ting Legionnaires' disease and the amount of time spent in the Bellevue's lobby, or drinking water in that hotel. But it's just a correlation and none of the evidence fits all of the cases, or even most. The disease was more likely to strike those who are older and who have some preexisting heart or lung condition, but that is no surprise.

The possibility that Legionnaires' disease was no accident has been raised and everyone concedes that it could have been sabotage. Murphy, at the Congressional hearing, expects testimony to the effect that if it were deliberate, a protein extract of castor beans called ricin, that was studied by the military, would be a candidate. But no one has any evidence that it was sabotage, and no one can prove that it was not.

It is logical to ask what one would do if a situation like this developed again. What would happen next time? CDC has said that it would like more money to beef up its capabilities in toxicology, but there is apparently no strong feeling that substantial changes in procedure are in order. But surely there will be suggestions and, for a while at least, pressure from the outside for plans to preclude another such epidemic from slipping away unapprehended.

Telephone interviews with individuals who have been asked to testify at the hearing provided *Science* with an indication of what those suggestions will be. First and foremost, of course, is the idea that epidemiologists must in the future take toxins into account from the start. Another is that one should call immediately on the expertise of the FBI, the CIA, and the army's authorities on biological and chemical warfare. A representative of the Armed Forces Institute of Pathology will suggest that it routinely be considered as a source of expert advice on toxicology and data analysis. And Murphy himself is reported to be thinking about establishing some central authority, perhaps in the office of the secretary of Health, Education, and Welfare, to coordinate the activities of several relevant agencies and oversee the whole show.

"Thinking toxicology" certainly makes sense, not just in anticipation of some mysterious epidemic but also in terms of the broad relationship between environmental chemicals and health. But it is not immediately obvious that a massive legislative effort for bureaucratic reorganization is needed, because it is possible that even if this investigation had gone off without a single hitch, the mystery would remain. As Dull says quite aptly, "It is just so hard to accept the fact that in 1976 there are some things we don't know."

—BARBARA J. CULLITON

Amphetamines: Tighter Controls on the Horizon

The abuse of the central nervous system stimulants known as amphetamines has dropped since "speed" had its heyday in the 1960's. But amphetamine abuse is still a major problem in terms of physical damage and emotional dependency. And despite the fact that manufacture and distribution of the most dangerous varieties of the drug have been under strict federal controls since 1971, it still seems to be available to anyone who wants it.

That's what Senator Gaylord Nelson (D–Wis.), chairman of the monopoly subcommittee of the Senate Small Business Committee, heard in 5 days of hearings he conducted last month on the safety and efficacy of antiobesity drugs.

The major condition for which amphetamines and ampetamine-like drugs (amphetamine congeners) are legally prescribed is obesity. But the evidence is strong that for most of the 2.25 million Americans estimated regularly to take prescribed amphetamines—not to mention uncounted users who buy them on the street—the drugs are not primarily being used for legitimate medical purposes.

It has been 6 years since Congress passed the Controlled Substances Act, which enabled the government to put restrictions on the production and distribution of licit drugs that are subject to abuse. Amphetamines and their congeners are controlled under the law, which has sharply reduced prescriptions of the formulations thought to be most dangerous. But the act seems to have reached the limits of its effectiveness, because the level of amphetamine consumption, according to Food and Drug Administration (FDA) statistics, has remained constant over the past 3 years. Furthermore, consumption of amphetamine-like drugs has gone up and there are many experts who believe their potential for abuse is almost as great as it is for amphetamines.

This phenomenon, combined with accumulating evidence to the effect that diet pills are of marginal use in combating fat, has led Nelson to conclude that, according to an aide, "the time is ripe" for amphetamines to be wiped off the market altogether, and for stricter controls to be put on other sympathomimetic diet drugs. There remain two respectable applications for at least one amphetamine congener—Ritalin (methylphenidate)—which are narcolepsy and childhood hyperkinesis. Ritalin is not used as a diet drug but it and Preludin (whose only indication is for obesity) are said to be the most heavily abused drugs in the amphetamine family.

It has been 4 years since an FDA advisory panel concluded that amphetamine-type diet drugs were "clinically trivial." The preponderance of testimony from nongovernment witnesses at the hearings was to the effect that the drugs are neither safe nor efficacious. They curb appetite for a short time, but tolerance is quickly built, and if the pills are withdrawn the appetite returns in full force. Tentative evidence was also presented that these pills taken in the early weeks of pregnancy may cause fetal heart defects and other malformations.

Now, judging from what government witnesses said at the hearings, it appears that the FDA and the Drug Enforcement Administration (DEA) are getting ready to agree that the abuse potential of many of these drugs outweighs whatever short-term benefits they have in helping obese people change their eating habits.

As J. Richard Crout, director of the FDA's Bureau of Drugs, testified, in view of the failure of the Controlled Substances Act to minimize abuse, "the only meaningful next step which can be taken is to remove the indication for obesity from the labeling for amphetamines or to remove them from the market." Since obesity is the only indication for some, changing the label would be tantamount to outlawing them altogether.

It has been more than a dozen years since various groups, including members of Congress, have been attempting to

curb or even ban entirely the marketing of anorectic (appetite-suppressing) drugs. But the success has been limited in the face of dedicated resistance on the part of pharmaceutical manufacturers—amphetamines and their relatives are the backbone of the diet pill business—and undiscriminating prescription practices on the part of some physicians—all catering to voracious public demand for fast-acting means to thinness and happiness.

The 1970 act sharply reduced production of diet pills—which reached an all-time high of 12 billion in 1971—by putting the most dangerous substances, amphetamine, methamphetamine, and phenmetrazine (otherwise known as Preludin) on Schedule II of the Controlled Substances Act. This is the most restrictive category for licit drugs. It lays down production quotas, requires detailed monitoring and record-keeping, and forbids renewal of a prescription without a physician's approval. Other amphetamine-like drugs were put on Schedules III and IV, a move that recognizes their abuse potential but doesn't restrict distribution other than through prescription requirements.

The regulatory problem has become increasingly complex in recent years as companies have come out with new drugs that are amphetamine-like in varying degrees. Some of these have been put on Schedule III or IV even though their abuse potential would seem to warrant tighter restrictions. For example, Pennwalt Corporation, the country's biggest manufacturer of diet pills, rechanneled its energies to marketing a drug called Ionamin after its big seller, Biphetamine, was put on Schedule II. Pennwalt claims that Ionamin is not an amphetamine and does not have the associated side effects. Lester Grinspoon, psychiatrist at Massachusetts Mental Health Center and the lead-off witness at the Nelson hearings, says, however, that the chemical structure is similar to amphetamine, and any minor chemical change is unlikely to change the drug's action much. [There is a class of amphetamine-like compounds that exert effects that are more sedative than stimulant, and sometimes hallucinogenic. Fenfluramine (marketed as Pondimin) is an example. These are not subject to much abuse, but neither is their anorectic value clearly established.] The fact is, say Grinspoon and others, the search for a drug that reduces appetite without producing the side effects characteristic of amphetamine has met with failure. (He says the situation is analogous to what happened when researchers tried to synthesize a nonaddicting opiate analgesic. The "hero" drug they came up with in 1898 was named heroin.)

There is a distinct division of opinion on this matter. Government officials believe some congeners are reasonably safe and Crout said, "I suspect a strong safety case against the nonamphetamines can't be made at this time." The best supporting data for their low addiction potential are government statistics showing that, indeed, Schedule II drugs are much more widely and heavily abused than those subjected to more lenient controls.

The popularity of amphetamines and their sympathomimetic relatives has been phenomenal since they first became available in pill form in the 1950's. And, says Grinspoon, "there's been nothing like this in the way it's been embraced by the medical profession and pushed by industry."

According to testimony of Frederick A. Rody, Jr., of the DEA, some pharmaceutical companies have raised strenuous resistance to having their drugs more tightly controlled, even in the face of massive abuse of their product. Some have asked for an expansion of their production quotas to meet expected demand, said Rody, even though the demand projections were considerably higher than DEA estimates of legitimate medical need.

Rody related how one company, Pennwalt Corporation, responded to forthcoming restrictions on its amphetamine drug Biphetamine. Just before it was put into Schedule II, the company exported large quantities of the raw materials to its subsidiary in Mexico City. There the stuff was encapsulated, under the name Bifetamina, presumably for sale in Mexico. So much of the substance was smuggled back into the United States and sold on the black market that DEA had to mount a special operation, "Operation Blackjack," to clamp down on the traffic. Subsequently, under pressure from DEA, Pennwalt agreed to get out of the amphetamine export business. But then, in what a DEA agent called a "deadly parallel" to the Biphetamine episode, Pennwalt has exported over the past 2 years 600 kilograms of the bulk powder from which Ionamin (a Schedule IV drug) is manufactured—enough for 20 to 40 million pills. There has recently been found to be heavy trafficking and abuse of "Ionamina" in states adjacent to the Mexican border. "Discussions" with DEA have recently been held, and Pennwalt has now agreed to stop shipments of Ionamin powder to Mexico.

The president of Pennwalt's pharmaceutical division, Isaac R. McGraw, defended his company, saying it had always scrupulously obeyed the law and eagerly cooperated with the government. "We do not believe there is any probative evidence that our anti-obesity products show any meaningful statistical or other factual evidence of abuse," testified McGraw. And, "Pennwalt is not aware of any significant illegal use of its anti-obesity products."

Other witnesses, including those dealing with street level addicts, in fact agreed that most "uppers" are obtained through legal channels. Rody said illicit manufacture and diversion of the drugs is on the decrease, so the increasing availability of supplies are created "largely by prescriptions and direct dispensing by physicians," who are apparently "prescribing and dispensing well over the patients' actual medical needs." Such practitioners include the small but notorious handful of "fat doctors" in Long Island who, witnesses said, minister to the needs of 800 to 1200 people a week, very few of whom are fat.

The American Medical Association has not tried very hard to curb such practices, according to Grinspoon. AMA spokesman Frank Chapple says its manual, *AMA Drug Evaluations*, recommends against prescribing amphetamines and like substances for weight control, but that otherwise the organization is not preoccupied with the problem. The AMA disbanded its Council on Drugs in 1971 after that body issued a strong warning about amphetamines, and Grinspoon notes that it has generally tried to avoid offending the drug industry, which, he estimates, is supplying over half the AMA budget with $15 million worth of drug advertising a year.

Grinspoon believes a total ban on amphetamine-like substances—such as has been enacted in Sweden and Japan—is unfeasible. The stuff is too easy to manufacture illicitly and, as with Prohibition, it just wouldn't work. Frank Reynolds, director of Teen Challenge Youth Centers and another witness at the Nelson hearings, deals with drug problems at the street level. From his vantage point neither prohibition nor tighter restrictions on drugs are going to make much of a dent on the problem so long as the belief prevails from Park Avenue to the ghetto that if you have a problem you solve it with a pill. The technological approach to solving human problems was implicitly confirmed by other witnesses who persisted in referring to obesity as a "disease." Obesity is a condition, and for most people it is no more a "disease" than is loneliness or any of the other emotional factors that cause people to overeat.

—CONSTANCE HOLDEN