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TO: HON. Mr. Justice Woodward, Commissioner  
Royal Commission into Drug Trafficking  
New South Wales

FROM: Max Fink, M.D.  
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I am pleased to respond to the invitation to discuss my experience with dependence producing drugs to assist the Commission in its recommendations regarding the trafficking of proscribed drugs. My experience is based on a six year study of the pharmacologic effects of cannabis and cannabis derivatives, both in volunteers in the U.S. and in chronic users in Athens, Greece. I have also studied the efficacy of narcotic antagonists in the treatment of opiate dependence. In these studies, begun in 1966 and continued to 1973, I have administered heroin, methadone and levomethadyl to opiate dependent subjects; and examined the pharmacologic effects and interactions of the narcotic antagonists cyclazocine and naloxone with opioids.

I am Professor of Psychiatry at the School of Medicine at the State University of New York at Stony Brook. At the time of the studies discussed today, I was Professor of Psychiatry and Director, Division of Biological Psychiatry at the New York Medical College; and a consultant to the National Commission on Marihuana and Drug Abuse, the Veterans Administration, and the National Institute on Drug Abuse.

At this time permit me to make a number of generalizations about the pharmacology of these compounds. There is an important distinction between opioids and cannabis which is immediately apparent in the studies. The administration of the opioids, even under controlled conditions, is fraught with risk. Our subjects have fallen into stupor and evinced grand mal convulsions after dosages of heroin which we deemed safe for the individual. Seizures occurred in three subjects, a finding that was sufficiently striking for us to report it in the scientific literature. In my clinical experience, three patients died on our wards after opiate overdoses. In two instances, we had made the proper diagnosis and administered naloxone, a proper narcotic antagonist. But our dosages were not sustained with sufficient frequency and the subjects died during the night. A third instance, a young man who had been detoxified by decreasing doses of methadone was drug-free on our ward. He was to be discharged the next day. A visitor passed him some heroin which he injected that night. The dose was higher than he anticipated (or his tolerance had been reduced by our treatment) and he died during the night, on a medical service.

Such tales are common. There was a time, when the methadone programs in New York were still new, that we read of a methadone death almost every day in the city. It was said then that the likelihood of a young addict achieving the age of 30 if he were taking opioids at the age of 21 was less than one in ten.

By contrast, we have found cannabis to be relatively benign. We have reported the central nervous system effects in its administration as well as the development of tissue tolerance; but the principal effects

in the cardiovascular and nervous systems are well tolerated, well within the ability of most subjects to accept and survive.

For this difference alone, the response of Society to cannabis ought to be different than the response to opioids.

In the studies of long term users of hashish in Athens, we were struck by their focussed interest on cannabis (hashish). Despite the fact that they had used hashish for more than 20 years, their interest in and experimentation with opioids was insignificant. They did smoke tobacco in large quantities and did use alcohol. In no instance were we able to document the combined use of hashish and opioids. While such observations are not compelling, they do suggest that the connection between opioids and cannabis is probably not inherent in the pharmacology of the drugs, but in the propinquity of the distribution systems. If one is looking for a synergistic use of drugs, we can suggest that cannabis and tobacco are clearly used together by long-term users.

Perhaps the most interesting studies are those with narcotic antagonists. When I first became acquainted with the subject of opiate dependence, four competing theories of treatment were current: abstinence after detoxification, abstinence in the framework of group therapy, cross tolerance to methadone, and blockade by narcotic antagonists, chiefly cyclazocine. Abstinence after detoxification was a temporary expedient with an unacceptable relapse rate; abstinence in a group therapy setting was helpful to a very small sample of users and very expensive to implement. The principal treatments were methadone and the narcotic antagonists. Working with methadone and its long acting analog, levomethadyl, I found these regimens of limited usefulness. Proper use of methadone did not preclude the use of other drugs such as opiates, barbiturates, alcohol,

and cocaine, and these drugs were used extensively. Spillage of methadone into the community was an additional source of opioid deaths and dependence. We did find methadone and levomethadyl substitution useful in some patients, but our successes were few --- too few to be gratifying or to be considered a success in relation to our costs. Our greatest energy was dedicated to cyclazocine therapy, which I thought was a logical treatment and prophylaxis. In this regimen, patients are first detoxified and after a few days in a drug-free state, are gradually introduced to single daily doses of cyclazocine. This narcotic antagonist has a long duration of action and after a few weeks, single doses of four to five mg are sufficient to block the effects of up to 25 mg heroin for more than 24 hours. Thus, patients who are on a maintenance dose of cyclazocine have no euphoria or sense of well being after heroin and we believed that this negative reinforcement would lead to disuse of heroin and eventually to an end of dependence. But we found many problems with the treatment, the principal one being the need for voluntary compliance by the subject --- he must take the medication daily for a number of years, and few patients are so cooperative as to complete a satisfactory treatment course. Lately, other antagonists have been studied, the best known being naltrexone, which is safer and easier to use than cyclazocine. The reason for raising the question of the antagonists is the perspective they give to the medical management of opiate dependence -- there are ways to treat dependent subjects but each method ultimately depends on the cooperation of the subject, something that is difficult to achieve.

These experiences with users have made me pessimistic about our ability to solve the opiate dependence problems by present medical or legal means. Opiates are dangerous substances and they should be

controlled in their distribution. One wonders, however, whether driving users to the streets has been successful, and whether relaxing controls for greater medical usage may not have some benefits. I am acquainted by reading only with the mixed picture presented by the English regulations for the use of opioids, and despite their difficulty, on balance I think that ~~they~~ they are more sensible than the laws in New York, where physicians are enjoined from using opioids other than for methadone maintenance in established clinics. I think the present rules have driven most practitioners away from any experience with opioids and made most users dependent on the illicit marketplace.

Finally, the most extensive experience I have had is with chronic users of hashish in Athens. There, a team of scientists from the New York Medical College and the University of Athens worked together to study a group of 47 hashish users and a matched sample of controls. The users were the survivors of a larger sample of chronic users of hashish which was known to the scientists at the University of Athens at the end of the second World War. We found that the users showed little evidence of toxicity -- they were no different from controls in medical or neurologic status, or in tests of brain function. There were some differences in psychologic tests which seemed related to their education. But they were individuals we would probably classify as psychopaths -- they were willing to flaunt the law for gratification of their senses. We did find that they had developed a tolerance to the pharmacologic effects of cannabis. They could smoke hashish containing more than 150 mg THC-delta-9 and develop euphoria and cardiovascular responses no greater than the effects of 10 to 20 mg doses in our volunteers. Such doses (over 100 mg THC-delta-9) are known to cause vascular collapse in naive subjects. We attempted to demonstrate withdrawal symptoms, but

the subjects were willing only to remain under our care for three days without smoking cannabis. In this time, we could not demonstrate the classic signs of physiologic withdrawal, but then, perhaps, their very inability to cooperate was in itself a symptom of withdrawal.

The conclusions of that study were many, but the principal one was that we had failed to find evidence of toxicity for cannabis use. Similar findings in Costa Rica and Jamaica reassure us that our observations were not spurious. Further studies of this nature were reported at the conference on chronic hashish use held in 1976 at the New York Academy of Sciences (volume 282).

These are my experiences. I have lectured often on the problems of cannabis use, and I have come to believe that the greatest risk in my community from the use of cannabis is the risk of legal penalties and imprisonment. There is also a risk of other substance use, since the present distributors of cannabis are acting in defiance of the law, and they seem as willing to sell and distribute opioids, cocaine, and other abuse substances as to sell cannabis. A society which legalized alcohol and tobacco -- substances with well defined toxicity and medical risks -- should legalize cannabis as well. For consistency, proscription of cannabis should be accompanied by proscription of tobacco and alcohol; legalization of the latter two drugs should lead to the same treatment for cannabis. There is no other rational position based on the available evidence.