

CHEMISTRY

Quinine Synthesized

Exact duplication of malaria remedy achieved for the first time by chemists. May point way to development of better anti-malarial than quinine or atabrin.

► FOR THE FIRST time in history quinine, important malaria remedy found in the bark of the cinchona tree, has been put together in the laboratory.

This total synthesis of quinine has been accomplished by two 27-year-old American chemists, Dr. Robert B. Woodward, of Harvard, and Dr. William E. Doering, of Columbia University, working for the Polaroid Corporation.

Their success in achieving what chemists the world over have attempted for almost 100 years was announced simultaneously with publication of details of the method in the *Journal of the American Chemical Society*. (May)

This chemical feat may point the way to another important achievement, the development of a better anti-malarial than quinine itself or the synthetic chemical, atabrine, now also widely used in malaria treatment. Although both quinine and atabrine are effective in treating malaria, neither of them is a true prophylactic or preventive of a malaria attack. This is because neither attacks the malaria germ in its earliest, pre-infective stage as injected by the mosquito. Nor is either of them very effective in preventing relapses.

The Woodward-Doering process for synthesizing quinine has already led to synthesis of another entirely new substance, an optical isomer of quinine. The structure of this substance looks like the reflection in a mirror of the quinine molecule. Tests to determine whether it has value as a remedy are planned.

The synthesis started with a coal-tar derivative, 7-hydroxyisoquinoline, and proceeded through nearly a score of chemical processes until the scientists had succeeded in creating quinotoxine. This chemical had originally been produced from quinine by Pasteur and in 1918 a German chemist, Rabe, had reconverted it into quinine. When Dr. Woodward and Dr. Doering, had reached the total synthesis of quinotoxine, they knew they could reach their goal by following Rabe's method for converting this chemical into quinine.

Whether the laboratory synthesis can be made commercially practicable has not

yet been determined. The Polaroid Corporation does not intend, states Edwin H. Land, president and director of research, to manufacture the products involved but to license the process, after consultation with government authorities, to such organizations as are best fitted to assure the broadest usefulness for the scientific discovery.

Commercial production of synthetic quinine might be pushed if we did not have enough atabrine and totaquine for military and essential civilian needs. Totaquine is a mixture of chemicals from cinchona bark and contains quinine.

When the Japs seized Java in March, 1942, they also gained almost the entire world's supply of quinine, which for about three-quarters of a century had come from the Dutch cinchona plantations there. At the same time quinine was desperately needed by American and

other United Nations forces fighting in the jungles of the Southwest Pacific and other malaria-ridden regions.

Cinchona trees, however, are native to South America, where the anti-malarial action of their bark was first discovered. Since the war steps have been taken to reestablish these cinchona plantations. Our supplies of totaquine are coming now from Latin America.

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VOLCANOLOGY

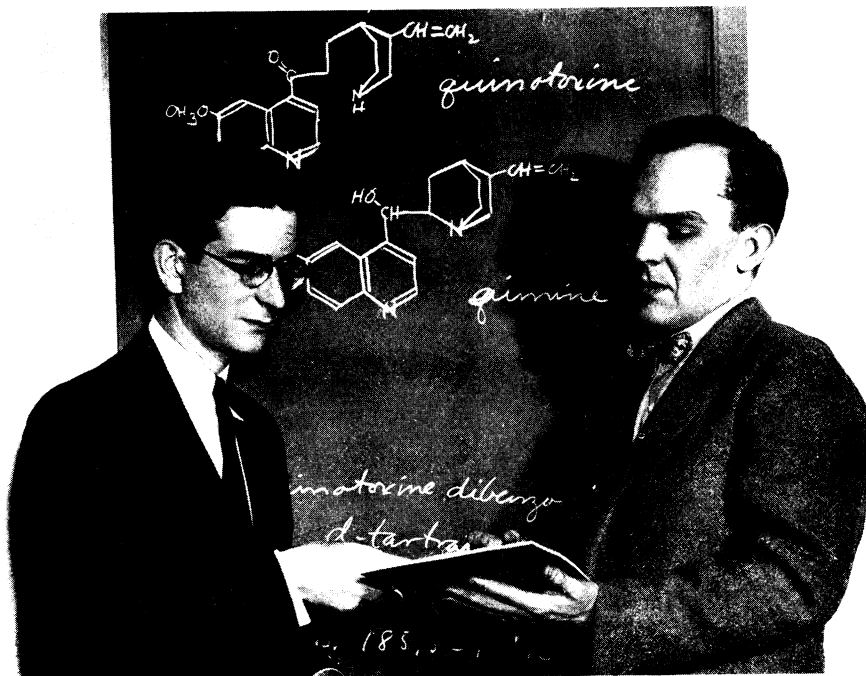
Lava From Paricutin Threatens to Engulf Town

By WATSON DAVIS

Writing From Mexico City

► SLOWLY CREEPING lava from Paricutin volcano is threatening to engulf the town of San Juan Parangaricutiro, nearly five miles away, and to drive 2,500 people from their homes. Engineer Ezequiel Ordóñez, 77-year-old dean of Mexican geology, recently left on his 26th trip to Paricutin, to determine how soon the town must be evacuated.

Moving six feet hourly, the flow has now reached a little valley 120 feet wide



SUCCESSFUL—An exact duplicate of quinine has been synthesized by chemists Robert B. Woodward (left) and William E. Doering, working for the Polaroid Corporation. That very valuable natural drug had defied duplication for nearly a century. But after less than 14 months of work the two young chemists completed the synthesis.

and six feet deep on the outskirts of San Juan. Whether lava engulfs the town is a race between the ability of this valley to hold lava without spilling and the continued outpouring from the volcano. Strangely enough, this new flow comes from the southern side of the volcano, which is the far side from the threatened town. The new stream of liquid and hot rock curves around old flows which engulfed the little village of Paricutin last year.

Eruption of the volcano itself is at present somewhat subdued, probably due to the effort of ejecting lava, but it still erupts every nine to ten seconds.

"Explosions occur very deep within the crater and vapors of explosions issue from the crater's mouth, with noises like

waves breaking against a rocky shore," Senor Ordonez reported in Mexico City, where he was trying to arrange government assistance for the Indian population facing eviction by the flow.

Senor Ordonez and his observers, constantly at the volcano's side day and night, are watching and recording what happens as carefully as they did in the weeks just after the volcano was born out of a cornfield on Feb. 20, 1943—first such event to be witnessed by human beings during recorded history.

Even if the lava fails to invade the town, the countryside for 20 miles around will not grow crops for decades to come and the Indian farmers must eventually be resettled elsewhere.

Science News Letter, May 13, 1944

MEDICINE

Mold Put Into Body

New kind of penicillin treatment consists of injection of the hyphae themselves. Tests on humans and animals show quick results with no bad reaction.

► A NEW and apparently better way of using penicillin, putting part of the mold itself directly into the body where it goes on producing its anti-germ chemicals, is suggested in a report by Dr. H. E. Enoch and Dr. W. K. S. Wallerstein, of London, in a report to the scientific journal, *Nature*. (March 25)

No harmful effects resulted in animals or humans from this method of using penicillin, the scientists report. The response to treatment is prompt, usually within three or four hours after the first injection. Fever dropped and there was immediate relief of pain in the trials on laboratory animals.

Results have already been obtained in human cases of pneumonia that failed to respond to sulfa drugs, and in acute staphylococcal, streptococcal and other infections.

In most of the animal cases one or at most two injections of the material were enough to completely clear an infection. Penicillin itself is rapidly eliminated from the body via the kidneys, which has necessitated giving frequent and usually large doses in order to have enough of it in the body to fight the invading germs. It may have to be given as often as every three or four hours. One injection of the living mold material, however, has an effect that appears to last for 36 to 48 hours.

The material used is a suspension in fluid medium of the hyphae, or filaments, of the mold. They are taken from below the mycelium, or mat of mold filaments, on top of the culture at the stage of its highest rate of penicillin production.

The material is freed of fever-inducing substances and other impurities and is equally efficient whether injected into the veins or the muscles. It seemed "exceptionally potent" when used in treating open wounds with mixed, fever-causing infections.

The effects of this material in checking infection, the scientists believe, are due not only to penicillin, which the mold goes on producing in the body, but to the presence or production of other anti-germ chemicals which are destroyed or left behind in penicillin manufacture.

In 21 cases of animal infections, positive results were obtained in 14. There was some doubt about three cases and four others failed to respond. Even when the living mold material was injected directly into the animal's veins, no harm resulted.

The infections which responded to treatment were gastro-intestinal (the colon bacillus), staphylococcal, streptococcal and pneumococcal. Virus infections did not respond to the treatment.

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CHEMISTRY

Anti-Bleeding Vitamin Receives U. S. Patent

► VITAMIN K, the anti-bleeding vitamin, is now covered by U. S. patent 2,348,037, issued to the group of five scientists who first isolated the compound in pure form, determined its chemical structure, and duplicated it synthetically in the laboratory. Rights in the patent have been assigned to St. Louis University, and any proceeds from licenses to manufacture it commercially will be plowed back into scientific investigation. The five-man

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