

The Pharmacologist

Vol. 66 • Number 1 • January 2024

Goodman and Gilman:

Pioneers of Cancer Pharmacology



A Publication by The American Society for
Pharmacology and Experimental Therapeutics

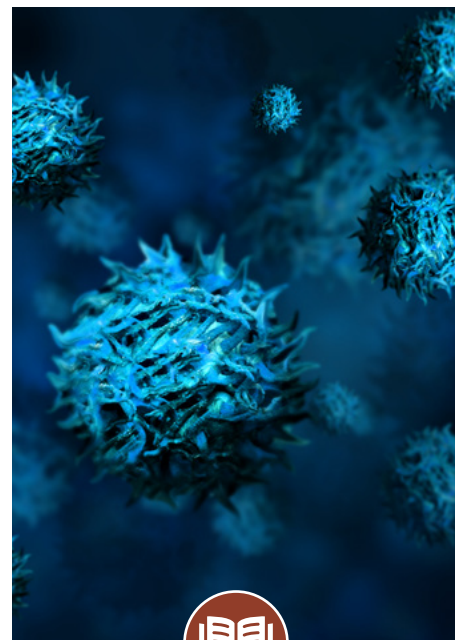
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Message from the President



Listen to [ASPET](#) President Namandjé N. Bumpus, PhD as she discusses the new look of *The Pharmacologist*, important happenings within ASPET and some upcoming highlights on the ASPET 2024 Annual Meeting.

Watch the video online

Visit *The Pharmacologist* companion website for digital-only features and extras. thepharmacologist.org



A Note from Dave's Desk



TPharm's Evolution

As your Executive Officer, it is my privilege to “be handed the torch” from ASPET’s storied and accomplished past and carry it into the next phase for our Society. It is truly inspiring to think about the many revered programs, products and services that ASPET has been carrying on for decades to benefit the pharmacology community. Among them, we’re excited for this January 2024 issue to serve as the latest evolution of *The Pharmacologist*.

Also known as “TPharm,” *The Pharmacologist* has served as one of ASPET’s primary methods of communicating with our members since its launch in 1959. In the first issue in spring of 1959, the authors admitted that “it has not been easy to get this venture off the ground,” noting the response to its proposal was “less than enthusiastic.” Nonetheless, *The Pharmacologist* was launched “to give helpful non-technical information to people who are interested in pharmacology and toxicology” and address the “growing needs for better communication between scientists as their numbers increase.” For context, ASPET had about 800 members in 1959 compared to more than 4,000 today. Originally, TPharm was printed and sent to all members twice a year in the spring and fall. The fall issue’s focus was “chiefly the abstracts for the fall scientific sessions of the Society.”

After proving its usefulness to the ASPET membership, *The Pharmacologist* moved to a printed, quarterly magazine to provide more timely information about ASPET and its members. In 2003, ASPET started a PDF version of the magazine versus a print version, while maintaining a print option for those willing to pay an extra fee. Since then, as you might expect, the number of members who opted for the print version has declined from thousands to approximately 100 print subscribers in 2023. As a result, the [ASPET Council](#) voted in May 2023 to make the full transition of *The Pharmacologist* to a digital-only magazine starting in 2024, which brings us to this issue.

This monthly, digital-only version of TPharm, designed for our members and the broader pharmacology community, will provide timelier, human-interest stories about pharmacology. Based on readership feedback, we’re planning new features but we’ll also continue some of the traditional features of *The Pharmacologist* that our members value. For example, we’re elated that Dr. Rebecca Anderson, who has been writing in-depth featured articles that tell the fascinating stories behind pharmacology discoveries and the people who make them happen since 2013, will continue to provide science stories that take us on an adventure in pharmacology.

As *The Pharmacologist* begins its latest iteration in 2024, we hope you’ll find TPharm both meets ever-changing communication preferences in this digital age, while also continuing to meet the original goal *The Pharmacologist* established more than 60 years ago to benefit the pharmacology community.



Dave Jackson, MBA, CAE
Executive Officer, ASPET



Cover Story

Goodman and Gilman:
Pioneers
of Cancer
Pharmacology

Read and share this story online
thepharmacologist.org



By Rebecca J. Anderson, PhD

Mention Goodman and Gilman to any pharmacologist, and they will automatically think of their graduate school textbook. Generations of pharmacologists have indelibly linked the duo as naturally as Mercedes-Benz and Baskin-Robbins. Actually, Louis Goodman and Alfred Gilman carved distinctly separate career paths, except for two key activities. We can be grateful that their two joint ventures were major contributions to pharmacology and experimental therapeutics.

The Textbook

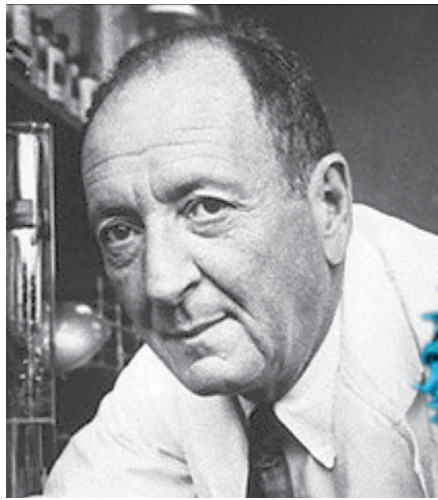
Alfred Gilman was born in 1908 in Bridgeport, Conn., the son of a music store owner.^{1,2} He received his undergraduate and graduate education at Yale University, earning a PhD in physiological chemistry in 1931.^{1,3,4} Gilman stayed at Yale as a postdoctoral fellow in pharmacology and then joined the faculty in 1932, with eight published papers already to his credit. He was slender, and in those days, played tennis and squash. He also enjoyed sailing and fishing.²

Gilman was generous and quick to praise his colleagues. Years later, as a senior researcher, he would cut his modest office in half to make room for a junior faculty member. He eventually closed his lab when he decided another member of the department could make better use of the space.¹

Louis S. Goodman (the one with the mustache) was born in 1906 in Portland, Ore., the son of an optometrist. He graduated from Reed College, earned his MD from the University of Oregon in 1932, and then served his internship at Johns Hopkins Hospital.^{2,5,6} Goodman's first publications were chapters that he was invited to write for medical textbooks. He was



Louis S. Goodman



Alfred Z. Gilman



somewhat taller and heavier than Gilman, and his idea of exercise was picking up and reading a book or journal.²

Goodman had a keen wit, was sometimes gruff and held strong opinions. His often-colorful quips earned him the nickname, Louie the Lewd.^{1,6} He constantly coaxed and cajoled everyone to work harder. One colleague said, “If you didn’t do well, you heard about it.”⁵

The pair met in 1934, when Goodman was awarded a fellowship by the National Research Council to conduct research in the pharmacology department at Yale. Lackluster medical student attendance in the pharmacology course (due to poor quality lectures) prompted Milton Winternitz, Dean of the Medical School, to ask Goodman and Gilman to run the course.² Even as assistant professors, they were recognized as excellent lecturers.

They found both of the available pharmacology textbooks unsatisfactory. One was unreadable, and the other was out of date.^{2,4} Instead, they compiled their lecture notes largely from contemporary journal articles and combined basic pharmacology, physiology and biochemistry with clinical medicine.⁵

Goodman had always been interested in pharmacology, read widely and remembered everything he read.² By all accounts, he was also an excellent writer. Having written book chapters and monographs, he thought he could write a much better pharmacology textbook, especially if he had help from Gilman. Gilman was less eager and probably would not have considered writing a textbook on his own.^{2,5}

Goodman drafted the first few chapters and sent them to colleagues for feedback. They not only encouraged him but also alerted a publisher, Macmillan Company.^{4,5} When Macmillan presented the two lecturers with a publishing contract in 1938, Gilman enthusiastically joined Goodman as a full partner in the work.^{2,5}

They wrote every chapter themselves. Mirroring their lectures, the book described pharmacology in the context of clinical therapeutics, a novel approach at the time.^{6,7}

Macmillan wanted a 450,000-word textbook, but Goodman and Gilman submitted a manuscript of nearly 1,000,000 words.^{2,4,6} The publisher balked because comparable textbooks were never that lengthy or expensive. The authors held firm, saying “take it or leave it.”⁴

Macmillan printed 3,000 copies and agreed to publish a second edition, if the book sold out within four years. Gilman confidently bet a case of Teacher's Highland Cream whisky that the high-priced, four-pound textbook would reach that goal.^{2,5,6}

The first edition of *The Pharmacological Basis of Therapeutics* was published on January 7, 1941. Just six weeks later, Goodman and Gilman received their case of scotch.^{2,5} In total, about 115,000 copies were sold.²

As a footnote to this achievement, Gilman's son was born six months later, on July 1, 1941, and was named Alfred Goodman Gilman, in honor of Gilman's good friend. Years later, the younger Gilman was chided by classmates, who proclaimed that he was the only person ever named for a textbook.¹

World War I Gases

Although Milton Winternitz retired as dean in 1935, he remained at Yale. World War II was raging in Europe and would soon involve the United States. Of great concern was the potential use of chemical weapons, and Winternitz was chairman of the Committee on the Treatment of War Gas Casualties, a group of respected academic scientists who were advising the government. Winternitz had written and edited sections of the definitive monograph on pathology of war gases and was generally regarded as the most prominent expert in the field.⁸

Modern chemical warfare began on April 22, 1915, when the German army used chlorine gas for the first time in large-scale offensive action.⁸⁻¹¹ Subsequently, both sides in World War I developed chemical weapons, including phosgene and Lewisite.⁹

On July 12, 1917, German forces first used mustard gas against the British at Ypres, Belgium.⁹⁻¹⁴ Within a year, the Allies were also

deploying mustard gas, and both sides soon realized that the best way to deliver the gas was in artillery shells.¹⁰

Victor Meyer first prepared dichloroethyl sulfide in 1886.^{12,13,15} The yellow-brown chemical had a very characteristic odor suggestive of garlic or mustard, hence its common name.^{10,13,15}

Mustard gas is actually an oily liquid at room temperature. When exploded via bombs over enemy troops and trenches, it dispersed as an aerosol. The aerosol stuck to skin, clothing and surfaces, and could pass through leather, rubber and most textiles. It could also persist on the contaminated ground for weeks.^{9,10}

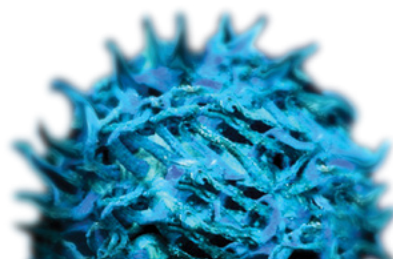
Mustard gas caused no immediate effects. Consequently, troops marched through contaminated areas unaware that they were being exposed. About 12 hours later, their skin, eyes and mucous membranes became irritated.^{9-11,13}

The extreme eye irritation felt like gritty sand, and some troops were temporarily blinded. Exposed skin developed large, painful blisters and ulcers. Without quick washing, the ulcers festered. The inhaled aerosol caused respiratory distress, pulmonary edema and damage to the bronchial tubes.^{9,10}

There was no antidote, and victims were incapacitated for weeks, sometimes months. Those who received prompt and diligent nursing care generally recovered. The fatality rate was just 2–3%. But because of the slow recovery, mustard gas severely diminished the army's ability to fight.^{10,13}

The effectiveness of mustard gas made it the chemical weapon of choice from 1917 onward.^{8,13} It accounted for nearly 400,000 casualties, more than any other chemical weapon.^{10,13}

Continued on page 18



ASPET Celebrates Mentoring Month

By Lynne Harris, MA, APR

January is [National Mentoring Month](#). This annual observance focuses on increasing the number of mentors, recognizing mentoring importance and impacting lives to help them reach their full potential. Established in 2002, National Mentoring Month is recognized every year and provides an opportunity for individuals and organizations to engage in various ways such as sharing personal experiences, connecting with mentoring partners or promoting mentoring programs.

The ASPET Mentoring Network: Coaching for Career Development is a program designed to supplement the training that graduate students and postdoctoral trainees receive through their university programs. The ASPET Mentoring Network focuses on developing skills

needed to succeed scientifically, professionally and psychologically. In a [mentoring network](#) format, participants share experiences and discuss the pressures faced by groups that are underrepresented in the sciences. As a professional development experience, the program uses a coaching model to help participants develop success skills for a variety of careers, including academia, industry, government and policy.

Graduate students and postdoctoral scientists accepted into the program each year attend several events in association with the ASPET annual meeting. These include training, guided discussions, an informal reception and an interactive program. During this time, trainees also meet coaches and other trainees and become part of a six-person coaching group. Monthly conference calls or webinars are also scheduled. Group events are tailored to the specific needs of each coaching group but may focus on work/life balance, interview skills, job searches, networking, grant writing and other topics frequently identified as important to professional growth. [Learn more at \[aspet.org\]\(http://aspet.org\).](#)

Upcoming Days to Remember

January 17 – International Mentoring Day

January 21 – Thank Your Mentor Day



Graduate Students & Postdoctoral Scientists:

Do you need some help planning your future? Do you have all the skills you need to succeed? Are you trying to decide among careers in academia, government, or industry?

[Learn more](#)



Leadership Profile

A Conversation with ASPET's President-Elect Carol Beck, PharmD, PhD



[Carol Beck](#), PharmD, PhD, is an Associate Professor in the Department of Pharmacology, Physiology and Cancer Biology at Sidney Kimmel Medical College at Thomas Jefferson University. Dr. Beck is also the Associate Dean of Curriculum and

Master of Science Programs, Program Director, Master of Science-Pharmacology at Jefferson College of Life Sciences. Dr. Beck shares her background and advice for young scientists with *The Pharmacologist*.

How did you get started in pharmacology?

I started my sophomore year of college as a pre-pharmacy major, having decided that pharmacy would be an interesting application of all of the science courses I was taking. (I knew that I did not want to go to medical school.) I went to pharmacy school at the University of Kentucky and completed the Bachelor of Science and PharmD degrees, and then did a residency. After residency, I was a clinical faculty member at North Dakota State University College of Pharmacy. I took many pharmacology courses as a pharmacy student but became serious about pharmacology as a discipline when I went back to graduate school at Vanderbilt for a PhD in Pharmacology.

How did you first get involved with ASPET?

Some people are serial entrepreneurs. I am a serial volunteer. I have always been involved in volunteer groups since high school.

Professionally, I have been involved with the pharmacy fraternity Lambda Kappa Sigma, the Biophysical Society, and Sigma Xi. I moved to Philadelphia to have a research lab and teach pharmacology to medical students at Thomas Jefferson University. When my career focus shifted from research activities to education activities, I wanted to become involved with the regional pharmacology society, Mid-Atlantic Pharmacology Society (MAPS), to connect with local pharmacologists. After one year on their board as a Councilor, I volunteered to serve as president. The MAPS by-laws required that the president of MAPS had to be a member of ASPET. So, I became a member. What kept me as an ASPET member was getting involved in one of the divisions, Division for Pharmacology Education, and also needing some professional involvement outside of my university for my promotion packet.

What do you want the ASPET membership to know about you and your ideas on how to move the organization forward during your term?

I really like the goals in our current strategic plan, and I am excited about ASPET being the Home for Pharmacology. I would like us to be seen as a welcoming group that provides opportunities for professional networking and friendships. ASPET should also continue to involve volunteers across all sections of pharmacology. To do all of these things will require us to increase our transparency about how to become involved and the pathways to leadership roles; ASPET can do this and I will push for us to do this!

What has been your proudest accomplishment in your career so far?

My first project as a postdoc was to study the genetic basis of myotonia congenita in an animal model known as “fainting goats.” Using cDNA libraries and sequencing techniques, we identified a mutation in the skeletal muscle chloride channel, the same channel involved in the human disease myotonia congenita. The mutations result in decreased and delayed chloride conductance in skeletal muscle, resulting in temporary immobility. The goats and their story have been very good to me and my career.

What advice would you give young scientists who are just starting out in their careers?

Build your own network and community. If these are available to you (like ASPET), then definitely be a part of them. If they are not available to you, create your own (and know that it is ok to need more than one).

When job-hunting, be yourself. Don't try to guess what the market wants in terms of background or personality or skillsets. Somewhere out there is a position that specifically wants and values your unique mix of interests and training.



From left, ASPET President-Elect Dr. Carol Beck and ASPET Secretary Treasurer-Elect Dr. Pamela Hornby, visiting Capitol Hill.



ASPET 2024

Advocacy. Diversity. Discovery.

May 16-19 • Arlington, VA

ASPET 2024 Annual Meeting

Save the Date!

Advocate for science funding and policy issues important to you and the pharmacology community.

Join ASPET for its
inaugural Capitol Hill Day!
Wednesday, May 15, 2024

Abstract submissions:

January 22–February 22, 2024

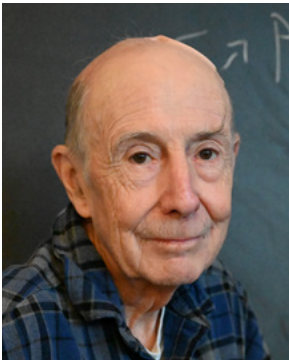
NEW THIS YEAR The Policy and **ADVOCACY** abstract category explores science policy issues that pertain to pharmacology and the broader scientific community. Topics include social, economic and/or regulatory policy issues on drug policy, animal research, artificial intelligence and workforce policy.

ASPET values pharmacology research from all disciplines regardless of social identities or career levels. The Society is committed to creating a **DIVERSITY**-centered environment that includes all age groups, ethnicities, races, cultures and genders.

ASPET 2024 is an opportunity for scientific **DISCOVERY**. Showcase your latest, cutting-edge science at the home for pharmacology.



Member Highlights



The California Academy of Sciences Inducts ASPET Member Bruce Hammock

Bruce Hammock, PhD, has been inducted as a Fellow of the California Academy of Sciences. Dr. Hammock, an ASPET member since 2003, is a Distinguished Professor at the University of California (UC), Davis. An expert in chemistry, toxicology, biochemistry and entomology, he holds a joint appointment with the Department of Entomology and Nematology and the UC Davis Comprehensive Cancer Center.

Dr. Hammock has been internationally recognized for discovering a new group of human chemical mediators that have contributed to treating arthritis, cancer and Alzheimer's Disease. He also co-discovered the human enzyme, Soluble Epoxide Hydrolase, a key regulatory enzyme involved in the metabolism of fatty acids.

Hammock is a member of the ASPET Division for Toxicology, and in 2014, he received ASPET's Bernard B. Brodie Award in Drug Metabolism and Disposition.

MSU Recognizes ASPET Member Carolina Restini for Excellence in Teaching

Michigan State University (MSU) recently awarded Carolina Restini, PharmD, PhD, the Department of Pharmacology and Toxicology's Award for Excellence in Teaching. Dr. Restini is recognized for exemplifying a commitment to excellence in teaching and implementing creative and effective ways to foster student learning. She received this honor as a faculty member who has earned the respect of medical students, peers and staff for her devotion to and skill in teaching.



Restini is an Assistant Professor at MSU, College of Osteopathic Medicine, where she teaches basic and clinical pharmacology. Dr. Restini develops research projects and investigations considering the humanistic aspects of therapeutics. She joined ASPET in 2019 and is a member of the ASPET Divisions for Pharmacology Education, Cardiovascular Pharmacology, and Translational and Clinical Pharmacology.



ASPET Fellow Dr. V. Craig Jordan Receives the Sir Henry Wellcome Gold Medal

ASPET Fellow [Dr. V. Craig Jordan](#) has been awarded the Sir Henry Wellcome Gold Medal from the British Pharmacological Society, for his outstanding lifetime research commitment to pharmacology. He has focused his 50-year career on the mechanisms of estrogen-regulated breast cancer growth and resistance to anti-estrogen therapies.

Jordan helped to revolutionize women's health with an in-depth translational research program that initially took a failed contraceptive ICI46,474, and developed the successful research strategy for the medicine that became tamoxifen. This would later be used for the treatment and prevention of breast cancer.

Jordan went on to discover a new group of medicines referred to as Selective Estrogen Receptor Modulators (SERMs). Five SERMs that switch on or switch off sites around a woman's body are FDA-approved with discovery origins in Jordan's laboratory.

Dr. Jordan was selected as an ASPET Fellow (FASPET) in 2022 and has been a member since 1981. He has received numerous awards from the Society, including the ASPET Award for Experimental Therapeutics (1993), the Goodman and Gilman Award (2012), and the Reynold Spector Award (2019). He joined the British Pharmacological Society in 1976 and was selected as an inaugural Fellow in 2004.

Interested in Being a Contributing Writer?

ASPET's *Pharmaco Corner* blog and flagship magazine *The Pharmacologist* seek contributing writers on a rolling basis.



Discussing Science. Discovering Cures.

The
Pharmacologist

[Pharmaco Corner](#) is a dedicated space where pharmacology experts can discuss issues that affect them professionally and personally. The blog connects science and society through various pharmacology disciplines. Send your pitches to pharmacocorner@aspet.org.

[The Pharmacologist](#) wants writers interested in contributing human interest and science stories focused on pharmacology. Contact us at thepharmacologist@aspet.org. Please include links to writing samples.



Advocacy Impact



Become an Advocate and Get Involved

By Catherine Davis-Takacs, PhD

Some public policy decisions can make us feel out of control. Events happening outside of our classrooms, laboratories and offices have a profound impact on our ability to conduct rigorous cutting-edge research, deliver high-quality learning experiences to our students, bring more effective treatments to patients, and continue to move scientific ideas forward. We can watch lawmakers decide on policies that will affect biomedical research for years to come or we can become involved. As scientists, and importantly citizens, we have the opportunity to shape policy in an evidenced-based way to help solve critical problems. But how? Engaging our political leaders seems to be a rather daunting task when added to our lengthy lists of laboratory and administrative duties, but it becomes our responsibility.

As distrust in science grows, we must develop skills to translate our research into easily accessible information for a lay audience. This task can be difficult and time consuming, as learning any new skill often is; but becoming an active member of a professional society like [ASPET](#) is an excellent way to engage political leaders and contribute to science policy decisions that affect how pharmacologists do their work. For example, [ASPET Council](#) members recently visited congressional offices to advocate for biomedical research funding, and registrants for ASPET's inaugural Hill Day can participate the day before the [2024 Annual Meeting](#).

[ASPET's Science Policy Committee](#) engages in many issues, including regulations for research animals, data management and open science



Dr. Dianicha Santana speaks with Rep. Jesus Garcia's legislative staffer on advocating NIH funding and animal research



ASPET Past President, Dr. Michael Jarvis (left) and Dr. Dianicha Santana, Chair of ASPET's Young Scientist Committee speak with Legislative staffer Kody Keckler of Rep. Mike Quigley (IL)

initiatives, and drug scheduling. Further, our committee has responded to requests for information from federal agencies, working with our members to explain how changes to policies, procedures and other regulations impact the important work of pharmacologists. ASPET's decade-old [Washington Fellows program](#) has trained young scientists to be advocates for pharmacology. Many of these alumni, including me, have continued to engage in public policy through our careers or with ASPET.

Policy issues are ever-changing, and we must empower one another to be advocates for pharmacology and overall biomedical research. Getting involved is as simple as finding an issue you are passionate about and sharing your expertise with lawmakers. This can be done through ASPET's activities, but you don't need to wait for ASPET to lead the way. You can use your expertise by responding to requests for information from federal agencies, contacting your lawmakers and engaging your community members in constructive dialogue through science cafes or other outreach events.

Now and in the near future, pharmacologists will be needed to explore changes in the medical use and decriminalization of psychedelic drugs and collaborate with federal

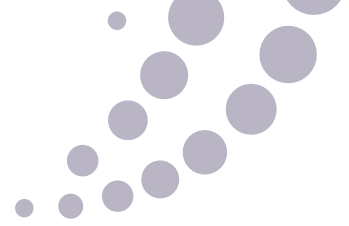
agencies to understand the possible medical uses and potential harm of novel compounds. Pharmacologists must continue to articulate the important role animals have in the development of pharmacological therapies and help to determine guidelines and best practices for the use of novel alternative technologies in pharmacological research. We will be needed to find ways to realize a more equitable research enterprise that cultivates scientific inquiry in our youngest minds, while providing a path for a diverse and skilled workforce to engage in pharmacology research. We will be needed to understand how our current methods might amplify inequality, and we will be expected to devise novel and innovative strategies to create an inclusive environment that values each individual for their unique contributions. Now is an exciting time to [get involved!](#)



Catherine Davis-Takacs, PhD

[Catherine Davis-Takacs](#), PhD, currently serves as ASPET's Science Policy Committee Chair. She is a Lead Lab Investigator at Uniformed Services University of the Health Sciences in Bethesda, MD. She holds a PhD in Behavior, Cognition and Neuroscience and a MA in Experimental Psychology, both from American University in Washington, D.C. She completed her postdoctoral training at Johns Hopkins University School of Medicine.

On Their Way...



Each month, the editors of three of the American Society for Pharmacology and Experimental Therapeutics (ASPET) journals choose who they call their Highlighted Trainee Authors. These early-career scientists are recognized for their innovative research published in [*The Journal of Pharmacology and Experimental Therapeutics*](#), [*Drug Metabolism and Disposition*](#), and [*Molecular Pharmacology*](#). This feature showcases these young scientists, demonstrates what drives them and reveals why pharmacology is important to them.



Rahil Eftekhari

Rahil Eftekhari is Postdoctoral Research Associate at Memorial Sloan Kettering Cancer Center in New York City. Eftekhari is passionate about developing a treatment for patients

through regulating the immune system. Her voluntary work with the Multiple Sclerosis (MS) Society of Canada has influenced her commitment to develop treatments that enhance the quality of life for patients.

Eftekhari hopes that her research will inspire further investigation and the development of PAR2 antagonists, paving the way for innovative pharmacological approaches to treat MS and other neuroinflammatory diseases.

“My goal is to bridge the gap between cutting-edge research and practical, patient-centered applications. I plan to engage in clinical trials, contributing to the development and evaluation of efficient immunotherapies that can be transformed into impactful and innovative clinical interventions,” said Eftekhari.

Eftekhari believes that publication in an ASPET journal signifies an active contribution to its extensive reservoir of knowledge, sharing insights

with peers and, ultimately, participating in shaping the future of pharmacological research.

“ASPET stands as a distinguished and esteemed institution in the field of pharmacology. [Having my work featured](#) in one of their journals would not only represent acknowledgment within the scientific community but also validate the rigor and quality of my research,” Eftekhari added.



Jan Jakub Lica

Jan Jakub Lica is a postdoctoral student at Medical University of Warsaw in Poland. Lica plans to engage in research within the realm of onco-hematological molecular and cellular

pharmacology, focusing on technology, oncology and cellular biology. He has met and learned from great experts throughout all stages of his education, progressing successively through medical, scientific and technical aspects.

“My mentor in the realm of molecular and cellular pharmacology, especially in studying the drug mechanism of action, has been supervisor of my PhD thesis, Professor Andrzej Składnowski from Department of Pharmaceutical Technology and Biochemistry, Gdańsk University of Technology. He passed

away last March, but his generous investment of time, knowledge, skills and patience has been invaluable for my development,” said Lica.

Lica aims to enhance the effectiveness of anti-leukemic agents and develop improved methods for *in vitro* cultivation, detection and collection of leukemia cells displaying primitive cell stage phenotype.

“[Having my work published](#) in the ASPET journal is a significant recognition and an opportunity to attract broader attention to the scientific problems I have authored,” Lica stated.



Agustos Ozbey

Agustos Ozbey, PharmD is a PhD Student, F. Hoffmann-La Roche Ltd., affiliated with the Katholieke Universiteit Leuven in Belgium. Ozbey is planning to pursue a postdoctoral

position after completing his PhD to further hone his skills. He wants to make substantial

contributions to drug development and pharmaceutical industries by enhancing the utilization of modeling tools. He hopes this research illuminates the current gaps in non-CYP enzyme PBPK modeling, prompting fellow scientists in the field to reevaluate their approaches and innovate better modeling strategies.

Ozbey has always wanted to work in a medical setting, driven by the desire to comprehend diverse diseases and offer enhanced treatments to patients every day. He has a strong conviction that lies in the power of modeling and simulation to advance drug development. Ozbey firmly believes that a predictive approach is key to providing patients with more effective and safer treatments.

“[Having our work published](#) in an ASPET journal like *Drug Metabolism and Disposition* is an incredible honor. All my collaborators and I are avid readers of this journal, and this achievement means our work will gain significant visibility, which is truly gratifying,” Ozbey pointed out.

CALL FOR PAPERS

New Therapeutic Targets for Post Traumatic Stress Disorder and Related Sequelae for *JPET*



A special section for the December 2024 issue of *The Journal for Pharmacology and Experimental Therapeutics* is seeking original research on potential new therapies for PTSD and/or any associated comorbid conditions, such as:

- Depression
- Substance-use disorder
- Pain
- Anxiety
- Cardiovascular disease
- Sleep disorder
- Traumatic brain injury
- A limited number of commentaries and/or minireview articles addressing the new approach or lack of therapies for comorbid conditions with PTSD

Submission deadline: February 16, 2024

Authors are encouraged to submit a [presubmission inquiry](#) to [Dr. Kelly Standifer](#) and [Dr. Susan Wood](#). All submissions must refer to *JPET*'s [Instructions for Authors](#).



Cover Story

Continued from page 7



But by the end of World War I, researchers had devised clothing and masks that offered adequate protection.⁹

Between the Wars

Funding for chemical weapon research, understandably, was greatly reduced following the war.^{16,17} The work and researchers were consolidated at Edgewood Arsenal in Maryland under the U.S. Army’s Chemical Warfare Service.^{8,10,13}

Edward Krumbhaar, a captain in the U.S. Army Medical Corps, studied victims who survived mustard gas intoxication and saw that they suffered a profound loss of white blood cells.^{11,12} His findings, which were published in 1919, were the first clinical report of this effect. In the 1920s, a few other researchers reported sulfur mustard’s effect on blood-forming tissues.¹⁶

During this time, chemists developed nitrogen-substituted analogs of sulfur mustard. In 1931, clinicians at New York’s Memorial Hospital successfully treated 13 patients by applying nitrogen mustard directly to superficial skin cancer.¹⁷

No investigator delivered the mustard agents systemically for any type of cancer, and these few isolated reports went largely unnoticed.^{16,18}

Reviving Research

At the dawn of World War II, the Chemical Warfare Service was revitalized to investigate, develop, manufacture, and supply both chemical weapons and protective anti-gas equipment. The U.S. and its Allies did not intend to use chemical weapons, but they maintained stockpiles as a precaution and to retaliate in case they were attacked with chemical agents.^{8,11,13}

Early in 1942, Winternitz, chairman of the Committee on the Treatment of War Gas Casualties, brokered a military contract for Yale. He assigned Goodman and Gilman to study sulfur and nitrogen mustards.

A young military physician, Stewart Alexander, took over as director of the Medical Division at the Chemical Warfare Service. His large laboratory group conducted secret research on the chemical agents’ toxicity and ointments that might protect against skin blistering.^{8,11,13}

In April 1942, Alexander began a two-month series of experiments to study nitrogen mustard. The effects on the skin, eyes and lungs of rabbits were similar to the well-known effects of sulfur mustard used in World War I.⁸

Alexander also coordinated the military’s research contracts on behalf of the National Defense Research Committee. About two dozen contracts were awarded to academic researchers around the country. Those researchers conducted a wide range of secret experiments on chemical weapons and possible antidotes. The Committee on the Treatment of War Gas Casualties assisted with administering and supervising the contracts.^{8,13}

The Yale Contract

Early in 1942, Winternitz, chairman of the Committee on the Treatment of War Gas Casualties, brokered a military contract for Yale.^{11,13,18,19} He assigned Goodman and Gilman to study sulfur and nitrogen mustards.¹⁹

The Yale researchers maintained close communications with the other groups holding classified military contracts. They shared their results and met frequently. This permitted the researchers to rapidly elucidate the mustard agents’ “unique and fascinating properties.”¹⁹

← *U.S. soldiers in trench putting on gas masks, World War I*

Goodman and Gilman focused their studies on the pharmacological actions and toxicity of mustard agents, primarily in rabbits. They showed that toxicity was due to the mustards' extreme chemical reactivity.

When given systemically, the sulfur and nitrogen mustards produced a wide range of pharmacological effects on cells, tissues, and enzymes.¹⁶ At “threshold doses” (that is, the lowest dose that produced an effect), the compounds damaged only cells and tissues with high rates of growth and proliferation: blood cells, blood-forming organs (bone marrow and lymphatic tissue), and the mucosa of the gastrointestinal tract. The damage to circulating white blood cells (lymphocytes and granulocytes) was rapid and dose-dependent.^{16,19}

They could not elucidate the molecular mechanism of action, but they did make one insightful observation. The mustards produced “profound disturbances” on the structure and function of fruit fly chromosomes.¹⁶

Goodman and Gilman focused their studies on the pharmacological actions and toxicity of mustard agents, primarily in rabbits.^{13,19} They showed that toxicity was due to the mustards' extreme chemical reactivity. Sulfur mustard forms a highly reactive sulfonium ion, and the nitrogen mustards form a reactive imonium ion.^{9,16,20}

We now know that these reactive ions alkylate DNA, forming covalent bonds that prevent cell proliferation. The reactive ions can also alkylate any other tissues, proteins and biochemicals that they contact.¹²

The mustards' actions were unlike any other chemical compound, but the effects resembled X-ray exposure.^{16,17,21}

Goodman and Gilman also conducted experiments aimed at finding an effective antidote. To evaluate the efficacy of each potential antidote, they measured its ability to protect against the decrease in white blood cell counts, which was the most sensitive measure of mustard toxicity.¹⁶

They found that thiosulfate pretreatment seemed to protect rabbits the best. This suggested that thiosulfate could be an effective antidote, at least under ideal laboratory conditions.¹⁹

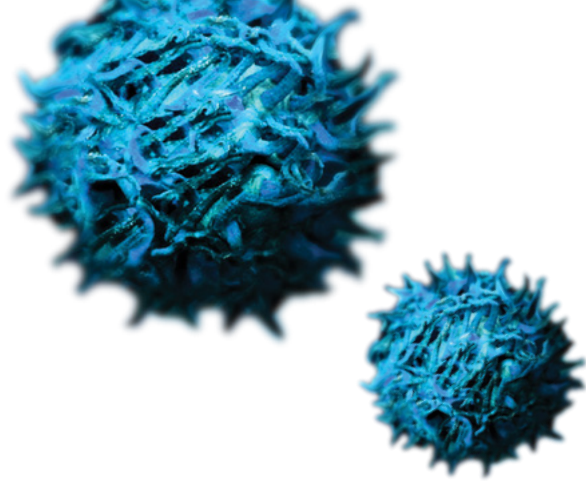
In parallel, Stewart Alexander's group at Edgewood Arsenal also observed that systemically administered nitrogen mustard caused deterioration of lymph nodes and bone marrow in rabbits, as well as a severe decrease in white blood cell counts. They saw the same effects in various animals. On June 30, 1942, Alexander described his results in a classified memorandum, which was shared with Yale and the other research groups.⁸

Mouse Lymphoma

The remarkable sensitivity and vulnerability of rapidly proliferating cells and lymphoid tissues suggested that the mustards might effectively treat lymphoid tumors. Goodman and Gilman showed their rabbit data to Thomas Dougherty, a Yale anatomy professor, and he agreed to assist with the first efficacy studies.^{16,19}

Sulfur mustard had undesirable physical properties for these studies.¹⁶ It was volatile, quite insoluble, unstable in water, dangerous to handle and difficult to administer.¹⁷

The nitrogen mustard analogs were slightly less reactive than sulfur mustard.^{16,21} They formed non-volatile, water-soluble hydrochloride salts, could be handled safely, and could be administered intravenously.^{16,17}



In the first series of experiments, they injected mice to determine the acute lethal dose and the dose that could be given daily without drastically affecting bone marrow.¹⁹

By chance, Dougherty had implanted a mouse with lymphoma, and the tumor was fairly advanced. Lymphoma tumors had little tendency to metastasize. They grew to an enormous size, often weighing as much as the mouse at the time of death.^{16,19} Lymphoma, therefore, was an ideal model for testing anticancer efficacy.

Not wanting to wait to establish a whole group of tumor-bearing mice, they gave nitrogen mustard to this single mouse. After just two daily doses, the tumor had softened and begun to shrink. It eventually disappeared. They stopped treatment, and the remission lasted about a month.¹⁹

When they detected a slight re-growth of the tumor, they treated the mouse again. The tumor shrank again, but not as completely as the first time. When it began regrowing, further treatments had no effect.¹⁹

The typical lifespan of a mouse following a lymphoma implant was about three weeks. The mustard-treated mouse lived for 84 days following implantation.¹⁹

Following this, Goodman and Gilman treated various tumors in mice, adjusting the dose, number of administrations, etc., attempting to optimize the dosing regimen. Many of these tumors regressed, but not all, and none completely disappeared like the original mouse's tumor.¹⁹ These mouse experiments were never published, but the results were sufficiently encouraging to consider a therapeutic trial in people.¹⁶

The consortium of wartime researchers had compiled a comprehensive pharmacological profile of nitrogen mustard.¹⁶ They knew the

bone marrow suppression was completely reversible, and there was a fairly wide safety margin between the effect on lymphoid tissue and the acute lethal dose.¹⁹

Also, they knew that thiosulfate was an effective, although imperfect, antidote.¹⁹ All of this raised Goodman and Gilman's confidence that they could safely move forward with a clinical trial, despite nitrogen mustard's classification as a poison.

The Pivotal Patient

Up to the 1940s, surgery and radiation were the only cancer treatment options.^{11,18} Most physicians thought that treating cancer with a drug (other than painkillers) was akin to malpractice.¹⁹

But when Gilman showed the data to Gustaf Lindskog, he was impressed. Lindskog, an assistant professor of surgery at Yale, thought any drug with promise of controlling cancer (even a cytotoxic compound like nitrogen mustard) was worth trying.^{13,19} He agreed to supervise the trial, and he soon identified a suitable patient.

JD was 47 when a couple of rapidly growing masses appeared beneath his jawbone. Those fluid-filled masses were removed, but they soon reappeared, and JD could barely open his mouth. A biopsy confirmed that the neck tumor was a lymphosarcoma, and JD entered Yale Medical Center for X-ray therapy on February 23, 1941.²²

Radiation treatment initially shrank the tumor, but eventually the lymphosarcoma spread to his lymph nodes, creating large masses in his armpits. Repeated radiation helped, but by August 1942, JD had difficulty breathing and swallowing, and he had lost weight.²²

Radiation was no longer effective, and surgery was out of the question. This type of cancer was known to be rapidly fatal, and the doctors considered JD's condition "hopeless."²²

JD was not Gustaf Lindskog's private patient, but he was interested in JD's management and took responsibility for overseeing his care. On August 25, 1942, Lindskog presented JD's case to the Yale Tumor Conference. The committee agreed that JD had no other therapeutic options and gave Lindskog permission to begin treatment with the experimental compound.²² Because Goodman and Gilman's work was still classified, nitrogen mustard was referred to exclusively as "substance X."^{8,22}

Lindskog fully explained the situation to JD, who understood that all conventional treatments had been exhausted and that "substance X" was experimental. Lindskog said that JD "readily agreed to accept the chance for help, whatever the risk."²²

At 10:00 a.m. on August 27, 1942, JD received the first dose of "substance X." It was an intravenous injection of 0.1 mg/kg.^{19,22} The dose had been extrapolated from the studies in rabbits and mice, and it was roughly 2.5 times what would become the standard dose.¹⁸ Unfortunately, the animal studies had not optimized the duration of therapy. They decided to give JD 10 daily injections.²²

By August 31 (day 3 after the first dose), JD was feeling better and able to sleep, eat, move his head, and cross his arms across his chest. His condition continued to improve, but on September 6, his white blood cell count had

fallen from 10,000 to 5,000 (barely within the normal range). Two days later, his white blood cell count dropped to 1,300. His platelet count was 22,000 (normal range is 200,000–500,000), and his gums began to bleed. He was given a unit of whole blood on September 21, and his blood counts recovered.²²

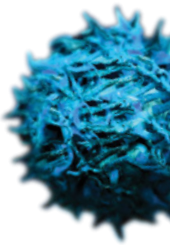
On September 27 (day 31), all of JD's neck and armpit tumors had disappeared. Unfortunately, JD experienced sporadic fevers and coughing, and his white blood cell count had dropped to 200–400. He was given another transfusion on September 30, and his white cell count rebounded to 2,200.²²

In October and November 1942, JD received additional rounds of "substance X" infusions, which produced dramatic but short-lived regressions. Unfortunately, he also experienced profound bone marrow depression, bleeding gums and multiple peripheral hematomas. JD died on December 1, 1942 (day 96); however, the discoveries observed by Goodman and Gilman was considered a medical milestone.²²

Goodman, Gilman and Lindskog had demonstrated, for the first time, successful chemotherapy treatment of a cancer patient.⁷ But in addition to inducing tumor regression, they also showed that resistance to chemotherapy could occur after multiple doses, and that chemotherapy could cause profound bone marrow suppression, immunosuppression, and death.²²

The Yale Clinical Trial

In their enthusiasm (and what Gilman later admitted was "a serious error"), the Yale team began treating a second patient before JD had completed his first series of injections.¹⁹ By the time they fully appreciated JD's profound bone marrow depression, they had completed the 10-day treatment of the second patient. This



patient's white blood cell count decreased, but unfortunately his tumor did not respond to treatment.^{16,19}

The Yale group treated five additional patients using more conservative therapeutic regimens.¹⁶ All of these patients were in the terminal stages of various cancers, and the results were similar to what Goodman and Gilman had seen in mice with various tumors.¹⁹ Some patients responded, but none of them achieved the complete remission they had seen in JD.

Like the animal responses, the patients' tumors reappeared as the bone marrow recovered, and there was no long-lasting cure.^{13,16} Considering that all of these patients had no therapeutic alternatives, the results were nevertheless encouraging and justified further clinical experimentation.

In June 1943, the Yale group dispersed.^{13,19} Gilman joined the U.S. Army and went to Edgewood Arsenal to work in the Chemical Warfare Service.²

Goodman went to the University of Vermont, where he headed the Department of Pharmacology and Physiology.^{3,6,23} In 1944, he moved to Salt Lake City to become the founding chairman of the Department of Pharmacology and was instrumental in building the full, four-year medical school curriculum at the University of Utah.^{5,6,23}

Lindskog stayed at Yale, eventually became chairman of surgery, and was widely recognized for his contributions to thoracic surgery.^{3,18}

Further Clinical Trials

After the Yale investigation, three other academic institutions with wartime government contracts conducted clinical trials with the nitrogen mustards.²¹

At the University of Utah, Louis Goodman coordinated the work of a team of clinicians, who recruited 34 patients at Salt Lake County General Hospital and 16 at Tufts Medical School. He also convinced his brother, Morton, a physician at the University of Oregon Medical School, to treat 10 patients.²⁴

Lenn Jacobsen led the University of Chicago group, who treated 59 terminally ill cancer patients. David Karnofsky treated patients at Memorial Hospital in New York.⁸

Their greatest challenge was establishing a regimen that would kill cancer cells completely but preserve enough of the bone marrow to regenerate healthy blood cells. In addition, they tried to determine which types of cancer would be most susceptible to nitrogen mustard therapy.¹³

The Utah, Chicago and New York clinical groups treated a total of 160 patients, most of whom suffered from Hodgkin's disease, lymphosarcoma or leukemia. After dose-ranging studies, they settled on a four-day course of treatment with 0.1 mg/kg. But despite their best efforts, the toxic effect of nitrogen mustard on white blood cell counts was "usually evident," and loss of platelets caused bleeding gums. Other common side effects included nausea and vomiting, damage to blood-forming organs, and sometimes anorexia, weight loss, weakness and headaches.^{16,17,21}

Patients with Hodgkin's disease, which at that time was invariably fatal, responded most favorably to treatment.^{16,21} Many of them experienced rapid remissions, including some patients who no longer responded to radiation treatment. The remissions typically lasted 4–8 months.^{16,17,21,24} Enlarged lymph nodes, spleen, and liver decreased. In addition, most patients enjoyed a better quality of life (increased appetite, weight, strength, and sense of well-being).^{16,21,24}

Less favorable results were obtained in treating lymphosarcoma, which is characterized by elevated lymphocytes and enlarged lymph nodes. Some patients, like JD, responded similarly to those with Hodgkin's disease. But in many cases, nitrogen mustard treatment failed, and the investigators could not determine why some patients benefitted and others did not.^{16,21,24}

A few patients with chronic leukemia showed modest improvement, but the results with acute leukemia were "disappointing."^{16,24}

These findings did little more than confirm the clinical results at Yale. The greatest effect of the nitrogen mustards was always on rapidly proliferating tissues, whether normal or cancerous. Unfortunately, nitrogen mustard was no cure. All patients eventually relapsed.^{16,17,21,24}

The Italian Connection

Despite the extensive research and protective countermeasures, chemical weapons were not used by either side during World War II.^{11,13} But there was one massive accidental exposure.

As the Allied forces drove north in Italy, they established a storage depot at the port of Bari on the Adriatic coast.^{11,25} Mustard gas was stored in special ammunition dumps, ready to retaliate in case of a chemical attack.⁸

In the fall of 1943, Bari Harbor was crowded with supply ships and merchant vessels. Included in this flotilla was the *USS John Harvey*, a Liberty ship laden with ammunition, gasoline, military supplies, and a secret cargo of 2,000 chemical bombs.^{11,14,25} Each bomb contained 60–70 pounds of sulfur mustard.¹³

On December 2, 1943, Bari Harbor was attacked by German bombers. Although the air raid lasted only 20 minutes, 17 Allied ships were sunk. The *John Harvey* took a direct hit, setting off a chain reaction of ammunition explosions in its cargo bay and releasing sulfur mustard from

some of the broken mustard bombs. Everyone aboard the *John Harvey* perished, including the specialists who knew about the secret cargo and had been trained to safely handle chemical weapons.^{8,11,13,25}

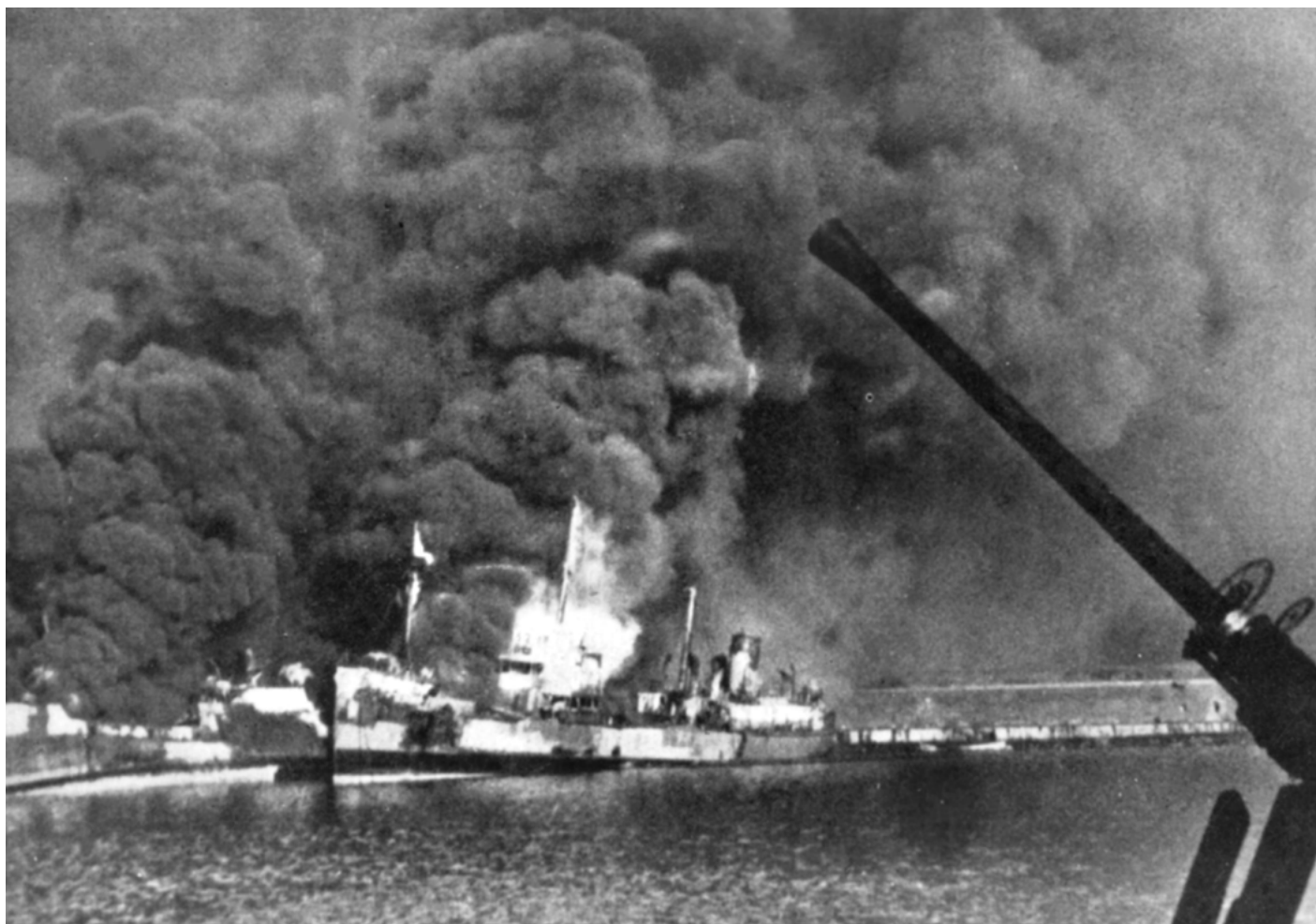
Some of the sulfur mustard vaporized, exposing personnel aboard the burning ships, in rescue vessels, and at the field hospitals. By the next morning, these casualties began showing the signs and symptoms of mustard gas poisoning, which were well-known from World War I: eye irritation, skin blistering, and lung inflammation.²⁵

Gasoline and fuel oil gushed from the ships and flooded the harbor, creating a thick oily slick.^{13,25} Liquid sulfur mustard that was not burned mixed and dissolved in the oil slick. Many sailors and merchantmen jumped or were thrown from their damaged ships. The soaking wet men who showed no obvious signs of blast injuries sat unattended for hours in the field hospitals.²⁵

Unfortunately, extended exposure of the skin to sulfur mustard in their wet clothes provided ideal conditions for systemic absorption of the chemical.²⁵ Over the next few days, these men exhibited a syndrome unlike the World War I victims but strikingly similar to the effects already documented by Goodman and Gilman at Yale and Alexander's group at Edgewood Arsenal.

The victims' white blood cell counts dropped as low as 100. Not all of the mustard-exposed casualties suffered a fall in white blood cell counts, but all of those with extremely low counts died. At autopsy, these victims had small, shrunken spleens, pale lymph nodes and bone marrow devoid of its normal red color.²⁵

At this time, Stewart Alexander had been posted to the Allied Headquarters in Algiers as General Eisenhower's personal consultant on chemical warfare and the care and treatment of chemical casualties. As the casualties mounted in Bari, Alexander was dispatched as a medical advisor.⁸



commons.wikimedia.org/wiki/File:SS_John_Harvey_on_fire_12-2-1943_Italian_port_of_Bari.JPG

The SS John Harvey on fire after a German attack on 12/2/1943 in the Italian port of Bari

By the time he arrived in Bari on December 7, 1943, many of the patients were suffering mustard poisoning too severe for any treatment to reverse.^{8,25} He could only offer medical advice to optimize nursing care. He carefully reviewed all of the patients' medical records, ordered additional laboratory tests, preserved tissue samples and ensured that this accidental chemical exposure was thoroughly documented.⁸

Of the 617 Bari casualties exposed to sulfur mustard, 83 died. This death rate (~14%) was much higher than the 2% fatalities from mustard gas in World War I. The major difference was the severe physiological damage caused by systemic absorption of the oily mustard solution.²⁵

Although unfortunate, this large-scale accidental exposure provided an independent confirmation of the cytotoxic effects that Goodman, Gilman, and the other investigators had seen in their clinical trials of nitrogen mustard.

Published at Last

During the war, chemical weapons researchers filed their results in classified documents, which were circulated to only a limited number of people with the proper security clearance. Beginning in 1946, they were permitted to publish their work in the open literature.^{11,16,21,24,25}

Goodman and Gilman published the results of their seven Yale patients in *JAMA* on September 21, 1946.²⁴ This report documented the 1942

Louis Goodman remained at the University of Utah for the rest of his career. In 1949, he became the founding editor of ASPET's newly launched Pharmacological Reviews.

treatment of JD, the first cancer patient successfully treated with a chemical. Goodman and Gilman were universally hailed as the pioneers of cancer chemotherapy.^{1,6,8,11,12,14,18,22}

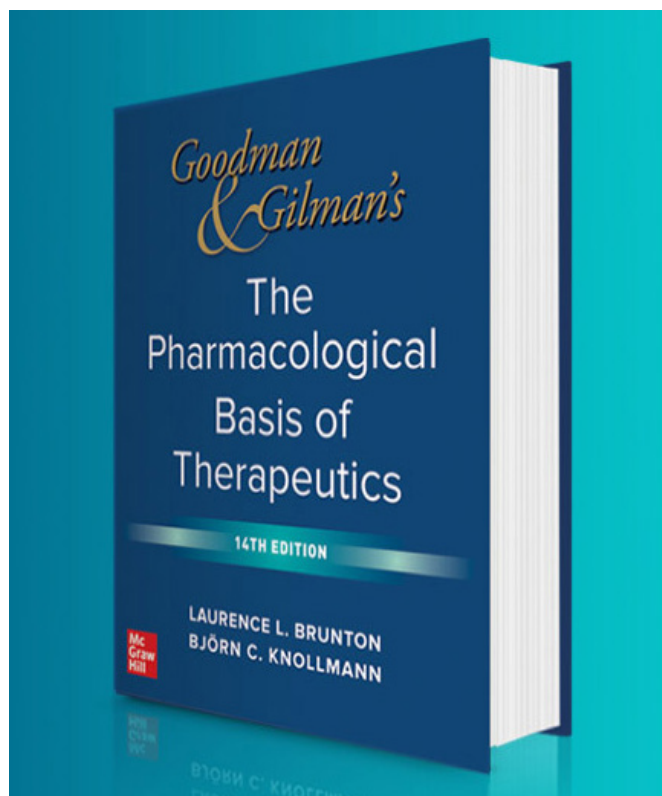
Lenn Jacobson at the University of Chicago, David Karnofsky at New York's Memorial Hospital, and Stewart Alexander also published their findings.^{17,21,25} All of these wartime investigators acknowledged that their results were preliminary. They urged further clinical trials to confirm which types of cancer would respond best to nitrogen mustard treatment.

The National Research Council offered free nitrogen mustard "to qualified institutions for investigational purposes."²¹ Many researchers requested it.¹¹ In 1949 the Food and Drug Administration approved the use of nitrogen mustard to treat cancer, despite its side effects and short duration of action.⁷

Wartime clinical studies had been conducted using two nitrogen mustards: bis(2-chloroethyl) methylamine and tris(2-chloroethyl) amine. Both were the product of a screening program designed to find the most potent chemical warfare weapons, not therapeutic drugs.^{16,21}

After the war, chemists synthesized hundreds of analogs, hoping to find compounds that had a wider safety margin and a longer duration of action.^{7,12,19,21,24} They found that adding an aromatic side chain to the nitrogen mustard backbone produced compounds that were more stable and had more favorable pharmacological properties.¹²

The first clinically useful analog was chlorambucil, which was introduced in 1953.^{12,20} Cyclophosphamide (the most successful and



The Pharmacological Basis of Therapeutics, 14th Ed.

www.amazon.com/Goodman-Gilman's-Pharmacological-Basis-Therapeutics/dp/12642588070

widely used nitrogen mustard) was introduced in 1958. These analogs could be taken orally, a significant advantage. They were well tolerated in small daily doses and provided flexible titration, which avoided depletion of blood cell counts.^{21,26}

The aromatic nitrogen mustard analogs soon formed the cornerstone of anticancer treatment and are now routinely incorporated into multidrug chemotherapy.^{12,13,18}

The Second Edition

Louis Goodman remained at the University of Utah for the rest of his career. In 1949, he became the founding editor of ASPET's newly launched *Pharmacological Reviews*.^{2,6,7}

After Alfred Gilman's discharge from the Army, he joined the College of Physicians and Surgeons at Columbia University as a professor of pharmacology. In 1956, he became the founding chairman of the Pharmacology Department at

the newly established Albert Einstein College of Medicine. In 1973, Gilman returned to Yale as a lecturer in pharmacology.^{2,3,23}

Goodman and Gilman realized that an updated edition of their textbook was long overdue. The first edition had contained three chapters describing the treatment of syphilis with arsenic, bismuth, and mercury. There were only cursory references to cancer treatment with painkillers.⁶

The intensive investment in wartime research produced advances in pharmacology that also benefited peacetime patients, such as chloroquine for malaria and mass production of penicillin, as well as nitrogen mustards for cancer.^{2,13} This explosion in pharmacology subject matter continued after the war and made updating the textbook challenging. By the time they finished a section of the book, it was already out of date. They rewrote some chapters multiple times.^{2,4}

In 1955, after nearly a decade of repeated revisions, the second edition of the textbook was finally published. It included descriptions of newly introduced drugs: nitrogen mustard and other anticancer drugs, the first effective treatments for hypertension, the first antihistamines, the first antibiotics (penicillin, streptomycin, tetracycline, and chloramphenicol), and new diuretics.⁶ In addition, Goodman and Gilman incorporated the cellular mechanisms of action for the older drugs.⁴

They realized that they could not keep up with the rapidly expanding pharmacology literature for future editions of the book, alongside the demands of their regular jobs. For the third edition, they invited 42 trusted colleagues and former students to write the various chapters.^{2,4} But Goodman and Gilman maintained tight

Goodman served as ASPET president in 1959, and Gilman followed as president in 1960.

control over the quality of the text and were actively involved as the book's editors.

Now in its 14th edition, the textbook's section on alkylating agents begins with: "In 1942, Louis Goodman and Alfred Gilman, the originators of this text, demonstrated the activity of nitrogen mustards against mouse lymphoma. Their clinical studies of intravenous nitrogen mustards in patients with lymphoma launched the modern era of cancer chemotherapy."²⁶

The two coauthors maintained a long-distance friendship, connected by their textbook's many editions. But they pursued separate research interests. They frequently served as consultants and advisors, and among their many honors was election to the National Academy of Sciences. Goodman served as president of ASPET in 1959, and Gilman followed as president in 1960.²

In a 1980 interview Goodman reminisced, "We bonded like brothers, never quarreled, had a lot of fun, and learned from each other."⁵

References can be found on page 33.



Rebecca J. Anderson, PhD

Rebecca J. Anderson holds a bachelor's in chemistry from Coe College and earned her doctorate in pharmacology from Georgetown University. She has 25 years of experience in pharmaceutical research and development and now works as a technical writer. Her most recent book is *Nevirapine and the Quest to End Pediatric AIDS*.



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Breaking Barriers in Women's Cancer Treatment: Innovative Approaches and Experimental Therapeutics



A special section for the January 2025 issue of *The Journal for Pharmacology and Experimental Therapeutics* is accepting original research on women's cancers including breast, endometrial, uterine and ovarian, such as:

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Submission deadline: March 13, 2024

Authors are encouraged to submit a presubmission inquiry to Dr. Elizabeth Yeh. All submissions must refer to *JPET's* Instructions for Authors.

PR&P Names New Editor-in-Chief and Deputy Editor-in-Chief

By Lynne Harris, MA, APR



Jennifer Martin, FRACP, PhD, MA (Oxon.), has been named the new Editor-in-Chief for the Pharmacology Research & Perspectives (PR&P). PR&P, the outlet for fundamental and applied pharmacology, is the official journal of the

American Society for Pharmacology and Experimental Therapeutics (ASPET) and the British Pharmacological Society (BPS).

Dr. Martin is a clinical pharmacologist and physician at the University of Newcastle, New South Wales, Australia. She brings extensive knowledge from her research in the field to her new role as PR&P Editor-in-Chief. Dr. Martin has held several positions in clinical pharmacology since 2000, including in pharmacovigilance, pharmacoconomics, pharmaceutical pricing and regulation at the national, state and local levels in Australia and New Zealand. Her editorship started January 1.



Ross Corriden, PhD, RAPT Therapeutics, South San Francisco, Calif., was selected to serve as Deputy Editor-in-Chief of PR&P. Dr. Corriden specializes in immunology, inflammation and molecular/translational

pharmacology. He currently serves as Director of Inflammation Discovery Biology Group at RAPT Therapeutics. Dr. Corriden has more than 3,700 citations and works published in

high-impact journals, including *Science*, *Nature Communications* and *Trends in Immunology*. He is a 2019 recipient of ASPET's Early Career Award and Past Chair of the Society's Translational and Clinical Pharmacology division. Dr. Corriden moved from PR&P Senior Editor to Deputy Editor-in-Chief on January 1.

PR&P is a collaboration between ASPET, the BPS and Wiley. It is a Gold Open Access journal that publishes original research, reviews and perspectives in all areas of preclinical and clinical pharmacology, therapeutics, education and related research areas. PR&P's growth has risen significantly in recent years. The 2022 Impact Factor was 2.6.



Outgoing PR&P Editor-in-Chief Michael Jarvis, PhD, FBPhS, served as Deputy Editor and Editor-in-Chief from 2018-2023, consecutively. Dr. Jarvis spent his career in all phases of drug discovery research, including target identification through

clinical candidate selection and clinical development. He has provided scientific and medical oversight for established drug therapies in multiple therapeutic areas including epilepsy, chronic pain, dyslipidemia, hypertension and metabolic disorders. Dr. Jarvis has authored or co-authored more than 250 peer-reviewed publications. He currently serves as ASPET's Past President, having served as president from July 2022 to June 2023. Dr. Jarvis has received numerous awards and recognition over his career. His service and work are appreciated.

A-POPS Encourages Team-Learning to Solve Clinical Problems

By Mark A. Simmons, PhD

Five exercises from the Patient-Oriented Problem-Solving (POPS) in Pharmacology are now available as an online learning tool, the [A-POPS](#). This unique, online system includes extensive analytics, student performance metrics and ease of scheduling. To assist students in learning through the A-POPS, the instructor groups students by four. Within a group, each student is assigned one of four unique License Keys for their role as either Student 1, Student 2, Student 3, or Student 4.

The POPS is a series of exercises consisting of simulations of clinical problems. Available as sets of PDFs, the POPS are organized and distributed by the instructor who runs the group sessions. The exercises are designed for small group meeting sessions to supplement the teaching of pharmacology to first- or second-year students in the health professions.

The new automated A-POPS streamlines the POPS process, eliminating the need for scheduling breakout rooms and distributing

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handouts. The system automatically records and scores student responses on the pretest, posttest, and group quiz. The system also provides instructors with survey data regarding the group's performance and student evaluations of the exercise.

Before the group meeting, students complete a pretest and review the assigned learning objectives. During the group meeting, the students proceed through the four episodes, finishing with a Group Pop Quiz. After the group meeting, students complete a posttest individually.

[ASPET](#) partnered with [DeckChair Learning Systems, Inc.](#) to develop the A-POPS. The five A-POPS workshops that are available, include "Treatment of Essential Hypertension," "Therapy of Diabetes Mellitus," "Drug Treatment of Heart Failure," "Pharmacokinetics Applied to the Treatment of Asthma," and "Chemotherapeutic Challenges (Antimicrobials)."

The workshops require the students to collaborate to formulate effective solutions to clinical problems using peer-to-peer learning. With the A-POPS, students can meet face-to-face or virtually, allowing the workshops to be completed anytime, anywhere, online.

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The A-POPS not only presents the text but also guides the students as a group through the pharmacology-centered cases consisting of a series of clinical scenarios. Each student is given the opportunity to serve as a leader while facilitating the discussion of a clinical scenario.

Each student takes a turn leading the group discussion to solve the problems posed during the four clinical episodes of the workshop. During each episode, only the leader has the information related to that episode. They must effectively communicate the details of the

[This brief video](#) provides an overview of the A-POPS, workshop outlines and learning objectives.

[Watch ASPET's Focus on Pharmacology webinar](#) on the A-POPS system.

clinical scenario to their colleagues and guide the discussion about the case.

The A-POPS provide a structured format for student-directed (peer-to-peer teaching) learning of topics in pharmacology. The POPS are written by pharmacologists and have been peer reviewed by both a basic scientist and a clinician. The exercises are consistent with the ASPET/[Association of Medical School Pharmacology Chairs](#) Pharmacology Knowledge Objectives and address accreditation standards. They are updated regularly and include consideration of diversity, equity and

inclusion in both content, development and interprofessional learning.

The United Nations marks [International Day of Education](#) annually on January 24, focusing on making education accessible to everyone. A-POPS exercises break down barriers and transform pharmacology education by harnessing the value of collaborative learning. This is important for pharmacology education because real-life scenarios demand team analysis and decision making. By matching students in groups, educators are able to maximize inclusive and quality education.

The A-POPS workshops are available to the entire pharmacology community, i.e. not restricted to ASPET members. The exercises are available for sale, either one exercise at a time or as a package of five exercises at a considerable discount (less than \$6 per student, per exercise).

Mark A. Simmons, PhD

Dr. Mark Simmons teaches pharmacology at the University of Maryland Eastern Shore (UMES). Prior to joining UMES, he was on the faculty at Northeast Ohio Medical University and Kent State University and, prior to that, at Marshall University School of Medicine. The focus of Dr. Simmons' research is on the molecular, cellular, and behavioral actions of drugs that affect the cardiovascular and nervous systems.

ASPET Congratulates the 2023 FASPET Class

The American Society for Pharmacology and Experimental Therapeutics (ASPET) recently recognized 16 individuals as ASPET Fellows (FASPET) for their exceptional contributions to the advancement of pharmacology including research, drug discovery, teaching, policy and industry. The FASPET designation is a prestigious honor bestowed on ASPET's most distinguished members to recognize their efforts through their scientific achievements, mentorship, service to ASPET and a demonstrated commitment to education and diversity.

Congratulations to the 2023 FASPET Class:

- [Xiaodong Cheng, PhD](#)
- [Janet E. Clark, PhD](#)
- [Lynette C. Daws, PhD](#)
- [Ted M. Dawson, MD, PhD](#)
- [Xinxin Ding, PhD](#)
- [Henrik G. Dohlman, PhD](#)
- [Margaret E. Gnegy, PhD](#)
- [John R. Hepler, PhD](#)
- [Michael F. Jarvis, PhD, FBPhS](#)
- [José E. Manautou, PhD, ATS](#)
- [Donald P. McDonnell, PhD](#)
- [Michael A. Nader, PhD](#)
- [John J. G. Tesmer, PhD](#)
- [Styliani-Anna \(Stella\) E. Tsirka, PhD](#)
- [Robert H. Tukey, PhD](#)
- [David J. Waxman, PhD](#)



References

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1. Gilman AG (2012) Silver spoons and other personal reflections. *Annu Rev Pharmacol Toxicol* **52**: 1–19.
2. Swain HH (1984) G&G: The textbook which structured American pharmacology. *The Pharmacologist* **26**: 41–44.
3. Schiff JA (May/June 2011) Pioneers in chemotherapy. Yale Alumni Magazine; available from: <https://yalealumnimagazine.org/articles/3173-pioneers-in-chemotherapy>.
4. Green H (1980) Interview with Alfred Gilman.
5. Green H (1980) Interview with Louis S. Goodman.
6. Altman LK (November 28, 2000) Dr. Louis S. Goodman, 94, chemotherapy pioneer, dies. *New York Times*; available from: <https://www.nytimes.com/2000/11/28/us/dr-louis-s-goodman-94-chemotherapy-pioneer-dies.html>.
7. ASPET (December 2007) First Edition, *Mol Interv* **7(6)**: 305.
8. Conant J (2020) *The great secret: the classified World War II disaster that launched the war on cancer*. WW Norton & Co., New York.
9. Cox BM (2007) Torald Sollmann's studies of mustard gas. *Mol Interv* **7(3)**: 124–128.
10. Everts S (February 23, 2015) When chemicals became weapons of war. *C&E News* **93(8)**: 9–23.
11. Hirsch J (2006) An anniversary for cancer chemotherapy. *JAMA* **296(12)**: 1518–1520.
12. Highley MS, Landuyt B, Prenen H, Harper PG, and De Bruijn EA (2022) The nitrogen mustards. *Pharmacol Rev* **74**: 552–599.
13. Institute of Medicine (1993) *Veterans at Risk: The Health Effects of Mustard Gas and Lewisite*. Washington, DC: The National Academies Press; available from: <https://doi.org/10.17226/2058>.
14. Gerald MC (2013) *The Drug Book*. Sterling, New York, p 220.
15. Lynch V, Smith HW, and Marshall EK Jr (1918) On dichloroethylsulphide (mustard gas), I. The systemic effects and mechanism of action. *J Pharmacol Exp Ther* **12(5)**: 265–290.
16. Gilman A and Philips FS (1946) The biological actions and therapeutic applications of the B-chloroethyl amines and sulfides. *Science* **103(2675)**: 409–436.
17. Karnofsky DA (1947) The nitrogen mustards and their application in neoplastic diseases. *New York State J Med* **47(9)**: 992–993.
18. Curtis J (Summer 2005) From the field of battle, an early strike at cancer, *Yale Medicine*; available from: <https://medicine.yale.edu/news/yale-medicine-magazine/article/from-the-field-of-battle-an-early-strike/#:~:text=At%20the%20start%20of%20World,first%20effective%20chemotherapy%20for%20cancer>.
19. Gilman A (1963) The initial clinical trial of nitrogen mustard. *Am J Surg* **105(5)**: 574–578.
20. Neidle S and Thurston DE (2005) Chemical approaches to the discovery and development of cancer therapies. *Nature Reviews* **5**: 285–296.
21. Rhoads CP (June 22, 1946) Nitrogen mustards in the treatment of neoplastic disease. *JAMA* **131(8)**: 656–658.
22. Fenn JE and Udelsman R (2011) First use of intravenous chemotherapy cancer treatment: rectifying the record. *J Am Coll Surg* **212(3)**: 413–417.
23. New York Times (January 14, 1984) Dr. Alfred Gilman dies at 75; Authority on pharmacology; available from: <https://www.nytimes.com/1984/01/14/obituaries/dr-alfred-gilman-dies-at-75-authority-on-pharmacology.html>.
24. Goodman LS, Wintrobe MM, Dameshek W, Goodman MJ, and Gilman A (1946) Nitrogen mustard therapy. *JAMA* **132(3)**: 126–132.
25. Alexander SF (July 1947) Medical report of the Bari Harbor mustard casualties. *Mil Surg* **101(1)**: 1–17.
26. Goodman & Gilman's *The Pharmacological Basis of Therapeutics* (Brunton LL and Knollmann BC, eds.) 14th Edition, McGraw Hill, New York.