The apricot pit bit

On April 20, Dr. Earl Meyers of the Food and Drug Administration wrote a letter to Andrew McNaughton, president of a private research foundation that bears his name. The foundation's investigational new drug application, Dr. Meyers said, had been received and assigned number 6734. McNaughton was asked to identify all future communications to FDA with that number; he was also told that human trials of the new drug could commence at once.

The drug is Laetrile, also called amygdalin, a compound derived from apricot pits. For close to half a century it has been alleged to be effective in both preventing and treating cancer, though it has never been accepted by the scientific community.

A week after it issued the IND, the FDA wrote McNaughton again. It said that, on closer look, it had found deficiencies in the initial application and that new data would have to be submitted within 10 days of receipt of the letter. Among other things, the FDA asked for additional animal data, biochemical evidence of efficacy and some clarification on the names and locations of physicians slated to conduct the proposed trials in man.

On May 12, FDA Commissioner Charles C. Edwards sent McNaughton a registered air mail letter. IND 6734, he said, "is hereby terminated."

In the interim, the McNaughton Foundation did, in fact, submit new data as requested. FDA scientists have got to complete their review of that material. According to McNaughton, the FDA's April 28 letter was not received until May 6 and the agency's termination was premature; formally, FDA still has the application and the new data under consideration.

A Congressional subcommittee that rides herd on FDA is curious about the flipflop.

In early June, Commissioner Edwards had referred to the Laetrile case in testimony before the group, the House Subcommittee on Intergovernmental Relations. "Laetrile," he said, "is a drug which is not generally recognized among qualified experts as safe and effective for any use. . . . No well documented case of therapeutic efficacy ascribed to Laetrile has ever been presented to FDA."

A spokesman for the subcommittee headed by Rep. L. H. Fountain (D-N.C.) says Congressmen want to know why the FDA granted IND 6734 in the first place. A full-scale investigation is slated, possibly for mid-August if Congress does not recess.

McNaughton and his supporters are eager for a hearing, anxious to present their side of the story. So anxious are they, in fact, that on July 13 McNaughton cabled the subcommittee, requesting permission to testify at hearings on the FDA held July 15. He was told that it was unlikely he could be scheduled for the 15th and that, in any case, he would have to submit written testimony 24 hours in advance. That he did. And, on the day of the hearing, a McNaughton representative distributed to the press two documents labeled "prepared for" presentation before the subcommittee. When a subcommittee officer informed him he had no authority to distribute information which the subcommittee had not scheduled for hearing, he departed, but by then several copies had already been given out. McNaughton is likely to be heard when the hearings resume.

The situation is complicated and messy. As in most issues involving the treatment of cancer, emotions run deep, especially so in this case because proponents of an unorthodox drug, one the American Cancer Society frankly labels phony, are pitted against what they see as the scientific establishment.

Laetrile has never, with the exception of those few days this spring, won any Federal stamp of approval for even preliminary testing in human beings in the United States. It is, however, legal in other countries and has been used by physicians in Japan, Germany and Mexico among others. According to McNaughton, whose Sausalito, Calif., foundation makes a policy of supporting research that lacks sufficient professional acceptance to win funds from traditional sources, foreign doctors report that Laetrile is effective in treating virtually all types of cancer except cancer of the brain. However, there appears to be a dearth of controlled clinical studies of Laetrile even abroad, and a clear explanation of just what is meant by effective is elusive. Many respected cancer researchers view these claims of effectiveness with skepticism—often Laetrile patients are taking other anticancer drugs as well—and consider Laetrile's supporters disreputable scientists who raise false hopes in their patients. Defenders of Laetrile counter that traditional forms of cancer therapy are hardly ideal and that their drug cannot do any harm.

In the last few years, however, one investigator of some reputation has entered the Laetrile controversy, throwing his weight behind demands that it be allowed a clinical trial in the United States. The maverick, who has so far failed to win his colleagues' support in the matter, is Dr. Dean Burk, head of the cytochemistry section of the National Cancer Institute in Bethesda, Md.

NCI

Dr. Burk: Laetrile deserves a try.

Dr. Burk claims neither that Laetrile is a cure for cancer nor that he, personally, has data substantiating claims of its effectiveness. But on the basis of what claims there are that it works, and on his own studies of its toxicity, he says, "The stuff is absolutely harmless, so why not give it a try?" It is, he claims, no more dangerous than sugar and could be taken daily as a prophylactic—like a vitamin.

Dr. Burk administered 150,000 milligrams per kilo of body weight to tumor-bearing mice for a three-month period. At the end of the experiment, all the mice were alive, leading him to conclude that, "If they live that long on such massive doses of drug, they're pretty healthy."

Admittedly, he has no data indicating that these large doses of Laetrile induced tumor regression. Nor did he perform what traditional toxicologists consider crucial examinations of body tissues, such as liver and kidney, to determine whether Laetrile induced cell damage. He stands on his statement: The fact that the animals were still alive is evidence that Laetrile does no harm.

Officials of the National Cancer Institute, somewhat embarrassed by a colleague who they declare has no special scientific competence in toxicology or pharmacology, have indicated that regardless of FDA's final decision in the Laetrile matter, the drug will not be tested on their cancer patients.

In a statement prepared for SCIENCE NEWS, Dr. Carl G. Baker, newly appointed director of the Cancer Institute, says: "Dr. Burk's views and recommendations concerning Laetrile do not reflect the position of the Institute. At this point, as previously, the Institute does not feel that there is a scientific, ethical or legal basis for

recommending the clinical use of Laetrile. . . . The experimental results reported by Dr. Burk, while of interest, have no implications in respect to the advantages, disadvantages or desirability of the clinical use of Laetrile."

In addition to his toxicity studies, Dr. Burk reports work showing that Laetrile, which is a combination of cyanide, benzyaldehyde and sugar, selectively kills cancer cells of virtually all types, possibly because those cells lack an unspecified enzyme that protects normal cells from the effects of cyanide. Laetrile itself, he says, is broken down in the body by the enzyme betaglucosidase.

According to Dr. Burk, the existence of enzymatic differences between normal and cancerous cells is theory, not a phenomenon he puts forward as fact. Charging the FDA with being unfair in its handling of the Laetrile application, he cites the fact that the agency declared IND 6734 deficient in part because the theory of mechanism is inadequately decumented. Conceding that mechanism is not proved, Dr. Burk rightly points out that FDA frequently approves drugs whose mechanism of action is not precisely known. Aspirin, penicillin and tranquilizers are among compounds approved without prior specific knowledge of their mechanism of action.

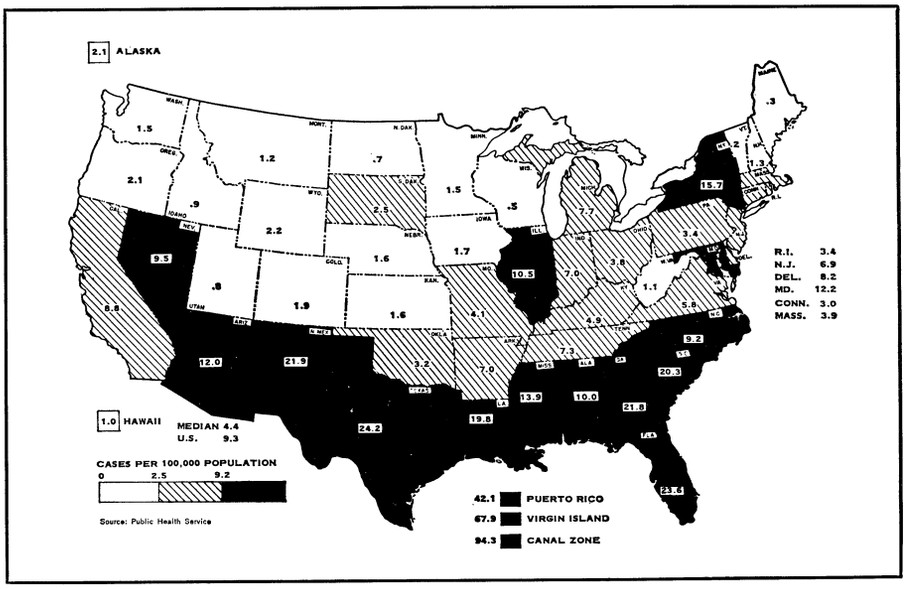
While the arguments are being weighed by the FDA, Laetrile is, at present, in limbo. Its use now is illegal, but until the agency brings forth a verdict on the supplementary data submitted in May, its proponents continue to hope for approval. Says Dr. Henry Simmons, director of FDA's Bureau of Drugs, "In this country Laetrile has not had its day in court and I intend to see that it gets it if the evidence justifies it. That is the law."

By way of explanation of FDA's initial granting of an IND number, Dr. Simmons says that the application first submitted by the McNaughton Foundation looked acceptable; that is, it followed the prescribed form and appeared to contain data covering the essential scientific questions and protocols for human trials. On second glance, FDA changed its mind.

In the past, when a scientist received an IND number for his application for a new drug study, he was automatically free to begin work. Partly as a result of the Laetrile fiasco, FDA is altering that policy and a new regulation has been promulgated. In the future, assignment of an IND number will carry with it a 30-day hold, giving the FDA time to scrutinize applications for clear deficiencies before work begins. After that time, when the agency undertakes a serious and careful review of the application, INDs can still be terminated if defects are uncovered. □

VENEREAL DISEASE

In epidemic proportions



The incidence of syphilis in the United States is rising dramatically.

The advent of penicillin in the 1940's lulled many authorities into a complacent state regarding venereal disease. For the first time, syphilis and gonorrhea could be cured; gonorrhea, in some circles, even acquired a reputation for being no worse than a bad cold. Clearly, this is untrue. Both syphilis and gonorrhea, transmitted by sexual contact, have serious, even fatal effects. And the incidence of both of these infectious diseases is on the rise.

According to a study released by the American Social Health Association, the incidence of syphilis in the United States in June of this year was 27.3 percent higher than it was in June 1969. In a year's time, the syphilis rate in New Jersey rose 55.3 percent; in Georgia it was up 28.5 percent; in California, up 20.5 percent, giving those three states the dubious distinction of having the highest increase-rates in the country. Nationwide, the incidence of reported cases of gonorrhea has jumped 15 percent in the last year. As with syphilis, epidemiologists agree that the actual incidence of venereal disease is even higher because many cases go either undetected or unreported by practicing physicians.

According to Dr. James McKenzie-Pollock, venereal disease director of the ASHA, "During the last months of the fiscal year, the increase of syphilis has been so dramatic that national emergency action is needed." Such action, he declares, could be provided if Congress passes legislation slated to go up for a vote within the next few weeks. Sponsored by Rep. Paul Rogers (D-Fla.), it would give cities and states funds to be used specifically for communicable disease programs—$75 million in fiscal 1971 and $90 million in fiscal 1972. Chances of passage are estimated to be 50-50.

In its VD report, the ASHA, with the backing of the American Public Health Association and the American Venereal Disease Association, called on the Secretary of the Department of Health, Education and Welfare to appoint a group to develop a national program for the control of venereal disease, emphasizing prevention through education and improved efforts at diagnosis and treatment.

Though transmitted in the same way, syphilis and gonorrhea are distinct diseases. Syphilis, caused by a spiral-shaped organism, *Treponema pallidum*, first manifests itself, between 10 days and 10 weeks after infection, by sores which disappear slowly even if the patient is untreated. The organism, however, remains in the body, causing, after 10 years or more, damage to blood vessels, the brain, heart, eyes and other organs.

Gonorrhea's symptoms include burning at urination and a discharge of pus, usually apparent in males but sometimes undetected in females. Ultimately the infection can lead to sterility, arthritis and heart disease, among other disorders. Both syphilis and gonorrhea can be passed from a mother to her unborn child.

The ever-increasing mobility of the population and relaxed sexual mores are cited by public health officials as the causes of the epidemic of venereal diseases. These same factors, Dr. McKenzie-Pollack says make control extremely difficult. □