Since its founding in February 1916, The JI has reflected a world outside of the laboratory. Indeed, with an inaugural issue published 18 months into WWI, papers in that first year included research on war-related diseases. With the arrival of WWII, this trend continued more rapidly and in more far-reaching ways, in content and production.

As timely and on point as The JI is today, the same held true yesterday, as well.

**WWI: Reshaping a Young AAI**

Although the United States stayed out of WWI until April 1917, the fighting had an impact on the formation of The JI and the shape of AAI, which had been founded only a few years earlier, in 1913.

Of the latter, medical service in the military was important enough to AAI leadership that at the second annual meeting in 1915, well before American involvement in the war, AAI extended “active memberships, without the payment of dues” to the directors and assistant directors of the laboratories of the Army Medical School, the Navy Medical School, and the Hygienic Laboratory of the U.S. Public Health Service (renamed the National Institute of Health in 1930).  

With regard to The JI, the founders envisioned it as an international journal, but the state of world affairs precluded participation with subscribers, contributors, and editors from the countries of the Central Powers (Germany, Austria-Hungary, Bulgaria, and the Ottoman Empire). By March of 1917, The JI, with 439 subscribers, went to “practically every foreign country,” in Europe except the Central Powers countries.

A month later, on April 6, 1917, the U.S. Congress issued a formal declaration of war and plunged the country into the Western Front in Europe. The AAI Council passed a resolution offering the “services of trained bacteriologists and immunologists and the facilities of their respective laboratories” to federal and state government. Many AAI members, including future presidents and editors of The JI, responded to the call and enlisted in the U.S. Army Medical Reserve Corps (MRC). So many volunteered that the 1919 annual meeting was very short on abstract submissions. AAI President William H. Park (AAI ’16, president 1918–19) sent a letter to the membership, in which he asked that “all who have had a chance to do experimental work, will feel it a duty to present a report of this at the annual meeting.” Nonetheless, only 16 abstracts were presented that year, down from 38 the year before.

Answering the call of duty obviously had an impact on the structure of the AAI Council. When Council member Richard Weil died in the line of duty as a member of the MRC, his seat was filled by George McCoy, who had been given membership as director of the Hygienic Laboratory of the Public Health Service. In 1918, the first editor-in-chief of The JI, Arthur Coca (AAI ’16, editor-in-chief, The JI, 1916–48, secretary-treasurer 1918–45), was appointed both treasurer pro tem and secretary to replace Willard J. Stone (AAI ’13, treasurer 1913–18) and Martin J. Synnott (AAI ’13, secretary 1913–18), both of whom were serving in the MRC.

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4. Minutes of the Fourth Annual Meeting, April 7, 1917, AAI-Rockville.  
5. For more information about AAI members in WWI, see “Immunologists during the First World War: One Soldier-Scientist’s Experience—Stanhope Bayne-Jones,” AAI Newsletter (December 2012): 16-23.  
7. Commissioned into the MRC when the United States entered WWI in 1917, Weil was appointed chief of medical staff at Camp Wheeler near Macon, Georgia. While attending hospitalized troops there, Weil contracted pneumonia and died on November 19, 1917.  
Immunology on the Battlefields

In his president’s address, published in the September 1, 1918, issue of *The JI*, John A. Kolmer (AAI ’13, president 1917–18) expressed optimism regarding how the science of immunology would affect the conduct of the war.9 He predicted that “a notable victory over the common enemy, disease, will be recorded as one of the greatest triumphs in this greatest of all conflicts” through improvements in sanitation, immunization, and treatment.10 Immunologists had made advances in combating many diseases that once plagued battlefields, including smallpox, typhoid, tetanus, diphtheria, and syphilis. Typhoid, in particular, was no longer the threat it had once been: as late as 1898, 85 percent of all U.S. deaths in the Spanish-American War were from typhoid, but with mandatory immunization against the disease for all U.S. troops in WWI, the disease claimed only 227 soldiers, one-quarter of one percent of all U.S. deaths in the war.11 Kolmer’s prediction was proven largely true, as WWI was the first U.S. war in which the death rate from disease was lower than that from battle.12

Kolmer also recognized major challenges that could be exacerbated by the war. Most pressing to him were the development of tests for immunity to pneumonia, tuberculosis, and meningococcal meningitis, along with immunizations against measles, anterior poliomyelitis, syphilis, and gonorrhea.13 Tuberculosis and meningitis were among the top wartime killers of American soldiers, although pneumonia overshadowed these two by far, accounting for 83.6 percent of deaths from disease.14

Of these 40,000 deaths from pneumonia, 25,000 were attributable to pandemic influenza, a development that Kolmer could not have predicted.

Even before the pandemic of 1918–19, influenza had captured the interest of immunologists. The winter of 1915–16 had seen a sharp increase in the mortality rate from influenza, as an epidemic of the disease swept through most of the nation, killing thousands of people.15 The mortality rate from influenza in 1916 was 26.4 per 100,000, the highest it had been since 1900.16 During the pandemic, this ballooned to 400 per 100,000 among American soldiers in the United States in the second week of October 1918 alone. In response to these conditions, *The JI*, in the July 1919 issue, carried three articles focusing on influenza research. All three described experiments with Bacillus influenzae, or Pfeiffer’s bacillus (now Haemophilus influenzae), then suspected to be the cause of influenza rather than an opportunistic pathogen. An article by F. M. Huntoon (AAI ’18) and S. Hannum considered both the causal and opportunistic roles and also attempted to understand the relationships between the various strains of influenza “in order to account for the epidemiological features of the pandemic.”17 *The JI* continued to publish research that sought to address the causes of the pandemic for years after.18

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9. Kolmer’s address was delivered at the fifth annual meeting of AAI in Philadelphia, PA, on March 29, 1918.
Venereal Disease

Another perennial health problem highlighted by the war was sexually transmitted infection. With over four million troops mobilized, the American armed forces needed to educate their personnel on the dangers of venereal disease, specifically syphilis and gonorrhea. Pamphlets published for the War Department contended that because “such diseases as small-pox, yellow fever and typhoid have been practically wiped out...the greatest menace to the country is venereal disease.” From 1916 to 1920, 17 articles on syphilis and various tests for the disease appeared within the pages of The JI. Kolmer was especially optimistic about the recent advances in the management of syphilis, as the older mercury-based treatments had largely been replaced with the first chemotherapy drug, arsphenamine, also known by its trade name Salvarsan or “compound 606.” This arsenic-based medication was painful to the patient, required more than 18 months of treatment and at least 50 injections, bore unpleasant side effects (such as nausea and vomiting), and had to be stored in sealed vials of nitrogen—but it worked. Ikuzo Toyama and Kolmer published an article on their work to explain the mechanisms of both arsphenamine and the older treatment of mercuric chloride. They determined that both drugs worked by increasing antibody production in small doses, whereas massive doses would have the opposite effect.

Research on the treatment of syphilis and gonorrhea led to effective public health education campaigns, as was evidenced early on in research concerning the incidence of these diseases among members of the armed forces. Although venereal diseases were still the most frequent cause for soldiers to be out of commission, a study found that, of the 48,167 cases treated at five army camps in the United States in the year ending May 21, 1919, 96 percent had been contracted before the patient enlisted. The constant bombardment of soldiers with information about these diseases produced an army with far lower rates of infection than the general public.

Interwar Years

After the Armistice of November 11, 1918, both the United States and the AAI returned to a normal state of affairs. By early 1920, The JI had a subscription agent in Berlin to distribute the journal in Germany. In the decades that followed, the economic fortunes of most post-war countries were in a state of flux, but the United States thrived during the Roaring Twenties until Black Tuesday, October 29, 1929, when the stock market crashed, and the Great Depression began.

On June, 16, 1933, President Franklin D. Roosevelt established the National Recovery Administration (NRA) as his first large-scale legislative attempt to begin righting the country’s economic ship. The goal of the new agency was to bring fair, regulated competition to the market and better working conditions to laborers through the creation of codes to stabilize production; set price controls; and regulate collective bargaining, wages, and maximum work hours for laborers. The NRA emblem, a blue eagle clutching a gear in one talon and lightning bolts in the other, symbolized industry and power. The symbol quickly gained a foothold in the American consciousness and was displayed in shop windows and printed on the packaging of goods to demonstrate support for the agency. Although use of the emblem was voluntary, businesses that did not display or use it were often boycotted.

Scientific publishers were not immune to the public pressure to include the NRA logo on their journals. Thus, the NRA eagle first appeared prominently on the cover of the October 1933 issue of The JI.
**WWII: Supporting the Effort**

By the late 1930s, immunology had become an established field of research that was both growing and diversifying, and *The JI* was the preeminent journal for immunology in North America. At that time, the journal was publishing one issue each month and nearly 1,000 pages of research each year.

When WWII broke out in Europe in 1939, the first visual clue of the war in *The JI* was a full-page notice from the Medical and Surgical Supply Committee of America in the November 1940 issue. A large, bold headline exclaimed that “Great Britain Needs Surgical Equipment,” in its solicitation of donations of medical supplies from medical professionals and institutions. After the United States entered the war, *The JI* voluntarily and proactively took steps to conserve paper in anticipation of restrictions on supplies. In January 1942, *The JI* published an “Explanation to Subscribers,” explaining the new format of the journal, with smaller type and narrower margins to fit the same amount of content into roughly 20 percent fewer pages. In 1943, the War Production Board codified such efforts, issuing regulations limiting publishers to 90 percent of the weight of paper they had used in 1941. In early 1944, a “V” logo (“'V' for Victory”) appeared on the cover, indicating that the journal was complying with wartime paper restrictions.

Paper wasn’t the only commodity that *The JI* was asked to help conserve. The August 1942 issue included a visually arresting headline over a message from the publisher, Williams and Wilkins: “URGENT: Notice of War Production Board Order Related to Obsolete Plates.” The War Production Board had issued Conservation Order M-99, which required the owners of obsolete printing plates to turn them over so their metals could be used in the war effort. Williams and Wilkins had previously provided authors published in *The JI* with the plates used to print their figures. The announcement informed authors that they were subject to “fine or imprisonment” if they did not comply with the government order. Such penalties, however, were likely intended for businesses, not individuals with a single plate here and there.

The expansion of War Production Board restrictions affected the scientific enterprise more broadly, as travel restrictions caused the cancellation of scientific meetings, including the AAI annual meetings in 1943, 1944, and 1945.

**Funding War-Related Research**

On June 28, 1941, President Roosevelt issued Executive Order No. 8807 to establish the Office of Scientific Research and Development (OSRD) “for the purpose of assuring adequate provision for research on scientific and medical problems relating to the national defense.” This new agency would spend over half a billion dollars on scientific research during the course of the war.

Many contributors to *The JI* benefited from OSRD funding during the war. A total of 23 articles described research funded in whole or in part by OSRD contracts, and the May 1946 issue featured five articles with OSRD funding—one-half of the content for that issue. The OSRD-funded articles in *The JI* reflected the changing needs of the military; the earliest of these articles described research on perennial threats, such as tetanus, typhus, and syphilis, whereas later articles dealt with diseases faced by soldiers fighting in the Pacific, such as dysentery and malaria. These papers were studies in basic research, as well as new and improved diagnostic and treatment options, including vaccine and penicillin research.

Seymour Halbert (AAI ’47), Stuart Mudd (AAI ’27), and Joseph Smolens (AAI ’43) of the University of Pennsylvania published three articles on aspects of Shigella, which had caused several severe outbreaks of dysentery in all theaters of the war. Two OSRD-funded articles described methods of producing the *Clostridium perfringens* alpha-toxin, the agent responsible for gas gangrene. Although both incidence and mortality of gas gangrene had declined sharply since WWI, prevention of the debilitating condition remained a priority for

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27. The wording of Order M-99, while technically including individuals, was clearly intended to apply to companies, as its primary effect was to compel printers and publishers to certify that they had no obsolete plates in their possession before obtaining new metal.
the military.\textsuperscript{31} Michael Heidelberger (AAI ‘35, president 1946–47, 1948–49) and various co-authors, including Manfred Mayer (AAI ‘46, president 1976–77), published a series of five articles detailing their unsuccessful quest to find a malaria vaccine. Even with the relative luxury of a large population of volunteer subjects for research and over $5.5 million spent on malaria research, that goal remained out of reach.\textsuperscript{32}

At the outset of the war in Europe, penicillin had not yet been used to successfully treat bacterial infections in humans. A few years into the war, however, this changed, and there was an urgent need to understand the antibiotic properties of penicillin and to ramp up production of the new drug. In the United States, the OSRD and pharmaceutical companies were largely responsible for initiating this research.

Although there was only one OSRD-funded paper on penicillin research,\textsuperscript{33} the OSRD recommended or supplied penicillin for two other experiments that were published in The JI.\textsuperscript{34} Werner Henle (AAI ’38, president 1962–63) and Gertrude Henle focused their research on influenza during WWII from their lab at the University of Chicago; the pair received OSRD contracts for human subject research that resulted in two articles in The JI.\textsuperscript{35}

### The Army Epidemiological Board

Many contributors to The JI, the Henles among them, received wartime funding from the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army (later shortened to the Army Epidemiological Board). At the urging of Brigadier General James S. Simmons, Chief of Preventive Medicine in the Office of the Surgeon General during WWII, and his deputy, Stanhope Bayne-Jones (AAI ’17, president 1930–31), the War Department approved the Board in January 1941 to “prevent catastrophic outbreaks of disease.”\textsuperscript{36}

Influenza was a high priority for the military, as the pandemic during WWI had been one of the largest sources of medical non-battle casualties in the U.S. Army abroad and at home. Among the 17 initial board members and commission directors were nine AAI members, including four past presidents, two future presidents, and six long-time members of The JI editorial staff, four of whom were editing the journal throughout the war. Bayne-Jones served as the first administrator of the Board, and Francis G. Blake (AAI ’21, president 1934–35) was its first president. Among the other prominent AAI members and editors of The JI who served with the Board were Oswald T. Avery (AAI ’20, president 1929–30), Alphonse R. Dochez (AAI ’20, president 1931–32), and Thomas Francis, Jr. (AAI ’30, president 1949–50). In the next two years, John F. Enders (AAI ’36, president 1952–53) joined the Commission on Measles and Mumps, and Karl F. Meyer (AAI ’22, president 1940–41) joined the Commission on Tropical Diseases, adding two more active editors of The JI to the Board.

Albert Sabin (AAI ’46) served on the Board’s Commission on Neurotropical Virus Diseases and in 1943, went to Cairo to set up a lab for the study of sandfly fever, infectious hepatitis, and poliomyelitis.\textsuperscript{37} Sabin was very pleased with the results of his research in the field, especially on sandfly fever, which also shed light on other mosquito-borne diseases, such as dengue.\textsuperscript{38}


\textsuperscript{36} Theodore E. Woodward and Center of Excellence in Military Medical Research and Education, The Armed Forces Epidemiological Board: Its First Fifty Years (Falls Church, VA.: Office of the Surgeon General, Department of the Army, 1990), 15.

\textsuperscript{37} Woodward and Center of Excellence, 57.

\textsuperscript{38} Letter from Sabin, Albert B., to Riley, William A., dated 1944-04-28, found in Correspondence, General—1943–63—Military Service, Sandfly Fever, Hauck Center for the Albert B. Sabin Archives, Henry R. Winkler Center for the History of the Health Professions, University of Cincinnati, Cincinnati, OH.
Among the many accomplishments of the board were successful treatments or vaccines for pneumonia, influenza, typhoid, typhus, tetanus, diphtheria, and numerous tropical diseases, as well as new understanding of the transferability of cellular immunity and the technique for fluorescent labeling of antibodies. The II was among the journals publishing research produced by the various commissions.

Non-military Research

The II continued to publish research, independent of the military, on a broad spectrum of topics, including allergic reactions, new technologies, bacteriophages, polio, and the discovery of a new disease. During the war, Mary Hewitt Loveless (AAI '41) completed her influential five-part series, “Immunological Studies of Pollinosis.” The power of the electron microscope, invented the previous decade, was harnessed to begin the investigation of the processes, mechanisms, and structure of antibodies. Alfred D. Hershey (AAI '42) completed his six-part series on “Specific Precipitation” and multiple papers on phage-antiphage reaction.

Polio remained a disease of constant concern on the homefront during the war. Although no major discoveries regarding polio were made during the war, the research helped set the stage for the post-war breakthroughs. In The II, 12 papers on polio were published with contributions from 12 different authors at seven institutions. The authors included Beatrice F. Howitt; Joseph L. Melnick (AAI '48), a pioneering virologist; and Ulrich Friedemann, a refugee of Nazi Germany. All of the articles were funded by the National Foundation for Infantile Paralysis (commonly known as the March of Dimes), an organization that quickly became a major sponsor of polio treatment and research.

In the September 1944 issue, the discovery of the Semliki Forest Virus (SFV) by Kenneth C. Smithburn (AAI '37) and Alexander J. Haddow of the Yellow Fever Research Institute in Entebbe, Uganda, was published. Although the discovery of SFV might not have been recognized as a major breakthrough at the time, it has since become a workhorse in immunology. Generally, non-lethal in humans, the virus makes an excellent vector and is used extensively in biological research because it has broad host range and incredibly efficient replication. It is used as a vector to transmit genes encoding vaccines (for viruses of public health interest, such as Chikungunya) and vaccines for cancers that are virally induced. SFV has also been used to treat cancer because it has high anti-tumor properties and therefore, enhances the immune response against solid tumors.

Wartime Diversity

The II became a home for a greater diversity of authors and institutions from around the world during the war. It published papers from Jonas Salk (AAI ’47) and Alfred Hershey well before they were internationally recognized. Five papers were published to complete a Ph.D. requirement, including that of Abram B. Stavitsky (AAI '50). It published papers from a wide range of institutions, including universities, government facilities, and pharmaceutical companies. Of the 124 articles published during the WWII, 35.9 percent had at least one female author.

Manuscripts were accepted from Australia, Brazil, Chile, Egypt, Ireland, Iceland, Israel, Mexico, Sweden, Turkey, and Uganda. The II also published papers from scientists who had fled the Nazi regime, including immunologists Werner and Gertrude Henle, Manfred M. Mayer, Felix Haurowitz (AAI '48), Hilary Koprowski (AAI '46), Ernest Witebsky (AAI '35), and pioneering biomathematician Felix Bernstein.

Faced with changes in research caused by two world wars, The II held true to its mission of publishing peer-reviewed articles at the forefront of immunological research. Following the return to peacetime after WWII, the Cold War would soon begin, and a “Doctor Draft” would affect the research of the next generation of immunologists; this will be explored in the next AAI Newsletter.

Authors: John S. Emrich, Ph.D., AAI Historian; Charles Richter, AAI History Intern

Editors: Mary I. Bradshaw, Senior Director of Communications and Development; Daniel S. Patrell, Director of Communications


41. Established in 1938, the organization was officially renamed the March of Dimes Birth Defects Foundation in 1976 and March of Dimes Birth Foundation in 2007.

42. Kenneth C. Smithburn and Alexander J. Haddow, “Semliki Forest Virus I. Isolation and Pathologic Properties,” The Journal of Immunology 49, no. 3 (1944): 141–57. The Yellow Fever Research Institute, Entebbe, Uganda, was supported jointly by the Medical Department of the Uganda Protectorate and the International Health Division of The Rockefeller Foundation.