CANNABIS UPDATE

- *are patterns of use peaking?*
- *latest evidence of effects*
- *cannabis and driving.*

POST note 113 March 1998

POST reviewed the extent of use, health and psychological effects of cannabis in a 1996 report[1]. Since then, debate has continued on its legal status, and the Lords' Science and Technology Committee is starting an inquiry into scientific aspects of this drug and its effects.

This briefing summarises findings relevant to the current parliamentary debate over cannabis.

TRENDS IN THE EXTENT OF USE

Because of cannabis's illegality, the picture on consumption has to be pieced together from official statistics on seizures and offenders, and some on-going social surveys. The Home Office's (HO) records **of illegal drug seizures and offenders** are in **Figure 1**, and show numbers starting to grow rapidly in 1988, with a 'pause' from 1990-2. The latest figures show upward trends continuing during 1995, but rather more slowly than from 1992-4. Thus, cannabis seizures and offenders rose by 3% and 6% respectively - well below the 27%-28% increase during the 2 years 1993 and 1994. Cannabis still accounts for the vast majority of both illegal drug seizures (~80%) and offenders (~82%). Cannabis comes in various forms, and 'fashions' appear to be changing (**Figure 2**) with nearly ten times as many plants seized now as in 1991 / 2 (seizures of herbal and resin forms are relatively unchanged). These statistics suggest a shift towards users growing their own plants, helped by high yielding seeds being on sale, and high intensity UV lamps and hydroponics allowing more 'commercial' plant production.

While on the legal statistics, one of the trends highlighted in POST's earlier report was the trend towards police cautions. More detailed HO figures now confirm a massive increase in cautions for unlawful possession of cannabis (up tenfold between 1986 (4,048 cautions) and 1995 (40,391)), while prosecutions for this offence only doubled (from 11,493 to 24,386).

Turning to the **social surveys,** the 'baseline' against which all other surveys have to be judged remains the British Crime Survey (BCS), a comprehensive **national** survey among 16-59 year olds. Highlights from the 1994 BCS included:

- just over 1 in 3 (34%) people in the 16-29 age group had tried cannabis at some point in their lives ('ever tried'), including some 12% within the last month;
- 15% of people in the 30-59 age group had 'ever tried' cannabis (2% within the last month);
- across all ages (16-59), 21% had 'ever tried' cannabis, and 5% had done so in the previous month.

FIGURE 1 DRUG SEIZURES AND OFFENDERS

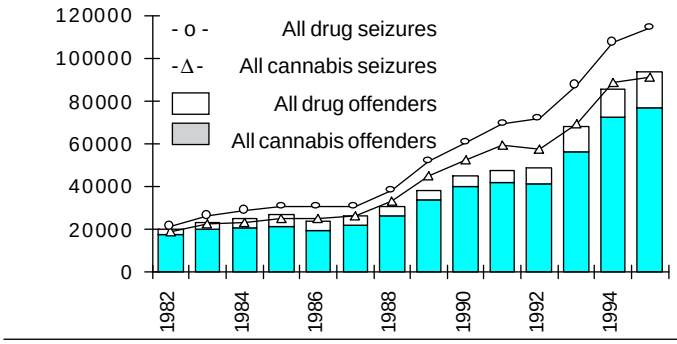


FIGURE 2 DIFFERENT FORMS OF CANNABIS

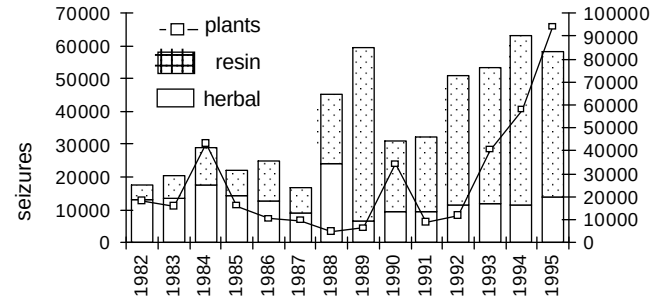
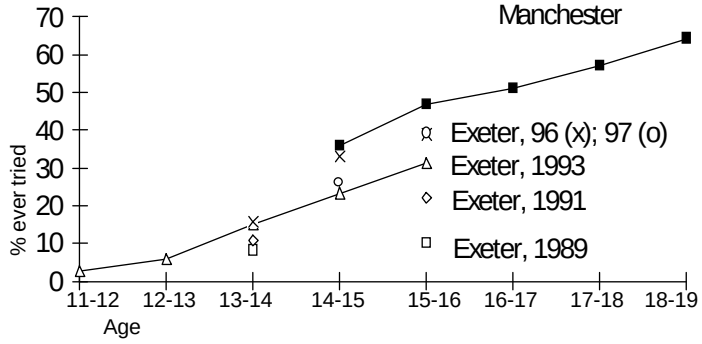


FIGURE 3 YOUNG PEOPLE AND ILLEGAL DRUGS



Other social surveys look at subsets of the population. For instance, surveys by Exeter University's School Health Education Unit now involve 27,000 young people in 122 schools nationwide, and have shown a consistent rise in experience of drugs with age (**Figure 3**), while the number of children with lifetime experience of drugs at a given age has also been rising - from ~10% of 15-16 year olds in 1989 to some 39% in 1996. The most recent results suggest that **this trend may have peaked**, since the 1997 figure for lifetime experience of any drug remained at 39% for 15-16 year olds (Figure 3). Indeed, figures for 14-15 year olds declined between 1996 (33%) and 1997 (26%).

1. POST, 1996. "Common Illegal Drugs and Their Effects".

A second survey is the 'longitudinal' study by the University of Manchester, which follows a group of schoolchildren from a cross-section of schools in NW England. The pattern again is one of increasing experience of drugs with age (Figure 3), with the proportion of young people trying any illegal drug rising from 36% at age 14-15 to near two thirds by age 18-19. Figures for lifetime experience of drugs emerging from surveys such as these tend to be somewhat higher than those reported nationally by the BCS, but in the 1994 BCS the gap was closing, suggesting the regional surveys are not seriously out of line. A clearer idea of the overall picture should emerge in the next 12 months or so, with the results of the 1996 BCS, and of a local study of 2,500 young people in the NorthEast.

The 'headline' figures on people who have 'ever tried' cannabis do not tell us how many are taking it and other illegal drugs on a regular basis. Not surprisingly, this varies greatly with the setting[2], but the national BCS suggests that for cannabis, a general rule of thumb is that 30% of young people who have 'ever tried' cannabis continue to take it once or more a month - indeed, outside of the opiates, cannabis is the illegal drug most likely to be taken frequently, with 9% reporting daily use and a further 14% several times a week. Recent figures also confirm that 46% of those who have tried cannabis have also experimented with other illegal drugs.

Drug-taking is not one-way, and many people stop taking them of their own volition - for example, of the 17-18 year-olds in the Manchester study, 10% had tried drugs and had positively stopped taking them, while other studies suggest that most of those who continue past 20 give up of their own accord by the age of 30.

HOW CANNABIS 'WORKS'

Psychoactive drugs exert their effects by affecting the processes by which cells in the brain (neurons) transmit messages to each other. In the normal course of things, neurons communicate by releasing neurotransmitters (dopamine, serotonin, noradrenaline, etc.) into the gap (synapse) between cells. The neurotransmitters travel across the gap and bind to receptors on the next cell, triggering specific cellular response; multiplied across the many millions of active cells across the brain, these chemical processes are the foundation of our thoughts, memory, mood, decision-making, etc. Psychoactive drugs can interfere with such processes in several different ways:

- they can mimic the natural neurotransmitter(s);
- they can release extra neurotransmitter;
- they can block receptors on the receiving cells so that the normal message is changed or blocked;
- they can also stop the neurotransmitter being 'cleared' from the gap, amplifying its effect.

Thus opiates mimic the natural endorphins and enkephalins normally released in response to pain and stress; stimulants such as amphetamine and cocaine flood synapses with dopamine and noradrenaline (stimulating the affected neurons for several hours), whereas hallucinogens such as LSD work by mimicking serotonin (involved in mood regulation). Ecstasy is unusual in that it has a dual action, acting as both stimulant (by boosting dopamine levels) and mood alterant (through its effects on serotonin pathways).

It has proved relatively difficult to pin cannabis's mode of action down to effects on a particular neurotransmitter system. One obvious assumption is that the active ingredient of cannabis (THC[3]) exerts its effects by mimicking chemicals that are naturally present in the brain (so-called 'natural cannabinoids'), and a key research target has been to discover these and work out their role. Researchers used 'tagged' cannabinoids to identify potential binding sites within the brain, and found one type of receptor (CB1) which bound only to THC and which was widely distributed throughout the brain. This led to the discovery of a natural cannabinoid (anandamide) which uses the CB1 site.

Quite what anandamide normally does in the brain is still uncertain. Research suggests that it may be involved in the release of a factor which causes blood vessels to relax, and it may also play a role in sleep induction. A recent World Health Organisation (WHO) report notes that while it appears to have similar actions to cannabis in some respects, anandamide is considerably less potent in its psychotropic impact, and has a more transient action than THC. Overall, the distribution of the CB1 receptors (found largely in the basal ganglia, cerebellum, cerbral cortex and hippocampus) coupled with the known effects of cannabis (see POST report) imply roles in cognition, memory, reward, pain perception and motor coordination.

More recently, a second type of cannabinoid receptor (CB2) has been discovered away from the brain which has a similar affinity for anandamide. CB2 receptors were first isolated in macrophages (large cells which are part of the immune system and defend against infection and tissue damage), and their presence here may help to shed light on some of the suppressive effects that cannabis has on the immune system.

The CB2 receptor is also present on the surface of mouse embryo cells and interacts with anandamide produced by the uterus to control implantation of the embryo. The evidence suggests that anandamide 'holds

2. For example, 98% of young people in the Glasgow 'dance scene' used cannabis on a more-or-less daily basis in one study, while 23% of 18-19 year-olds in the Manchester study had used an illegal drug (mostly cannabis) within the last week.

3. The main active ingredient of cannabis is generally accepted to be tetrahydrocannabinol (THC).

back' implantation until the uterus is at its most receptive (a point which coincides with lowest anandamide production). If this is the mechanism in women, then cannabis might act to prevent embryo implantation, reducing fertility.

The discovery of the CB2 receptor in sites away from the brain opens up the possibility of designing cannabanoid drugs that bind only to this receptor. Such drugs might be able to deliver some of the wide range of potential therapeutic applications currently claimed for cannabis (see below) via interactions with the CB2 receptor, without the psychotropic effects (presumed to stem from the CB1 receptor in the brain).

EFFECTS OF CANNABIS

A wide variety of therapeutic and harmful effects are claimed for cannabis, the main ones being listed in **Table 1**. Potential **therapeutic effects** include control of nausea and vomiting in the advanced stages of cancer and AIDS, anti-depressant and anti-convulsant effects. While only some of these effects have been validated in clinical trials, a recent review by the BMA[4] concluded that "*although cannabis itself is unsuitable for medical use, individual cannabinoids have a therapeutic potential in a number of medical conditions in which present drugs or other treatments are not fully adequate*".

Turning to the **harmful effects**, these were summarised in the earlier POST report and more recent authoritative reviews by national and international bodies include the 1997 WHO Report. Among recent research highlights in this area are:

- increasing evidence that **long-term cannabis use impairs memory processes and frontal lobe function** (e.g. problem solving), and that the effects may not be readily reversible (e.g. by quitting cannabis). There is also evidence of such effects occurring at relatively low (e.g. 'social') levels of use.
- **'Heavy' cannabis use impairs performance in tests of attention /executive function** (tasks such as card-sorting and learning word lists) more than 'light' cannabis use.
- **There are similar levels of bronchitis and damage to cells lining the lungs between daily tobacco smokers and daily cannabis smokers**, despite the fact that the latter smoke many fewer 'joints' each day compared to the cigarettes. This damage does not show up in measures of lung function.
- Cannabis increases dopamine levels in the nucleus accumbens - part of the so-called dopamine pathway, a component of the brain reward system implicated in **dependency**. Drugs associated with dependency (opiates, cocaine, amphetamines, etc.) all stimulate dopamine release through this pathway. Similarly, physical symptoms of withdrawal from opiates, alcohol and cocaine have been linked with the production of corticotropin releasing factor (CRF) in a related part of the brain, and recent studies have shown that sudden withdrawal from cannabinoids also results in CRF production. **This provides mechanisms through which dependency may be induced**.
- Studies on twins suggests that the subjective effects (degree of pleasure or dislike) are partly determined by genetics.

TABLE 1 EFFECTS OF CANNABIS AND CANNABINOIDS

Therapeutic (of Cannabinoids)

- Nausea/vomiting associated with cancer chemotherapy
- Muscle spasticity (e.g. associated with MS, cerebral palsy and spinal chord injuries)
- Pain management (e.g. analgesic, anti-inflammatory)
- Anti-convulsant (e.g. epilepsy)
- Treatment of gluacoma
- Bronchodilation (asthma treatment)

Harmful (of Cannabis)

- Effects on memory, learning and cognition, and higher order cognitive processes
- Short-term cardio-vascular effects
- Long-term risks of bronchial disease and cancers of the aerodigestive tract
- Links with psychotic conditions such as schizophrenia in vulnerable individuals
- Dependency - cannabis fulfills the modern (psychologically-based) criteria for a drug of dependency
- Effects on the immune and reproductive systems

The Lords Science and Technology Committee is currently considering both potential therapeutic and harmful effects of cannabis and cannabinoids, and is expected to report later in the year

CANNABIS AND DRIVING

Questions over the effects of cannabis on driving have resurfaced recently as Governments look to tackle what is perceived to be a growing problem with drug-driving. As described in the earlier POST report, there are good reasons for presuming that cannabis may impair driving, since laboratory studies show it to affect driving-related performance measures such as psychomotor tasks, visual perception, divided attention tests, braking times, perception and reaction to red lights, etc. Such effects have been confirmed in the limited number of actual driving studies conducted to date, but the extent of impairment is generally lower than might be expected. One possible reason might be that people intoxicated by cannabis appear to be more aware of their impairment, and able to compensate for it (take fewer risks, drive more slowly, etc.), at least to some extent. This contrasts with the effects of alcohol intoxication, which tends to encourage people to take greater risks. Overall, a major Australian review[5] concluded that there is probably a 2 to 4-fold increase in the risk of being involved in an accident when driving when intoxicated with cannabis, and higher still when in combination with alcohol.

4. British Medical Association, 1998. Therapeutic Use of Cannabis. Harwood Academic Publishers.

5. Hall, W., et al, 1994. Australian National Drug Strategy Monograph No 25, Government Publishing Service, Canberra.

One criticism of such studies is that they do not simulate real emergencies, and a parallel approach to assessing the role of cannabis (and other drugs) in accidents is to test victims for drug residues. Figures released in February 1998 (the results of the first 15 months of a three year DTER UK study) showed that 99 (16%) of 619 fatalities tested positive for illegal drugs, three-quarters of them for cannabis. Among driver fatalities only, 51 (18%) out of 284 tested positive for drugs, with cannabis again accounting for most positive results. These figures represent a big increase in drug use when compared to the previous UK survey of road accident victims (1985-87), where only around 3% tested positive for illegal drugs.

The rate at which cannabis is cleared from the body varies between people and may take up to a month, while its intoxicating effects wear off within a few hours, although effects on reaction time etc., may persist for up to 12 hours. Detecting cannabinoids in the blood may thus merely confirm use within the last month, and does not in itself demonstrate that the individual was affected at the time of the accident. The test results have therefore to be interpreted with caution, but there do appear to be more fatalities testing positive than might be expected if there were no extra risk. Thus 12-13% of driver fatalities tested positive for cannabis, while the average proportion of the 16-59 age group having used cannabis in the last month is only 5% in the 1994 BCS. These figures are consistent with an increased risk but not proof of it.

With the availability of roadside tests for various drugs (both illegal and medicinal), there is debate over how far these should be deployed along the same lines as the breathalyser. Some cite the growth in the high positive results for cannabis as making it a high priority for many police forces to deploy such tests, and tests that detect cannabis and other illegal drugs (in sweat or via mouth swabs) are undergoing trials at the present time[6]. Others point to earlier (1995) estimates which suggested that drivers involved in traffic accidents were just as likely to have taken prescribed drugs such as benzodiazepines and antihistamines as cannabis, and that the long residence time of cannabis confuses measures of its importance in road accidents.

Basically, the detailed understanding of the relationship between levels in the body and fitness to drive we have for alcohol has not been developed for cannabis, so the levels in the body do not reveal the degree of unfitness to drive. Until a better understanding of such effects is gained, police may need to rely in physical and behavioural measures of intoxication - speech, alertness, mood, physical signs such as enlarged pupils or rapid eye movements, and tests of coordination, balance, ability to follow simple instructions etc.

DIFFERENT PERSPECTIVES

While science can reveal the risks associated with cannabis use, putting them in perspective is another matter! From one view, recent findings are tending to confirm risks previously dismissed as theoretical by some. Thus respiratory risks are not proportionately smaller than for tobacco (taking into account relative numbers smoked); the discovery that cannabis may act on chemical pathways involved in dependency and withdrawal is also leading to calls for the dependency potential of cannabis to be re-evaluated (upwards). The findings on higher order cognitive performance may have implications for the effectiveness with which individuals contribute to intellectually demanding tasks (e.g. at work). Meanwhile the high proportion of cannabis users who try other drugs makes it difficult to debate the risks of cannabis in isolation.

On the other hand, cannabis risks still appear to compare favourably on many criteria with those from socially acceptable yardsticks such as tobacco or alcohol. As pointed out in the Australian and other reviews, tobacco creates more dependency than cannabis and, from a public health perspective, the risks from cannabis smoking are less than for tobacco because there are many more daily tobacco smokers (25-30%) than daily cannabis smokers (1-3%), many of whom discontinue their use by age 30. As the WHO has noted however, such comparisons are fraught with difficulty - for instance, alcohol is thought to have beneficial effects at moderate intakes. This **question of comparative risks is particularly contentious**, and different conclusions are reached on cannabis depending on whether its risks are compared with tobacco smoking or with the much lower risks tolerated for many other activities (e.g. in foods or medicines). With medicinal use, one challenge is to develop means of administration which avoid the harmful side-effects - for instance, by using individual cannabinoids under prescription.

Scientific opinion on the likely outcome of future research is divided. Some see the full long-term risks of cannabis only likely to emerge over the next few years, as more sophisticated research techniques are applied, and as the first generation of chronic cannabis users from the late 1960s and early 70s reach an age where more harmful effects may manifest themselves. There is also concern over the potential risks accompanying the increase in potency of cannabis (up from 1.5% in the late 1960s to as high as 15-20% now). Others continue to see limited scope for 'hidden' dangers in view of the long history of use in some societies.

6. The tests will involve some 5,000 motorists in the four police force areas, and started in March 1998.