MEDICINE

More Penicillin Coming

Distillers, mushroom and molasses firms all join in the increasing production of the germ-killing mold. Present production figures are a secret.

By JANE STAFFORD

➤ MORE PENICILLIN, germ-killing chemical from mold, is on the way. Distillers, mushroom and molasses firms have joined the ranks of drug manufacturers, and all of them are rapidly swinging into large-scale production of this life-saving medicine which a bacteriologist discovered in a mold that was spoiling some of his experiments.

Actual production figures are a secret. The armed services get first call on all the penicillin that manufacturers can turn out, and the Army is said to be demanding 10 times as much penicillin for 1944 as it got in 1943. Nevertheless, one of the manufacturers, Dr. Theodore G. Klumpp, president of the Winthrop Chemical Company, predicts that within the next 12 months enough penicillin will be produced "to more nearly provide for civilian as well as military needs."

Prof. Alexander Fleming, a British bacteriologist, discovered penicillin, but it was a team of scientists in the U. S. Department of Agriculture who solved the bottleneck in penicillin production. Housewives fighting to keep food from getting moldy in warm, damp weather may wonder how there could be a bottleneck in producing anything that seems to grow so fast. The answer is that the problem is not only one of growing tremendous quantities of the mold, but of growing it in such a way that it will produce large amounts of the germ-fighting chemical, penicillin. It must also be grown in pure culture, free from other molds, bacteria or the like. This makes it necessary to grow it in small units, carefully protected from other organisms, which is hard to do in large-scale commercial practice.

The discovery that the mold, *Penicillium notatum,* produced a chemical of some kind which can destroy certain disease germs was made by Professor Fleming in 1929. Little was heard about penicillin from then until 1940 and 1941, when Prof. H. W. Florey and associates at Oxford University announced to the medical world the curative possibilities of penicillin. England, however, was in the middle of the blitz and no British chemical firm was able at that time to take on large-scale production of penicillin.

Professor Florey and Dr. N. G. Heatley, therefore, came to the United States, in the summer of 1941, to consult American chemical and drug manufacturing houses. The manufacturers were not very encouraging, but scientists at the National Research Council referred the British scientists to the Department of Agriculture, and particularly to its Northern Regional Research Laboratory at Peoria, Ill.

HELPING TO PRODUCE PENICILLIN—Extensive studies conducted with the vast mold collection, part of which is shown here, in the Northern Regional Research Laboratory of the U. S. Department of Agriculture, have aided the mass production of penicillin.

Has Large Mold Collection

This laboratory has one of the largest collections of molds in the world and its staff has had wide experience in the use of molds in the fermentation field. Most persons know that the fermentation which produces vinegar is done by bacteria. Less well known is the fact that certain molds also are fermenters, producing such substances as citric acid, gluconic acid, oxalic acid and sake, or rice wine. Department of Agriculture scientists were pioneers in this field. Without their knowledge, experience and facilities, it would not have been possible to develop penicillin production on a commercial scale.

The first thing these scientists did was to work out better methods of feeding and growing the mold. Then they developed new strains of mold which were more efficient penicillin producers. The result of this was to increase the penicillin yield one hundredfold.

In the early days of penicillin production, the mold was grown in large glass bottles on the surface of the nourishing medium. It is still being grown that way in some plants. Department of Agriculture scientists, however, showed that *Penicillium,* the mold, could also be grown in submerged cultures and that penicillin could be produced by the fermentation process.

This brought the whisky distillers and the mushroom and molasses firms into the field of penicillin production. Mushroom cultures, it may surprise you to

know, are produced by a fermentation method. Some of the drug and chemical manufacturers are now also using the fermentation process for producing penicillin, among them Merck, Squibb and Pfizer.

The fermentation processes, W. J. McManus, chief of the drugs and penicillin unit of the War Production Board, points out, give a much lower yield of penicillin per ounce, but this is more than made up for by the mass production and speed. Instead of having to wait eight to ten days for the mold to be ready for harvesting, the cycle is now four days. Instead of working with half-pint amounts and yields in the range of about 30,000 units of penicillin the fermentation process producers work on a scale of 10,000-gallon quantities and yields of 300,000 units are handled.

Further speed-up in penicillin production is expected by a new high vacuum diffusion process for drying it. The chemical is very unstable in liquid form. Steam ejectors, mechanical pumps and a freezing method utilizing a cold trap have heretofore been used on a limited scale in vacuum dehydration.

Many difficulties have been encountered, however, and the drying process has required from 20 to 40 hours. A new method, which preliminary tests suggest will reduce this time to six hours, has been announced by the National Research Corporation of Boston. Besides the saving in time, the method is said to be capable of cutting the cost of dehydration to one-sixth that of any conventional method.

After the mold has been grown and harvested, the penicillin extracted and dried, the fluffy yellow or brown powder must be assayed for potency. The Department of Agriculture scientists gave valuable assistance here, too, working out and improving methods of assay and carrying on in the Peoria laboratory all assays of commercial products until the Food, Drug and Cosmetic Administration could set up facilities for doing this.

First Step

First step toward a synthetic penicillin that might be produced on a large scale from chemicals, as sulfa drugs are manufactured, has been taken with the isolation of penicillin in pure crystalline form. Before manufacture of a synthetic penicillin will be possible, however, scientists must learn its exact chemical composition and then find methods of making the chemical on a commercial scale.

At a guess, and an optimistic one at that, this will take at least a year and a half, as Mr. McManus sees it, and he is in a position to see all there is on penicillin production. Commercial manufacture of a synthetic penicillin, even when scientists find how to do it, may be too expensive to be practical.

Penicillin for civilians may be slightly more readily available as a result of kitchen stove and hospital laboratory methods of production developed by Dr. George H. Robinson and Dr. James E. Wallace, of Pittsburgh, and Dr. Julius A. Vogel, of Jones and Laughlin Steel Corportation. (*See SNL,* Oct. 23)

Drs. Robinson and Wallace first suggested that small amounts of crude penicillin, suitable for treating wounds, sinus infections, boils and other infections of the skin and mucous membranes, could be obtained by growing the mold directly on gauze dressings which had been saturated with a solution of yeast, sugar, starch and glycerin. After saturation with this mold-food solution, the gauze is sterilized, inoculated

with the mold and subsequently used for dressings on infected wounds.

Dr. Vogel adapted this method to one which could be carried out in the average home by anyone having only a rudimentary knowledge of sterile procedure. The bake oven of the kitchen stove, a glass coffee pot, and a tea cup are among the familiar pieces of equipment used in this process. (*See SNL,* Nov. 27)

Disadvantages of the method are: 1. The penicillin gauze can be used only between the ages of four and 12 days, the period during which the mold on the gauze is actively producing penicillin. The penicillin is in the crude state and is present in such small quantity that it cannot be refined and used intravenously for septicemia (blood poisoning) or pneumonia or for any infection that is not in or near the surface of the skin.

Syphilis, gonorrhea, pneumonia, staphylococcus infections such as acute and chronic osteomyelitis, cellulitis, carbuncles of the lip and face, empyema, infected wounds and burns, pneumonia and hemolytic streptococcus infections are all vulnerable to attack by the potent mold chemical which 19 drug, chemical and other manufacturing firms are now producing as speedily and in as large quantities as possible.

Penicillin is still a new word; the pronunciation which seems to be most prevalent places the accent on the penult (next to the last syllable). This would be the natural thing to do, in deriving the word from the generic name of the mold which is its source, *Penicillium.* A good rule-of-thumb, memory aid is to say it as a lisping child might try to say "penny-shilling"—"penny-sillin'."

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MEDICINE

$5 Penicillin Factory

Physician who reported a new method for producing the valuable germ-fighter tells the story of how and why he started his own private mold culture.

➤ WITH AN INITIAL outlay of less than $5 and at a production cost of less than five cents per petrie dishful, any doctor can manufacture penicillin, the germ-fighter from mold which money cannot buy.

These production cost figures come from Dr. Julius A. Vogel, of Aliquippa, Pa., who adapted for a kitchen production line (*See SNL,* Nov. 27) the method of producing crude penicillin on gauze dressings devised by Dr. George H. Robinson and Dr. James E. Wallace, of the Allegheny General Hospital, Pittsburgh. (*See SNL,* Oct. 23)

As soon as he read their report in a scientific publication, Dr. Vogel related at the Industrial Hygiene Foundation conference, the idea of growing his own penicillin intrigued him greatly. His evenings were free and producing penicillin at home promised both diversion and, if successful, the reward of having the precious medicine for his practice.

Remembering that he had saved from medical school days his platinum loop holder, an instrument used by bacteriologists for handling microorganisms of all kinds, Dr. Vogel first sought for and found it.

Next he telephoned Dr. Robinson who "very graciously consented" to present him with a pure culture of his strain of the mold, *Penicillium notatum.*

"Without pausing to catch my breath, I immediately arranged to be relieved of my duties the next day," Dr. Vogel related. "Accordingly at 10:45 on the morning of the 12th (of October, four days after publication of the Robinson-Wallace report) I had safely tucked away in my vest pocket my culture of *Penicillium* which Dr. Robinson himself implanted upon the medium.

"With my precious cargo carefully protected, I secured from a surgical supply house five 75-millimeter petrie dishes, a length of platinum wire and a glass marking pencil. From my druggist I secured the ingredients for preparing the nutrient medium.

"On the evening of the 13th, with the mold grown sufficiently to be discernible on the surface of the medium in my test tube, I inoculated the petrie dishes and sat down to wait results. By the morning of the 18th the cultures were sufficiently mature to take them along with me and look for trouble—and in a plant employing 10,000 men it does not take long for trouble to appear. Thus was I embarked upon the course in which 'deep (*Turn to next page.*)

Do You Know?

Mahogany, formerly used in fine furniture, is now used to build light, speedy submarine chasers.

Most *animals* living in the wild are vegetarians, the bulk of their food being plants, seeds, fruits and berries.

Sweet potato meal may be used as a substitute for corn in cattle feeding; it is made from dehydrated *sweet potatoes.*

The *jerboa,* which looks and leaps like an eight-inch kangaroo, has excited the interest of American soldiers in North Africa.

The basking shark and the whale shark are the two biggest *fishes;* they are dull, sluggish monsters sometimes 50 feet in length.

Fighting *frigates* being built by the Maritime Commission are 306-foot boats for convoy escort duty; over 100 are under construction or already completed and in service.

Clothing after the war may be treated with a chemical now used by the Army to make it resist water, stains and spots; the chemical impregnates each fiber and is not lost in washing.

The American *soybean* crop this year will yield approximately 209,000,000 bushels, most of which, because of its high nutrient value, will go into human and stock food.

Boron was once thought by agricultural chemists to be a plant poison; now it is known that it must be present in soil in small quantities if plants are to grow properly.

The 1943-44 *wheat* crop in Australia, which will be harvested around New Year, is estimated at 89,000,000 bushels; this is 57% of last year's yield, and about 55% of the average yield for the past ten years.

Nearly $100,000,000 worth of *gold* has been produced annually in recent years in Latin America, the greatest quantities coming from Mexico, Colombia, Chile, Peru, Brazil, Venezuela, Ecuador and Bolivia.