Penicillin and the War Years

As it turned out, it was unnecessary to wait as long as the Secretary of Agriculture had predicted for exciting and meaningful research results. The four regional laboratories had been in operation for only about a year when, on December 7, 1941, Japan attacked Pearl Harbor. On December 8, the United States declared war on Japan, and the goals of the researchers were soon altered to meet urgent needs of the military. But the story of wartime research actually began several months earlier. On July 9, 1941, Percy Wells, on detail from the Eastern lab to Washington, received two visitors from war-beleaguered England. They had with them a small but valuable package. The Britishers were Howard Florey, a future Nobel Laureate, and Norman Heatley, an Oxford University bacteriologist, and their package contained a small amount of penicillin, a drug unfamiliar to Dr. Wells. The two scientists wanted U.S. help in mass-producing it.

Penicillin was discovered in 1928 by Alexander Fleming at St. Mary's Hospital in London. He observed that a plate culture of *Staphylococcus* had been contaminated by a blue-green mold and that colonies of bacteria adjacent to the mold were being dissolved. Curious, he grew the mold in a pure culture and found that it produced a substance that killed a number of disease-causing bacteria. It was still effective, he found, when diluted as much as 800 times. The mold was eventually identified as *Penicillium notatum*. Naming the substance "penicillin," Dr. Fleming in 1929 published the results of his investigations, pointing out that his discovery was relatively nontoxic and might well have therapeutic value if it could be produced in quantity.

Until 1939, penicillin was almost forgotten. Then Florey and three colleagues, searching for better infection fighters as Great Britain faced the imminent threat of war with Germany, began work to see if they couldn't develop penicillin for medical use. By 1940, with war a reality, they had succeeded in converting penicillin into a stable, dry, brown powder. By 1941, the team

During World War II, Andrew J. Moyer, a chemist at the Northern lab, developed the industrial process—deep vat fermentation—that made mass production of penicillin possible. The technique was subsequently used to produce other antibiotics, vitamins, and other drugs and chemicals.

of scientists became convinced that if penicillin could be produced in quantity, it could be invaluable in preventing infections in war casualties. Unfortunately, hard-pressed British drug manufacturers were unable to undertake the necessary research.

That was the problem that Drs. Florey and Heatley brought to the United States in the summer of 1941, and USDA's Dr. Wells promptly directed them to the Northern laboratory in Peoria. Several researchers there, he assured them, were experienced in industrial fermentation and in growing molds. Work on the project began on July 14. By November 26, 1941, Andrew J. Moyer, the lab's expert on the nutrition of molds, had succeeded, with the assistance of Dr. Heatley, in increasing the Oxford yields of penicillin 10 times.

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What Moyer had done was to grow the mold in a medium that included corn steep liquor, an inexpensive (nonalcoholic) byproduct of the wet corn milling process. Inclusion of the steep liquor, which was full of nutrients, provided a better growth medium then any tried in England. Dissatisfied, Moyer experimented until he had improved the medium with the addition of milk sugar, and *Penicillium* growth doubled again. Moyer also used deep vats to grow the cultures; his innovations with submerged culture fermentation became the basis for many industry practices to come. Results were so encouraging that Robert D. Coghill, head of NRRC's fermentation division, met in New York that winter with representatives of four major U.S. drug companies, who agreed to attempt large-scale production of penicillin. The meeting was held 8 days after the United States entered the war. By the end of 1942, 17 U.S. firms were working on penicillin.

In March, 1942, only enough of the drug was available to treat a single case. But the Peoria researchers soon made another breakthrough. Searching for a superior strain of *Penicillium*, they found it on a moldy cantaloupe from a local market. Named *Penicillium chrysogenum*, it was made available to the drug companies and greatly increased production of the antibiotic. Thanks to the combined efforts of many people, penicillin was available in quantity by June 6, 1944, to treat Allied soldiers wounded on D-Day.

In the years that followed the pioneer work in Peoria, new and better strains of penicillin were discovered, manufacturing techniques were improved, and yields were increased several thousand times. But years later, in 1970, George E. Ward, a member of the USDA research team, put the Peoria contributions in perspective in *Advances in Applied Microbiology*: "Hundreds of new antibiotics have been discovered...about 20 have had sufficient merit to justify their industrial production...Corn steep water is used in most media and submerged culture methods similar to those developed for penicillin are usually employed."

In 1987, Dr. Andrew Jackson Moyer was inducted posthumously into the National Inventors Hall of Fame in Arlington, Virginia. He was cited for his work in growing *Penicillium* mold in deep fermentation in corn steep liquor and milk sugar. He was the first inventor to be inducted for achievements in government research, and he joined such other prominent members of the Hall of Fame as Thomas A. Edison, Luther Burbank, and the Wright Brothers.

Other wartime research at the four regional laboratories, while less dramatic than the penicillin story, also proved productive. Several projects laid the groundwork for important postwar discoveries to come. Many new or improved products were needed for the war effort, and much of the work of the scientists was classified. They continued to work with agricultural materials, including possible new sources of rubber. At the Eastern lab, fruit aromas and flavors were captured in fruit essences, which, while not quite essential to the war effort, did help improve drinks and jellies for the crews of U.S. submarines.

Wartime Rubber Research

Natural rubber comes from the plant *Hevea brasiliensis,* a native of the Amazon Valley of Brazil. In 1876, its seeds were planted in a greenhouse near London, and the seedlings grown there were transplanted to plantations in Southeast Asia, the source of most U.S. rubber imports. During World War II, when Southeast Asia was overrun by the Japanese, rubber supplies to this country were cut off. The United States was forced to find other sources of rubber or risk losing the war.

The most promising source was Buna S, a general-purpose synthetic rubber resulting from U.S. and pre-war German research. It was produced from butadiene (a petroleum derivative) and styrene (produced from coal tar or petroleum). The U.S. Government built plants to produce Buna S and the styrene and butadiene to supply them. Rubber and chemical industries ran the plants and made the rubber.

The project succeeded. When the United States entered the war, this country was producing only about 18 million pounds of synthetic rubber a year. By the end of the war in 1945, production capacity had jumped to about 2 billion pounds a year, an incredible achievement and one essential to the Allied victory. The Government sold its synthetic rubber manufacturing plants to private companies in 1945.

A major contribution to the development of Buna S was made by scientists at the Eastern lab. Soap made from inedible grades of animal fats was the emulsifier used to manufacture synthetic rubber. In the critical year of 1943, wide variations in the rate of rubber formation indicated that unknown chemicals were retarding the process. The slowdown was most pronounced when soaps from low-grade tallow and grease were used, but excluding them failed to correct the problem. Eastern lab researchers found that two fatty acids—linoleic and linolenic—were responsible for slowing the rubbermaking process. Since both were polyunsaturated acids, partial hydrogenization of the fats (similar to a process for making margarine) remedied the situation. The ERRC also developed a sensitive method for detecting the presence of very small amounts of the two fatty acids. The technique proved useful, not only in the synthetic rubber industry, but also in carrying out subsequent research on fats and oils.

Three million pounds of natural rubber were made during World War II from U.S.-grown guayule, a desert plant.

While carrying out its crash program to make synthetic rubber, the Government also conducted an intensive search for rubber-producing plants that could be cultivated in the United States. *Hevea,* still the best source, wouldn't grow outside the Tropics and was unproductive even in Florida. Several promising plants were studied and tested by the regional laboratories, including goldenrod, guayule, and Russian dandelion. The latter plant, which was investigated at the Eastern lab, had been discovered in eastern Russia in 1929 near the Chinese border. In early 1942, two sacks of Russian dandelion seed were flown into the United States, and 600 acres were planted as an experiment in Michigan and Minnesota. Scientists found that the dandelions could produce rubber in 15 months or less and could be grown in most parts of the United States. A process for extracting rubber from the plant was developed by Eastern lab researchers, and enough rubber was produced to permit the fabrication of experimental car and truck tires. They proved of high quality. Research stopped, however, when the Government's Emergency Rubber Project was terminated in 1944. At that time, processing costs were not competitive with either *Hevea* or the new synthetic rubbers.

Another rubber-bearing plant studied was goldenrod, a source that had aroused the interest years before of Thomas A. Edison. Of all the alternatives to *Hevea* examined by USDA, however, the plant with the highest rubber content was guayule, a perennial desert shrub and a member of the sunflower family. After 4 years of growth under favorable conditions, the rubber content of a guayule plant will run as high as 20 percent. During World War II, as part of the emergency rubber project, 3 million pounds of guayule rubber were produced. After the war ended, with imports of natural rubber restored from Southeast Asia, work on the less cost-effective guayule, as well as on Russian dandelion, was dropped. Synthetic rubber, however, was here to stay. (See p. 94 for the story on domestic rubber research after the war.)

The Southern lab came up with mildewproof and rotproof fabrics for use by troops in the South Pacific and in improved cotton bandage. At the request of the U.S. Army, the Western lab mounted a large-scale project to dehydrate fruits and vegetables, not only to preserve them but also to decrease the weight and bulk of military rations. Dehydration proved successful for many products, including potatoes, eggs, and milk. Prepackaged soups and stews were compressed into small packages for shipping.

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In the Northern lab, a batter process for separating starch and gluten from low-grade wheat flours was developed after starch from corn was diverted to increase the production of industrial alcohol. The process provided wheat starch to meet demands for sweeteners when beet and cane sugar were scarce. (In the late 1950's, NRRC improved the batter process to reduce the amount of water required to separate the starch.) This process formed the basis of the wheat gluten industry today. In other wartime research in Peoria, wheat replaced corn in the production of industrial alcohol, with the process tested in a converted whisky distillery.

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Cotton Goes to War

Guncotton, the nitrocellulose explosive used to fire shells from big Navy guns, is made in part from cotton linters, the short fibers that cling to cottonseeds after the first ginning. As America's involvement in World War II began, the military foresaw a shortage of linters, but noted that there was a surplus of long cotton fibers. SRRC technical people went to work to transform long fibers into fuzzy short ones. They developed a machine to cut the cotton into short lengths, but found it could chop up the fiber faster than they could supply it—350 pounds of cotton a minute. So SRRC engineers invented a machine that could tear a mass of cotton apart and feed it in a thin, even sheet to the cutting disks. The high-speed process worked.

As it turned out, the artificial linters were never needed by the Navy, but the experimentation that went into the machines in New Orleans wasn't wasted. It led after the war directly to development of the granular card, an innovative machine for disentangling cotton fibers prior to spinning. It turned out to be one of the most important inventions for cotton processing.

In much the same way, wartime research to develop better cotton bandages led after the war to commercialization of stretch cottons. And a process for making oil-repellent fabrics, called for by the Army Chemical Warfare Service to protect military clothing from liquid chemical weapons, was later used by the Air Force for the clothing worn by rocket handlers who worked with liquid missile fuels.

One of the oddest discoveries, which appeared to have no application at the time, came about at the New Orleans lab during research to make firehoses out of treated cotton instead of linen. To prepare a cotton that would swell like linen when wet, researchers tried attaching hydrophilic, or water-loving, molecules to the cellulose chain of cotton.

Years later, a scientist on the project recalled: "We experimented using strong solutions of reactants to treat the cotton fabric. Then we left it to wash in running water. But when we came back to see how our product was doing, there was nothing left to inspect. The fabric had disintegrated and gone down the drain."

Eventually, however, a use was found for the disappearing cotton. In one manufacturing process, a machine makes lace by embroidering it on a backing cloth. What was needed was an inexpensive cloth that could be dissolved when no longer needed, leaving undamaged lace behind. The SRRC chemist reactivated his old experiment and found that cotton backing for the lace would dissolve readily in water containing alkali. The application led to production of millions of yards of cotton-backing cloth for lacemakers.