmised daily injections might have the same effect on humans. “Many people thought that my collaborators and I were crackpots,” Neer recalls. But a multicenter study proved the hypothesis, and such injections are now a standard treatment to reduce fractures in osteoporosis patients.



NEER EXAMINES AN ARM X-RAY OF A HYPER-PARATHYROID PATIENT IN 1983.

The General Clinical Research Center

In 1978 Ward 4 was retitled the General Clinical Research Center, one of many NIH-supported GCRCs. After decades in the Bulfinch Building the center moved in 1985 to a larger space in the White Building.

➤ **Reproductive disorders.** Endocrinologist William F. Crowley, Jr., MD, worked with the Salk Institute team that shared the 1977 Nobel Prize for the discovery of the brain peptide GnRH, which controls sexual maturation, puberty and fertility in mammals. Studying MGH patients with reproductive disorders, he found that these peptides could suppress reproductive hormones in a safe, reversible way. GnRH remains the treatment of choice for precocious puberty 45 years later, and it has proven to play a major therapeutic role in the suppression of testosterone in men with prostate cancer and estrogen in women with breast cancer, and during in vitro fertilization.

➤ **Advances in diabetes.** Today a world-renowned diabetes specialist and founder of the MGH Diabetes Research Center, David M. Nathan, MD, arrived at the GCRC in 1978. Nathan’s early research included establishing a connection between elevated hemoglobin A1c and elevated blood sugar (leading to the first accurate testing of patients with diabetes) and helping pioneer implantable insulin pumps. For a researcher with plenty of curiosity but no funding, the GCRC “defined my career,” Nathan says. “They had a dedicated, incredibly well-trained group of experts, including nurses, dietitians and a medical assistant, who carried out research for you.”



NATHAN (RIGHT) DISCUSSES INSULIN PUMPS WITH COLLEAGUES IN 1983.

Timely research today

The GCRC shortened its name to CRC in 2008 and in 2016 added the new Translational Research Center (directed by Dr. Mason Freeman, with the goal of increased collaboration with industry) to form the Translational and Clinical Research Centers. As Neer’s successor since 1990, Nathan has guided the center into a new era of remarkable discovery.

Research nurses continue to serve as the “eyes and ears” for researchers, overseeing clinical care of patients while adhering to strict protocols for a wide range of studies, says Kathryn E. Hall, DNP, MS, ANP-BC, NE-BC, who since 2008 has served as Nurse Director for what is now the TCRC. “Every day is different on this unit,” Hall says. “We all stay engaged because the work we’re doing is cutting edge. We’ve never turned down a study. If somebody comes with an idea, we figure out how to support it.”

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– Kathryn E. Hall, DNP, MS, ANP-BC, NE-BC, TCRC Nurse Director

> Peanut allergies. The growing prevalence of food allergies is “a feature of modernity and industrialization,” says Wayne Shreffler, MD, PhD, chief of Pediatric Allergy & Immunology and director of the Food Allergy Center at MGH. About 1.5% of U.S. children suffer from potentially life-threatening peanut allergies. The traditional medical approach, advising at-risk patients and families to avoid peanuts altogether, only intensified the risks, Shreffler says. Hence the bins of finely ground peanut powder on hand at the TCRC. Nutritionists use a precision scale to measure doses as small as 300 micrograms (one thousandth the size of a peanut kernel). Administered to children with allergies in a clinical setting, these tiny doses, gradually increased over time, help desensitize the immune system to the allergen.

Conducted in concert with the National Institute of Allergy and Infectious Diseases, this research helped pave the way for new immunotherapy drugs that are bringing relief to children.



“WE OFTEN FOLLOW PATIENTS OVER THE COURSE OF MONTHS OR YEARS. I’VE OVERHEARD PARENTS, WITH TEARS OF JOY, TELLING THE NURSE ‘I NO LONGER HAVE TO WORRY ABOUT MY SON GOING TO A FRIEND’S HOUSE AND HAVING AN ANAPHYLACTIC REACTION,’” SAYS HALL.

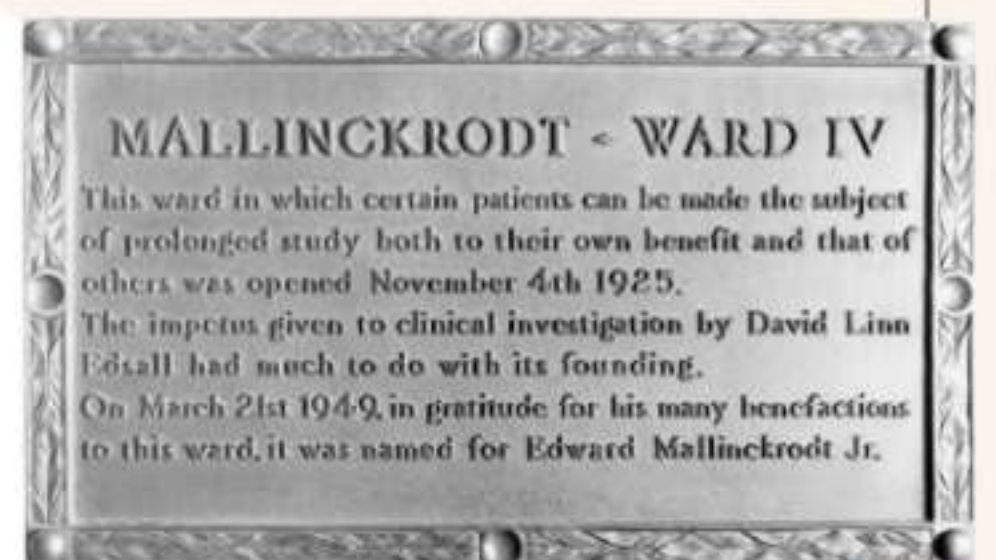
> Attacking ALS. Amyotrophic lateral sclerosis, or ALS, is a neurodegenerative disease affecting some 35,000 Americans. Researchers such as Merit Cudkowicz, MD, MSC, director of the Sean M. Healey and AMG Center for ALS at MGH, have made great strides in developing therapies that slow the disease’s progress, making diagnosis faster and more accurate, and slashing drug development time. Since 1995, Cudkowicz and her team have conducted many of their trials at the GCRC and CRC. Staff have taken the time to learn about ALS at a deep level to support the research, she says. Just as important is the shared commitment to patients’ wellbeing. “Our patients love the nurses there,” says Cudkowicz. “They feel comfortable and cared for.”

Ward 4 and the Tradition of MGH Research

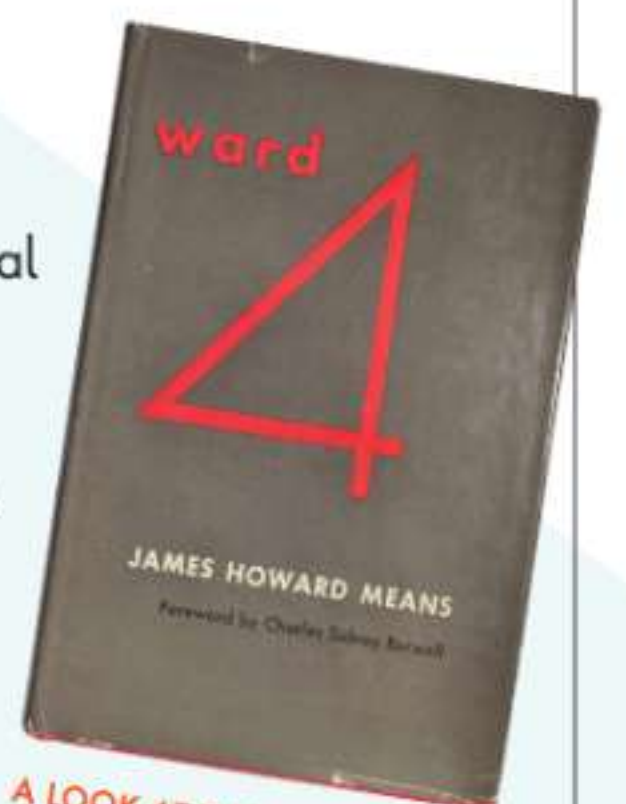
- 1821 — Massachusetts General Hospital opens with the dual purpose of caring for the sick and creating a bedside teaching environment for Harvard Medical School.
- 1891 — Brothers Charles H. and Henry C. Dalton donate \$10,000 for stipends to encourage young researchers. Starting in the 1920s, several "Dalton Scholars" will use Ward 4.
- 1910 -1911 — Charles H. Lawrence, MD, operates a four-bed "study ward" in the MGH Outpatient Building.
- 1923 — James Howard Means, MD, is appointed Jackson Professor of Clinical Medicine and chief of medical services at MGH.
- 1924 — A Rockefeller Foundation grant secured by Means's mentor and predecessor David Linn Edsall, MD, enables Ward 4 construction amid renovations of the historic Bulfinch Building.
- 1925 — Ward 4 opens on November 4. Research begins with studies on lead poisoning, led by Joseph Aub, MD.
- 1932 — Ward 4 closes in July due to a lack of funding amid the Great Depression and reopens in December 1933, thanks to an \$8,000 grant from the Hyams Foundation.
- 1940-1945 — Ward 4 conducts war-related research on malaria drugs and other projects for the U.S. Office of Scientific Research and Development (OSRD).
- 1949 — Ward 4 is renamed Mallinckrodt Ward 4 for Harvard alum, industrialist and donor Edward Mallinckrodt, Jr.
- 1951 — Means retires from active work as chief of medical services at MGH.
- 1953 — Mallinckrodt creates an endowment to ensure continuous operations of the ward.
- 1958 — Means publishes his definitive history of the ward.
- 1958 — In a twist, Mallinckrodt Ward 4 becomes a General Clinical Research Center (GCRC) supported by the NIH, whose early national clinics were inspired by Ward 4.
- 1985 — After more than 50 years in the Bulfinch Building, the clinic moves to a larger, more modern space in the White Building.
- 2000 — The GCRC is expanded and MGH becomes one of the nation's first GCRCs with an imaging facility.
- 2008 — The unit's name changes to the CRC because of NIH funding changes.
- 2016 — The facility is renamed the Translational and Clinical Research Centers (TCRC), reflecting clinical research and the growing collaboration with industry.



THE LAB CIRCA 1940S



WARD 4'S FIRST NAME CHANGE, 1949



A LOOK AT THE WARD'S FIRST 30 YEARS

"The patient is always first.
The protocol is a close second.
You must follow every detail.
It makes a difference
in the outcome of the science."

— Mary E. Larkin, MS, RN



SAMPLES AWAIT USE IN SKIN PRICK TESTING FOR ALLERGIC REACTIONS.



MARIAN ROPES, MD, SECOND FROM RIGHT, HAD BEEN MGH'S FIRST FEMALE MEDICAL RESIDENT.



AMY MACLEOD, RN, CONFERS WITH A COLLEAGUE ABOUT TIMED SAMPLE COLLECTION.