



# *Adverse Health Consequences of Cannabis Use*

*A Survey of Scientific Studies Published up to and  
including the Autumn of 2003*

*Jan Ramström*

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## *Foreword*

During a succession of years, there has been a discussion as to whether – or to what extent – cannabis can cause harm and dependence, and thoughts have also been advanced on the legalisation, in different guises, of cannabis use. The statements made in this context differ in terms of the solidity of their scientific foundations, which is why the National Institute of Public Health Sweden has found it important to present an overview of the range of possible harmful effects caused by cannabis use as presented today in the scientific literature.

Jan Ramström has previously compiled a similar knowledge overview. In connection with the United Nations' General Assembly Special Session (UNGASS) on drugs in 1998, that overview was published in English as well.

The report which is presented now has the same starting-points, but it includes the scientific data and findings that have come into existence since the previous survey was made. It is intended for health-care organisations, information officers such as drugs advisers and drug counsellors, and others in need of knowledge-based information on the consequences of cannabis use. The author is responsible for the interpretation of the knowledge survey presented and for the conclusions drawn from this.

*GUNNAR ÅGREN*  
*DIRECTOR-GENERAL*



## Introduction

In 1996 I compiled, as asked by the Swedish National Board of Health and Welfare, a report entitled *Skador av hasch och marijuana: En genomgång av vetenskapliga studier av skadepanoramats hos cannabis* (subsequently translated into English as *Adverse Health Consequences of Cannabis Use: A Survey of Scientific Studies into the Range of Damage to Health Caused by Cannabis*). In that report I tried to cover all that had been published up to and including February of 1996. The present version is an update covering the scientific studies published up to and including the autumn of 2003. In principle, then, this reworked version is intended to have the same structure as the previous one. In other words, the additions are not intended to form a supplement but to be integrated with the earlier material.

### *Trends over the Past Seven-Year Period*

Notwithstanding this aim, which will inform my work, the approach used and the instructions I have been given enable me to emphasise important trends and shifts that I have observed in this research field over the past seven-year period. In this context, it is important to stress that these reflections, unlike the rest of what is presented in the report, constitute my subjective impressions.

#### *Growing Interest in the Harmful Effects of Cannabis*

In the mid-1990s, there were signs that researchers' interest in cannabis-related questions was declining. When reviewing scientific reports now, however, my impression has been that, especially over the past few years, interest has increased and studies have multiplied. An attempt to quantify these trends, by means of wide-ranging searches, confirms this impression of greater activity: the number of publications has indeed grown strongly in the past few years. In 1991–1996 there were a total of 1,460 publications, whereas in the next six-year period, 1997–2002, there were 2,500. It may be added that there is no inherent automatic mechanism that will yield a constant increase in the number of studies. In the first half of the 1990s, the number of studies produced each year was more or less constant (ranging from 215 to 264). However, in the later period, the number of articles accepted for publication increases almost every year, reaching 511 in 2002 – i.e. more than twice the annual production in the first half of the 1990s. Part of this increase is presumably attributable to growing interest in medical uses of cannabis, but it is my definite impression that stronger interest in harmful effects has had an impact as well.



### *Greater Concern over the Increase in Cannabis Abuse*

As I have been reading scientific works, particularly reviews, during this later period, I have formed the impression that it is now considerably more common for authors to make concerned statements about the current situation. Three circumstances in particular tend to underpin this: first, the increase in the number of smokers, especially among the young (in certain age groups in the United States, cannabis smoking is almost as common as tobacco smoking); second, the increase in studies confirming previously suspected or proven links between cannabis and psychological or social harmful effects; and third, the increase in the THC content of cannabis preparations – an issue which is mentioned ever more frequently.

This trend among researchers and clinicians may be illustrated by two 2002 issues of scientific journals. First, one issue of the *British Medical Journal* devotes its “editorial page” to these problems and also presents four studies shedding light on this theme (Rey & Tennant, 2002). Second, *Addiction* – which is probably the world’s leading journal in this field – published a 140-page supplement on the treatment of cannabis abuse in December 2002. This supplement begins with a thorough and concerned overview of the increased number of scientific studies demonstrating the harmful effects, particularly the psychological ones, of cannabis. It then devotes thirteen articles to presenting two very large (over 1,000 patients) research projects evaluating a range of treatment approaches used within these projects (Dennis et al., 2002).

### *Increasing Demand for Treatment of Cannabis Abuse*

The above is linked to what I see as a third trend: an increasing need for treatment among abusers. This development has been pointed out not least by clinicians and researchers. There is a demand both for treatment projects and for high-quality evaluations. Awareness that the treatment of cannabis abuse requires an approach different from those currently used to treat dependence on other drugs has brought about the methodological development now seen in the United States, Australia and the Nordic countries, where Sweden plays a leading role. However, it is mainly a question of methodological work; evaluation activities still tend to lag behind. In Sweden and the other Nordic countries, though, professional interest in the treatment of cannabis problems has increased strongly over the last ten-year period. Methodological development has mainly taken place in Lund, where over 1,000 cannabis abusers have been treated (Lundqvist & Ericsson, 1988; Lundqvist, 1995). With the Stockholm Dependence Centre (*Beroendecentrum*) as the hub, a network has been built for the development of knowledge about this type of treatment. This network now includes social and health-care workers from approximately 25 teams in Sweden.

In my opinion, the falling age at first drug use among abusers, a growing number of well-made harm reports (especially the clarification of the risks of psychological and

psychosocial disturbances in cannabis-smoking young people) and the increasing strength of the preparations combine to form the background to a tendency in the scientific community which can be summed up as: “we must take this more seriously than we used to”. While it is true that many researchers have emphasised, from time to time, the importance of not underestimating the harmful effects, such researchers seem to be growing more numerous. *At present, we find ourselves in a curious situation where researchers and clinicians are becoming ever more concerned, while the general public, not least in Europe, seems to grow less concerned.*

### *Some Shifts in Perspective*

While research continues in all fields, there seems to be an incipient interest in a few special perspectives. Concern about the effects of combining alcohol and cannabis, which is not new, has yielded a few studies investigating this combination. The findings give particular cause for concern as regards driving (see Chapter 16). The other theme attracting greater interest is the importance of co-morbidity for violence – i.e. where violence is mediated by a cannabis-induced mental disorder in the form of acute psychosis, delirium or deterioration of personality disorders (see Chapter 13).



# Part One – General Remarks

## 1. Background and Aims. Facts about the Cannabis Drug

### *Purpose of This Report*

This report sums up the state of knowledge regarding the harmful effects of cannabis. “Knowledge” here refers to insights based substantially on research reports, research findings published according to the procedures described in Chapter 2. There is only exceptionally a reason to rely on other sources of knowledge, namely in those cases where no decent scientific studies have in fact been carried out or where on-going long-term research projects have not yet yielded answers to certain questions. In these exceptional cases, it is sometimes possible to use clinical experience (preferably documented in writing), i.e. experience acquired, and agreed upon, by professionals in health care, drug services and similar fields.

This is an update of the Swedish National Board of Health and Welfare report *Skador av hasch och marijuana: En genomgång av vetenskapliga studier av skadepanoramats hos cannabis* (subsequently translated into English as *Adverse Health Consequences of Cannabis Use: A Survey of Scientific Studies into the Range of Damage to Health Caused by Cannabis*). The earlier version covered research reports published up to and including February of 1996. The report is now updated to cover research published up to and including the autumn of 2003, and it will be made available as a PDF file on the website of the National Institute of Public Health Sweden.

In other words, this is *not* a report about cannabis in general, about how widespread it is, how it is used, its legal status, its medical use and so on. Nor is it a guide on how to treat cannabis abuse, or a treatise on the very important social interaction between abuse and social environment. Moreover, this report is not intended as a direct contribution, for or against, to the debate on the legalisation of cannabis – even though I do think its contents are eminently suited to inform such a debate.

At the same time, in the initial chapter, I will argue that those who have to deal with issues concerning cannabis abuse in individuals or groups should try to place their knowledge about the harmful effects of cannabis in a wider context – or, as I put it, specify the problem picture. To facilitate that process somewhat, I will bring up a few aspects of direct relevance to the assessment of the abuse situation. However, this can of course never replace the individual-psychological, family-dynamics or social assessments that often need to be carried out as well!

It is my impression that there is a great deal of uncertainty among policy-makers, drugs advisers, youth counsellors, some treatment staff and the general public as regards the risks associated with cannabis smoking. This situation is exacerbated by the fact that a great deal of nonsense intended for young people is disseminated over the Internet while the media bring a considerable amount of objectively unfounded information/propaganda into Sweden from several other European countries in connection with the liberalisation trends that emerge from time to time.

At the same time, it is young people who are the most exposed to cannabis and other drugs, often in settings where we as adults are in practice barred from entry. Unfortunately, it is also the case – as the reader of this report will realise – that teenagers are in fact more sensitive than other groups to many of the side-effects of cannabis.

Cannabis smoking (and other forms of cannabis consumption) is increasing in those European countries that have not yet reached saturation (“saturation” here means that about half the members of the groups concerned are using or have used the drug) as well as in the United States, Australia and New Zealand. In Sweden, the proportion of ninth-year school pupils (aged 15–16) who have tried drugs (generally cannabis) increased from 1992–1993 but has levelled off in the past few years, although at a higher level than in the late 1980s. Preliminary figures for 2003, however, suggest a new increase (CAN, Reports No 71 & 73, 2003; Dennis et al., 2002). This is a very worrying development!

### *The Dangerousness of Cannabis – Three Questions*

The consumption of cannabis is associated with a number of risks of harm. Cannabis presents a specific range of harmful effects, which is why it is usually not meaningful to make comparisons with alcohol abuse or tobacco smoking, each of which has its specific range of harmful effects. Some effects are acute and obvious while others develop insidiously and do not manifest themselves for weeks or months, possibly years.

To pin down the problems involved in a specific case, the following three questions need to be considered:

1. *Who is the abuser?* An adult or a teenager? Mentally stable and well integrated, or mentally fragile? What are the social circumstances of his or her life?
2. *What is the pattern of abuse?* Are we looking at occasional or highly frequent smoking? Is the abuser dependent? A poly-drug abuser? Does the person appear to identify himself or herself as a drug user?
3. *What is the strength (in general) of the preparation?* Are we dealing with preparations whose THC concentration (see below) is low, or with strong cannabis preparations?

### *Structure of the Report and Advice to the Reader*

*The aim has been to account, in a single report, both for conclusions on harmful effects (proven, suspected and excluded) and for the scientific data which support these conclusions. The reader will also receive advice on where to find the original presentations of the research findings to which reference is made (or, in some cases, where to find a previous and generally accepted review).*

The major problem has been to produce a text meeting a double requirement: it should be accessible to the interested public, and it should also account for scientific and other facts relating to the effects of cannabis. These facts can be hard to convey without making the text difficult to read and without using an excessive number of technical terms. To facilitate the reading and the understanding of the more technical discussions, a glossary has been added at the end.

Part One of the report (“General Remarks”) serves as a kind of introduction. As it has proved difficult to summarise the contents in a brief yet meaningful way, I would recommend the reader to take the time to read the two chapters making up this first part. In the three parts which deal only with the harmful effects of cannabis (“Cannabis and Mental Disorders”, “Some Psychological and Psychosocial Harmful Effects” and “Physical Harm”), I have inserted **summary boxes** at the beginning of each of the 19 chapters to facilitate a quick reading. If the summary given in a box should prove insufficient, a presentation of the relevant research projects – sometimes along with discussion and analysis – can be found in the text. For those who wish to go further, there is of course a list of references, indicating where the various studies can be found. In addition, the table of contents provides an overview of the kinds of harm treated in the report.

After a brief presentation of the cannabis drug and its intoxicating effects, I describe different cannabis preparations and, very briefly, the metabolism of cannabis in the body. In the section called “Specifying the Problem Picture”, I try to argue for greater exactitude and awareness of what we are talking about on any given occasion. As has been mentioned above, it is possible to adopt various perspectives within the framework of the overall question. Part One then concludes with an account of how scientific findings on the damage to health caused by cannabis are documented. Part Two looks at the psychiatric damage caused by cannabis, Part Three considers certain risks of psychological and psychosocial harm (long-term effects on intellectual faculties, effects on the development of teenagers and traffic risks), and Part Four provides a description of the main kinds of bodily damage caused by the drug.

## *On the Cannabis Drug*

“Cannabis” is a generic name for various preparations obtained from the hemp plant, *Cannabis sativa*. While *marijuana* consists of dried plant parts, the main ingredient in *hashish* is the resin secreted by the glandular hairs found all over the plant but mainly around the flowers. In addition to these two kinds of preparation, which have been used since time immemorial, *hashish oil* is produced by means of extraction. Marijuana and hashish are smoked in cigarettes or pipes. Hashish oil can be used to add strength to the preparations used for smoking, or can be mixed into food and drink. In our part of the world, the absolutely predominant method of taking cannabis is by smoking.

Of the more than 400 substances contained in cannabis,  $\Delta$ -9-tetrahydrocannabinol (THC) is the most psychoactive and is also the main cause of several of the harmful effects of the drug. The THC concentration (together with the intensity and duration of smoking) is important in determining not only the intensity of intoxication but also the risk of harm. Discussions of THC concentrations are thus a recurrent feature of this report.

A little less than two decades ago, the THC concentration of marijuana was generally between 0.1 and 4 per cent, while hashish typically tended to be stronger, at 3–8 per cent. The THC concentration of hashish oil – both in Sweden and abroad – varies greatly, ranging from 20 to 50 per cent. In Sweden, hashish has been the dominant preparation, while the most usual one in the United States and certain other countries has been marijuana. Through manipulation of growing conditions, varieties of *Cannabis sativa* with a considerably higher THC content than before have been developed. However, it is only since the late 1980s that these stronger varieties seem to have become more widespread. This causes problems both for individuals making risk assessments and for researchers trying to compare research findings.

In the opinion of several researchers and clinicians, all the evidence seems to suggest that quite a few of the differences as regards the existence and frequency of harmful effects found by different researchers (especially when comparisons are made between research findings from different countries) can be explained by the fact that the groups studied have been using preparations of differing strength. For instance, the variation between countries in the prevalence of cannabis psychoses (for definition, see Chapter 7) is deemed to be caused by differing strength of preparations (Newman & Miller, 1992; Meyer, 1975; Ghodse, 1986; Rolfe et al., 1993; Wylie et al., 1995).

### **Stronger Cannabis Preparations**

A relatively large proportion of existing scientific reports concern studies carried out in the United States in the 1960s and 1970s. The drug abusers studied had typically been using marijuana with a THC content of 0.5–3 per cent, whereas marijuana smokers in the late 1980s and in the 1990s have had access to cannabis plants (such as *sinsemilla*) with a

considerably higher THC concentration (7–11 per cent according to Schwartz, 1991). These earlier studies may therefore be of a fairly limited value in helping us to understand the harmful effects caused by present-day cannabis abuse in the United States or by both past and present hashish abuse in Europe. In the United States and other countries, it is common in scientific contexts for mention to be made both of the increasing risks and of the influence on research findings. According to official federal statistics, the average THC concentration of cannabis seized in the United States tripled between 1980 and 1997 (Dennis, 2002).

C.H. Ashton reviewed scientific reports and other information from the United States and the United Kingdom. She concluded that all preparations (except hashish oil) are stronger today than they were in the 1960s and 1970s:

- marijuana cigarettes, before: 1–3 per cent THC (approx. 10 mg per cigarette – “reefer”);
- marijuana cigarettes, now: 6–20 per cent THC (approx. 60–200 mg per cigarette – “joint”);
- hashish cakes, now: 10–20 per cent THC.

(Ashton, 2001)

It may be added here that the THC concentration of hashish cakes mentioned by Ashton is slightly over double that found in the 1960s and 1970s.

At the Swedish National Laboratory of Forensic Science, there is a long-established practice of performing concentration analyses on (random samples of) cannabis which is seized in large quantities. As a result, it is possible, to some extent, to chart changes in the THC concentration levels of preparations available on the Swedish market. When I contacted the laboratory in 1996, I was told that over a ten-year period, considerable changes had been noted in the THC concentration: first, the difference which had previously existed across the board between the stronger hashish and the weaker marijuana had disappeared; second, marijuana was no longer available with the very low concentration levels (< 1 per cent) previously found and its average THC concentration was considerably higher than before, meaning that seizures might be found where the hashish had a THC concentration of 6–8 per cent while the marijuana contained 13–14 per cent THC; and third, both hashish and marijuana now showed a greater spread in their THC concentration – from 1 per cent to 15 per cent (20 per cent) (von Wachenfelt, 1996).

A marijuana cigarette weighing 0.5 to 1 g thus contains 5–200 mg THC. If it has been treated with hashish oil, the quantity of THC may be much greater.

### **Cannabis Intoxication**

With a slight generalisation, cannabis can be said to produce two kinds of intoxicating effect. On the one hand, there are euphoric and calming effects (similar to those of other



drugs with a sedative effect, such as alcohol and benzodiazepines) – the taker experiences calm, relaxation, a feeling of happiness and of distance from everyday life. On the other hand, there are more dramatic impacts on the taker's emotions and cognitive functions – e.g. fragmentation of thought processes, major disruption of temporal perception, distortion of sensory impressions (sound, touch, light, etc.), reduced ability to maintain attention, considerable deterioration of short-term memory/imprinting ability and, in certain cases, a noticeable introversion and dissociation of the taker from other people. At high doses, there appear – in some people, perhaps not in all – hallucinations and delusions, during which the taker does not, however, lose contact with reality.

### **How Cannabis Produces Its Effects on the Brain**

Despite intensive research we are still, in many respects, dealing with hypotheses when we discuss the mechanism by means of which cannabis affects the brain. In recent years, however, considerable progress has been made, including the discovery of specific cannabis receptors in the brain. The exact significance of this discovery is not yet known. Researchers have also identified THC-like substances produced by the body itself (endocannabinoids) which bind to these receptors. The two most important endocannabinoids are anandamide and 2-arachidonylglycerol. The receptors are located primarily in specific parts of the brain: the basal ganglia, the hippocampus and the cerebral cortex. These findings tie in with certain of the effects and side-effects produced by cannabis, above all its effects on psychomotor and cognitive functions.

### **The Metabolism of THC – Duration of Intoxication**

Partly stimulated by growing interest in possible medical uses for cannabis, extensive research is being carried out on both THC and the numerous other substances contained in cannabis. As a spill-over effect, this research sometimes yields information of importance to the understanding of cannabis as a drug of abuse. One example concerns the complex metabolism of THC and its relation to, in particular, the acute psychological effects.

When cannabis is smoked, the THC level in the blood rises quickly, reaching its maximum within a few minutes. If the drug is taken by mouth and stomach (e.g. by eating cookies or chocolate containing cannabis), the maximum THC level is achieved after 30 to 60 minutes (depending on whether the taker is fasting or not). The *maximum* subjective effect more or less coincides with the blood level, even though a minor delay has been observed. The duration of intoxication is directly dependent on the size of the dose. If the dose is low, the effect lasts for a few hours if the drug is inhaled and for twice as long if it is eaten. The blood level of THC falls rather quickly, partly because of conversion into metabolites and partly because of distribution to fatty tissue (Grotenhermen, 2003).

Relatively little is known about this phase of the metabolism; for instance, it is unknown what quantities of THC and metabolites are stored in fatty tissue. The THC later secreted back into the blood *probably* does not reach concentrations that cause any psychological

effects of importance for normal human activities. There is, however, not complete agreement on that claim, and given the limitations of our present knowledge it is advisable to be very cautious and to operate with wide margins. There are two particular reasons for this: first, the metabolism of the cannabinoids is affected to a large extent by individual – unknown – factors; and second, some of us are involved in activities that seem to be extremely sensitive to THC and certain of its metabolites. Special mention should be made of the (aircraft) pilot profession, which requires the ability to remember and combine a number of different signals into a whole and to carry out a series of manoeuvres correctly and in correct order. As will be seen in Chapter 16, pilots showed impaired ability 24 hours after taking cannabis (Leirer, 1991).

Ashton (2001) points out that, to some extent, professionals such as anaesthetist doctors and nurses have similar tasks: to carry out, during a short period of time, a series of actions, in correct order and precisely “dosed”. Indeed, our high-speed and high-tech society is based on a large number of people having roles involving similar requirements. Still, I would like to emphasise that there are very large differences between individuals as regards the rate at which THC is distributed, broken down and secreted. Moreover, the duration of the metabolism is dose-dependent, which is why the above indications of time should be seen as averages.

Because of the process of storage in fatty tissue and the subsequent slow secretion via the liver and kidneys, low levels of THC and its metabolites can be detected in urine for as long as six weeks after consumption of cannabis.

THC has a large number of metabolites. In volume terms, the predominant one is THC-COOH, which is non-psychoactive. One of the intermediate steps in its formation is 11-OH-THC. Both THC and 11-OH-THC are short-lived but psychoactive, whereas the non-psychoactive THC-COOH remains considerably longer in the blood – from days to weeks.

The importance of distinguishing between the non-psychoactive metabolite THC-COOH and the psychoactive THC is a relatively recent insight, one of whose consequences has been something of a breakthrough in the research on the risks of cannabis and driving (Ramaekers et al., 2004; Kane et al., 2002; Grotenhermen, 2003). Examples of this will be seen for instance in the presentation of traffic research given in Chapter 16.

### **Cannabis Smoking – A Potent Symbol**

In the 1960s and 1970s, when cannabis became a widely spread drug in the industrialised societies of the Western world, the use of cannabis took on a potent symbolic force for large groups of young people. I will not here discuss the links between cannabis and flower power, the hippie movement, different music styles and youth revolt in general. It is, however, obvious that some of this symbolic force remains even today, and that an awareness of the main features of the origins of cannabis abuse as a societal phenomenon is important if

we are to be able to understand the situation facing us today. One of the very best books available describing the interaction between individuals' needs on the one hand and cultural and economic conditions on the other is *Hasch: Romantik och fakta* ["Hashish: Romanticism and Facts"] by Thomas Nordegren and Kerstin Tunving (1984).

### *Specifying the Problem Picture*

It is a far too common occurrence that the dangerousness of cannabis is discussed in general terms, without any form of specification. What are the circumstances? Who is the abuser? What does the pattern of abuse look like?

### **THC Content**

As was mentioned in the section on the different preparations, the THC content of cannabis varies considerably, depending, among other factors, on the kind of preparation. Differences are also found between different sorts of the same preparation, especially between different types of marijuana. Many of the harmful effects are dose-dependent – which is not to say that this is the only factor determining the intensity and other characteristics of a side-effect..

### **Sporadic or Chronic Abuse**

The acute effects of cannabis intoxication, especially where the THC concentration is high, have a very clear impact on the taker's experiences and functional ability in different respects. Certain subjective intoxication experiences, which are characteristic of isolated occasions of intoxication, disappear or change when the abuse becomes chronic in nature. However, the same *functional impairments remain*, and new functional impairments make their appearance as manifestations of chronic effects. Whether or not the taker is dependent (see Chapter 4) seems to be fairly important in determining how difficult it is to stop abusing.

### **Differential Risk of Harm from Cannabis**

The risk that cannabis abuse will cause harm varies from individual to individual, because people's vulnerability varies. This interplay between stress or trauma on the one hand and vulnerability on the other is valid for many diseases and kinds of harm. The problem is that individual vulnerability to any given type of stress or trauma is usually unknown. That being said, as far as the effects produced by cannabis on humans are concerned, we do know that certain groups are significantly more likely than others to be harmed. This applies mainly to the following three groups:

#### *1) Teenagers*

Anything in excess of occasional cannabis smoking presents a threat to the development of young people, owing to the way in which THC interacts with the inner psychological processes that characterise the teenage years. Several factors, not least the inner mental

imbalance which is a feature of that developmental period, make teenagers more likely than adults to react with psychiatric symptoms. Since the teenage organism is still under development, it can also be suspected that young people are more susceptible to bodily harm. Moreover, as teenagers struggle to break free from their parents, the support they can count on from adults is often weaker than it would otherwise have been.

### *2) Pregnant women/unborn children*

Since THC passes from the mother's blood into that of the foetus, the latter is exposed to an increased risk of harm if the mother smokes cannabis while pregnant. If the mother also uses or abuses other substances that are noxious to the foetus, for instance if she smokes tobacco or drinks alcohol, we can expect a summation effect.

### *3) People with a disposition towards mental disorder*

Cannabis smoking can provoke, cause relapses into and worsen a number of mental illnesses and disorders. This is clearly illustrated in the chapters on psychosis and depression. For example, cannabis smoking entails a very large risk of deterioration and relapse in people with a schizophrenic condition.

Generally speaking, problems caused by cannabis smoking and its interaction with fragile or manifestly ill people are encountered on a daily basis at our psychiatric clinics.

## *Medical Uses of Cannabis*

Intensive research is being carried out to test the hypothesis that the cannabinoids (and other substances contained in cannabis) have curative effects – or, rather, to determine whether their curative effects, if any, are better than those of available pharmaceutical preparations. Even though there is no direct link between this research and that on the harmful effects of cannabis, the two fields are sometimes confused in the public debate, which I think is unfortunate. In fact, what we are dealing with here are two entirely separate medical fields which could, at best, cross-fertilise each other.

The opiates (including morphine) have long been, and still are, our most effective analgesics, and they have formed the basis for a series of synthetic preparations with a strong analgesic effect. This use of morphine and preparations derived from morphine to relieve pain, however, only exceptionally gives rise to drug-policy discussions where comparisons are made, or contrasts drawn, between the abuse of morphine or heroin and the medical prescription of opiates.

## 2. *How to Find Information about the Harmful Effects of Cannabis*

There are grounds for dwelling on the question of how to acquire reasonably comprehensive information about the harmful effects of cannabis. Is there any guarantee that I have not overlooked any important research findings? What is the proper course of action if there are no research results in a certain field? And what should you do if different teams of researchers have obtained different results?

First of all, I wish to stress that, although the central source of knowledge is research findings, primarily from research carried out during the last 40 years, there is an additional source: clinical experience. However, I refer to this second source of knowledge only as a second expedient, usually in situations where there are no research findings or where what research there is does not yield much information. Furthermore, the clinical experience referred to should have been acquired by several clinicians and there should be no known record of divergence within the clinical sphere in question. It is preferable if the clinical experience is documented in written form, and it is a minimum requirement that the experience in question does not run contrary to the written reports which are available. The term “clinical experience” as used here refers to the experiences made by people working in health care or social services in their encounters with a large number of abusers or families and relatives of abusers.

### *Systematised Scientific Documentation*

By going through previously published summaries of the state of research and by searching for information in scientific databases, I have been able to obtain a satisfactory coverage of research reports published up to and including the autumn of 2003.

Since most of the side-effects of cannabis are directly or indirectly medical, my approach has been to carry out literature searches of the medical database MEDLINE, including the additional resources contained in PubMed. (MEDLINE is the US National Library of Medicine in computerised form.) I have also used the Swedish abuse directory Alcona, which is run by the Swedish Council for Information on Alcohol and Other Drugs (CAN).

Although the practice of storing articles from scientific journals in electronic databases has considerably facilitated the task of searching the literature, it would hardly be possible to find one’s bearings among the thousands of scientific works produced without also having access to a number of reviews compiled in previous years. These reviews have generally been produced by teams of experts working on instruction from national or international health-care organisations. Some of the most important such reviews (ordered by year of publication) are:

*Chronic Cannabis Use (1976);*

*Marijuana: Research Findings (1980);*

*Report of an ARF/WHO Scientific Meeting on Adverse Health and Behavioral Consequences of Cannabis Use (1981).* – This is a summary of Cannabis and Health Hazards;

*Marijuana and Health (1982);*

*Cannabis and Health Hazards: Proceedings of an ARF/WHO Scientific Meeting on Adverse Health and Behavioral Consequences of Cannabis Use (1983);*

*Cannabis och medicinska skador: En nordisk värdering* [“Cannabis and Adverse Medical Effects on Health: An Evaluation from the Nordic Countries”] (1984);

*The Health and Psychological Consequences of Cannabis Use (1994);*

*Cannabis: A Health Perspective and Research Agenda (WHO, 1997);*

*The Health Effects of Cannabis (1999).*

There are of course also many textbooks which provide a short account of the scientifically proven harmful effects of cannabis along with information about various other aspects of the drug. Mention will be made here of two such books:

*Marijuana* (Mark S. Gold, 1989);

*Hasch. Romantik och fakta* [“Hashish: Romanticism and Facts”] (Thomas Nordegren & Kerstin Tunving, 1984.)

The most comprehensive and most thorough of the reports is *Cannabis and Health Hazards* from 1983, which was produced by the Addiction Research Foundation (ARF) and the WHO. This report has served – for me as well as for many others – as a basis for comparisons with the situation obtaining at later dates. The Australian report *The Health and Psychological Consequences of Cannabis Use* is also impressive both as regards the volume of factual information contained in it and as regards many of its analyses, even though I disagree with some of its overall judgements. As can be seen from the list above, before the publication of the Australian report no reviews had been compiled for a decade. This reflects the fact that the number of research reports fell during the later half of the 1990s, as did the general level of interest in all aspects of cannabis. Since then, the trend has shifted.

In 1993 the WHO begun work, in collaboration with the ARF, on a follow-up to the 1983 report. In 1997, they produced a summary (*Cannabis: A Health Perspective and Research Agenda*) which, for some reason, was never printed or at least never disseminated. The full report (*The Health Effects of Cannabis*) turned out to be rather better and is likely to be available in medical libraries across the world.

In many cases, however, the knowledge overviews can be used only for general orientation; it is usually necessary to read the original articles in order to weigh up and analyse the research findings for oneself. A common approach to obtaining an all-round understanding of a scientific issue is to start with a recent, authoritative review article, which provides an overview, and then work one's way backwards in the traditional manner, using the review's list of references as a guide.

Finally, in cases where there is disagreement between researchers, it is my task to weigh their respective arguments. I may then conclude that the evidence on either side is overwhelming, or – a more common occurrence – that the question must still be considered open.

### *A Young Area of Research*

Research findings relating to cannabis are sometimes very uncertain – and sometimes there has been no research work at all on a particular aspect. In those cases, it is important to realise that this is a rather young area of research. A comparison between tobacco and cannabis research shows both that cannabis research seems to lag behind by several decades and that tobacco research is much more extensive.

Tobacco research had its major breakthrough during the first half of the 1960s, and the 1964 report by the Surgeon General (the head of the US Public Health Service) was based on over 7,000 scientific reports, a number of which referred to longitudinal studies. It was possible to point to a causal connection between smoking and a series of diseases, especially of the respiratory tract and the cardiovascular system. As early as at this stage, it was possible to show that smoking was the main cause of lung cancer in men, and the main cause of chronic bronchitis in both men and women. In 1989, 25 years later, the Surgeon General had access to more than 57,000 articles. Cannabis research, on the other hand, was very modest in scale in the early 1960s, and in 1996 the total number of scientific articles on the subject probably did not even exceed 10,000. As of today, tobacco research has yielded about 140,000 studies whereas cannabis research has produced only one-tenth of that number.

Another reason why the number of scientifically confirmed cases of certain expected harmful effects (for example on the respiratory organs) is still relatively limited compared with the findings of tobacco research may be that these are side-effects which often need decades to reach a clinically observable level.

### *Research Reports and Quality Assurance*

Is there any assurance that an article published in a prestigious journal is of acceptable quality? To begin with, before a research department allows an article to be sent off for publication, it is generally subjected to an internal process of review and criticism. Moreover, scientific journals also review articles submitted – not seldom in a heavy-handed way – with regard to their form and, in particular, their content. Most researchers have had articles returned to them accompanied by a letter from an editor suggesting a more or less extensive reworking of the article or turning it down flatly because of insufficient quality. At the same time, however, we have to realise that outside the laboratories, there is no such thing as an absolutely perfect study that cannot be questioned in any respect.

Scientific works that have been published, however, must be assessed and compared from the perspective of the quality of the design which has been used. Two studies relating to the same question may have entirely different weight as evidence. While it would carry us too far here to discuss in detail the considerations that have to be made when determining whether a study is high or low on the methodological scale, some of the factors that affect the weight which should be attributed to a study are the following: whether the study is prospective or retrospective; whether there is a control group; whether the membership of the study group and the control group has been randomised; the size of the study group; whether the study is longitudinal or more of a cross-sectional character; and the extent to which the researchers have taken into consideration other circumstances (known as confounding factors) that experience shows may affect the result of a study in the same direction as the influencing factor studied (in this case, cannabis smoking). If several studies have arrived at the same result, this may be of decisive importance.





## Part Two – Cannabis and Mental Disorders

### 3. Damage to Mental Health – An Overview

#### **Summary of Chapter 3:**

Cannabis is one of the most psychopathogenic of all narcotic preparations. For instance, compared with heroin abuse, cannabis smoking – excepting the strength of dependence development – is associated with far more serious risks regarding the development of mental disorders of various kinds.

The following mental disorders/illnesses are relevant here in that it is considered that they can be caused, precipitated from a latent state or exacerbated by cannabis abuse:

- Development of dependence
- Delirium (acute confusional states)
- Cannabis psychoses
- Schizophrenia
- Other psychoses
- Anxiety disorders
- Depersonalisation syndrome
- Depression
- Suicide
- Amotivational syndrome
- Impulsively violent behaviour

### *Introduction*

In addition to the “ordinary” effects (those common to all sedative drugs of abuse) of relaxation, calmness, a feeling of happiness and of distance from everyday concerns, cannabis also produces more dramatic effects on the psyche of the taker: fragmentation of thought processes, severe disruption of temporal perception, a feeling of being able to be in several places at the same time, a marked sense of separation from other people and from ordinary life (a “glass-wall feeling”), and where very high doses are involved also, if

not always, hallucinations and delusions. Given these very special – mind-fragmenting – effects, it is not surprising that associations are found between cannabis and various mental illnesses.

*Cannabis is one of the most psychopathogenic narcotic preparations. Owing to the widespread use of the drug, this fact has serious consequences for both individuals and society. It is worth mentioning that the opiates (heroin etc.), apart only from the development of dependence, produce far fewer toxic psychiatric complications than do cannabis preparations.*

Ever since cannabis became a widely spread drug in Western industrialised countries, we have seen psychiatric symptoms which in many respects resemble observations from countries (such as Egypt and India) where cannabis has a long history of use as a stimulant. There has also been extensive research carried out in this field. The following chapters present a number of studies where cannabis smoking is associated with mental damage. A couple of recent reviews may be mentioned here. Two veterans of the field, Joseph Rey and Christopher Tennant, wrote an article entitled *Cannabis and Mental Health: More Evidence Establishes Clear Link between Use of Cannabis and Psychiatric Illness*, which was published in the *British Medical Journal* at the end of 2002. Another example from the same year is *Changing the Focus: The Case for Recognizing and Treating Cannabis Use Disorders* by Dennis et al. (*Addiction*, 2000, Supplement No 1).

It is obviously crucial, for a variety of reasons, to have as comprehensive knowledge as possible about the association between cannabis abuse and mental disorders. This is important for all measures taken, from drug-policy perspectives to the design of treatment interventions aimed at individual abusers. Regardless of what is the cause and what is the effect – whether the abuse causes the mental disorder or whether a person with a mental disorder “self-medicates” by smoking cannabis –, the two conditions generally tend to have a negative influence on each other. Without digressing too far from the main theme of this report, it may be pointed out that the combination of drug abuse (including cannabis abuse) and mental disorders is now a major problem in psychiatric care and drug services. It is also well known that unless they are given specially designed treatment, these “dual diagnosis” (or “co-morbid”) patients generally have a worse prognosis than those who suffer only from either problem.

The following chapters may present some difficulty to readers who are not familiar with psychiatric terminology. However, I have not judged it possible to include an introduction to psychiatry in this report. I regret this and express my hope that the glossary added at the end of the report may be of some help.

### *Classification of Mental Disorders/Illnesses Precipitated, Caused or Exacerbated by Cannabis Smoking*

The following mental disorders are known or suspected to be more or less strongly associated with cannabis abuse in that the abuse may cause the mental disorder, precipitate a latent mental illness or severely exacerbate an existing illness/disorder:

- a) Development of dependence
- b) Delirium (acute confusional states)
- c) Cannabis psychosis
- d) Other psychoses
- e) Schizophrenia
- f) Anxiety disorders
- g) Depersonalisation syndrome
- h) Depression
- i) Suicide
- j) Amotivational syndrome
- k) Impulsively violent behaviour

## *4. Development of Dependence in Cannabis Abusers*

### ***Summary of Chapter 4:***

Cannabis abuse can evolve into cannabis dependence, which is characterised by a compulsive need for the drug, daily or almost daily consumption and difficulties in stopping. The dependence is not only psychological but also physical; the latter aspect is manifested during detoxification as withdrawal symptoms such as moderate anxiety, irritability and sleeplessness.

The proportion of cannabis abusers who become dependent has been found to vary considerably in different studies; on average, it is surprisingly high. Of those who smoke cannabis at least once, 10 per cent will develop dependence at some point in their lives.

Cannabis-dependent people are more at risk of being affected by the harmful effects of cannabis smoking, and they are also more likely to move on to other illegal drugs.

As regards the taking of drugs, a distinction is made between the concepts of *use*, *abuse* and *dependence*. Abuse involves individuals causing physical, mental or social harm – to themselves or to others – through their use of the drug. At the abuse stage, use of the drug is not constant; the individuals have a degree of control over their drug use and are periodically able to abstain from using the drug. At the dependence stage, the abuse has evolved into a compulsive need for frequent or constant intoxication. Social, mental or physical harm is ignored, and considerable time is devoted to obtaining the drug, taking it and dealing with the after-effects. Other interests are increasingly relegated to second place, and attempts to break the dependence often fail. Dependence (particularly physical dependence) entails *tolerance* – requiring the abuser to increase the dose in order to attain the same degree of intoxication – as well as *withdrawal symptoms* when attempts are made to end the abuse.

Whether a particular drug can or cannot give rise to dependence is a very important issue. The risk of harm increases considerably for an individual who is no longer able to control his or her drug use. The development of dependence is involved, in several ways, in other harmful effects, but dependence development is still usually considered a harmful effect in its own right. Similarly, abuse is considered and classified as a harmful effect or an illness in its own right, although at a lower and less alarming level than dependence. A distinction is made between psychological and physical dependence; many drugs give rise to both. Generally speaking, it can be said that the short-term difficulty in stopping the use of a drug is affected more by physical dependence, whereas psychological dependence is important in both the short and the long term.

Despite clinical observations of signs of both dependence and withdrawal symptoms, it took rather long to prove conclusively that cannabis smokers develop not only abuse but also dependence.

A relatively large number of experiments were carried out (cannabis was given to subjects for a certain period of time, and then the effects of interrupting the supply were studied) in an attempt to prove the occurrence of tolerance and withdrawal symptoms. Initially, these attempts failed. In many cases, for ethical and other reasons, the doses given were unrealistically low and the periods of study were short (Hollister, 1986). When Jones and Benowitz (Jones, 1983) gave significantly higher and more frequently administered doses during a three-week period, their subjects rapidly developed tolerance and manifested a withdrawal syndrome very similar to that observable in clinical work.

Since then, a large number of systematic observations and studies have been made that support the clinical picture and the experiments: dependence develops in association with long-term use (Miller & Gold, 1989; Gable, 1993). It is also a matter of general agreement that tolerance develops, in other words that there arise a physical dependence and a need to increase the dose in order to attain the same effect as before (Compton et al., 1990). In line

with this view, “cannabis dependence” is included as a diagnostic unit in the modern psychiatric diagnostic systems DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 1994) and ICD-10 (WHO, 1992).

Notwithstanding the above-mentioned studies, however, doubts have been expressed from many quarters as to whether there really occur withdrawal symptoms in association with cannabis dependence. However, among clinicians, including myself, it is well known that frequent use of cannabis over a relatively long period of time – especially where high doses are involved – leads to withdrawal symptoms when the taker undergoes detoxification. Commonly occurring such symptoms include sleeplessness, anxiety, irritability and occasionally perspiration, slight nausea, trembling and weight loss (Compton et al., 1990). The sleeplessness experienced can be especially troublesome and often causes relapse in people who try to give up cannabis. The intensity of the discomfort experienced depends on the size of the dose and on the frequency and duration of abuse (Compton et al., 1990). This is why a number of further studies have been carried out to investigate issues relating to dependence and withdrawal symptoms. All of these studies have arrived at the same result (Duffy & Milin, 1996; Crowley et al., 1998; Haney et al., 1999).

*In other words, there is now general agreement on the issue of cannabis and dependence, including the importance of withdrawal symptoms. In spite of this, it is not rare to find both physicians and abuse-treatment staff in the drug services who are unfamiliar with this fact and with its importance for issues of progression, complications and the treatment of cannabis abusers.*

In addition, some reports have been published which describe more serious withdrawal symptoms, especially psychotic symptoms of a manic-depressive nature (Teitel, 1971; Rohr et al., 1989).

### *How Widespread Is Cannabis Dependence?*

Within the framework of the Epidemiologic Catchment Area (ECA) Study, a large North American population study, an attempt has been made to determine the frequency (or prevalence) of cannabis dependence. Among the 20,000 people surveyed, 4.4 per cent showed signs of cannabis abuse. Roughly three-fifths of these were dependent according to the commonly accepted criteria (Hall et al., 1994, p. 116).

Newcomb (1992) monitored a large group of young Americans for thirteen years, starting when they were in the seventh, eighth or ninth year of school. In the thirteenth year of follow-up, when the subjects were aged 27–29, their situation in terms of abuse was examined again. Just under 24 per cent were users or abusers of cannabis; and of these, just over 25 per cent (8 per cent of the total group studied) were *dependent* according to the DSM-III-R criteria and displayed symptoms similar to those described at the beginning of this chapter. Kandel

and Davies (1992) found that 14.6 per cent of a group of 28–29-year-olds used cannabis very frequently (near-daily use).

In the cannabis monograph published by the Australian National Drug and Alcohol Research Centre (Hall et al., 1994), there is an extensive and very thoroughly drafted section on cannabis dependence. After stressing that certain groups (characterised by sex, age, social factors, etc.) are more or less likely to develop dependence, the authors claim that, based on their review of the literature, it is a well-founded rule of thumb that, of those who ever start smoking cannabis, about 10 per cent run the risk of developing dependence at some point in their lives.

### *Consequences*

As has previously been pointed out, most of the harmful effects dealt with in this report are determined by the frequency and duration of abuse. Therefore, those dependent on cannabis run particularly high risks. The tangible effects arising from long-term abuse are the kinds of cognitive damage discussed in Chapter 14. As pointed out in Chapter 15, dependence in teenagers puts important aspects of their development towards adulthood at risk. An abuser who has become dependent will often ignore social damage (such as damage relating to work, education and family relationships). Moreover, a cannabis-dependent person can be expected to act in a riskier manner towards others, for example when driving a car. Hendin (see Chapter 14) also stresses a number of risk factors which are exacerbated by long-term use.

Some researchers, including Kandel and Davies (1992) and Fergusson et al. (2000; 2002), have also shown that the link to other kinds of abuse – of both “hard” drugs and alcohol – becomes much stronger as a person progresses from sporadic to very frequent cannabis abuse.

A further aspect which it is important not to disregard is the “mental corruption” engendered by the life situation of the dependent persons: for years on end, as well as having to hide their abuse from outsiders, they must come up with explanations and excuses for themselves and their family in order to be able to continue their abuse.

## 5. Cannabis and Psychoses – An Overview

### **Summary of Chapter 5:**

A great many studies show that the group of cannabis smokers exhibits an increased prevalence both of psychotic symptoms and of short-lived psychotic illness in the strict sense.

Cannabis smoking can cause psychosis, activate latent psychosis and exacerbate manifest psychotic conditions.

This chapter discusses the following relationships between cannabis smoking and (near-) psychotic conditions:

- Cannabis-caused delirium (acute confusional state)
- Cannabis-caused toxic psychosis (cannabis psychosis)
- Cannabis-caused functional – non-schizophrenic – psychosis
- Can cannabis smoking cause schizophrenia?
- Interaction between the effects of cannabis and manifest schizophrenia

The interaction of cannabis with psychotic conditions is doubtless one of the most alarming aspects of what is gathered under the heading “harmful effects of cannabis”. I will here report on the prevailing scientific view of this interaction. Occasionally, I will also take my own clinical experience into account. The principal point to be made, though, is that several studies have found not only a statistical association but also a causal link between cannabis smoking and psychoses or psychotic symptoms.

At the same time, this is an elusive subject. Our knowledge about the nature of psychoses is defective, and the impact on the brain of the substances found in the cannabis plant is a subject we still do not know enough about, despite the great breakthroughs made in recent years. Moreover, there are major difficulties involved in carrying out the long-term studies required. One problematic factor is that until recently, there were discrepancies between countries in the terminology used. Furthermore, it is not always clear from a scientific article what psychotic manifestations are actually referred to in it.

Roughly speaking, what we are discussing here are two fundamentally different psychotic manifestations. Those in the first category are called *toxic* (they belong to the group of brain-damage syndromes) and involve a situation where cannabis consumption, generally intensive and/or long-term, causes the psychotic symptoms by means of the toxic effect of cannabis. In these cases, the symptoms are provoked in direct connection with cannabis consumption and subside once the supply of the drug is interrupted. Residual symptoms



can often easily be made to cease by means of antipsychotic medication, and the patient will recover fully if he or she abstains from further consumption of cannabis or other drugs.

The other category is that of *functional* psychoses/psychotic manifestations. The word “functional” refers to the absence of organic damage. (Today we would have to say that there probably is an organic component, but more in the form of a subtle vulnerability whose nature we know rather little about [Cullberg, 2000].) Above all, this category covers schizophrenia and schizophrenia-like psychoses, which not rarely run a chronic course.

In the toxic group, direct impact on the brain often manifests itself through the appearance of elements of delirium involving signs such as marked bewilderment and memory disturbance, and this delirium is sometimes so evident that it dominates the picture. In the functional conditions, these symptoms are absent, and – at least in the schizophrenic conditions – there is often a sensation of outside interference with thought. The other psychotic manifestations are often similar.

It should be underlined that what we are dealing with here are the most profound disturbances known to psychiatry; even when they are short-lived, such disturbances can leave marks on those affected and on their families which may remain for many years or even be of life-long duration. By definition, these conditions are of a combinatory nature: there is both an abuse condition and a serious mental disorder. These “dual disorders” are among the most difficult to assess in the whole of psychiatry. Moreover, conditions of this type not rarely make demands on the most costly resources available in the field of psychiatric care.

*The following relationships between cannabis and (near-) psychotic conditions are discussed here:*

- Cannabis-caused delirium (acute confusional state)
- Cannabis-caused toxic psychosis (cannabis psychosis)
- Cannabis-caused functional – non-schizophrenic – psychosis
- Can cannabis smoking cause schizophrenia?
- Interaction between the effects of cannabis and manifest schizophrenia

### *Older Scientific and Clinical Reports of an Overall Nature*

In addition to the more specific studies that have been carried out into the ability of cannabis to cause different specific psychotic conditions, and the studies of the interaction between cannabis abuse and psychotic conditions, especially schizophrenia, there also exist several reports – many of them from studies carried out in the Nordic countries – which should be seen above all as providing evidence that cannabis consumption can

profoundly destabilise neurophysiological processes, thereby causing danger to the individual concerned.

In her dissertation entitled *The Prognosis of Drug Abuse in a Sixteen-Year-Old Population*, Maj Britt Holmberg found that of those young people who had been consuming large quantities of drugs (almost exclusively cannabis) at the age of sixteen, 10 per cent had a case record as psychosis patients eleven years later. This proportion is of course many times larger than that which would be expected in a normal group of young adults (Holmberg, 1981). In another study, a group of 908 patients were examined from a number of different viewpoints in connection with their admission to two hospitals in London. Of the 496 patients who agreed to undergo an examination including a urine test for cannabis, it was found that among those testing negative for cannabis, 62 per cent were diagnosed as having psychosis, whereas 88 per cent of those testing positive for cannabis received such a diagnosis (Mathers et al., 1991).

Bier and Haastrup (1985) found, in their study of all patients admitted during one year to a psychiatric unit at one of Copenhagen's hospitals, that 30 patients had cannabis-provoked psychoses, i.e. psychoses where it was deemed that cannabis smoking had contributed to precipitating (or causing a relapse into) psychosis. The authors conclude that in a population of 100,000, it can be expected that 15 patients per year will be admitted to hospital with psychoses precipitated or caused by cannabis. The group of patients included both people with no other mental disorder (toxic cannabis psychoses), schizophrenics and people with personality disorders. In the late 1960s and early 1970s, Tennant and Groesbeck (1972) studied American soldiers stationed in Europe. In 1969 a major wave of drug abuse, dominated by strong cannabis preparations (hashish), started among these soldiers. During the years 1969–1971, the authors found that, in addition to a series of other acute negative reactions, the number of cases of “schizophrenic reactions” (acute psychotic reactions which did not necessarily have to lead to what we mean by schizophrenia) increased from 16 in 1968 to 77 in 1971 – i.e. an almost fivefold increase in four years. The researchers' impression was that the smoking of hashish was a major contributing factor in these psychotic reactions.

A North American study of cannabis-smoking young people in the first half of the 1970s (Weller & Halikas, 1985) can be mentioned as an older representative of that minority of studies where no association was found between cannabis smoking and psychosis (or other serious mental disorders). However, owing to the low THC concentrations prevailing at that time, marijuana smokers then ingested, on average, only one-third as much THC as present-day marijuana smokers in the United States.

### *Recent Studies*

Over the past 15 years, the studies showing cannabis to have been the stressor causing or inducing psychotic symptoms or psychotic illness in the proper sense (cannabis psychosis, delirium or schizophrenia) have both increased in number and grown ever more likely to use a refined methodology. All of the studies that I refer to in the following sections on psychosis are examples of this, but I would also like to mention some recent more comprehensive studies. On a general note, it is clear that it is above all because of several on-going prospective and longitudinal studies, which started over two decades ago, that we are able to make analyses and have findings at our disposal today.

Within a major longitudinal research project, a research team from New Zealand are monitoring 1,200 children/young people from birth to – at present – the age of 21 (Fergusson et al., 2003). It has been found that cannabis-dependent young people develop psychotic symptoms more often than those who are not dependent.

Arseneault et al. (2002) – also a New Zealand research team – participate in another longitudinal project which is monitoring 1,100 children/young people who are now 26 years old. Young adults who smoked cannabis at 15 run a greater risk of developing schizophrenia or schizophrenia-like illness: their risk is 10 per cent, as against 3 per cent for non-smokers. It is also interesting to note that the younger a person is when first using cannabis, the greater is the risk of psychotic manifestations.

It should be added that all studies cited in the following sections on psychosis obviously also support the existence of a causal link between cannabis and psychosis. Two of the most important of these studies are the Swedish one covering 45,000 military conscripts, which is mentioned in the chapter on cannabis and schizophrenia (Andréasson et al., 1987; 1989), and the recent and well-made Dutch study by van Os et al. (2002).

In order to complete the picture and provide a reminder of sorts that this remains a complex field, even though a great deal of clarity has been achieved in recent years, I would like to mention a study by Phillips et al. (2002). The researchers involved carried out a study – albeit of short duration (one year) – on a group of what one would perhaps call pre-psychotic young people, comparing those of them who had smoked cannabis in the year preceding the year of the study with those who had not. No differences were found in the frequency of illness, which is surprising in spite of several objections that the researchers themselves noted could be made against their study, e.g. that the patients were too few, that the doses of cannabis were low, that the patients' consumption of cannabis during the actual year of the study was unknown and that the study was of short duration.

## 6. Cannabis-Caused Delirium (*Acute Confusional State*)

### **Summary of Chapter 6:**

Cannabis smoking can cause an acute and short-lasting (between a few hours and a few days) state of profound delirium. The individuals affected experience complete or partial loss of their orientational ability, their memory and their sense of their own identity. An element of delirium is a common occurrence in cannabis psychosis.

This condition is probably more likely to arise if high doses of THC are involved or if the individual is in a weakened condition, for example owing to lack of sleep or to withdrawal symptoms relating to alcohol or other drugs.

Certain experts have calculated that delirium or cannabis psychosis occurs at one time or another in 10 per cent of all cannabis abusers.

There is widespread agreement that the use of cannabis, especially in high doses, can cause delirium (Hollister, 1986; Negrete, 1983; Tunving, 1985; Thornicroft, 1990; Chaudry et al., 1991), which is also known as acute brain syndrome or delirium. This is a short-lived condition, lasting from a few hours up to a few days. One characteristic of this condition is unclear consciousness: the persons affected have difficulty with spatial and temporal orientation, are unable to perceive correctly the situation in which they find themselves, and may fail to recognise close acquaintances. Not infrequently, this condition is difficult to distinguish from cannabis psychosis, which is described in the next chapter; and indeed it is not unlikely that one quite often encounters conditions which are a mix of delirium and cannabis psychosis. Castle and Ames (1996) subsume all transient confusional states, cannabis psychoses and psychosis-like conditions under the heading “acute brain syndromes” (or “encephalopathies”).

The main feature is profound confusion with regard to space, time, place and the people nearby, as well as uncertainty with regard to one’s own identity. Misjudgements of sense impressions and memory disturbance may also occur, as well as language disturbances (such as incoherent speech). Dramatic and rapid shifts in mental state are not unusual. There may also appear, in varying degrees, genuinely psychotic symptoms such as delusions and hallucinations.

In all probability, the degree of intoxication is important in determining whether or not this condition is provoked. Hollister (1986) is one of the researchers who claim that this

explains why cannabis-induced delirium was significantly more common outside North America in the mid-1980s, what with marijuana being the predominant cannabis preparation in Canada and the United States while hashish was (as it still is) the more common form in Europe.

The condition is probably more likely to be provoked in persons who are in a physically weakened state for a variety of reasons, such as physical illness, malnourishment, severe sleeplessness, the effects of other drugs or withdrawal symptoms.

The symptoms are frightening both to the individual and to those who witness them. Since a completely disoriented person may sometimes perform actions which are based on a totally erroneous perception of the surrounding reality, the condition can be serious and place the individual in dangerous – on occasion even fatal – situations. Under the heading “Cannabis and Suicide”, I account for a Swedish study of deaths caused by jumping from a height while under the influence of cannabis. In at least one of the cases reported, I have been able to conclude, by examining medical records, police reports and other material, that the suicide was carried out under the influence of severe disorientation/confusion, even though a (non-depressive) psychosis was present at the same time.

As has previously been mentioned, it is very difficult to calculate how likely cannabis abusers are to be affected by a given harmful effect. Based on general clinical experience as well as reports by abusers and their families, however, cannabis psychosis/delirium would seem to be a not entirely infrequent side-effect. Please refer to the next chapter, which deals with cannabis psychoses.

## 7. Cannabis Psychosis

### **Summary of Chapter 7:**

Cannabis smoking, especially of preparations with a high concentration of THC, can cause a toxic and short-lived (between a few days and six weeks) psychosis. Not infrequently, this psychosis has dramatic symptoms and requires hospitalisation, sometimes under constraint.

If the individual concerned stops smoking, the condition has a good prognosis. If he or she continues to use cannabis, however, the psychotic condition can probably remain for a very long time.

Different assessments and calculations to determine the frequency of this side-effect have yielded surprisingly similar results. As a “rule of thumb” it is considered that, on average, a person who smokes cannabis runs a 10 per cent risk of being affected at one time or another by cannabis psychosis or delirium.

Toxic cannabis-caused short-lived psychosis can sometimes be difficult to distinguish from the toxic cannabis-caused delirium described above; moreover, in the initial stage, the two conditions sometimes merge into each other. The essential difference between the delirium and the psychosis is the clouding of consciousness that accompanies the delirium; in the psychotic condition, the individual’s consciousness is by and large clear. Since the course of the psychosis generally lasts longer (one to six weeks) than the intoxication state, one may expect to find a delayed toxic effect. The duration indicated above is valid only if the individual stops smoking. If he or she persists in using cannabis, this psychotic condition, which otherwise responds very well to treatment, may continue for a very long period, perhaps for several years.

The clinical picture can sometimes be very difficult to distinguish from that of acute schizophrenia. However, some researchers maintain that the typical picture of cannabis psychosis does differ from that of schizophrenia and is characterised above all by what are known as “positive” symptoms such as paranoia and other delusions, hallucinations and, not rarely, sudden affective changes where aggressiveness alternates with euphoria. The clearest differentiating factor distinguishing cannabis psychosis from acute schizophrenia is the absence of disruption to thought, which is more or less the rule in schizophrenic patients (Thacore & Shukla, 1976). A further difference, which is also the primary one, lies in the subsequent course taken by the condition: cannabis psychosis is short-lived, while

by definition the course of schizophrenia lasts for at least six months (according to the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV]). Schizophrenia is often associated with a “premorbid personality”, which can manifest itself in various forms; the most common ones include extreme reserve, loss of earlier interests, vague delusions such as suspiciousness, and bizarre ideas. However, some of these symptoms may also characterise a chronic hashish smoker, which makes differential diagnosis more difficult. The absence of hereditary factors (for schizophrenia) is a further pointer towards identification as cannabis psychosis.

The most certain way of distinguishing between the two kinds of psychosis is to monitor the course taken by the psychosis. As mentioned above, provided that the person stops taking cannabis (as well as any other hallucinogenic or CNS stimulant drugs), cannabis psychosis is short-lived. However, this also means that, if the person continues to smoke hashish or marijuana, thus ensuring the persistence of the psychosis, there is sometimes no certain way of distinguishing cannabis psychosis from schizophrenia or other forms of functional psychosis.

This condition, like the delirium described above, is very frightening both to the individual concerned and to his or her family. Even though this is, from a psychiatric point of view, a condition whose prognosis is good and whose course is generally short-lived, the onset of cannabis psychosis must still be considered a very serious condition. It often requires hospital treatment, not rarely involving hospitalisation under restraint, and during the intensive phase of the psychosis there is probably an increased risk of suicide, for instance by jumping from a height (see the chapter on depression and suicide). Even where the course taken by the psychosis is not dramatic, the subjective impression of the person involved is that the condition represents a temporary mental breakdown, and this is an experience which can cast a shadow over a large part of that person’s future life.

### *Scientific and Clinical Reports*

The scientific literature has featured controversies about whether or not cannabis psychosis exists. In several cases, there has in fact been a mix-up with the delirium described above – a mix-up which is understandable since the two conditions, especially in the initial stages, tend to follow similar courses (Thorncroft, 1990). Most researchers, however, are of the opinion that the phenomenon as such – a toxically provoked psychotic reaction – does exist, and “cannabis-induced psychotic disorder” is indeed included as a diagnostic unit in DSM-IV.

And to complicate matters still further: in several research reports, especially older ones, “cannabis psychosis” refers to a longer-lived, functional and non-toxic (except possibly in the initial stages) condition. This means that in many cases, the lack of agreement has related to a condition other than the one I have described here. We will return to these issues in the following sections.

*In my opinion, “cannabis psychosis” is an excellent, clinically relevant and accurate term for a short-lived, mainly toxic, cannabis-caused psychosis.*

There is a large body of reports from researchers who have themselves studied the issue and from clinicians who have collected descriptions of groups of cannabis psychoses (as defined above). A few older examples of such descriptions are Weil, 1970; Bernardsson & Gunne, 1972; Pålsson, Thulin & Tunving, 1982; Tunving, 1985; Carney, 1984; and Brook, 1984. As the existence of this type of psychosis has been gaining acceptance, at least in the Nordic countries (Kristensen, 1994), such reports have become rarer, while the question of whether cannabis can cause *chronic* psychosis has come more to the fore. In the United Kingdom, however, where there has been more debate on whether cannabis is dangerous at all, a number of reports on cannabis psychosis have been published (Wylie, 1995; McBride & Thomas, 1995); both of these reports mention very high proportions of habitual smokers having developed delirious and/or psychotic reactions.

With regard to methodologically more advanced scientific studies showing that these psychoses exist and making comparisons with control groups of patients not affected by cannabis, it is above all the studies by Rottanburg et al. (1982) and Rolfe et al. (1993) that deserve mention. Chopra et al. (1974) have also, in a large-scale study, contributed extensive knowledge of cannabis psychoses. On the basis of in-depth analyses of published research findings, Ghodse (1986) and Thornicroft (1990) conclude that cannabis, especially in high doses, can provoke toxic psychoses.

An example from the author’s own clinical work:

*While I was collecting material for the first version of the present report, I was also professionally active in a private general psychiatric practice. A young patient (23 years old) was referred to me. He displayed the full range of signs described above: no history of mental illness, no divergent personality traits prior to this disturbance and no schizophrenia in close relatives. This patient’s illness had developed after a period of intensive cannabis smoking. He suffered from pronounced ideas of persecution, “magical” imaginings, pronounced suspiciousness and impulsive out-breaks involving aggressiveness towards members of his family as well as severe sleeplessness (being awake all through the night). By organising round-the-clock care and supervision within his family, making sure he saw me frequently and could phone me at more or less any time of the day or night, and quickly starting treatment with antipsychotic medication, it was possible to avoid having him admitted to a hospital. The psychotic symptoms proper faded after 7–10 days, after which there followed a convalescence period lasting for a couple of months, as well as a few relapses.*



### *Some Recent Studies*

As has been mentioned before, increasingly strong support has been found for an association between cannabis smoking and psychoses. Often, however, no clear distinction is made between different psychotic manifestations. In the above-mentioned studies (Fergusson et al., 2003; Arseneault et al., 2002), it can be assumed that some of the cases did indeed involve cannabis psychosis. As regards the Arseneault et al. study, though, this applies only in so far as the 26-year-olds studied were still cannabis consumers; the report is unclear on this point.

Two teams of researchers (Núñez et al., 2002; Debasish et al., 1999) have been able to confirm previous findings where a distinction, based on several features, had been drawn between two different groups of psychoses: acute schizophrenia on the one hand and short-lived toxic psychosis – cannabis psychosis – on the other.

### *How Common is Cannabis Psychosis?*

How common, then, is cannabis psychosis? We do not know for certain. There is probably some degree of underdiagnosis. Most studies from across the world show that there is a tendency at general psychiatric clinics to underestimate the prevalence of drug abuse (including alcohol abuse) in patients. It is a well-known fact at locked psychiatric wards and prisons that it is well-nigh impossible to keep the institution free from drugs; exceptions to this rule are specialised clinics and some special prison wards.

It is probably not unusual for patients to continue taking cannabis (unbeknownst to the staff) even when they have been admitted to a hospital. This will give rise to a longer-lived, schizophrenia-like course of illness. Another reason why the recorded diagnosis may not be cannabis psychosis is that poly-drug abuse is extremely common. If the individual concerned has been using, for instance, both cannabis and CNS stimulants – a frequent combination in Sweden –, we can no longer talk about a pure cannabis psychosis, and in such cases the diagnosis is usually determined by the “harder” abuse. Sometimes the condition can be dealt with in outpatient psychiatric care, and then – in Sweden at least – no note at all is made of the diagnosis in any central register.

For the above reasons, then, it is a difficult task to estimate the prevalence of this condition. Notwithstanding the difficulties involved in distinguishing cannabis psychosis from two neighbouring conditions – on the one hand, “psychotic symptoms” (serious enough, but not sufficiently so to warrant classification as a true illness), and on the other, acute schizophrenia –, several attempts have been made both to estimate and to measure the prevalence of cannabis psychosis.

Based on long experience and a literature review, Johnson (1991) estimated that 10 per cent of all those who had used cannabis on more than a single occasion experienced

cannabis psychosis or delirium. This proportion seemed high at the time, but later assessments have confirmed rather than refuted it. The most interesting study may be that carried out by Thomas (1996), who sent questionnaires to 1,000 New Zealanders aged 18–35 years, receiving a reply from 65 per cent. Of these, just under 40 per cent had used cannabis; and of these, 15 per cent had experienced psychotic symptoms. The now commonly accepted rule of thumb is that *10 per cent of those who smoke cannabis risk being affected by psychotic symptoms, which in many cases will amount to cannabis psychosis proper*. Johns (2001) also supports this assessment.

In a British report (Wylie et al., 1995) describing observations of a wave of psychosis and confusional states, it is emphasised that these observations were made in a group of abusers consuming (Dutch) cannabis with a very high THC content. In other words, the risk which is quantified above becomes greater as the intensity of smoking increases, i.e. if the individual concerned smokes more often or uses preparations with a higher THC concentration.

## 8. Cannabis and Chronic Non-Schizophrenic Psychoses

### **Summary of Chapter 8:**

On the basis of their studies, some researchers have maintained that cannabis smoking can also give rise to longer-lived psychoses, sometimes referred to as “cannabis psychoses”. The conditions in question have been psychoses whose clinical picture has differed in certain respects from that of schizophrenia.

Still, despite the fact that studies have been carried out which support this position, the overall impression is that there is not sufficient evidence to support the existence of this alleged side-effect of cannabis smoking. In other words: what appears to be a separate type of functional psychosis is probably schizophrenia.

A number of scientific studies have been carried out to answer the question of whether cannabis smoking can provoke long-lived, possibly chronic, psychoses. This, then, does not refer to a toxic psychosis which is maintained by means of continued cannabis smoking, but rather to psychotic conditions which remain after the toxic effect has ceased, often for a long period of time unless the condition is stopped through successful treatment. Simplifying slightly, it can be said that these reports and the discussions that they have given rise to have dealt with two different questions: a) Can cannabis smoking

lead to a protracted psychotic condition which is not schizophrenia? and b) Can cannabis smoking cause schizophrenia?

### *Cannabis Smoking and Functional Non-Schizophrenic Psychosis*

Here as elsewhere, there is a good deal of confusion as regards definitions. It is often difficult to understand what certain researchers consider themselves to have proved within the complex field of various kinds of psychosis and neighbouring conditions. Negrete (1983) has made an attempt to systematise the different conceivable psychotic conditions (including delirium), but this systematisation is too rarely used. Hall et al. (1985) make a thorough effort to bring order to the discussion. It is clear that some of the researchers who have talked about a short-lived cannabis-induced psychosis have been misunderstood and taken to have been claiming that there exists a functional and potentially (in the absence of treatment) protracted psychosis.

Thacore and Shukla (1976) have made the clearest attempt to demonstrate the occurrence of a specific cannabis-provoked functional psychosis. The psychoses described by them occurred, without exception, following a very long period of cannabis abuse; there was no evidence of delirium; and the picture presented by these psychoses differed from that found with schizophrenic patients in that there were no “negative” symptoms and a much lower degree of disturbance to thought. The researchers maintained that they could thus distinguish a variety of psychosis which differed both from the toxic cannabis psychoses and from schizophrenia. For various reasons, however, the attitude generally adopted towards this interpretation and other similar studies has been that the evidence does not yet allow any definite conclusions to be drawn.

Tsuang et al. (1982) – who, it should be added, studied patients with various types of drug abuse – were able to separate, in an interesting manner, the purely toxic psychoses from those where drugs had contributed to precipitating what had probably been a latent psychosis. One of the differences found between these two varieties of psychosis was that there were clear signs of a hereditary disposition towards (increased vulnerability to) schizophrenia whereas no such heredity could be observed for the toxic psychoses. Most of the evidence seems to suggest that the purportedly functional cannabis psychoses are in fact primary schizophrenic psychoses or schizophrenic psychoses precipitated by cannabis abuse (Hall et al., 1995). One potentially misleading circumstance is that cannabis smoking appears to affect the clinical picture exhibited by these probably schizophrenic patients.

It is difficult to find studies from recent years that reinforce – in a similar way as in the case of schizophrenia – the hypothesis that there is a specific cannabis-provoked (non-schizophrenic) chronic functional psychosis.

To conclude, then, the question of whether or not there exists a functional, non-toxic and non-schizophrenic cannabis-induced illness has not yet been answered.

## 9. Cannabis Smoking and Schizophrenia

### **Summary of Chapter 9:**

It is well known among clinicians that cannabis smoking interacts with manifest schizophrenia: cannabis smokers experience more relapses (more frequent hospitalisation), their symptoms are more dramatic, and they are less susceptible to the effects of neuroleptic medication.

It is also considered a well-established fact that intensive cannabis smoking can be the precipitating (in the sense of activating) factor when particularly sensitive individuals fall ill for the first time. In addition to this, some studies suggest that the onset of cannabis-precipitated schizophrenia occurs, on average, at a younger age (four years earlier, according to some calculations) than spontaneous onset of schizophrenia.

Can cannabis cause schizophrenia, i.e. provoke schizophrenia in individuals who would not otherwise have developed the illness? There is a growing body of indications in support of the claim that the answer to this question is “yes”. The largest study in this field is the Swedish one of military conscripts. Until recently, no other study had repeated it in order to contribute to corroborating its conclusions in a convincing way. However, given van Os’s (2002) thorough study of 5,000 randomly chosen Dutch people as well as a pair of longitudinal studies (lasting for 21 and 29 years, respectively) from New Zealand, it must now be considered proven that cannabis smoking can provoke a functional (non-toxic) schizophrenia-like psychosis.

### *Can Cannabis Smoking Cause Schizophrenia?*

The issue of how cannabis can cause relapses into schizophrenia and how it can interact negatively in different ways with schizophrenic illness is discussed in the following section. First, though, we will discuss the question of whether cannabis can literally cause schizophrenia, or in other words whether cannabis smoking, viewed from a stress-vulnerability angle, can exert such a heavy strain on the psyche that a schizophrenic illness – which would probably otherwise never have been provoked – breaks out.

Several of the findings from the above-mentioned studies (e.g. Holmberg, 1981; Bier & Haastруп, 1985; Tennant & Groesbeck, 1972) suggest that there may be such a connection. However, none of the studies meets the methodological requirements necessary for such a conclusion to be tenable. Already in the early 1970s, Breakey et al. (1974) pointed out that there was some form of association between drug abuse (including cannabis abuse) and the onset of schizophrenic illness. He considered that cannabis (and other drugs) precipitated latent schizophrenia, but also believed that there were grounds for suspecting that cannabis could precipitate schizophrenia in cases where the illness would otherwise not have become manifest. The reasons were that the onset of drug-induced schizophrenia occurred on average four years earlier than the onset of other forms of schizophrenia, that the onset was more sudden than in other schizophrenics, and that the patients' premorbid personality was consistently better than in a comparable group with non-drug-induced schizophrenia. Hereditary aspects were not touched upon in this study. Twenty years later, Eikmeier (1991) arrived at similar results in a larger-scale study which looked only at cannabis-induced schizophrenic psychoses as compared with drug-free schizophrenic psychoses. These studies, it should be stressed, do not prove that cannabis use really does increase the risk of developing schizophrenia; but they do suggest that cannabis use will cause the onset of the illness to occur earlier (which is serious enough in itself).

It is not difficult to understand why there are relatively few studies claiming to help answering this question. On a general note, the complexity of the question requires the use of an advanced scientific method, and probably also a very large study group which is monitored over a long period of time. There is a need not only for interest and skill in the research team, but also for endurance and financial resources.

Until recently, there has really been only a single study which comes close to meeting these requirements: the large-scale follow-up of 45,000 Swedish military conscripts carried out by Andréasson, Allebeck, Engström and Rydberg (1987). Information recorded at the time of the enrolment of the conscripts (typically at the age of 18 or 19), including on their drug-taking habits, was compared with recorded schizophrenia diagnoses over the subsequent fifteen years. It was found that a person who had claimed, at the age of 18 or 19, to have consumed a great deal of cannabis (on more than 50 occasions) was six times more likely to be diagnosed as schizophrenic during the subsequent fifteen-year period than a person who had claimed at enrolment that he had never used cannabis at all. When account was also taken of other factors which were recorded at the time of enrolment and which may increase the statistical likelihood of being diagnosed with schizophrenia, the cannabis-dependent risk became smaller, but there remained a statistically significant risk increase associated with cannabis use.

On publication, this study justifiably aroused considerable attention; and for the past fifteen years, it has probably been the most frequently cited study in the international research literature on the relationship between cannabis and psychosis. The initial

reactions to it ranged from total acceptance (Ottosson, 1992) to extensive criticism (Johnson et al., 1988). Negrete – the doyen of this field – judged the connection which was claimed to exist between cannabis and the precipitation of latent schizophrenia to be reasonable, on the basis of this study as well as previous ones (Negrete, 1989). At the same time, though, he was of the opinion that the study suffered from a number of weaknesses.

Andréasson et al. (1989) and, above all, Allebeck et al. (1993) have carried out a couple of supplementary studies in which they have tried, in large part successfully, to eliminate the weak points of the original study, thus adding further strength to their original findings. The latter study involved going through information from the medical records of 112 patients who had been diagnosed with both schizophrenia and cannabis dependence. This information was examined to determine such aspects as the clinical picture at the onset of illness, the temporal relationship between the cannabis abuse and the patient's falling ill, and the involvement of other drugs, above all amphetamine. In all significant respects, the findings which were made in these studies confirmed the conclusions reached in the original study.

Further support as regards one aspect of that study comes from an examination of 100 randomly chosen medical records of patients diagnosed as having schizophrenia in the period 1973–1977. The researchers found a large degree of consistency across regions and hospitals as well as over time, and also a large degree of conformity with the DSM-IV diagnostic criteria for schizophrenia (Dalman et al., 2002).

In the original Swedish study, the first analysis was performed fifteen years after the enrolment of the conscripts. In order to add further strength to their findings and to extend the study, the research team (reinforced by a few British researchers) performed another analysis 27 years after the time of enrolment. By comparing the group of people who had fallen ill within five years of enrolment with those who had fallen ill later, and by re-analysing the data provided at the enrolment interviews – in the light of twelve more years' worth of research into the importance of various background factors in the development of schizophrenia –, the researchers were able to dismiss a few more of the objections which had been made to the original study (Zammit et al., 2002).

### *Some Recent Studies*

A few studies published in the past five years support the Swedish study to some extent. J. van Os et al. (2002) claim to have replicated the Swedish study, which gives their study extra weight. This study doubtless occupies (along with the Swedish one) a particularly prominent place. There is no room here for a detailed description, but suffice it to say that even though the study group is smaller and the period of monitoring is shorter in the Dutch study – both considerably so –, most of the weaknesses hampering the Swedish study have been eliminated.

Within the framework of a national Dutch inventory study of psychiatric morbidity, a random sample of just over 7,000 people (reduced through dropouts and the application of exclusion criteria to 4,100) from 60 different localities was drawn. A baseline assessment and two follow-up assessments, the later one after three years, were made individually by means of questionnaires and, where necessary, in the form of clinical interviews. Those exhibiting psychotic manifestations at follow-up were divided into three groups, of which the “heaviest” one would appear to be rather close to the schizophrenia diagnosis in the Swedish study.

The study by J. van Os et al. shows the following:

- a) There is a causal link between cannabis taking and psychotic manifestations.
- b) The psychotic manifestations range from psychotic symptoms to mental illness (defined as “need for psychiatric treatment for psychotic illness”).
- c) The risk of developing psychosis increases with the amount of cannabis taken.
- d) The risk of developing psychosis seems to be greater where the individual has consumed cannabis earlier (before or at the start of the study) than where the individual has done so later (in direct connection with the follow-up after three years). This makes it possible to exclude, in large part, that the psychoses were caused by direct toxic effects.
- e) In cannabis-smoking individuals assessed, at the beginning of the study, as having a disposition towards psychosis, there is a synergistic risk increase, with a very high proportion exhibiting manifest psychotic illness at the three-year follow-up.

The studies mentioned in the previous chapter on cannabis psychosis (Arseneault et al., 2002; Fergusson et al., 2003) also support the existence of a causal link between cannabis and psychotic illness.

Arseneault et al. also consider their study as directly supporting the Swedish study. However, unlike that study, which is retrospective in several respects, the findings made by Arseneault et al. in New Zealand are based on a long-term prospective study (data on just over 1,000 children/young people, with the times of assessment including the ages of 11, 15 and 18 as well as the end of the study, when the subjects were 26 years old). Cannabis smoking during the teenage years was found to have a clear impact in that the risk of schizophreniform illness (including an unknown proportion of schizophrenia proper) was four times greater at the age of 26. The younger a person was when first using cannabis, the greater the risk was found to be (which may be because the early start has resulted in the overall consumed *amount* of cannabis being larger).

Fergusson et al. (2003) showed that cannabis dependence increases the frequency of psychotic symptoms. Degenhardt and Hall (2001) show, in a large study of 6,700 adult Australians, that cannabis dependence doubles the risk of developing psychotic symptoms.

### *Cannabis and Manifest Schizophrenia*

Naturally, the line of argument followed in the preceding section is also supported by the specific interaction between schizophrenia and cannabis smoking which has been observed by many psychiatrists and whose existence has been borne out by several scientific studies.

Treffert's case descriptions from 1974 of four schizophrenic patients have acquired almost classic status. He let four schizophrenic patients, all of whom were on antipsychotic medication, act as their own controls. They all smoked cannabis occasionally, despite having been warned not to, and regularly experienced deterioration in their condition, sometimes with very serious consequences. It was not difficult for Treffert to demonstrate a direct association between relapses into marijuana smoking and serious deterioration of the schizophrenic condition (Treffert, 1974).

Most psychiatrists have, over the years, found themselves able to make similar observations: cannabis smoking causes a deterioration regardless of antipsychotic medication.

According to Negrete et al. (1986), the interaction between cannabis smoking and schizophrenia has the following characteristics: cannabis smokers experience more relapses (more frequent hospitalisation), their ("positive") symptoms are more dramatic, and they are less susceptible to the effects of neuroleptic medication. The effects seem to be dose-dependent (Linszen, 1995). There are no significant discrepancies in the way different clinicians or different researchers view the problem. A further question, which however does not fall within the scope of my report, is why schizophrenics are so strongly attracted to cannabis (and amphetamine) despite the risks of deterioration involved.

In recent years, these different aspects of the interaction between cannabis and schizophrenia have also been demonstrated in a series of studies (Bersani et al., 2002; Verdoux et al., 2002; Caspari, 1999). Among the authors of reviews, Degerhardt and Hall (2001) may be mentioned.



## 10. Anxiety Conditions and Depersonalisation Syndrome

### **Summary of Chapter 10:**

Cannabis intoxication can induce anxiety attacks of varying strength. Such attacks of panic anxiety are probably a relatively frequent side-effect; they are believed to be more common in occasional smokers or smokers who ingest a larger amount of THC than they are used to.

Further, the anxiety attack may signal the beginning of a protracted panic-anxiety syndrome which does not differ from panic-anxiety illness that begins in some other way. Cannabis smoking can also provoke a relapse into panic-anxiety syndrome.

On occasion, experiences of unreality, which are a common feature of cannabis intoxication, may become so strong that they dominate the experience of intoxication. These anxiety-like “depersonalisation syndromes” generally abate rapidly after intoxication. There are, however, a number of published case studies where the feelings of unreality have persisted over a very long period after being provoked; in some cases, the disorder has had an invalidating effect and has been very difficult to treat.

In a survey of 117 patients with chronic/long-lived depersonalisation syndrome, cannabis was found to be the third most frequent provoking factor.

### *Anxiety Conditions*

One of the contradictory characteristics of cannabis is that it can both relieve anxiety and give rise to pronounced attacks of anxiety and panic. Such anxiety attacks are probably the most common side-effect experienced by smokers of cannabis (Hollister, 1986; Mathew et al., 1993), and all habitual smokers have themselves had them or seen their friends affected by them. While the condition is more frequent in beginners, it also occurs in more experienced users. This side-effect is almost certainly dose-dependent, although it is also to a large degree dependent on the mental condition of the smokers and on their perception of the social setting in which they find themselves. This is a well-known phenomenon in abuser circles, but it has also been demonstrated under experimental conditions (Sheehan & Sheehan, 1982). In a survey of 200 cannabis abusers, 22 per cent stated that they had experienced panic anxiety on at least one occasion (Thomas, 1996).

Like other attacks of panic anxiety, these attacks can be very frightening, with a strong feeling of losing control, going mad, and so on. Nevertheless, those affected seldom seek professional help – instead, the situation is dealt with within their circle of friends. The condition is generally short-lived, its only consequence being that the persons affected are subsequently more careful with doses and with the social setting in which they smoke, or that they stop using the drug completely.

However, an anxiety attack sometimes marks the beginning of a protracted panic-anxiety disorder which is indistinguishable from panic anxiety that has begun in some other way (Ströhle et al., 1998; Deas, 2000). Cannabis can also provoke a relapse into or a deterioration of panic-anxiety disorder (Szuster, 1988). In some cases, professional help may be required (Fishman, 1988).

### *Depersonalisation Syndrome*

Feelings of unreality are often part of the experience of an anxiety attack, and this holds true for cannabis-induced anxiety attacks as well. In cannabis smokers, though, these feelings of unreality may become more profound in nature, and sometimes they dominate the negative experience (Mathew et al., 1993). When these symptoms are provoked by cannabis, they are short-lived – as are like anxiety attacks in general.

When feelings of unreality dominate the symptom picture and become long-lived, we usually talk of “depersonalisation syndrome”. This condition appears to be closely related to the anxiety disorders, but there is a lack of consensus as regards its classification. From a psychodynamic point of view, it is seen as a defence against unbearable anxiety. This condition is rarely encountered as an independent disorder in general psychiatric practice.

It is worth noting, not least in view of the rarity of the condition, that a number of cases of prolonged depersonalisation syndrome induced by cannabis smoking have been reported in the scientific literature. Several of these cases have been difficult to treat (Szymanski, 1981; Keshaven & Lishman, 1986; Moran, 1986).

Prolonged depersonalisation syndrome subsequent to cannabis smoking (as opposed to depersonalisation experiences during intoxication) is rarely mentioned in reviews and summaries of the harmful effects caused by cannabis, and thus it was not primarily by studying the research literature that I became aware of the connection between these conditions. A patient who was referred to my general psychiatric practice exhibited the following clinical picture:

*A district doctor referred a young man to me with “anxiety disorder following cannabis psychosis”. It transpired that the young man had not had a psychosis; what he had in fact suffered from was a severe attack of*

*anxiety the last time he had smoked marijuana – roughly six months previously. After this attack, an anxiety syndrome (panic anxiety) had persisted and progressively become more dominated by feelings of unreality. The patient had smoked cannabis fewer than ten times in all, his social situation was very stable, and he had no history of mental problems and no hereditary tendency towards mental illness. Three years later, I was able to conclude that the patient's feelings of unreality had become a constant companion of his. Sporadically occurring anxiety proper had made its appearance, and the patient's tendency towards social phobia complicated the situation. The patient was not handicapped by the symptoms, but they were a great nuisance to him and also a cause of worry. In addition to the unpleasantness of having a symptom of this kind constantly present, certain important social activities were made much more difficult. For several years, the condition resisted all attempts to treat it.*

Daphne Simeon and co-workers have recently, in an informative survey (Simeon et al., 2003), examined 117 cases of depersonalisation syndrome – which is a larger number than I have found in earlier reports. When going through these cases, they found that the majority of the patients were suffering from a chronic condition that had persisted for 15 years on average. In no fewer than 57 of these patients, no provoking factor could be identified. The second most common provoking factor was found to be stress (29 cases), and in third place was cannabis (15 cases). A majority of the patients had a life story involving shorter or longer periods of other mental illness, mainly depression and anxiety.

## 11. Depression and Suicide

### **Summary of Chapter 11:**

Clinical observations suggest that cannabis smoking can provoke depressive reactions. Despite this, it is only recently that research has been able to show that cannabis has a specific depression-provoking effect.

In many of the groups which have been studied, cannabis interacts with other depression-provoking factors. In recent years, however, some longitudinal and prospective studies have managed to distinguish cannabis as a separate factor capable of provoking depressive symptoms and probably also “major depression”.

When it comes to suicide, what has been investigated are above all serious suicide attempts. It has not been possible to show with certainty that cannabis abuse, as an independent factor, causes suicide/suicide attempts. Cannabis abuse does, however, appear capable of causing, above all indirectly – through its association with harder drugs and by provoking psychosis and depression –, premature death through suicide.

A Swedish research team studying people who took their own lives by jumping from a height has found that a disproportionately large share of these people were under the influence of cannabis.

### *Cannabis and Depression*

In a well-known review article, H. Thomas (1993) looks at the question of depressive reactions. His conclusion is that it is not possible to find scientific proof that cannabis causes depressions of clinical importance. He does, however, consider that there is a large body of clinical observations showing that shorter-lived dysphoric episodes can be provoked by cannabis abuse.

The increased frequency of suicide among large-scale consumers of cannabis which was pointed out by Andréasson and Allebeck (1990) may, however, be a reflection of increased frequency of depression in cannabis abusers (see next section).

Weller et al. (1989) compared abusers, users and non-users of cannabis in a group of outpatients and found that of the abusers, 55 per cent had a clinical depression according to

the DSM-III criteria. However, it was unclear whether there was a causal connection. The cannabis abusers also exhibited a higher frequency of other problems – some of which have an established relationship with depression – such as parallel abuse of alcohol and/or sedatives. Moreover, the cannabis abusers had family backgrounds which featured a significantly higher level of drug abuse, alcohol abuse, criminality and suicide. The study by Rowe et al. (1995), which showed an association between marijuana smoking and depression in women, suffers from the same lack of simultaneous control for other depression-provoking factors.

### *Recent Studies*

The main difficulty involved in the non-longitudinal studies has indeed been determining what is cause and what is effect: has cannabis smoking caused depression, or have depressed people “self-medicated” by smoking cannabis? (When it comes to psychoses, there are examples of both relationships, but a sufficient number of studies have shown that cannabis can precede and provoke both temporally adjacent toxic psychoses and temporally more distant functional schizophreniform psychoses.)

Bovasso (2001) carried out a study whose main objective was to shed light on two questions: 1) To what extent does cannabis abuse constitute a risk factor for the development of depressive symptoms? and 2) To what extent do depressed people tend to self-medicate with cannabis? The study was based on data initially collected in 1980 within the framework of a major psychiatric inventory of the entire population of a region in the United States. In all, 1,920 persons of all ages were examined in 1995, on average 14 years after the start of the study. Two groups were studied more closely: those 849 who had no depressive symptoms at baseline and those 1,837 who had no cannabis abuse at baseline. At follow-up, it was found that among those “non-depressives” who were cannabis abusers at baseline (and for an unknown period thereafter), depressive symptoms were four times more common than among those not recorded as cannabis abusers. Further, it was found that depressive symptoms at baseline did not significantly increase the likelihood of exhibiting cannabis abuse at follow-up. The depressive symptoms involved were mainly anhedonia and suicidal thoughts.

Patton et al. (2002) studied a group of school students for seven years. A total of 1,600 students from 44 schools were monitored between the ages of 14–15 and 21–22 years. Particularly if they were using cannabis intensively (on a daily basis), the girls ran a 4–5 times greater risk of depression than if they had not been cannabis smokers. In line with the findings of the previous study, depressive problems during the teenage years did not give rise to increased cannabis use during early adulthood.

*Notwithstanding certain weaknesses, and despite the fact that it is not clear what types of depression have been provoked, these studies mark a distinct break in the trend evidenced*

*by previous studies. They show that there is a causal connection between cannabis smoking and subsequent depression/depressive symptoms.*

### *The Interaction between Cannabis and Antidepressants*

Stoll et al. (1991) have reported a case of mania which they suspected to be a manifestation of interaction between cannabis and fluoxetine, one of the now very widely used SSRI-type antidepressants (the Prozac group). This could be a reflection of the fact that cannabis has an effect on serotonin metabolism in the brain, as has been demonstrated in animal experiments. In any case, such a report represents a call for caution in prescribing this type of antidepressant to patients who are cannabis smokers. Previous clinical reports have suggested that cannabis smoking in a patient makes it more difficult to adjust the dose of lithium, which is used in treating manic-depressive illness (Nordegren & Tunving, 1984).

There are also descriptions of strongly negative effects in four cases involving older antidepressants (tricyclic antidepressants).

### *Cannabis and Suicide*

Few scientific studies have attempted to examine the relationship between cannabis and excessive mortality. Andréasson and Allebeck (1990) studied large-scale cannabis consumers in a group of 45,000 Swedish military conscripts. They found excessive mortality in the cannabis group (violent death was the dominant cause of death; 34 per cent had died from suicide or suspected suicide), but after controls were made for other factors, this excessive mortality could not be linked to cannabis as a sole cause of death. The authors point out that the association between cannabis and harder drugs (for which there is a documented increased mortality, not least from suicide) indirectly affects mortality. In a similar fashion, cannabis indirectly increases the risk of suicide as a result of its ability to precipitate, exacerbate and cause psychosis and depression.

There is reason to remind the reader of one of the findings from the study by Bovasso et al. (2001) mentioned above. Of the depression variables investigated in that study, two were particularly often reported by the subjects: anhedonia and suicidal thoughts.

Beautrais et al. (1999) find only a very limited independent association between cannabis and suicide. However, they do join Bovasso et al. in emphasising the indirect link by way of psychosis and depression – both of which are conditions involving increased mortality from suicide.

### *Suicide Committed by Jumping from a Height*

Fugelstad, Gerhardsson de Verdier and Rajs (1995) found, in a study of 53 suicides committed by means of jumping from a height, that a disproportionately large share

(11 per cent) of the jumps had occurred under the influence of cannabis. By taking into account the proportion of abusers in the age group concerned (20–34 years), the researchers were able to calculate the increased risk of committing suicide by jumping from a height: a cannabis smoker is 18.7 times more likely than a non-smoker to take his or her life by jumping from a height.

## 12. *Amotivational Syndrome*

### **Summary of Chapter 12:**

“Amotivational syndrome” is a well-established term which aptly describes the particular personality traits of many chronic cannabis abusers. Many clinicians and some researchers have described this syndrome as a specific, yet complex, illness provoked by cannabis.

However, scientific studies have shown that the syndrome is quite simply a reflection of chronic cannabis intoxication. Not least does the continual impact on cognitive functions lead to a mental state characterised by varying degrees of apathy, loss of effectiveness and reduced ability to carry out complex, long-term plans, to deal with frustration, to concentrate for any length of time, to follow routines or to deal successfully with new situations.

It seems reasonable to say that our modern high-tech society, with the demands it places on individuals and its rapid pace of change, is a social environment to which a chronically cannabis-intoxicated person is extremely ill adapted.

In 1968, Smith introduced the term “amotivational syndrome”, and in the same year McGlothlin and West described the particular personality traits of cannabis smokers under the heading of “amotivational personality characteristics”. These two notions referred to the same condition, which the researchers had observed mainly in North American young people (Cohen, 1982). Although it has been difficult to find scientific evidence for the existence of such a cannabis-induced syndrome, the ubiquity of the term “amotivational syndrome” is remarkable. It is clear that it has struck a chord as an apt description of particular personality traits frequently observed in chronic cannabis smokers.

At the scientific level, it has been difficult to pin down this condition, which refers to a cannabis-induced mental state characterised by “apathy, loss of effectiveness, and reduced

ability to carry out complex, long-term plans, deal with frustration, concentrate for any length of time, follow routines, or deal successfully with new situations” (Cohen, 1982).

The descriptions of the condition tally to a degree with older observations of large-scale consumers of cannabis preparations in certain developing countries. On the other hand, it is precisely studies from developing countries that have shown the absence of amotivational syndrome: Comitas (1976) in Jamaica, Carter and Doughty (1976) in Costa Rica, and Boulougouris, Liakos and Stefanis (1976) in Greece.

The clinical reports which support the existence of amotivational syndrome appear primarily to build on observations of young individuals in Western industrialised countries (Cohen in *Marijuana and Youth*, 1982; Tunving, 1987). Newcomb and Bentler (1988) also claimed to have found some evidence supporting the existence of amotivational syndrome in their longitudinal study of a large group of young people.

Cohen (1982) maintains – drawing part of the support for his claim from a study by Soueif (1976) – that chronic cannabis abuse does not produce these motivation-inhibiting effects in illiterate abusers who are manual labourers and live in a rural, intellectually less demanding culture. Instead, those affected by the condition are not least young people living in the complex, urban environments of the modern Western world, where considerable demands are made on people with regard to intellectual performance, a readiness to adapt rapidly to change and a willingness to re-learn quickly.

What Soueif (1976) discovered was that the differences (in terms of scores on tests of cognitive and psychomotor functions) observed in a large study between a group of chronic cannabis smokers and a group of non-smokers more or less disappeared when the subgroup of “illiterate rural people” within the broader group of cannabis smokers was compared with the non-smokers. On the other hand, the differences were amplified when the subgroup of “literate urban people” was compared with the non-smokers.

Musty and Kaback (1995) maintain that amotivational syndrome does exist, but that it is a manifestation of depression. However, their study is unclear on a number of points relating to the delimitation and definition of depression; and moreover, the methodology used to measure the study group’s poor level of motivation is open to question.

One circumstance worth drawing attention to is the fact that in many studies, including the two just mentioned, poor levels of motivation are equated with lower scores on tests which primarily measure cognitive and psychomotor ability. While the effect exerted by chronic cannabis smoking on cognitive functions undoubtedly affects mental processes which may contribute to “amotivation”, the processes we are dealing with here are probably not exclusively cognitive in nature.



In conclusion, then, it can be said that the term “amotivational syndrome” seems to be a strikingly apt description of the particular psychosocial personality traits of a not insignificant proportion of chronic cannabis abusers, especially among young cannabis smokers in Western industrialised countries. These traits, which seem to be elusive to scientific documentation, can be confused with – or reinforce – other states or conditions, including periods of regression during the teenage years which are appropriate to that phase from the perspective of developmental psychology, as well as depression, chronic tranquil schizophrenic psychosis and certain personality disorders.

*These psychosocial personality traits are in all probability nothing other than a manifestation of certain effects of chronic cannabis intoxication.* This would be consistent with the varying frequency of occurrence and with the way in which the syndrome is dependent on the psychosocial circumstances of the individual.

The markedness of these personality traits would seem to be dependent on the “cerebral reserve” at the individual’s disposal as well as on the social demands placed upon him or her. It seems reasonable to say that our modern high-tech society, with the many demands it places on individuals and its rapid pace of change, is a social environment which is more or less incompatible with chronic cannabis intoxication.

## 13. Cannabis and Violence

### **Summary of Chapter 13:**

Generally speaking, the effect of cannabis is to soothe and to calm rather than to stimulate aggression. Research into the relationship between the effects of cannabis and acts of violence, however, has produced ambiguous findings.

This chapter presents a few pilot studies showing an association between cannabis and serious violence (murder, manslaughter and aggravated battery). These studies, along with clinical observations, underline the importance of studying the co-morbidity of cannabis and personality disorders, and probably that of cannabis and psychosis as well. It is also very important to draw the appropriate conclusions from the studies (see the account of the study by van Os et al. in Chapter 9) which show how the combination of cannabis and a disposition towards psychosis strongly increases the risk of developing manifest schizophreniform psychosis.

The studies presented in this chapter once again highlight the need to study the interaction between cannabis and alcohol.

Niveau and Dang join many others in pointing out that both the increasing prevalence of abuse and the growing strength of preparations make the risks greater. Not least, stronger preparations seem more likely to cause toxic psychosis.

Most researchers agree that the effect of cannabis is normally (i.e. in the case of the average abuser) to calm and to induce passivity rather than to stimulate aggressiveness. However, owing to the dramatic nature of the effects produced by cannabis on the mind and to clinical observations of violent acts, the question of whether cannabis might be associated with aggressiveness and acts of violence has been raised repeatedly. A large number of commissions and conferences have focused on this issue (Abel, 1977; Rosenberg et al., 1984). In all cases, the conclusion reached has been a similar exonerative verdict of “not guilty”.

Abel (1977) does, however, point out that a weakness shared by all these commission reports is that in general, they have not looked at the question of the effect produced by cannabis on individuals who are especially vulnerable in this respect – above all, mentally

fragile people with low levels of impulse control and people with psychoses, borderline psychotic conditions, profound personality disorders and brain damage.

There seems to be no study that shows, in a methodologically satisfactory manner, that cannabis is in any way linked with violence. The explanation may have something to do with Abel's above-mentioned point of view. If you add in the fact that the primary objective of most studies is to identify pure effects of cannabis, the findings are easier to understand. In stable, mentally healthy people, the calming effects usually predominate. As can be seen from the pilot studies referred to below, it appears to be precisely the *combination* with a mental disorder that may sometimes lead to unfortunate consequences.

When it comes to alcohol and illegal drugs other than cannabis, we increasingly speak in terms of "dual diagnosis" or "co-morbidity", taking an interest in the interaction between two or more conditions. It seems to be time that we studied not only the interaction between cannabis and schizophrenia but also the connection between, for instance, cannabis and various personality disorders.

Moreover, the studies mentioned below remind us once again how important it is to reflect on the interaction between alcohol and cannabis.

### *A Few Pilot Studies in the Field of Cannabis and Violence*

Spunt et al. (1994) conducted a study which shows that in certain cases of aggravated violent crime there is probably a connection with cannabis intoxication. They interviewed 268 people sent to prison for murders committed in New York State during 1984. Of these inmates, 73 had been under the influence of cannabis when committing their murder; and of these, 18 were of the opinion that there was a link between the murder and the effects of cannabis. The persons interviewed were also asked how marijuana smoking affected them. Four of them gave answers along the lines of "it made me aggressive, violent", one answered "when I am high I just lose control ...", and another said "I don't think I had done anything if I hadn't been under the influence". Four interviewees gave answers of the type "it lowered my inhibitions", and two replied along the lines of "it made me feel paranoid".

Fifteen of the eighteen murderers who had been under the influence of cannabis were also under the influence of alcohol or an illegal drug other than cannabis at the time of the murder. Nine of these said that they thought the combination of cannabis with alcohol – or of cannabis with another drug – was an important factor in their committing the crime. One of the three who were under the influence of only cannabis and alcohol explained the effect in the following manner: "One alone you can handle – but two together confuse your mind." Another of them said: "The alcohol took away my inhibition and the pot made me crazy." And the third of them observed: "The combined effect made me lose self-control."

Niveau and Dang (2003) have accounted for twelve cases of aggravated violent crime, all committed in Geneva in the period 1996–2000. Initially, there was a much larger study group, but those with poly-drug abuse were excluded. When committing the crime, the individuals in question were under the influence of cannabis only. Of the twelve subjects, five had a previously known personality disorder and three had other psychiatric disorders.

At the time of the crime, all twelve were suffering from severe negative effects caused by cannabis consumption: four of them experienced acute psychotic conditions and one suffered a relapse into or an exacerbation of chronic paranoid psychosis. A further three of them experienced negative reactions such as intensive anxiety (the description is somewhat unclear on this point) and three were affected by delirium. One patient had a “mood disorder”.

The report is densely written and my space here is limited. What I wish to emphasise most of all is what appears to be, at least in some cases, an unfortunate combination of (mainly psychotic) vulnerability, cannabis and a stressful situation whose joint effect has been to provoke psychosis, delirium and attacks of rage, all with a strong element of aggression. It should be noted that some of the processes described here are given scientific explanations in Chapter 9. The account of the study by van Os et al. shows how great the risk of psychosis outbreak is in vulnerable people who have a history of psychiatric problems, especially in the psychotic direction.

These authors and others maintain that, given these insights, cannabis abuse must be taken more seriously.

In other words, here we see two shifts in perspective as regards the dangerousness of cannabis. There is growing interest in dual diagnoses involving cannabis abuse as one of the disorders, and there is also growing interest in the interaction between alcohol and cannabis. In addition to the discussion presented in this chapter, the reader should also refer to Chapter 16 on cannabis and traffic.



## *Part Three – Some Psychological and Psychosocial Harmful Effects*

### *14. Harmful Effects of Cannabis Smoking on Reasoning Ability, Memory and Sense of Coherence (Cognitive Functions)*

#### **Summary of Chapter 14:**

After a single instance of intoxication, the acute psychotoxic effects caused by cannabis smoking on cognitive functions (reasoning ability, memory functions, analysis and planning ability, etc.) will remain, in general, for a maximum of four to five hours. The duration of these effects is dependent on the level of THC in the blood, and there is a delay of an hour or so relative to the time of consumption. In the case of repeated consumption, i.e. on one or more occasions per day, the functional impairments will persist (even though the individual learns how to hide certain functional shortcomings) and the entire personality will eventually become marked by above all cognitive difficulties, and also by the social strategies to which the individual has recourse in order to cope. The manifestations of the chronic effects include the following: decreased ability to carry out complex thought operations, reduced ability to concentrate, decreased ability to process information, impairment of short-term memory, reduced intellectual flexibility and ability to learn from experience, lowered ability to carry out long-term strategic planning, and difficulties expressing oneself verbally in new, unfamiliar situations where old modes of thought and old knowledge are inadequate.

Chronic abuse also leads to a measurable deterioration in the individuals' "sense of coherence" (i.e. their perception and understanding of their environment), although this effect fades a number of weeks after abuse is discontinued – or sooner if treatment is given.

Systematic clinical observations of cannabis abusers yield a picture of a personality characterised by rigidity, inflexibility and memory problems – and consequently problems in dealing with change. Cannabis abusers are not seldom lonely and isolated people.

Studies of chronic abusers show that certain functional defects (typically subtle ones) persist for several years after the individual has discontinued his or her abuse. The functions affected relate mainly to memory and attention.

The effects of cannabis intoxication include diminished memory, changes in temporal perception and reduced ability to pay attention. This affects a number of sensorimotor functions such as reaction speed, co-ordination, the ability to assess lengths of time and the ability to carry out several tasks simultaneously. More complex functional impairments can also arise (probably through interaction between the above-mentioned defects), especially in the case of long-term – i.e. more than occasional – abuse.

The acute deterioration of these functions and its importance for (above all) driving will be discussed in Chapter 16. The cognitive disturbances might possibly be at the core of the mental weaknesses which provoke psychosis and depressive symptoms. Chapter 17 accounts for late mental effects on children whose mothers have smoked cannabis during pregnancy. The symptoms exhibited by these children are similar in many respects to some of the cognitive disturbances which arise in cannabis-smoking young people and adults.

This chapter looks at the question of how chronic cannabis abuse affects mental functions – i.e. what happens to human intellectual and psychomotor functions if the brain is exposed to constant and very prolonged cannabis intoxication. It is reasonable to assume that repeated poisoning, month after month and year after year, will produce some form of negative effects, and it is also reasonable to assume that those effects do not consist solely of the repetition of the effect of acute poisoning.

A particularly interesting aspect of this relates to the effects it may have on personality: on the experience of self, on the individuals' perception of their environment, on their ability to function psychosocially at the psychological and social levels, on their ability to develop personal maturity, and so on.

Studies and observations can be classified as laid out below, according to the types of harmful effects to which they refer:

- a) Permanent brain damage following cannabis smoking
- b) Damage to cognitive mental functions while under chronic cannabis influence
- c) Effects on complex mental functions such as the sense of coherence and the ability to process new impressions and one's own memories

### *a) Permanent Brain Damage following Cannabis Smoking*

The term “brain damage” as used here refers to permanent damage which can be demonstrated radiologically while the individual is alive or by means of microscopical investigation of the brain of a deceased abuser.

There are many clinical and anecdotal reports describing prolonged impairment of mental functions in chronic abusers of cannabis, not least from developing countries. These observations are supported by early scientific studies (e.g. Chopra, 1976; Soueif, 1976). Even though these studies have severe limitations due to unsatisfactory scientific design, they contributed strongly to placing the discussion of permanent brain damage on the scientific agenda at an early stage.

Campbell et al. (1971) caused something of a sensation by publishing a study where they showed the existence of cerebral atrophy (using air encephalography) in ten chronic cannabis abusers while thirteen controls of the same age returned normal results. However, in addition to the fact that this study was severely criticised on several counts from a methodological point of view and proved to be unrepeatable by other researchers, it has been shown in several studies using modern radiological methods (computer tomography) that cerebral atrophy cannot be detected in chronic cannabis abusers (e.g. Hannerz & Hindmarch, 1983).

### *b) Damage to Cognitive Mental Functions While under Chronic Cannabis Influence*

#### **Scientific Studies**

In 1986, Wert and Raulin made two wide-ranging reviews of all studies that had been carried out in this field up to that point. They found (Wert & Raulin, 1986a; 1986b) that neither neurological nor neuropsychological studies had shown unambiguously that chronic abusers suffered from structural or functional damage caused by their chronic abuse.

However, Wert and Raulin do discuss the possibility that the “differential impairment” (in groups equally exposed to cannabis abuse and having experienced similar conditions in other respects, some subjects exhibited damage while others did not) found in many studies might not be a consequence of faulty study design but rather a manifestation of varying vulnerability in different individuals. The authors write:

*It might well be that some individuals are predisposed to cerebral impairment as the result of cannabis use, either because of structural or biochemical characteristics which accentuate the possible damaging effects of the drug, or because they have little*



*of the cerebral reserve that most of us call on when we experience mild cerebral damage. That functional reserve can mask very real cerebral damage.*

This kind of interaction between stress/damage on the one hand and vulnerability on the other is now an accepted model for explaining both how many illnesses arise and why some people do not fall ill. Generally, however, we know very little about these vulnerability factors in each individual case. This line of thinking is obviously valid for many of the harmful effects dealt with in this report.

With regard to what were, after all, the dominant findings – no proven damage as a result of prolonged cannabis use –, it could not be excluded that the testing methods may not have been sensitive enough. However, Wert and Raulin's answer to that objection was that it was indeed possible, using the same testing methods, to detect brain damage in alcoholics.

Subsequent studies have proved them right: the damage caused by cannabis smoking is not only of a more subtle kind than had previously been expected, but it is also different in nature.

A couple of studies returned to earlier study groups where the original study had not been able to prove the existence of any cognitive damage. Renewed testing which made use of more sophisticated methods found clear differences between abusers and non-users, especially with regard to the ability to sustain attention and the ability to remember something just learned (short-term memory) (Page et al., 1988).

By using more specific testing methods and applying a more rigorous methodology, a number of studies have shown that prolonged use of cannabis causes damage in the cognitive sphere, particularly with regard to specific aspects of memory and attention as well as the organisation and integration of complex information. In order to exclude the effects of acute intoxication, the tests were carried out after at least 24 hours' abstinence from cannabis smoking. In general, there was found to be an association between the duration of the cannabis-smoking habit and the degree of functional impairment measured: the longer the period of abuse, the worse the test score.

Block et al. (1990) showed that intensive, prolonged cannabis smoking is detrimental above all to the ability to express oneself verbally and to solve mathematical problems. Solowij (1995a; 1995b; 1999) has shown that prolonged cannabis use leads to impaired ability to focus attention and to screen out irrelevant information. Schwartz et al. (1989) showed, in a study which is discussed in greater detail in the chapter on teenage development (Chapter 15), that cannabis smoking resulted in a significant impairment of short-term memory which persisted for at least six weeks after the individual stopped smoking. Leavitt et al. have presented their findings only at scientific conferences (reports which I have not had the opportunity to read), but their results are reported in reasonable

detail by Hall et al. (1994, p. 138) as well as by Lundqvist (1995, pp. 46–47), who concurs in the opinion of Leavitt et al. that they and other researchers have shown that long-term use of cannabis entails, among other effects, the following:

- impaired ability to carry out complex thought operations and impaired ability to screen out distracting impressions;
- reduced ability to process information;
- no effect on long-term memory but impaired short-term memory, particularly with regard to information which is of a kind unfamiliar to the individual or which is complex in nature;
- difficulty in carrying out tasks which require intellectual flexibility, long-term strategic planning and the ability to learn from experience;
- no effect on the ability to deal with the routine, familiar demands of everyday life, but problems when faced with the task of expressing oneself verbally in a new, unfamiliar situation or in a situation where old ways of thinking and old knowledge are inadequate.

With regard to the question of whether functional impairments can persist over a lengthy period of time after discontinuation of abuse, Solowij (1999) has shown that a “reduced ability to focus attention and to screen out irrelevant information” remains after the individual has stopped smoking cannabis. When Solowij’s study was carried out, the subjects had refrained from taking drugs for an average period of two years. There was found to be a direct relationship between the degree of impairment and the duration of cannabis abuse.

### **Clinical Observations**

In his PhD thesis, Thomas Lundqvist (1995) looked at the cognitive damage arising in connection with prolonged cannabis smoking. He presented a model for categorising the cognitive functions at issue, a model which he had been using for a number of years to organise clinical observations of cognitive functions in 400 long-term cannabis abusers who had sought care at an outpatient clinic. Together, these clinical observations provide a very informative illustration of and supplement to the scientific studies referred to above. In a small-scale study (which will be accounted for in the next section), Lundqvist sheds more light on the disturbances to chronic abusers’ experience of the surrounding world.

Lundqvist’s clinical observations regarding cognitive disturbances, when placed in relation to scientific studies, lead both to a treatment model for cannabis abusers and to a number of interesting hypotheses and figures of thought concerning the direct effects of cannabis on the various structures and functions of the brain. However, those parts of the thesis fall outside the scope of this report.

It is worth noting in its own right that over 1,000 cannabis abusers have sought help at the treatment centre where Lundqvist works. Even though the functions necessary to assess

their need to stop abusing will have deteriorated as a result of their abuse, many cannabis abusers still wish to make an attempt to change their life situation. This is a reflection of the fact that cannabis abusers suffer from their dependence and their functional impairments.

Lundqvist divides the cognitive functions which are impaired when the individual is under the influence of cannabis into the following categories:

***Verbal ability***

Having a vocabulary that corresponds to one's age, finding the words for what one wants to say, understanding others and having the ability for abstract thought.

***Logical-analytical ability***

Ability to analyse and draw logical conclusions, ability to understand causal connections and ability to judge oneself in a critical/logical manner.

***Psychomotility***

Ability to maintain attention and to vary the degree and focus of attention. Ability to understand other points of view and to change one's own point of view. Some degree of general flexibility with regard to different ways of looking at and interpreting societal phenomena.

***Memory***

- Short-term memory/working memory: Ability to remember what has just happened or been communicated, which is a prerequisite not only for the integration of what has just been communicated but also for the integration and organisation of a whole range of cognitive processes, as well as a precondition for a reasonably adequate temporal perception.
- Long-term memory: This consists of both "episodic memory", which makes it possible to remember events and their temporal context, and "semantic memory", which has more to do with what we call "knowledge", e.g. different facts and the inter-relationships between different phenomena.

***Analytical and synthetic ability***

Based on the ability to combine the other functions. Makes it possible to synthesise, sort out and organise mental material.

***Psychospacial ability***

Makes it possible to orient oneself, other people and various phenomena in time and space, which is a precondition for temporal organisation as well as one of the prerequisites for social orientation.

***Gestalt memory (holistic memory)***

Enables us to understand and form patterns – not only to understand that there is a connection, but also to understand its nature and structure. For example, enables us to make and maintain the connection between a person, a name and a social role.

All of these functions were disturbed, to a greater or lesser degree, in the cannabis abusers who sought help at the treatment centre. Systematic interviews were carried out with ten former chronic cannabis abusers, between 2 and 48 months after they had discontinued their abuse, about the changes they felt they had gone through. All of them said that their way of thinking and the way they perceived the world around them had changed after they had stopped smoking. Above all, they felt that their verbal ability, their logical-analytical ability and their psychomotility had improved.

***c) The Effect of Cannabis Abuse on the Abusers' Understanding of the Surrounding World as Expressed in Their "Sense of Coherence"***

Antonovsky (1987) has developed "sense of coherence" (SOC) into a clinical and scientific notion. He found that people who had been better than others at dealing with demanding, traumatic experiences in their lives had a more developed sense of coherence. SOC can be seen as constituted of three components: *comprehensibility* – being able to understand the situation in which one finds oneself and the traumas one is exposed to; *manageability* – being able to handle a situation or act upon it, or being certain that somebody whom one trusts will act in one's interests; and *meaningfulness* – in the sense that the strains to which one is subjected are in some way meaningful.

Antonovsky has developed a test which measures a person's degree of SOC. Lundqvist tested fifteen cannabis abusers on two occasions – when they were admitted and six weeks later, i.e. after six weeks of both abstinence and treatment. On admission, the average test score was 118.2; six weeks later it had risen to 141.9. This represents a statistically significant improvement, both for SOC as a whole and for each of its three components. Following treatment, the former abusers obtained scores close to those achieved by the control group consisting of non-abusers with university degrees, whose average score was 153. (According to Antonovsky, in such a country as Sweden, scores between 143 and 153 are to be seen as reflecting a good level of adaptation in these respects.) These improved levels were recorded although it can reasonably be assumed that the recently detoxified former abusers were not yet in a state of full mental balance – a circumstance which has been shown by experience to result in lower SOC scores. It was also found that cannabis abusers who had undergone a period of abstinence but had not received any treatment obtained a significantly worse score than the study group.

Even though this is a single study – and taking into account that it is not entirely clear exactly what is measured by the test –, this research into the understanding of the surrounding world supports the position that prolonged cannabis abuse weakens the individual's ability to maintain a functional relationship with the world around him or her.

### **What Is the Importance of the Cognitive Damage to the Individual?**

Even though the mechanisms involved are unknown to us, it seems reasonable to assume that the impairments in cognitive functionality play a significant part in several of the psychiatric harmful effects described in the opening chapters of this report.

In Chapter 15, “Cannabis Smoking in Teenagers”, I discuss the impact on the individual of prolonged cannabis smoking during the teenage years, especially as regards its effects on learning/schooling and on psychosocial development.

The impact of this cognitive damage on the individual’s ability to operate complex machinery in the processing industry and, above all, to operate vehicles – cars and aeroplanes – in traffic is the subject of Chapter 16, “Cannabis and Driving”.

Obviously, a reduction in memory capacity affects the learning ability, in a broad sense, of adults as well as that of children and young people. There is good reason to recall Wert and Raulin’s thoughts with regard to “differential impairment”, which we looked at in the previous section. The nature and severity of the harmful effects produced are doubtless dependent in large part on the extent to which the individual is able to compensate mentally and socially.

Lundqvist (1995) found, in his clinical assessment of the 400 chronic cannabis abusers, that most of them displayed more or less pronounced weaknesses in all seven cognitive categories (and certain emotional disturbances also seem to be part of the picture).

Moreover, Lundqvist claimed that he could distinguish a typical personality profile characteristic of cannabis-smoking clients. According to this profile, abusers typically:

- have difficulty in finding the words to express what they really mean;
- have a limited ability to be amused by or enjoy literature, film, theatre and the like;
- have a feeling of boredom and emptiness in everyday life, along with feelings of loneliness and of not being understood;
- externalise problems and are unable to take criticism;
- are convinced that they are functioning adequately;
- are unable to examine their own behaviour self-critically;
- feel that they have low capacity and are unsuccessful;
- are unable to carry on a dialogue;
- experience difficulty in concentrating and paying attention;
- have rigid (fixed) opinions and answers to questions;
- make statements such as “I’m different, other people don’t understand me, I don’t belong to society”;
- do not plan their day;

- think they are active because they have many on-going projects – which they seldom see through to completion;
- have no daily or weekly routines.

Lundqvist bases what he has to say on his extensive clinical experience of how a new identity develops in the chronic abuser. Even if one may not wish to be quite so categorical, what emerges is clearly a picture of rather special personality traits: rigidity, inflexibility, difficulty in remembering and thus generally in dealing with changes in the surrounding world, loneliness and a tendency towards isolation. These personality traits are doubtless dependent both on the size of the dose and on the duration of abuse; but the cognitive, emotional and social resources originally available to the individual also play an important part. The similarities with “amotivational syndrome” (see Chapter 12) are striking.

Having previously studied young people, Hendin et al. (1987) wished to determine the consequences of continued cannabis use in a group of adult habitual smokers. Subjects in a carefully selected group of 150 long-term users of cannabis were asked about their subjective impression of various effects caused by their long-term smoking. These subjects were white, did not abuse any other drugs or alcohol, and were not marginalised or socially disadvantaged. They had been using cannabis at least six days a week for at least two years. The aim of the study was to increase understanding of the role played by cannabis in these people’s lives, and special interest was directed towards adaptive aspects, which were later studied in greater detail in 15 specially selected subjects.

Alongside a number of aspects subjectively felt to be positive (of which, however, some were found, in the subsequent intensive study, to be objectively negative), two-thirds of the 150 subjects felt that the main disadvantage of chronic abuse was memory impairment. Just under half were of the opinion that their ability to concentrate on a complex task had deteriorated, and an equal proportion considered that an inability to get things done was one of the negative long-term effects. Further, 43 per cent felt that there had been a deterioration in their ability to think clearly, and 36 per cent considered that their level of ambition had become lower as a result of their chronic abuse. Moreover, some of the subjects interviewed felt that acute intoxication had an additional negative effect on functions such as memory (45 per cent) and ability to concentrate (41 per cent).

The intensive study of 15 specially selected chronic abusers, which Hendin et al. carried out within a psychoanalytic frame of reference, is of considerable interest; for the main part, though, it falls outside the scope of this report. One of the findings, however, will be mentioned here. Cannabis smoking is often claimed (by abusers themselves) to have the effect of increasing one’s self-awareness and of stimulating one to contemplate and gain a deeper understanding of one’s own and other people’s situation in life. The researchers were in fact struck by how consistently chronic marijuana smoking was found to have the opposite effect! Introspection was effectively inhibited, thought and feeling were

separated, and the individual became less able to see reality. *Cannabis was used, then, as a means of escaping from an awareness which might have provided the individual with a basis for maturing, for making conscious choices in life and for dealing with disturbed relationships.*

## 15. Cannabis Smoking in Teenagers

### **Summary of Chapter 15:**

1. Cannabis smoking disrupts the hormonal balance in both men/boys and women/girls. We do not know exactly how this affects teenagers, but the suspicion is that it can reduce fertility. There have been reports of disturbance in growth and of delayed sexual maturity.

2. **Cannabis as a gateway to harder drugs:** It has long been understood that cannabis use is one of several factors that increase the likelihood of starting to use other illegal drugs. One of the reasons for assuming there to be a causal connection has been that the intensity and duration of a person's cannabis smoking increase the risk that he or she will move on to harder drugs. Notwithstanding this, it is only recent and methodologically well-conducted studies (including prospective ones of long duration covering a large number of people) that have been able to show that, even after controlling for the effects of other known and suspected factors, there remains a strong association between cannabis smoking and moving on to harder drugs. *It would appear that we are close to proving the controversial gateway hypothesis – the hypothesis that, in many cases, cannabis use constitutes a gateway to harder drugs.*

3. The development of identity, according to accepted theory and experience, is a central aspect of the psychological development of young people. In turn, the development of identity is crucially dependent on a number of other factors, including certain aspects of cognitive development – which, as we know (see above), is put at risk by long-term cannabis smoking. A large number of clinical reports and a few extensive scientific studies also show that when a person uses cannabis, this is often one of the reasons why psychosocial teenage development slows down, comes to a standstill or even breaks down completely.

### *The Sensitive Teenage Years*

This is the most important chapter of this report. With most drugs – not least cannabis – the teenage years are of special importance. Vulnerability to various side-effects is generally highest in teenagers. Exposure to cannabis is also highest in the teenage years, as the early peer group takes on greater importance and a range of factors may tempt young people to “feel their way” and “just try it”.

Naturally, most of what is discussed in other chapters applies to teenagers as well. Therefore, this chapter looks mainly at those harmful effects that have specific importance in the teenage years. This often means the effects that interact with the teenager’s “developmental tasks” – the expectations that people around them (from parents to psychologists and sociologists) tend to subsume under headings such as “breaking free from one’s parents”, “finding oneself”, “finding one’s identity”, “finding a way to relate to the other sex”, “finding the meaning of life”, “conquering a new social arena – from the teenage peer group to a circle of adults” and “choosing and starting a career”. Or, quite simply, leaving – not without a certain sadness – childhood and maturing into an adult.

Database searches yield no avalanche of studies that deal with this complex of problems – the teenager’s encounter with cannabis abuse. Of course, there are on-going research projects, and the annual number of reports published in scientific articles seems to be on the increase at present. However, as regards the kind of research-report reviews in book form that I mentioned in Chapter 2, the situation is more troublesome. These reviews contain no sections on teenagers and cannabis. It is especially remarkable that the otherwise excellent *Cannabis and Health Hazards* (1983) does not devote a section to this issue; and it is perhaps even more surprising that no mention is made of this fact in the foreword. Similarly, there is no such section in the WHO’s most recent publication, *The Health Effects of Cannabis* (Kalant et al., 1999).

*The Health and Psychological Consequences of Cannabis Use* (Hall et al., 1994) represents an exception in that its authors discuss, in an integrated manner, the issue of the effects caused by cannabis on different aspects of youth development.

The “failure” of the other reports might be attributable to the fact that it is taken as a given that cannabis is a young people’s drug. It might also be that our culture’s bad conscience has put blinkers on the editors and authors. Perhaps this is just another reflection of our society’s inability to see the needs of young people and to take these needs into account?

To be fair, though, it must immediately be said once again that research teams all over the world have devoted decades to the youth-related issues. Denise Kandel and her co-workers constitute one of the best-known such teams.



This seemingly low-key interest from parts of the research community stands in stark contrast to the numerous worrying clinical observations concerning young people's relationship to cannabis. For example, at the Maria Ungdomsmottagning in Stockholm (a clinic specialising in young abusers), the impression gained by the staff is that it is, in fact, often easier to help a young heroin addict than it is to help a firmly addicted cannabis abuser. The reason why parents' anti-drug associations in e.g. Sweden and the United States have taken such a strong stand against cannabis is that they have seen so many cases where a teenager's development has come to a halt as a result of long-term hashish or marijuana smoking.

This chapter will deal with three aspects of the effects caused by cannabis abuse on the teenage individual:

- The effects of cannabis on the hormonal system during the teenage years
- Does cannabis abuse represent a gateway to harder drugs?
- Cannabis abuse and the teenager's psychosocial maturation

### *The Effects of Cannabis on the Hormonal System during the Teenage Years*

As is shown in the chapter on fertility (Chapter 20), cannabis can affect the hormonal balance in both men and women. However, this effect seems to be more relevant in men. The changes in hormonal balance which cannabis can provoke are suspected of being involved in a relative reduction of fertility in adult men. There is reason to suspect that such hormonal effects may be more important during puberty than later on in life. As is also pointed out in the chapter on fertility, gynaecomastia (development of breasts in men) has been observed in a small number of men who were intensive smokers of cannabis (Hollister, 1986; Harmon, 1972). The importance of these findings is uncertain. If intensive cannabis smoking in men always caused a hormonal imbalance resulting in gynaecomastia, this phenomenon ought to be better known both to the public and in the research community.

There is one reported case concerning a 16-year-old boy who had smoked marijuana since the age of 11. He was short in stature and had no pubic hair, his testicles and penis were small, and his blood testosterone level was low. When he stopped smoking, he started growing again and his blood testosterone increased to a normal level (Hollister, 1986). Although this observation refers to a single case, it ought to be seen as providing a warning signal, bearing in mind the occasional reports of children starting to smoke cannabis at a very young age.

In women, the menstrual cycle is affected. Taken together with findings from animal experiments, this is considered to suggest that cannabis can bring about a relative reduction of fertility.

*To sum up, we know that continual cannabis smoking disrupts the hormonal balance of the body. The effects of this disruption include a lowering of testosterone levels in men/boys and disturbances to the hormones which control the menstrual cycle in women/girls. While we do not know exactly how this affects teenagers, we suspect that it may disrupt sexual maturity and fertility, and possibly growth as well.*

### *Does Cannabis Abuse Represent a Gateway to Harder Drugs?*

The question of whether cannabis represents a gateway to harder drugs has occupied clinicians and researchers for 30 years. The reason for the interest in this question has been that a transition to harder drugs – heroin, amphetamines or cocaine – represents a significant increase in the degree of risk to which the individual is exposed. Even though cannabis is more psychotoxic than heroin, intravenous heroin abuse is in many other respects a considerably more serious condition than cannabis dependence. With heroin – which is also much more expensive than cannabis –, addiction not infrequently develops quickly, the dependence is strong, and mortality is considerably higher, mainly owing to overdoses. It is the rule rather than the exception that heroin-dependent individuals become socially marginalised. The abuse of both amphetamines and cocaine (not least in the form of “crack”) also leads to rapid development of severe dependence, with the risk of a series of mental side-effects and high mortality levels. Moreover, transition to intravenous abuse adds the risk of HIV infection.

The most extensive studies in this field have been carried out by Denise Kandel and her research team. They showed, at an early stage, how young people in the United States tended to progress through a sequence of increasingly strong drugs. A very large proportion of their subjects followed a series of graded steps, and very few deviated from the progressive sequence or hierarchy expected. Four stages were identified: 1) beer and wine; 2) cigarettes and spirits; 3) marijuana; and 4) other illegal drugs (Kandel, 1989). It was also found that the younger the age at which abuse started, the higher in the drug hierarchy the individual would climb; and the more intensive the abuse at any given stage, the greater was the risk that the individual concerned would progress to the next stage. Research carried out in the Nordic countries has found similar tendencies (Aas & Pedersen, 1993). Golub and Johnson (1994) have shown how the importance of alcohol as a gateway to abuse of hard drugs has declined while that of marijuana has increased. This is considered to be due primarily to the strong expansion of marijuana smoking observed in the United States over the past three decades. Yamaguchi and Kandel (1984) have also shown how extremely rare it is for abusers of hard drugs not to have progressed via marijuana. Here, though, it should be emphasised that it is only a small fraction of those who smoke cannabis that ever try other illegal drugs, and even fewer who continue using such other drugs.

In general, then, prior cannabis use seems to be a necessary condition for the use of hard drugs; but is cannabis also a gateway to harder drugs in the sense that cannabis abuse is

actually the cause of heroin, cocaine or amphetamine abuse? A great deal of effort has been devoted to answering this question. Since the vast majority of cannabis smokers do not become abusers of hard drugs, there is clearly no simple causal connection. What we can conclude from the various studies, in other words, is that cannabis is only one of the factors that seem to predispose an individual to the abuse of hard drugs. A range of other negative social and psychological background factors are also very important.

Kandel et al. (1986) demonstrated a direct association between the intensity of cannabis abuse and the risk of progression to hard drugs. Of the subjects in their study group who had used marijuana more than 1,000 times in the course of their lives, 90 per cent had also tried hard drugs; of those who had used marijuana between 100 and 1,000 times, 79 per cent had used hard drugs; and of those who had used marijuana fewer than 100 times but more than 10 times, 51 per cent had used hard drugs. Of those who had used marijuana between 1 and 9 times, 16 per cent had also used hard drugs. Among the subjects who had never used marijuana, though, only 6 per cent had used hard drugs.

This statistical association between the intensity of cannabis consumption and the likelihood of using hard drugs strengthens the case for assuming that there is a causal connection between cannabis smoking and progression to harder drugs, but it does not constitute proof of such a causal connection.

The association can also be demonstrated by means of the below findings from a more recent analysis of the study group from Newcomb's (1992) large-scale longitudinal study (of which an account will be given in the next section). However, this analysis concerns the proportion of the marijuana-dependent individuals in the group who also became *cocaine-dependent* – in other words, the proportion of the large-scale consumers/abusers of marijuana who also became large-scale consumers/abusers of cocaine. In all, marijuana-dependent subjects accounted for 8.1 per cent of the group of 27–29-year-olds studied. Of these, 36 per cent were dependent on cocaine as well. Kleber (1995) has pointed out that studies linked to the Center on Addiction and Substance Abuse at Columbia University have shown that 60 per cent of the young Americans who use marijuana before the age of 15 will use cocaine later in life. Further, it has been shown that young American between the ages of 12 and 17 who use cannabis are 85 times more likely to use cocaine than non-smokers of cannabis in the same age group.

The general impression, then, has been that the imperative role of cannabis in the “stepping-stone” model has resisted all attempts to prove it scientifically. On the other hand, a large body of circumstantial evidence has been gathered. It is found time and again that cannabis is a central component of the network of influencing factors that leads to the abuse of hard drugs.

This discussion has continued with unabated intensity. Some people claim that this is the crucial question of the debate on the dangerousness of cannabis: “If the gateway theory is

incorrect, cannabis cannot really be all that dangerous, can it?" The intensity of the defence of the gateway theory has often been based on the assumption that the correctness or otherwise of this theory determines what the correct view on cannabis should be. Since I account for many other suspected and proven harmful effects of cannabis abuse in this report, I obviously do not share that assumption.

### **Is the Question of the Role of Cannabis As a Gateway to Hard Drugs Now Being Answered?**

In a few recent research reports, Fergusson et al. (1997; 2000; 2002) account for a number of analyses from a study of young people where attempts are made to find links between cannabis smoking and a range of developmental problems that might conceivably be affected by cannabis abuse. The study monitors 1,265 New Zealand children from birth; the subjects were 20–21 years old at the time of the latest report. The researchers have unique knowledge about the children and their backgrounds, and their analyses are greatly facilitated and given considerably larger weight by the prospective and longitudinal design of the study.

We will here look at only one of the issues addressed by the project: the “gateway” question. At the time of the first analysis, the subjects were 18 years old. Like many researchers before them – not least Kandel’s team – Fergusson et al. found that the initial analysis showed associations which were not, when other known factors were controlled for, very strong at all. The researchers then joined above all Kandel, but many other researchers as well, in suggesting an alternative explanation.

As the young people came into contact with cannabis, the researchers claimed, the effects caused by cannabis on the mind, the culture surrounding the drug, new friends who had acquaintances in abuser circles as well as other circumstances all combined to amplify the impact of negative background conditions. This hypothetical process is called a “cascade effect” (Kandel et al., 1986). In this way, then, cannabis would indirectly have caused or contributed to a number of difficulties encountered by the young people, including progression to other illegal drugs. This was obviously bad enough in its own right, but there had been no convincing proof that cannabis constituted a specific causal factor.

At the time of the later analyses, the subjects were 21 years old. The researchers then had more data at their disposal and used more advanced methods of analysis. It was possible not only to take more careful account of other factors known to contribute to negative developments, but also to control, to a degree, for time-dependent and not fully known influencing factors. The more intensive the cannabis abuse, the stronger was the association with use of other drugs. For younger (14–15 years old) large-scale consumers in particular, there was found to be a very strong association even after controlling for other known or suspected causal factors (Fergusson et al., 2002).

Here, then, a different picture emerges. Cannabis abuse is here an independent specific factor, in all likelihood a cause of the progression to “hard drugs”. This is the first time that associations of this strength have been found, and the theory of cannabis as a gateway seems to be on its way to being proved. If this study is replicated by another research team, it will be hard to dismiss the conclusions that could be drawn from the findings. Still, though, while this makes it clearer that there is a causal connection, we do not yet know the *nature* of that causal connection.

Since the existence of a strong association between cannabis use and a negative effect tends to make one think in terms of some kind of neurophysiological process rather than the psychosocial mechanisms which are generally close at hand, I will mention an interesting line of research and its accompanying hypotheses. This relates to the phenomenon of sensitisation, a sort of “inverse tolerance effect” where an addictive substance increases a person’s sensitivity to the euphorising effects of that substance. Even though most of the research is based on animal experiments, similar phenomena exist in humans. Not least interesting is the occurrence of cross-sensitisation. This means that exposure to one preparation (e.g. cannabis) should be able to make a person more sensitive to another preparation (e.g. heroin). But let me repeat once again that this is hypothetical reasoning (Törngren, 1999).

### *Cannabis Abuse and the Teenager’s Psychosocial Maturation*

#### **Cannabis Abuse and Cognitive Development during the Teenage Years**

In Chapter 14, there is a discussion of the effects caused by long-term cannabis abuse on cognitive functions. From that discussion, it is clear that cannabis smoking has negative effects on a number of aspects, not least aspects which are of importance for more complicated thought operations, planning, and the integration of impressions and previous memories, etc. It is worth repeating here that short-term memory is also called working memory, and that it is not just a “memory function” but a central location for the co-ordination of a number of mental functions which play an important role in enabling individuals to orient themselves relative to the surrounding world, such as planning, reorientation and reacting to new and unexpected circumstances. The scientific studies and clinical observations previously referred to concerned mainly adults; here we will look at what these kinds of cognitive disturbance can entail for teenagers, who are in a dynamic developmental phase.

In order to emphasise that teenagers are at least as sensitive as adults to the effects produced by cannabis on cognitive functions, I would like to refer to a study which was carried out on teenage subjects. Schwartz (1989), in a very thorough study, showed that long-term cannabis smoking at those relatively high THC concentrations (7 per cent) which were found already in the late 1980s in the United States led to a significant

reduction in the short-term memory of the subjects. It is particularly noteworthy that some memory impairment remained six weeks after the first examination. Unfortunately, for financial reasons, the study did not continue beyond this point, but the findings are in line with the studies mentioned in Chapter 14 which showed that effects on cognitive functions persisted for a time after the abuse had ceased.

### **Identity Development, Formal Thinking and Cannabis Abuse**

In this section, I deviate – for reasons which I hope will be obvious – from the structure found elsewhere in this report. By means of a slightly more extensive discussion, I try to place the study findings to which I refer in a larger context.

Baumrind and Moselle (1985) maintain that many studies are not only deficient in terms of methodology, but also lack a theoretical foundation. With this type of research on complex relationships, it is necessary for studies to be based on an explicit theory of teenage development. This is necessary for the researchers to be able to draw up hypotheses, ask relevant questions and choose adequate study instruments. Without such a theoretical foundation, the risk is that studies will produce a bulk of disconnected statistical data which are difficult to deal with.

Having indicated some of the ways in which propitious youth development is made more difficult in the society of the 1980s, the authors go on to describe, stage by stage, the development which occurs during the teenage years. Baumrind and Moselle see a progressive transformation of “action schemas” from less integrated to more integrated systems as being the central thrust of youth development. They describe the manifestations of the maturation process within a range of different psychosocial categories. As in the psychoanalytically oriented development theories, the forging of a personal identity is a central element of this model. In this regard, this model resembles, in several ways, my own lines of thinking on the importance of social integration to the development of identity in the late teenage years (Ramström, 1991). In this context, we can also remind ourselves that several researchers from various disciplines have emphasised that the environment in which the teenagers of the Western industrialised societies of the 1980s and 1990s are to mature into adulthood seems to be hazardous in certain respects (Ramström, 1991; Ziehe, 1986; Lasch, 1983). If this is so, drug abuse which makes this maturation process more difficult, or delays it, takes on an even greater importance.

Given our knowledge that cannabis produces negative effects on cognitive and other functions, it is of considerable interest to note that Baumrind and Moselle, like Steingart (1969) and Ramström (1991), consider that certain stages of cognitive development – especially the ability for abstract thought – are crucial to the development of identity in the teenage years. According to Piaget, the child’s ability for concrete thinking is supplemented by the ability to perform formal thought operations at the age of 11–13 (though it has later been questioned whether this stage does not in fact normally occur somewhat later, at

the age of 15–16). The ability to perform formal thought operations is the basis of the ability for abstract thought. At this stage, unlike during the period of concrete thinking, the young person is able to conceive of a world different from the actual reality before his or her eyes at any given moment. One new possibility that this development opens up for the young person is the ability to hold up his or her parents' characters and mores to judgement, not rarely causing them pain.

But the ability for formal thinking also provides the foundation for long-term planning of the development of one's own personality. Once an individual has reached this stage of cognitive development, he or she can move on from the kind of planning typical of the child ("When I grow up I'm going to be a millionaire") to a kind of planning that reflects the increasing maturity of the adolescent ("By choosing a certain study programme at upper-secondary school and working to achieve certain grades, I can acquire the education I need for entry to the career that I want"). There is strong evidence that the functional shortcomings described in Chapter 14 as being characteristic of cannabis abusers are caused, in large part, by inadequate ability to perform formal thought operations (Lundqvist, 1995).

If the development of identity does not progress, the teenager remains at a childish level of development characterised by both a lack of independence and deficient integration in the adult world.

If we thus place our knowledge of the mechanisms by which cannabis produces its effects, mainly as regards its impact on cognitive functions, in relation to a central and crucial element of the mental development of the teenager (the forging of identity), we can see how prolonged smoking of hashish during the teenage years may result in the stagnation of psychosocial development. Still, even though the interaction just described affects the core of teenage development – the forging of identity – and is therefore very important, we must not forget that the impairment of mental functions can have a range of other effects. Deterioration of short-term memory obviously makes learning more difficult, but it also has a negative effect on the individual's ability to make plans, to establish new relationships and to make realistic assessments of the world around him or her.

In recent years, researchers have also found that the consumption of cannabis in the early teenage years has a causal connection with mental and social disturbances in the later teenage years and early adulthood. Quite a few of these disturbances have been mentioned already: psychosis (Arseneault, 2002), depression and suicidal thoughts (Bovasso, 2001; Patton et al., 2002), and criminality and unemployment (Fergusson & Horwood, 1997; Fergusson et al., 2000; Fergusson et al., 2002).

### *Clinical Experience*

In addition to accounts given of their experience by field-workers, doctors and nurses, teachers, police officers and not least parents, there are also more systematised and detailed descriptions of the long-term effects produced by cannabis on teenagers – for example textbooks (Heinemann, 1984; Ramström, 1987), a section of a research report (Lundqvist, 1995) and a clinical report in a scientific journal (Kolansky & Moore, 1971). Kerstin Tunving, a very experienced doctor in the field of drug-addiction treatment, wrote the following in her article *Psychiatric Aspects of Cannabis Use in Adolescents and Young Adults* (1987):

To sum up, the impression is, based on clinical observations, that teenagers who abuse cannabis “sleep away” their teens. They often do not develop at the same pace as youth of the same age, but stay childish and dependent.

It is also of interest to note that what induced Richard Schwartz and his co-workers to conduct a study into the effect of cannabis on short-term memory in young people was, in fact, repeated clinical experience of cannabis-dependent young people who, when admitted to a treatment programme, found it very difficult to remember information and instructions during the first three or four weeks.

### *Scientific Studies*

In addition to the previously mentioned problems involved in carrying out studies of this kind, it should also be noted that two of the studies described here were carried out in the United States in the 1970s and early 1980s, when the American market was still dominated by weaker cannabis preparations. Moreover, none of the studies makes any attempt to correlate outcome with varying intensity of cannabis abuse (Schwartz, 1991).

In the introductory chapter of their large study *Living High*, Hendin et al. sum up their findings from earlier studies of cannabis-smoking teenagers:

In all of its functions marijuana served to detach these adolescents from the problems of the real world – from their anger and unhappiness with their parents and from the need to work and compete to achieve success [...] Fantasies of being destined for a special fate, to become rich without work, and to excel at a sport they scarcely played were typical of the parody of success, achievement, and confidence that marijuana sustained in some of the young men [...] The young female marijuana abusers, although not usually expecting particular greatness, nevertheless maintained a magical belief that good things would happen to them: college acceptance while flunking out of high school, or happiness in love while dating unresponsive



or abusive young men. For all these adolescents, marijuana helped sustain in an unrealistic way the desire for power, control, achievement and emotional fullness (Hendin et al., 1987, p. 14).

In her dissertation *The Prognosis of Drug Abuse in a Sixteen-Year-Old Population*, Maj-Britt Holmberg (1981) studied over 1,000 Swedish pupils in the ninth year of school (aged 15–16). Of these, 14 per cent used cannabis (primarily). At a follow-up after eleven years, she found the following:

- The mortality rate was 5–8 times higher among those who were abusers at the time of the first interview in the ninth year of school.
- The abusers (together with those who had attended remedial classes or had left school prematurely) had had an above-average level of medical and social problems during their childhood and youth.
- Of the drug users, 10 per cent had been diagnosed as having a psychosis during the eleven-year follow-up period.
- The 2.4 per cent who had claimed a highly frequent use of drugs (with cannabis being the dominant drug) were more likely to develop drug addiction proper than the other abusers.

The most extensive and in-depth longitudinal study of young cannabis smokers carried out to date was conducted by Michael Newcomb and Peter Bentler (1988). In their main report, they concentrate on the effects of cannabis use on individuals' entry into young adulthood. They studied the consequences of use/abuse of alcohol, marijuana abuse and the abuse of hard drugs. In many respects, the three categories of drugs produced similar effects.

The findings reported include the following:

- Cannabis smoking increased the risk of impairment to mental functions in young adulthood. The researchers measured a higher degree of “psychoticism” and a reduced ability to make careful plans. *“This effect [...] indicates that teenage drug use interferes with organized cognitive functioning and increases thought disorganization into young adulthood.”*
- Only the use of hard drugs was found to be associated with an increase in suicidal thoughts during young adulthood. (See, however, the above section on the risk of transition from cannabis to hard drugs.)
- Smoking cannabis as a teenager was shown to have a clear association with a number of negative psychosocial factors during the teenage years, but above all during the early stages of adult life. The abusers in this study, like those in e.g. Kandel's (1986) study, were more likely to interrupt their training or education. Once they reach adulthood, abusers exhibit less stability on the labour market – i.e. they find it harder to hold down a job.

- Further, the abusers showed a significantly stronger tendency to fail in their marriages, as expressed in a higher divorce frequency.
- Finally, it was found that the social networks built by the abusers during these early years of their adult lives were worse than those of the non-abusers.

Newcomb and Bentler (1988) conclude that their large-scale study supports, in a number of respects, Baumrind and Moselle's theory that abuse (*of e.g. cannabis*) during the teenage years leaves teenagers less well equipped to integrate themselves into adult life.

Moreover, these data are supported in most respects by the analysis of young New Zealanders carried out by Fergusson and co-workers within the – over ten years more recent – Christchurch Study (Fergusson et al., 1997; 2000; 2002). In the most recent report (after monitoring their 1,265 pupils/young adults up to the age of 21), the researchers sum up their findings as follows:

*Cannabis use, and particularly regular or heavy use, was associated with increased rates of a range of adjustment problems in adolescence/young adulthood – other illicit drug use, crime, depression, and suicidal behaviors – with these adverse effects being most evident for school-aged regular users.*

## 16. Cannabis and Driving

### **Summary of Chapter 16:**

Experimental studies show that cannabis smoking has a negative effect on a number of mental functions. These functions are of importance for driving.

Studies making use of both simulators and real driving situations, on main roads in rural areas as well as in city traffic, show how cannabis, even in moderate doses, impairs the ability to drive a car.

Given that a person who is under the influence of THC can compensate for many of the functional impairments through an effort of will – if the circumstances are favourable and the person is motivated –, it is suspected that most experimental studies produce findings which underestimate the risks involved in combining driving and cannabis smoking.

Owing to improved understanding of the metabolism of THC, it has been possible in recent years to carry out considerably better and more reliable epidemiological studies (involving blood testing). These studies have clarified the risks and support the experimental studies.

One study shows that the combination of cannabis with alcohol, by giving rise to a strong synergism, can affect a driver in a very dangerous manner.

To conclude, experimental studies show that moderate cannabis intoxication impairs driving ability to an extent comparable with that found in the case of a dangerous alcohol intoxication.

### *Introduction*

What is said in this chapter with regard to driving a car naturally also applies to the driving of a bus or a train, and to an even larger degree with regard to the piloting of an aircraft. Further, it seems reasonable to assume that demands similar to those placed on a driver are made of persons required to operate certain machines/appliances used in modern processing industry, and also, in certain aspects of their work, of those employed in certain other professions, such as doctors, nurses and air-traffic controllers.

The focus here is not on the negative effects caused by daily or near-daily abuse on intellectual performance in general; what is discussed in this chapter are the immediate effects which cannabis intoxication has on mental functions of importance for driving. These effects seem to be roughly the same irrespective of whether the cannabis user is a beginner or a habitual smoker. For intensive smokers, though, there are additional long-term effects, primarily affecting cognitive functions, as described in Chapter 14.

### *The Effects of Cannabis Intoxication on Psychomotor Functions*

As is explained in the description of cannabis and THC given in Chapter 1, cannabis intoxication produces, alongside euphoric effects common to many drugs of abuse, a cannabis-specific effect on functions such as perception, temporal understanding and memory. I will begin this section with a very condensed overview of the psychomotor functions considered to be most important for the ability to operate complex machinery, especially cars in traffic.

Herbert Moskowitz – one of the leading researchers in this field – presented a wide-ranging review, extending up to the mid-1980s, of scientific studies that deal with the acute effects of cannabis, focusing in particular on those psychomotor effects that can be assumed to be of importance for driving (Moskowitz, 1985). He maintains that, beyond all doubt, cannabis, even in moderate doses, impairs functional ability with regard to *coordination*, tracking (i.e. the ability to rapidly follow, by means of an instrument, an irregularly moving object), *perception and vigilance* (roughly speaking, the readiness to react quickly to unexpected events).

He also accounts for a number of studies demonstrating a deterioration of the ability to judge the length of an interval of time as well as a deterioration of short-term memory. This latter is the most constant finding in studies of the acute effects of cannabis intoxication (Miller & Branconier, 1983). However, Moskowitz expresses some doubts, not least based on several of his own studies, as to the importance of these two functions for driving. On the other hand, a correctly functioning short-term memory is very important for an aircraft pilot, who has to carry out a series of interconnected actions (and remember where in the series he or she is!) both while flying and during take-off and landing.

With regard to a few other functions – *reaction time* being one example of major importance for driving –, the findings were less definite. Wilson et al. (1993) did however, at a later date, demonstrate the existence of a clear association between a more realistic dose of cannabis (15–35 mg) and reaction time.

### *Studies of the Ability to Drive When under the Influence of Cannabis*

The findings described above show only how cannabis affects individual functions. With regard to judging the traffic risks, if any, posed by cannabis smoking, a more important

contribution has been made by the studies which have assessed the direct effect caused by cannabis intoxication on individuals driving cars or using car-driving simulators.

In this context, the following kinds of study have been carried out:

- Studies using a driving simulator
- Studies using a flight simulator
- Experimental studies of intoxicated persons driving a car:
  - on a test track free of other traffic
  - in traffic
- Studies of the presence of cannabis in the blood of drivers involved in road accidents (generally, fatal accidents)
- Anonymous telephone interviews with cannabis abusers on the subject of their involvement in road accidents

### *Simulator Studies*

An overall assessment of simulator studies carried out up until the mid-1980s is included in Moskowitz's research review. The studies conducted in car-driving simulators show both a reduced ability as regards direct control of the car and a deterioration of the ability to make correct interpretations of visual and aural input which is of importance when driving. In one study, whose participants included Moskowitz, the researchers suddenly introduced an obstacle which entailed a collision risk. At higher doses of marijuana, several subjects were unable to avoid a crash (Smiley, 1986).

The flight simulator is considered to be the most sensitive instrument for laboratory studies of the relationship between humans and complex machinery, and the effects caused by various drugs on this relationship. In certain respects, of course, flying an aircraft is a more complex task than driving a car; but since the laboratory situation probably entails, in several respects, an underestimation (see below) of the effects caused by the drug compared with real-life situations, the findings of flight-simulator studies should be seen as providing an important contribution to our understanding of the risks involved in driving. Naturally, these studies are carried out on experienced aeroplane pilots.

Janowsky et al. (1976) – also mentioned by Moskowitz – tested the ability of pilots who were under the influence of cannabis to carry out various sequences of actions typical of instrument flying. Even though the dose of THC given was low (8 mg), the pilots showed clear functional impairment, which appeared to be due above all to reduced short-term memory. Leirer et al. (1991) conducted a well-known flight-simulator study using higher – but still very moderate – doses of THC (20 mg). The nine test pilots' performance deteriorated in several respects, during flight as well as during take-off and landing. The researchers also found small but distinct impairments as long as 24 hours after the

administration of cannabis, although none of the pilots felt that they were still under the influence and only one of them perceived that diminished functionality remained after 24 hours.

### *Studies of Driving on Test Tracks and in Traffic*

In three studies (Hansteen, 1976; Klonoff, 1974; Attwood et al., 1981) of car driving on tracks free of other traffic, it was found that cannabis caused slight to moderate impairment to driving ability. One of the studies also looked at driving in traffic, but the findings made were inconclusive. In all of these cases, however, low or very low THC doses were used.

Robbe (1994) carried out an extensive research programme whose central focus was car driving, both on a closed-off road and on a motorway with normal traffic. The subjects in one study group (people who smoked cannabis more than once a month but not on a daily basis) were instructed to determine experimentally their optimal dose for “getting high”, and the average of what they found was used to set the highest dose given in the experiment at approximately 20 mg (300 µg/kg body weight). This is probably a relatively low dose: habitual smokers can consume 200 mg, and sometimes twice as much, in one day (Moskowitz, 1985); and with the strong varieties of marijuana in use today, a single 1-gram cigarette can contain up to 200 mg THC.

Robbe’s study shows that cannabis smoking causes a significant deterioration of driving ability. The most sensitive of the factors studied – influenced at all three dose levels used: 7, 14 and 20 mg – was the standard deviation of lateral position (SDLP). This is a variable which has previously been used in studies of the effects on driving of alcohol and other drugs, and it is a function of the ability to keep the car steadily in the middle of the lane at a constant distance from the verge of the road. Results were obtained only for driving on a road free of other traffic. In the experiments carried out on roads with other traffic, only the lowest dose (6–7 mg) was used (for safety reasons), and at that dose no significant impairment of driving ability could be identified.

Comparisons were made with identical studies concerning the effects of alcohol on driving ability. The SDLP deviations recorded for the 20 mg dose were very close to the deterioration in the same variable observed in persons with a blood alcohol level of 1.0 grams per litre. Robbe concludes that his studies confirm previous studies carried out using driving simulators and experimental driving on traffic-free roads: *cannabis in moderate doses impairs the taker’s ability to drive a car.*

At the same time, however, Robbe found that the effect of cannabis on driving ability was in most respects relatively moderate. A possible reason for this, he claims, could be that a person under the influence of THC is largely able to compensate for most functional impairments, provided that he or she is motivated to do so, is not distracted by other

impressions, and does not encounter overly complicated traffic situations. This view also finds support in experimental studies (Cappel & Pliner, 1973). According to Robbe, this circumstance entails a risk that experimental studies can lead to an underestimation of the risks associated with driving in “normal” conditions while under the influence of cannabis.

### *Presence of Cannabis in the Blood of Persons Involved in Road Accidents*

It has proved very difficult to carry out studies relating to the presence of cannabis in the blood of victims of traffic accident and to draw any firm conclusions from such studies, in particular those which were carried out a few years ago. The main reasons are problems concerning legal aspects, practical difficulties (above all relating to measurement techniques) and issues of research methodology. At one point, it seemed that the most fruitful approach in this field of research was to calculate a “culpability index”: comparing, in a group of drivers involved in accidents, those who were under the influence of cannabis and those who were not with regard to the extent to which they caused the accident. Warren’s study (1981) found that, if the risk index of drivers not under the influence of cannabis was set at 1.0, that of cannabis-intoxicated drivers was 1.7 – the same risk index as for drivers under the influence of alcohol. In other words, this study showed that a driver under the influence of cannabis was almost twice as likely as a non-intoxicated driver to cause a serious road accident. Certain studies, however, have failed to find that association; and in general, this method has yielded contradictory results. The reason for this inconsistency of findings is probably, according to a recently published analysis (Ramaekers et al., 2004), that not all researchers have measured the level of the relevant substance, but tested instead for non-psychoactive metabolites of THC which are irrelevant to determining whether the individual is under the influence of cannabis. The problem is that these metabolites (above all THC-COOH) remain in the body for much longer than THC itself. While the presence of such metabolites obviously indicates consumption of cannabis on the part of the individual, this consumption may have taken place several days before the time of driving.

Reviewing earlier studies using more modern techniques and methods, Ramaekers et al. have found that there is in fact a stronger link between cannabis consumption before (or during) driving and an increased risk of accidents than there was previously thought to be. These more recent studies found that drivers under the influence of cannabis were 3–7 times more likely to be the cause of an accident in which they were involved than were drivers not under the influence of cannabis or alcohol. In his review, Ramaekers also emphasises that both experimental and epidemiological data clearly show that the combination of cannabis with alcohol entails a strong further increase in the risks associated with driving. In this context, he refers to a study carried out by members of his team (Ramaekers et al., 2002), showing that the combination of clearly moderate amounts of alcohol with moderate amounts of cannabis caused a very strong increase in the risk of making mistakes while driving.

Incidentally, Ramaekers advocates a return to a more traditional type of study where injured or killed drivers are compared with an appropriate control group. Two such studies – one older and one from last year – may be mentioned here:

Gieringer (1988) found that cannabis abusers were 3–5 times more likely to be involved in a road accident than those who did not use cannabis. A recent French study (Mura et al., 2003) compared blood samples from 900 car drivers who had sustained injuries as a result of road accidents with blood samples from 900 controls. The control group consisted of patients who had been transported to or sought help at the same emergency ward as the road-accident victims but for reasons other than traffic injuries. One of the findings made was that the most frequent “drug” was alcohol, which was detected (at a level above the French legal limit of 0.5 g/litre) in 26 per cent of the drivers (and in 9.5 per cent of the controls). In the youngest age group (18–27 years), the corresponding figures for alcohol were 17 per cent of the drivers and 6.7 per cent of the controls. For cannabis alone (i.e. no other drug nor alcohol present), the proportions were 10 per cent for the drivers and 5 per cent for the controls.

#### *Anonymous Telephone Interviews with Cannabis Abusers*

In a survey of 6,000 young people aged 16–19 based on anonymous telephone interviews (Hingson et al., 1982), it was found that driving a car after either drinking alcohol or smoking cannabis increased the risk of being involved in a road accident. Those who drove after smoking marijuana at least six times a month were 2.4 times more likely to have a road accident than those who never drove after smoking cannabis. While the study method used is probably rather unreliable, the findings are consistent with those made in the studies presented above.

#### ***Concluding Remarks***

One of Moskowitz’s (1985) conclusions is that almost all the studies described by him used comparatively low doses of THC. Thus, the effect produced by more “realistic” doses could be considerably larger.

Moreover, many researchers emphasise that the combination of cannabis with alcohol is a frequent occurrence and that there is a need for further study of the effects produced by this combination, for example on driving. While some researchers claim that what we are dealing with is probably a simple summation of the effects of the two drugs (e.g. Hall et al., 1994), others, including Robbe (1994), warn us against making this assumption. To some extent, alcohol and cannabis give rise to functional impairments of completely different kinds, which means that there is a risk – as shown by Robbe and Ramaekers – that their combination is very hazardous. One effect may be that the tendency towards more careful driving displayed by those under the influence of cannabis is cancelled out by the tendency of alcohol to impair judgement and make the individual more inclined to take risks.



Generally speaking, there is a risk that alcohol's more palpable effect on psychomotor functions and the effects produced by cannabis on cognitive functions (information processing, attention) may combine to form a disastrous mix in a complicated traffic situation (Ramaekers et al., 2000).

*In conclusion, we can say that extensive research into the effects produced by cannabis on humans' ability to operate complex machinery has shown that even a moderate dose of cannabis impairs a number of functions which are crucially important if the individual is to be able to drive a motor vehicle safely. Experimental studies have been carried out and subsequently been confirmed by epidemiological and other field studies. One study shows that the combination of a moderate amount of alcohol and a moderate amount of cannabis causes a very strong deterioration of driving ability.*

## Part Four – Physical Harm

### 17. Cannabis and Pregnancy

#### **Summary of Chapter 17:**

THC (see page 3) is a substance which passes from the mother's blood system to that of the foetus, which means that THC can produce direct harmful effects on the foetus during pregnancy.

There is a risk that habitual cannabis abuse during pregnancy may affect the foetus, with resulting lower birth weight and shorter birth height.

As regards the risk of foetal damage in the proper sense, research findings are contradictory, but most studies show that cannabis smoking does not increase the risk. However, researchers warn us against excluding cannabis as a cause of malformations before larger and methodologically better-conceived studies have been conducted. That being said, it does seem that we can exclude the risk of malformations being caused by chromosomal damage produced by cannabis.

The most worrying scientific findings concern – not surprisingly – damage to the child's central nervous system. A very long-term Canadian study found that children of cannabis-smoking mothers had sustained damage to cognitive functions which did not become noticeable until the children reached the age of four. The reason for the late appearance of this damage is assumed to be that the functions involved are “executive” cognitive functions which are not taken into use until the child is four to six years old.

Another long-term study shows similar associations between exposure during the foetal stage and relatively late (at age 6 and 10, respectively) behavioural disturbances.

THC is a substance which passes from the mother's blood to that of the foetus. This means that THC can cause direct damage to the foetus during pregnancy. (THC is also passed on to the infant via breast-milk.) Animal experiments have shown a number of very serious effects on the gestation of, and on the young born to, females which have been given cannabis or THC during gestation. These findings have naturally given rise to questions concerning the risks to which the human foetus is exposed if the mother smokes hashish or marijuana during pregnancy (Abel, 1985).

Researchers are here confronted with the usual problems of finding a reliable design for their studies, including comparable control groups. Further, research of this type is faced with particular difficulties as regards finding means of excluding other factors that might explain damage that has been observed, such as other drugs (including alcohol and tobacco), inadequate nutrition and infections during pregnancy. Moreover, it is also difficult to find suitable methods of measurement with sufficient sensitivity to detect even damage of a subtle nature.

The conceivable – and suspected – harmful effects of cannabis can be divided into the following categories:

- Effects on birth weight, birth height, etc. (similar to the effects of tobacco smoking during pregnancy)
- Increased risk of malformation
- Effects on the central nervous system of the foetus
- Other effects on the foetus

#### *Effects on Birth Weight etc.*

Until the mid-1980s, there were doubts as to the effects of cannabis on factors such as birth weight. Early studies produced varying results and were not always conducted with sufficient thoroughness. A series of later studies have shown that cannabis smoking during pregnancy is statistically associated with a lower average birth weight (Hatch & Bracken, 1986; Zuckerman et al., 1989) and a shorter average body height (Zuckerman et al., 1989; Tennes et al., 1985).

However, findings which in certain respects call into question the effect of both cocaine and marijuana on birth weight have been reported in a multi-centre study (Shiono et al., 1995). This study does not find any significant association between marijuana smoking during pregnancy and a lower birth weight of the child. If one looks solely at the association between mothers found to have marijuana in their blood during pregnancy and the birth weight of their children, though, there turns out to be a clear tendency which points in the same direction as the studies mentioned above. The overall picture is that – when account is taken of the quality of different studies, the methods they use to establish current abuse and the selection of pregnant women for the respective studies – *cannabis*

*use, at least habitual cannabis use, during pregnancy represents a risk that the pregnancy and the foetus will be affected, with reduced birth weight and birth height as a consequence.*

The importance of these effects for the children's further development, however, is not known. The central result achieved is that it has been demonstrated that THC, by affecting the mother's hormonal system (and reducing the duration of pregnancy) or by its direct toxic action, produces such a clear and measurable effect on foetal development.

### *Increased Risk of Malformation*

The term "malformation" here refers to abnormal anatomical developments of parts of the body and/or internal organs that are visible to the naked eye or can be detected by means of traditional examination methods used in radiology or laboratory diagnosis (to determine functional disturbance).

The increased frequency of malformation shown in animal experiments has not been as striking as the inhibition of growth mentioned above; and moreover, it has been necessary to use very high doses to provoke that increased rate of malformation.

The research findings in this area are somewhat contradictory. While there are a few studies (e.g. Linn et al., 1983) which suggest a higher risk of malformation, most studies – and indeed the best-designed and best-executed ones – have produced findings which contradict the suspicion that the smoking of cannabis preparations increases the risk for malformation of parts of the body or of internal organs (Zuckerman et al., 1989).

That being said, since there do exist studies which have arrived at a different conclusion, since the "exonerative" studies have certain methodological shortcomings, and since most of the "exonerative" studies relate to marijuana and were carried out during the first half of the 1980s or earlier – when marijuana with low THC concentrations was still in widespread use – *it would be unwise to exclude cannabis as a cause of malformation until larger and better-controlled studies have been carried out* (Hall et al., 1994).

### **Malformation as a Result of Chromosomal Damage Caused by Cannabis**

Malformation can also be caused in other ways than through a direct toxic effect on the foetus. By damaging the genetic material of either parent, poisons capable of affecting the genes can cause malformation genetically.

It has not been possible to prove that THC can produce such effects, and this risk has been dismissed in several reviews of research (Marijuana and Health, 1982; Hollister, 1986; Hall et al., 1994).

### *Damage to the Central Nervous System of the Foetus*

It seems a reasonable suspicion that cognitive damage could arise at the foetal stage, bearing in mind the acute effects of cannabis on cognitive functions as well as the damage to cognitive functions caused in adults and young people by long-term exposure to cannabis (see Chapter 14). It is indeed within the area of effects on the central nervous system that the most disturbing scientific findings have been made.

A central position in this field of research is occupied by the Ottawa Prenatal Prospective Study (OPPS), carried out by a research team led by Peter Fried. This study of the children of mothers who smoked marijuana while pregnant is unique, not least because of its long-term nature. The mothers were recruited to the research programme during the period 1978–1983. The children were examined from a neurological point of view immediately after birth and on several occasions during their first year; thereafter, they have been tested with regard to cognitive and psychomotor functions once a year up to the age of 16.

The researchers initially found signs of deficiencies in the children's neurological development, or signs of withdrawal effects. These symptoms disappeared during the first year, and when the children were examined with regard to motor development, perception and motor functions at the ages of one, two and three years, no deficiencies were found which could be related to their exposure to cannabis during the foetal stage. However, when the children were examined at the age of four, deficiencies were found in their memory and verbal ability. These deficiencies were no longer detectable at the ages of five and six – although the six-year-olds were found to have impaired ability to maintain attention. In the examinations at ages six to nine, several manifestations of deficiencies in cognitive functions were identified. The parents of the children who had been exposed to marijuana were also more likely to report behavioural disturbance in their children.

When the children were examined at ages nine to twelve, moderate functional impairment of a specific type was discovered: the children had reduced ability as regards *memory in connection with visual stimuli, analytical ability and integrative ability*. Moreover, attention disturbances were found. The same pattern recurred at ages 13–16 (Fried et al., 2003). It could be mentioned that the disturbances exhibited by children whose mothers had smoked cannabis while pregnant were different from the disturbances manifested by children whose mothers had smoked regular cigarettes only; the latter children were affected as regards overall intelligence and certain functions related to hearing.

*To sum up, the research team found that – in addition to slight, transitory neurological deficiencies at birth – the children showed a slight disturbance to cognitive functions which was not detectable until they reached the age of four, and which subsequently disappeared. Other kinds of disturbance to cognitive functions, together with behavioural problems, appeared during the children's first school years and have proved possible to follow until the age of 13–16.*

Fried (1995; 2003) presents a hypothesis – which tallies well with the kinds of cognitive damage sustained by adults following long-term cannabis smoking – as to why the deficiencies are not detectable until a few years after birth: the damage caused at the foetal stage is assumed not to become important until the child needs to function at a higher level with regard to “executive” functions (integrative cognitive functions of importance for processes such as problem-solving and planning). Indeed, cognitive disturbances of these kinds are among those found in adults (Leavitt et al., 1994).

Most studies of the effects resulting from cannabis use during pregnancy do not follow the child beyond the age of one year. This is why there is only a very limited amount of scientific data either supporting the findings reported by Fried et al. or calling them into question. Day et al. (1993) found an association between marijuana smoking during pregnancy and lower intelligence-test scores at the age of three (but not before that age); this finding supports those of Fried. An association between marijuana smoking during pregnancy and sleeping problems in three-year-olds detected by Dahl (1995) also points in the same direction.

Peter Fried (1995) warns us against underestimating the risks to the foetus from cannabis exposure during pregnancy. He emphasises that his study looked at the effects arising from marijuana smoking in the 1970s, reminding us that the marijuana in use today has a considerably higher THC content.

Recently, however, another long-term study has become available to us, even though the children included in it are five to six years younger. Goldschmidt et al. (2002) studied a group of just over 600 pregnant women, of whom slightly less than half smoked marijuana in different amounts while pregnant. Careful assessments of aspects such as the situation in the women’s homes were carried out during the pregnancy and after they had given birth, in order to isolate the effects, if any, of cannabis. During the first years, the main emphasis was placed on reports from parents and, later, teachers. At the age of six, an association was found between exposure to marijuana and teacher reports of delinquent-behaviour problems.

When the children were ten years old, a more extensive assessment was carried out, including interviews with parents and teachers as well as standardised questionnaires. A clear association was found between exposure and “delinquency”. Further, it was found that these behavioural disturbances were mediated by pronounced hyperactivity, impulsiveness and deficiencies in attention. These characteristics proved to be associated with the degree of exposure to marijuana.

A comparison of these two long-term studies – probably the only ones of their kind in the world – yields several similar tendencies. One of them is that test-score differences and behavioural disturbances, respectively, appear at a relatively late stage, as a manifestation

of the fact that the damaged functions do not develop and start to be used until then. Further similarities include reports by parents and teachers, respectively, of disturbed/restless behaviour, which appear at more or less the same age. While Fried has focused more on measuring cognitive functions, Goldschmidt records behaviour.

### *Other Effects on the Foetus*

Several researchers have recorded a few cases of rare cancers in children of mothers who smoked marijuana while pregnant. While these findings do not prove anything, they do signal a need to be more observant and represent a call for more research (Cannabis: A Health Perspective and Research Agenda, 1997, p. 25).

## *18. The Effects of Cannabis on the Respiratory Organs*

### **Summary of Chapter 18:**

The most important of the known long-term harmful effects on the respiratory organs are chronic bronchitis and cancer of the respiratory tract.

There is a causal connection between long-term cannabis smoking and chronic bronchitis. Chronic bronchitis not rarely leads to chronic obstructive pulmonary disease (COPD).

Cannabis smoke has a documented content of carcinogenic substances, and the discovery of preliminary stages of cancer in studies of large groups of cannabis smokers suggests that cannabis can cause cancer. These research findings, together with the numerous reports on the association between early onset of cancer in the respiratory tract and cannabis smoking, imply that the carcinogenic properties of cannabis smoke must be considered nearly proven.

Bearing in mind the well-documented harmful effects of tobacco smoking on the human respiratory tract (above all chronic bronchitis, emphysema and cancer), researchers have long been interested in finding out whether cannabis smoke has similar or other effects on this system of organs. In this context, we can start by noting that cannabis is sometimes smoked mixed with tobacco, in which case the cannabis smoker is subject to the risks of harm associated with tobacco smoking. Further, there are many similarities between

cannabis smoke and tobacco smoke, and so we could expect the side-effects to be similar (Gold, 1989). The main difference between the two is of course the presence of nicotine in tobacco and that of THC and other cannabinoids in cannabis.

In general, a tobacco smoker has more nicotine cigarettes a day than a cannabis smoker has cannabis cigarettes or pipefuls. On the other hand, cannabis is smoked – at least in the Western world – using an inhalation technique different from that commonly used by tobacco smokers who inhale. This technique, which ensures that “fuller use” is made of the cigarette or pipeful, consists of drawing the smoke deeper into the lungs and keeping it there for as long as possible. Furthermore, cannabis smokers tend to smoke as much of the cigarette as possible, while tobacco smokers often have filter-tips on their cigarettes and stub them out before it is absolutely necessary. This means that the amount of tar ingested by someone who smokes cannabis at a dependence level for several years (i.e. several “joints” or pipefuls on a daily or near-daily basis) is very probably comparable with the amount ingested by a habitual tobacco smoker (Tennant, 1983).

The explanation as to why research concerning these expected harmful effects has produced, to date, only a limited number of findings compared with the body of findings yielded by tobacco research may be that:

- the harmful effects in question are side-effects which generally need decades before their development reaches a clinically observable level;
- cannabis research is a young field compared with tobacco research.

Tobacco research is far ahead of cannabis research, both temporally and quantitatively. The great breakthrough of tobacco research occurred in the first half of the 1960s, and the 1964 report by the American Surgeon General (the head of the US Public Health Service) was based on over 7,000 scientific reports, a number of which referred to longitudinal studies. It was possible to point to both a statistical association and a causal connection between smoking and a series of diseases, especially of the respiratory tract and the cardiovascular system. As early as at this stage, it was possible to show that smoking was the main cause of lung cancer in men, and the main cause of chronic bronchitis in both men and women. In 1989, 25 years later, the Surgeon General had access to more than 57,000 scientific works for the report published in that year. Cannabis research, on the other hand, was rather modest in scale in the early 1960s, and in 1996 the total number of scientific articles published on the subject probably still did not exceed 10,000. As of today, tobacco research has yielded about 140,000 scientific works whereas the total body of cannabis research amounts to no more than roughly one-tenth of that number.

Clinical observations of how cannabis smoking increases the risk of acute infections of the nose, sinuses, pharynx and bronchi are common (Tennant, 1983).



The main long-term harmful effects on the respiratory (and adjacent) organs are: 1) *chronic bronchitis* (which may be followed by COPD, chronic obstructive pulmonary disease); and 2) *cancer of the respiratory tract*.

### *Chronic Bronchitis*

Clinical experience of chronic bronchitis in young cannabis smokers is so common that doctors are advised always to suspect cannabis abuse when encountering bronchitis in young people.

Tashkin (1993) showed there to be a clear association between chronic bronchitis and regular, large-scale (3–4 “joints” daily over a period of at least five years) consumption of cannabis.

Chronic bronchitis not rarely leads to COPD. Bloom et al. (1987) found that chronic marijuana smoking “had a striking effect on pulmonary symptoms and function”. One manifestation of this effect on the lungs was that cannabis smokers were significantly more likely to exhibit the kind of impaired lung function characteristic of the preliminary stages of COPD. This functional impairment was more pronounced in marijuana-smoking men than in comparable tobacco smokers.

### *Cancer of the Lungs, Bronchi, Larynx, Oral Cavity, Pharynx and Oesophagus*

Tashkin (1993) lists a series of factors which point towards cannabis smoking being associated with an increased risk of cancer of the respiratory tract:

- The tar found in cannabis smoke contains a 50 per cent larger amount of certain carcinogenic substances (among them the highly carcinogenic benzopyrene) than tobacco-smoke tar.
- The smoking of a marijuana cigarette produces four times as much tar as the smoking of a tobacco cigarette.
- Experiments on animals have shown that cannabis smoke or the tar from cannabis smoke has a carcinogenic effect.
- Large-scale consumers of cannabis exhibit a significantly higher frequency of cellular changes constituting a preliminary stage of cancer. This has been shown by e.g. Tennant (1983) and Tashkin (1993).
- There are several reported observations of groups of young patients exhibiting both cannabis abuse and cancer development. In these cases, the tumours have made their appearance 10–30 years earlier than in those patients whose cancer was caused solely by tobacco:

Of 887 patients with cancer of the upper or lower respiratory tract, Taylor (1988) found ten who were under 40 years old. Of these, five were

large-scale consumers of cannabis, two smoked cannabis frequently but not daily, and one was probably a cannabis smoker. Two of them had cancer of the lungs, four had cancer of the larynx and four had cancer of the tongue.

Endicott (1991), in a retrospective review of patients with cancer of the throat and head at two centres in the United States, found 26 patients who were 41 years old or younger when their tumour was discovered. The average age of these patients was 32 (range: 17–41); the normal average age at which these cancers make their appearance is 57. All 26 patients were current or former marijuana smokers.

Donald (1993), when examining the records of his patients with cancer of the head and throat over a 20-year period, found 22 patients who had squamous-cell cancer and were 40 years old or younger when their tumour was discovered. Their average age was 26, and 19 of them were cannabis smokers, including 16 large-scale consumers. In 13 of these 22 patients, the tumour was located in the tongue or elsewhere in the oral cavity. Only half of these patients were tobacco smokers as well.

Caplan et al. (1990), who has reported two cases of tongue cancer in two marijuana smokers (who did not use alcohol or tobacco), has put forward the hypothesis that cannabis may be responsible, as the sole factor, for tumours, especially in the upper respiratory tract.

Since Tashkin's review was made, further reports have been published. Sridhar et al. (1994) studied the connection between cannabis smoking and early onset of lung cancer. Of 110 patients with lung cancer, 13 were younger than 45 (range: 27–45); the average age of onset for lung cancer is 55 years or older. All of these thirteen patients were cannabis smokers, compared with 6 per cent in the older group. Twelve of the thirteen were tobacco smokers as well.

In a recent review, Tashkin – who is the leading researcher in this field – looks again at the question of cancer and other risks to long-term cannabis smokers (Tashkin et al., 2002). In addition to the circumstances mentioned above, he presents further risk factors. First, he emphasises that examinations of mucous membrane in long-term smokers suggest that THC weakens the immune defence against tumour cells. He goes on to account for five separate series of young men having developed cancer of the respiratory tract; all or a majority of the patients were cannabis smokers. In a genuine scientific study, a comparison had been made between 170 patients who had been diagnosed as having cancer and 170 matched controls without such a diagnosis. The proportion of cannabis smokers was clearly larger in the cancer group. The risk increased with the total amount of cannabis ingested by a person. The finding with the most serious implications was perhaps that those

who had smoked both tobacco and cannabis ran a many times higher (36-fold) risk of developing cancer. There is reason to suspect that the combination of tobacco and cannabis leads not only to a summation effect but also to a synergistic effect.

*To conclude, there now exists a considerable body of documentation showing that cannabis smoke contains carcinogenic substances and probably has negative immunological effects. The discoveries of preliminary stages of cancer made in studies of large groups of cannabis smokers suggest that cannabis has carcinogenic effects. These research findings, together with the numerous reports about a probable connection between early onset of cancer in the respiratory tract and cannabis smoking, imply that the carcinogenic properties of cannabis smoke must be considered nearly proven.*

## 19. Cannabis and the Cardiovascular System

### **Summary of Chapter 19:**

It was previously thought that the acute effects of cannabis intoxication on the cardiovascular system did not constitute a risk for a healthy young person. Albeit few in number, however, there are now reports of myocardial infarction, other acute heart conditions and stroke in young persons as well.

For people with coronary disease or hypertension, marijuana smoking constitutes an obvious risk. In other words, elderly people and people with a heart disease and/or high blood pressure have further reasons not to use cannabis.

It is not known how long-term exposure to cannabis smoke (and its 400 substances) may affect the cardiovascular system. We should wait to see the results of large-scale longitudinal studies before we decide whether or not to acquit cannabis as not guilty of producing tobacco-like or other long-term effects.

### *Risks Owing to Acute Effects*

Cannabis intoxication initially causes palpitations of the heart and a certain drop in blood pressure; there is also often a phase characterised by a certain rise in blood pressure. These cardiovascular effects may contribute to provoking a state of anxiety, particularly in inexperienced smokers, but they are not otherwise considered to represent any risk to a

young person with a healthy heart. However, our knowledge of the effects caused by cannabis on the heart and the blood vessels is very limited (Sidney, 2002).

Overall, it would seem that cannabis smoking at a moderate dose represents no risk to young and physically healthy people. However, elderly people as well as people with a heart disease and/or high blood pressure should obviously abstain from cannabis smoking (Tennant, 1983). A decade or so ago, there were few reports to support such a warning. Today, however, there is a substantial body of reports on myocardial infarction – a sufficiently large number to show that cannabis can provoke both angina pectoris and infarction (Sidney, 2002). However, it would appear that it is not the often moderate drop in blood pressure that constitutes a threat. Kosior et al. (2000) reported two cases of cardiac arrhythmia – one of atrial fibrillation and the other of recurrent paroxysmal tachycardia – in young people. Besides, there were also reports of atrioventricular (AV) blocks and other cardiac events.

It also seems that the changes in blood pressure can result in cerebral events: there are reports of both transient ischaemic attacks (TIAs) and strokes, including in young people (Jones, 2002).

A noteworthy example – to remind the reader of the limited nature of our knowledge with regard to how the cardiovascular system is affected by the substances contained in cannabis smoke – is provided by the two reported cases of myocardial infarction in very young and otherwise healthy cannabis smokers (Podczeck et al., 1990). Since then, there have been further reports of young people dying of myocardial infarction in connection with cannabis smoking (Jones, 2002).

### *Risks Owing to More Long-Term Effects*

Although we have, at present, no scientific proof that cannabis use causes cardiovascular diseases in the longer term, on closer inspection there are certain disturbing facts which should give us food for thought. We may, for example, recall what was said in Chapter 18 with regard to the difference in developmental level between the research into tobacco smoking and that into cannabis smoking; and also with regard to the different smoking techniques, where it was said that, because of the method used to smoke cannabis, the lungs of the smoker are exposed to four times as much tar from a cannabis cigarette as from a tobacco cigarette.

We still know very little about the effects on the cardiovascular system of several years' exposure to cannabis smoke and the 400 substances it contains. Because of the similarities between tobacco smoking and cannabis smoking, and for other reasons, we ought to await the results of large-scale longitudinal studies before we clear cannabis of the accusation of having tobacco-like or other long-term effects.

## 20. Cannabis and Fertility

### **Summary of Chapter 20:**

Cannabis smoking disrupts the hormonal balance of both men and women. Research into the consequences that this effect may have on the fertility of men and women has yielded contradictory results. There does, however, remain a suspicion that cannabis smoking may lead, in both sexes, to a relative reduction of fertility which is of importance above all in people who already have a tendency towards low fertility owing to other factors.

More than three decades ago, the suspicion arose that cannabis smoking might have a negative effect on the fertility of men. Harmon and Aliapoulios (1972) reported three cases of gynaecomastia (development of breasts in men) in three large-scale consumers of cannabis. The researchers held that the hormonal effects (particularly a reduction in testosterone) suggested by the gynaecomastia ought to have a negative impact on sperm production. Subsequent animal experiments have pointed in the same direction, while direct studies of the sperm production of cannabis-smoking men have yielded contradictory results (Bloch, 1983). Both Hollister (1986) and Gold (1989) maintain that it is very uncertain what this effect on testosterone levels means in terms of sperm production. It is probably the case that these disturbances matter the most in teenagers and in men who already have a low level of sperm production owing to other factors.

The effect of cannabis on fertility in women is also uncertain. Research has shown disturbances to hormone secretion whose effects include disruptions to the menstrual cycle. These findings, together with those from animal experiments, suggest that cannabis probably has a certain fertility-reducing effect which, as in the case of men, may be of importance above all in those cases where the individual already exhibits other tendencies towards reduced fertility (Gold, 1989).

## 21. The Effects of Cannabis on the Immune System

### **Summary of Chapter 21:**

Despite almost three decades of research, the question as to the effect of cannabis smoke on the human immune system must be considered to be unanswered.

The human immune system involves several organs or parts of organ systems. The immune system is of decisive importance for the body's defence against infection (bacteria, viruses and other micro-organisms) as well as against certain types of cancer. It is also involved in the development of allergies and auto-immune diseases.

In his review article *Marijuana and Immunity*, Hollister (1992) begins by saying that few areas of research are as filled with controversy as the question of the effect caused by marijuana on the immune system. He goes through the findings of studies carried out at the different levels where the various components of the immune system operate, and his conclusion is that *the question of the effect caused by cannabinoids on the immune system remains unanswered after more than 15 years of research*. Nobody has been able to call this conclusion into question in a convincing manner. Quite simply, we do not know what importance, if any, the changes observed have with regard to the body's defence against infection and the development of cancer.

Hollister also noted that the level of interest directed towards this area of research fell over the latter part of the 1980s. The probable explanation is that questions related to AIDS occupied the attention of immunology researchers at the same time as the relationship of cannabis to the immune system appeared to be a less fruitful subject of research than it previously did. At the time of writing (in 2004), it can be added that this research seems to have gained momentum again in connection with different attempts to make medicinal use of cannabis.

Despite intensive study of the effects caused by cannabinoids on various aspects of the immune system, Klein et al. (1998) sum up the situation by saying that the questions put to researchers still cannot be answered.



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# Glossary

## A

<b>Amotivational syndrome</b>	Certain personality traits caused by chronic cannabis abuse.
<b>Anandamide</b>	A substance similar to cannabinoids which occurs normally in the human body.
<b>Anhedonia</b>	The inability to feel joy or pleasure.
<b>Antipsychotic</b>	Having the quality of counteracting psychotic symptoms (usually said of medicinal drugs).
<b>2-arachidonylglycerol</b>	A substance similar to cannabinoids which occurs normally in the human body.
<b>Atrioventricular block (AT block)</b>	A serious disturbance to the conduction system of the heart.

## B

<b>Bronchitis</b>	An inflammation or irritability of the mucous membrane of the bronchial tubes.
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## C

<b>CAN</b>	The Swedish Council for Information on Alcohol and Other Drugs ( <i>Centraförbundet för alkohol- och narkotikaupplysning</i> ).
<b>Cannabinoids</b>	Substances contained in the cannabis plant.

<b>Cannabis receptors</b>	<i>See Receptors.</i> The cannabis receptors can be stimulated both by exogenous (not occurring naturally in the body) cannabinoids such as THC and by endogenous (occurring naturally in the body) cannabinoids such as anandamide.
<b>Cardiac</b>	Of or relating to the heart.
<b>Cardiac arrhythmia</b>	Irregular rhythm of the heart. If more than temporary, it is a <b>manifestation of damage to the conduction system of the heart.</b>
<b>Cerebral</b>	Of or relating to the brain (cerebrum).
<b>Cerebral atrophy</b>	A shrivelling of the brain.
<b>Cognitive functions</b>	Intellectual functions such as thought and memory.
<b>Confounding factor</b>	The scientific term for an interfering factor which, if not controlled for, may disturb the study of a relationship or connection.
<b>Confusion</b>	A profound state of bewilderment; disorientation.
<b>D</b>	
<b>Delirium</b>	An acute confusional state.
<b>Depersonalisation syndrome</b>	A mental disorder characterised by a profound sense of unreality as regards the surrounding world and/or oneself.
<b>Dysphoria</b>	A feeling of dissatisfaction and irritation.
<b>E</b>	
<b>Endocannabinoids</b>	Substance similar to cannabinoids which occur normally in the human body.
<b>Euphoria</b>	A pronounced sense of well-being.

**I****Interaction**

Refers here to the mutual effects that two substances (such as a medicinal drug and a narcotic drug) have on each other, possibly with a negative outcome for the individual.

**L****Latent**

The opposite of *manifest*. Refers to a predisposition towards an illness which has not broken out.

**M****Manifest**

The opposite of *latent*. Refers to a disease which has broken out.

**Metabolite**

A product of the body's processes for breaking down substances.

**N****Neuroleptics**

Medicinal drugs for the treatment of psychoses.

**O****Opiates**

Drugs (narcotic and medicinal) derived from the opium poppy.

**Opioids**

Opiates and synthetically produced narcotic and medicinal drugs which are closely related to the opiates.

**P****Paroxysmal tachycardia**

A suddenly occurring, rapid but regular heart rhythm.

<b>Prepsychotic</b>	Close to the breakout of psychotic illness.
<b>Prospective study</b>	A longitudinal, long-term, study which is started before the influencing factor whose effect is to be studied has started affecting the study group.
<b>Psychoactive substances</b>	Substances producing an effect on mental functions.
<b>Psychomotor functions</b>	The functions responsible for co-ordinating the brain and the locomotor system (the organs used to move the body: the skeleton, the muscles and the nerves).
<b>Psychotoxic substances</b>	Substances producing a noxious/toxic effect on mental functions (usually by affecting brain cells).
<b>R</b>	
<b>Randomisation</b>	(Scientific term.) Random distribution of study subjects to a study group and a control group.
<b>Receptors</b>	Structures at the surface of nerve cells which receive signals from neurotransmitter substances (mainly secreted from other nerve cells). Together, the signals from thousands of receptors generate outgoing signals from the nerve cell.
<b>S</b>	
<b>Synergism</b>	A situation where the joint effect of two or more factors is greater than the sum of the effects of the individual factors.
<b>T</b>	
<b>THC</b>	Abbreviation for <i>_9-tetrahydrocannabinol</i> , which is the most psychoactive of the cannabinoids.
<b>THC-COOH</b>	A non-psychoactive metabolite of THC.

<b>TIA</b>	Förkortning av <i>transient ischemic attac</i> . Kortvarig, övergående blodbrist lokalt i hjärnan.
<b>Tolerance</b>	A consequence of the development of dependence, meaning that the individual needs ever-higher doses to achieve the same effect.
<b>Transient ischaemic attack (TIA)</b>	A consequence of the development of dependence, meaning that the individual needs ever-higher doses to achieve the same effect.
<b>W</b>	
<b>Withdrawal symptoms</b>	Discomfort felt as the supply of an addictive substance is broken off.





*The mission of the National Institute of Public Health Sweden is to promote health and to prevent illness and harm. Its mandate includes the synthesis and dissemination of research findings.*

This report is a survey of the harmful effects – mental as well as physical – which can arise as a consequence of cannabis use.

The author, Jan Ramström, is a psychiatrist with several years' experience of specialised drug-abuse services. A long-time Head of Clinic in the field of general psychiatry, he has been affiliated with the Swedish National Board of Health and Welfare for nine years in the capacity of Scientific Adviser on issues of psychiatry and substance abuse. His previous publications include other reports as well as several textbooks in the field of substance abuse, psychiatry and youth development.

The report is intended for health-care organisations, information officers such as drugs advisers and drug counsellors, and others in need of knowledge-based information on the consequences of cannabis use.



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