much easier to sequence than RNA, this provides an easy way to obtain RNA sequences.

Tom Maniatis of Harvard University and, independently, Nina Fedoroff of the Carnegie Institute of Washington in Baltimore, are developing a modification of the enzymatic method of Sanger and Coulson for the direct sequencing of restriction enzyme fragments. Maniatis has obtained relatively large quantities of the hemoglobin gene by molecular cloning methods (*Science*, 19 March 1976, page 1160), and is now sequencing regions of this gene that are not transcribed into protein. He and his associates are also sequencing another class of DNA sequences —the satellite (small DNA) sequences— that do not consist of genes and that are present in huge amounts in cells of higher organisms. Winston Salser and his associates at the University of California at Los Angeles are using the chemical method to sequence the hemoglobin gene and satellite sequences. Salser, Randolph Wall, and their colleagues are, in addition, cloning and sequencing immunoglobulin genes. Fedoroff is sequencing the control regions of a set of genes, the 5*S* ribosomal RNA genes, that are repeated many times in cells of toads. Other investigators are now beginning to sequence nearly any DNA that they can obtain in large amounts.

The new interest in DNA sequencing does not mean that RNA sequences are no longer of interest. Since RNA molecules carry important biological information, work on their sequences is continuing unabated at a number of laboratories. However, because DNA sequencing is now so extremely simple the direction of research in molecular biology will surely change. Useful information can now be quickly gathered—information that a few years ago investigators had little hope of gathering.

—GINA BARI KOLATA

Marihuana: A Conversation with NIDA's Robert L. DuPont

Robert L. DuPont, director of the National Institute on Drug Abuse (NIDA), made headlines recently when he became one of the first Administration officials publicly to recommend a liberalization of marihuana laws. The occasion was a press conference accompanying the release of *Marihuana and Health*, NIDA's fifth annual report to the Congress on marihuana research. Recently, *Science* talked with DuPont and asked him to elaborate on those views.

DuPont, a 40-year-old Harvard M.D., served as Director of the District of Columbia's Narcotics Treatment Administration from 1970 to 1973, where he conducted a comprehensive program for treatment of heroin addiction. In June 1973, Richard Nixon appointed him director of the White House Special Action Office for Drug Abuse Prevention. He held that position until the office was terminated on 30 June 1975. He has been director of NIDA since September 1973.—THOMAS H. MAUGH II

How would you summarize the new report to the Congress?

I think that it is hard to summarize. People are looking for simple statements that marihuana is safe or that it is dangerous, and the report defies that kind of summary. But there is a broad range of biological concerns reflected in the report, from the decrease in testosterone levels and effects on cell-mediated immunity to bronchitis and the potential for cancer. There is a growing concern about the seriousness of these negative health effects—although they are something less than has been searched for by many, such as some tremendous evidence that marihuana users' ears fall off or that their noses turn green, or something like that. Also, we have overlooked the problems of marihuana intoxication in the past. They are related most urgently to driving performance, but they are also related to work performance, to studying, and to interpersonal relations—to the activities where, we are aware, most of the problems of alcohol are concentrated. We've just ignored that in the past discussion of marihuana's health hazards.

Is the pattern of marihuana use changing?

There is evidence not merely of more widespread use, but of much more frequent use. This is highlighted in the report. Those people who do use marihuana tend to use it more frequently than most of us thought. In a study of high school seniors who used marihuana at the time of the survey, 23 percent of the user group reported daily use. Now that's different from alcohol, where the equivalent figure was about 9 percent. It suggests that there is a tendency to more frequent use if there is any use. I've talked to many marihuana users who report that they have to make an effort to limit their use—and it is not all that easy for many people to do that. In this way marihuana use is more like cigarette smoking than it is like alcohol. And I think we've been, perhaps, misled, or have misled ourselves, into thinking that there is not a very large potential for a lot of people to be on the very heavy use end of the spectrum.

Is the potency of street marihuana changing?

There has been a tendency toward rising potency levels. The conventional wisdom is that marihuana is of low potency—often said to be less than 1 percent THC [tetrahydrocannabinol]—and that the THC content of hashish is around 10 percent. But more recent evidence suggests that much marihuana in the United States has 2 or 3 percent THC and that most hashish is down around 4 or 5 percent; so the distinction between marihuana and hashish is not as great as people had thought. And there is good reason to believe that we're going to have marihuana in the potency range of 5 or 6 percent in the near future.

Is the more potent form potentially more hazardous?

Of course, all the effects are exaggerated with the more potent form. But the most important effect is an increased likelihood of having an acute adverse reaction—a panic reaction. But that's largely compensated for by the experience of the user.

Are marihuana use and alcohol use mutually exclusive?

The old idea was that somehow marihuana was *replacing* alcohol for young people—that if people used one, they wouldn't use the other. The argument was that marihuana is a safer drug than alcohol so, therefore, let them smoke pot. All of the available evidence, unfortunately, cuts the other way. It suggests that people who use alcohol are more likely to use marihuana and that people who use marihuana are more likely to use alcohol. So what we have is a drug-using behavior, particularly as exemplified in the two most common intoxicating substances, marihuana and alcohol, advancing as a front rather than moving like two ends of a teeter-totter. The effects on driving appear to be partic-

ularly disastrous when these two drugs are used together. The driver's ability to compensate for the deficits associated with one of these substances appears to involve mental mechanisms that are distorted by the other substance. So the driving performance deteriorates very rapidly at relatively low levels of simultaneous use of the two.

There has been some controversy lately about a study on marihuana and sex. What is that study?

It is a very complex study to be conducted at Carbondale, Illinois. Basically, what we're interested in is whether—as is the case with alcohol—there is a negative effect on sexual responding associated with marihuana use. We want to learn more about the biological effects of marihuana. That's an important part of our overall marihuana research strategy. Then if negative effects should be found, it might have a deterrent effect in terms of marihuana consumption.

How did this study become notorious?

It was singled out by Senator William Proxmire [D–Wis.] last summer around the issue of waste. He picked five studies, but this is the one that got the media coverage. Then it was picked up on the issue of offensiveness to community standards—the whole business of giving pot to college students and showing them pornography. That issue has had a life of its own, and Congressman Robert Michel [R–Ill.] has become the focal point. He has now inserted into the House appropriations bill language denying HEW [Department of Health, Education, and Welfare] the right to fund that program this year. But there have been meetings of various scientific groups within HEW and NIDA and we've supported going ahead with the project [unless the law specifically forbids it].

Should the laws reflect the potential hazards of marihuana?

It is very important to separate the legal and the medical problems. There has been a tendency for people in both areas to look to the other area for solutions to their problems. For example, many people who are dealing with marihuana laws look to the scientific evidence for a solution to their dilemmas. I have discouraged that and suggested that legislators are not going to hear from the scientists anything, ever, that is going to resolve the problem for them. It will never happen.

What I do think, though, is that legislators need to recognize that marihuana is a substance in widespread use now, and that it does pose some important health hazards. Of course, then what do you do about it? My impression is that the debate on the legal side has narrowed tremendously and that the only question now before us is this: When a marihuana user—not a seller, but a user—comes in contact with law enforcement officials, what happens to him? And I would say that on the hard line, if you will, the anti-marihuana line, the argument is that he ought to be put on probation or some such thing. But there is no support, not even on the hardline side, for putting the

Reassurance from Foreign Studies

The only extensive studies of long-term use of marihuana have been conducted in Jamaica, Costa Rica, and Greece. Only the Jamaica results have been published so far,* but preliminary results from the other two studies are summarized in *Marihuana and Health*. Thirty marihuana users were studied in Jamaica, 41 in Costa Rica, and 47 in Greece. All three studies produced roughly similar results.

The investigators found few physiological differences between marihuana users and the control group. There was no evidence, for example, of impairment of the heart, liver, or kidney. There was also no evidence of chromosomal abnormalities, although there may have been technical deficiencies in the methods used to determine this. In the Jamaican studies, the only apparent physiological differences between the users and the controls were modest decreases in lung function and slight alterations in hemoglobin levels among the users; both these changes might result from tobacco use.

After smoking marihuana, subjects in the Jamaica study produced less work—weeding, hoeing, and digging—than normal with more movements; but there was no other evidence of the so-called amotivation syndrome. Other differences between Jamaican and American users were also apparent. The Jamaican subjects, for example, reported no increase in appetite, no enhancement of hearing, and no alteration of time sense after marihuana use. Most of the subjects said they used marihuana simply to work better.

Studies by many techniques, such as electroencephalograms and echo-electroencephalograms, in both Costa Rica and Greece indicated that there were no physical deterioration or mental abnormalities of the brains of marihuana users. Unpleasant psychological symptoms did develop in many of the users, however, when they were given doses of tetrahydrocannabinol higher than their normal tolerance levels. The investigators in Greece also observed a slightly higher incidence of personality disorders among hashish users, but concluded that these were more related to psychosocial variables than to marihuana use.

These findings have been very reassuring to marihuana proponents since they indicate that there are no major health problems that affect all users. But the findings should not be overinterpreted to indicate that there are no hazards. The findings have been derived from studies on a small group of carefully selected users, so that the chances are good that rare consequences such as brain atrophy or psychosis might not have been detected if they did occur. The subjects, furthermore, were laborers and farmers in cultures where intellectual impairment would be difficult to detect with standard U.S. tests.

The only conclusive way to determine whether deleterious effects are associated with long-term marihuana use would be a large-scale prospective study, conducted in the United States, similar to those which identified the determinants of heart disease and the hazards of tobacco. The National Institute on Drug Abuse is working with its consultants to design such a study, but it will be at least a year before they have developed a comprehensive plan. Implementation of such a study would probably require at least a $2-million increase in NIDA's budget for marihuana research, so Congress would probably have to approve the plan. It will thus be at least 2 years before such a study could begin and at least five more years before any results could be obtained.—T.H.M.

*V. Rubin and L. Comitas, *Ganja in Jamaica: A Medical Anthropological Study of Chronic Marihuana Use* (Mouton, The Hague, 1975).

typical marihuana user in prison. On the soft side, to continue that analogy, the argument is that the user ought to get a fine, some kind of noncriminal fine, to let him know that society considers this to be undesirable behavior. Now my argument is that there is not a very wide margin between those two points of view, and the fact that the debate has narrowed down that much, I think, is a measure of the progress that has been made in clarifying the issues. It's interesting how much effort is now going into compromising those two narrowly different points of view in state capitals all over the country. Personally, my view is that we do not need to threaten young people with imprisonment to discourage their use of marihuana.

Have political concerns influenced your opinions on this?

I have experienced remarkably few political pressures. First of all, I couldn't say the things I have said under President Nixon. He really felt very strongly, personally, about this subject and it was not possible to make statements like this and work for him. Gerald Ford has been much more open to the expression of a wider range of opinions on a variety of subjects. I've had no pressure about taking back anything I've said, for example, even when my views have been publicly contrasted with the President's own position. I suspect that President Ford is familiar with a fair range of opinions on marihuana even within his family. This may partly explain his tolerance to different points of view on this issue. But it needs to be clearly understood, and it often isn't understood, that I am not speaking for the President on the subject. I'm speaking for me. The concern is that, when headlines reflect my statements, it makes political people very anxious, and the walls shake a little bit. But I haven't had any negative reactions.

Some people thought you were prepared to recommend liberalization of marihuana laws 2 years ago at a meeting of the National Organization for the Reform of Marihuana Laws (NORML), but that pressure from the White House stopped you.

My White House superiors had some suggestions for language changes as that speech went through several drafts. But these suggestions—which I accepted—were quite minor. I must say, the idea that I had thought this through in some definitive fashion for the NORML speech doesn't entirely describe reality. Frankly, I've done a lot of thinking about the national marihuana policy since the NORML speech, and I believe I am clearer about it in my thinking than I was then. I have not been a very daring person, in terms of my view on marihuana. I'm really very conservative about it, and I'm about as down on marihuana use as it is possible to be. I don't want to do anything to encourage its use. The problem is to find ways to discourage marihuana use which are not themselves as destructive as the marihuana use they are designed to discourage. I'm not a pro-drug kind of person, but the NORML people see me as something of an avant garde, flaming liberal on the subject in comparison to other people in the government.

Many people think that the recently published Jamaica study (see box) has shown that there are no health hazards associated with marihuana. True?

Well, I would have to put the Jamaican, the Costa Rican, and the Greek studies together; 117 people were studied in all three. It's a pretty small pool of subjects. The studies were important because they show that there aren't major health consequences that occur in a high percentage of chronic users of marihuana. But they are terribly limited studies. They were studies in less complex, more traditional societies. They were studies where people who had many of the health problems which might have been related to marihuana use were excluded through the sample selection process. If a chronic user had a serious health problem, he might have been excluded because we wanted to study fairly healthy people. We did this to eliminate contaminating variables, but it is possible that this process excluded some people who had negative health consequences of marihuana use. I'm not at all sure that if you took alcohol and tobacco and put them to the same test that they would show up bad either. But that's where we are in terms of those studies, so I think there has been a problem of overinterpreting those initial studies as showing that there are no serious health problems associated with marihuana use. That has been unfortunate.

Then why do such studies?

Because they narrow the parameters for the discussion. It's no longer credible to say that *all* marihuana smokers have an x or y negative health outcome. That's a limited but valuable finding.

Why should we worry about health problems that might affect only some users?

We have, as a nation, intellectual scales that we'll put issues into to try to weigh them. The scales on which we put recreational drugs are quite unique. They go something like this, as far as I can understand it: If 20 or 30 percent of the people who use a substance do not die within 1 year, it is a pretty safe substance and, therefore, we say that a person should have freedom of choice about whether or not he uses it. If he doesn't hurt anybody but himself, it's up to him to decide. Then we've got another scale that the people at FDA [Food and Drug Administration] just down the road have for pharmaceutical products. And that scale says that if three mice out of a thousand die of cancer when exposed to a substance, well, heck, you pull the darn thing right off the market. Never mind having any evidence of human toxicity whatsoever. We don't give people a choice of whether they want to use cyclamates in the United States. And I find this disparity between how the same people—liberal, right-thinking, progressive souls—in our country want to relax our prohibition against marihuana and, at the same time, increase our prohibition against cyclamates or red dye No. 2 or birth control pills, to be intellectually curious at best. I think we've got to get the two scales closer together before we can be realistic on either side.

Do you think marihuana is being emphasized to the detriment of other problems of drug abuse?

I used to think that it was. The first 5 years of my involvement in the drug field, I considered the marihuana issue a joke. But I have turned around completely on that subject. It's now clear to me that the leading edge of change in drug-using behavior for the American population—and I think this is true worldwide—is marihuana. Drug use is spreading very rapidly. We're now talking about 13 million regular marihuana users in the United States. When I think about how many people are exposed. . . . In the 18-to-25 age group, for example, 53 percent have used marihuana. Well, that's fantastic! I'll give you another figure that, to me, is incredible: 6.2 percent of last year's high school graduating class reported daily use of marihuana. That's 0.2 percent more than reported daily alcohol use. That level of exposure in our population, to me, merits the very greatest concern. The questions about the health consequences of marihuana use are of major importance. For example, if we were to find out that marihuana was associated with some major health problem, every year that goes by before we find out exposes millions of people to the substance. So I think it's very important to keep the priority.