Cannabis: The full facts scientifically referenced

STRENGTH:

The herbal cannabis smoked in the sixties and seventies had a THC (Tetrahydrocannabinol, the main psychoactive ingredient) content of 1-2%. The latest potency study of THC content was carried out in 2008. It found that skunk (produced by selective breeding of cannabis plants) had an average THC content of 16.2%, ranging up to 46% and occupying 80% of the market. Hash (resin) has consistently had a THC content of 4-6% and makes up the other 20%. Old-fashioned herbal cannabis is virtually unobtainable now.

CBD (Cannabidiol), an anti-psychotic substance was present in almost equal amounts in the old cannabis and helped to counteract the psychotic effects of THC (Morgan 2008). It is virtually absent (0.1%) in skunk.

Home Office Cannabis Potency Study 2008.
Morgan C, Curran HV, Effects of cannabidiol on schizophrenia-like symptoms in people who use cannabis. The British Journal of Psychiatry (2008) 192, 306–307. doi: 10.1192/bjp.bp.107.046649

Holland:

The Dutch Government plans to place cannabis with a THC content of 15% or more, in the same bracket as heroin and cocaine. i.e. the equivalent of our class A drugs and so to ban it.

Ministry of Security and Justice, Strong cannabis becomes a class A drug, Government of the Netherlands, 2011 United Kingdom Focal Point, UK Drug Situation 2012, London: Department of Health 2012.

PERSISTENCE in brain cell membranes:

Unlike the other common illegal drugs, THC is fat-soluble so persists in the fatty cell membranes of the brain cells for a long time. After a week 50% will remain, around 10% after a month *(*BMA 1997*)*. Traces can be detected in hair and urine for several weeks after that. The actions of the dozens of neurotransmitters (chemical messengers which pass information from cell to cell in the brain), are impeded by this THC, so normal functioning of the brain is badly affected (Katona et al 2000, Schliker and Kathmann 2001*)*. Repeated doses accumulate in the brain, affecting its performance over a long period of time.

BMA Therapeutic Uses of Cannabis Harwood Academic Publishers 1997.
Katona I, Sperlagh B, Magloczky Z et al GABAergic interneurons are the targets of cannabinoid actions in the human hippocampus Neuroscience 2000; 100: 797-804.
Schliker E, Kathmann M Modulation of transmitter release via presynaptic cannabinoid receptors Trends Pharmacol. Sci. 2001; 22: 565-72.

Academic performance:

The processes of learning and memory require new brain cell branches to be produced for the new connections. This is particularly important in adolescence when normally there is an upsurge in the formation of these new fibres (Robbe 2006, Ashtari 2009, Rubino 2009, Kucewicz 2012, Zalesky 2012). This is badly disrupted, and the younger the child, the worse the damage (Giedd 1999, Chambers 2003). A grade ‘D’ pupil is 4 times more likely

to use cannabis than one with 'A' grades (National Household Survey, USA 2002). IQ scores will drop by about 8 points if use is started in the teens and continued (Meir et al 2012).

Robbe D, Montgomery SM, Thome A, Rueda-Orozco PE, Mc Naughton BL, Buzsaki G Cannabinoids reveal the importance of spike timing coordination in hippocampal function. Nature Neuroscience 2006; 9: 1526-33.
Ashtari M, Cervellione K, Cottone J., Ardekani BA, Kumra S, Diffusion abnormalities in adolescents and young adults with a history of heavy cannabis use Journal of Psychiatric Research, 2009; 43(3): 189-204.
Kucewicz M, Tricklebank M, Bogacz R, Jones M, Dysfunctional Prefrontal Cortical Network Activity and Interactions following Cannabinoid Receptor Activation. The Journal of Neuroscience Oct 26th 2011; 31(43): 15560-15568
Zalesky A, Solowij N, Yucel M, Lubman DI, Takagi M, Harding IH, Lorenzetti V, Wang B, Searle K, Pantelis C, Seal M. Effect of long-term cannabis use on axonal fibre connectivity Brain 2012 135; 2245-2255
Giedd JN, Blumenthal J, Jeffries NO et al Brain development during childhood and adolescence: a longitudinal MRI study Nature Neuroscience 1999; 2(10): 861-3.
Chambers RA, Taylor JR, Potenza MN Developmental Neurocircuitry of Motivation in Adolescence: A Critical Period of Addiction Vulnerability Am J Psychiatry 2003; 160: 1041-52.
Meir MH, Caspi A, Ambler A, Harrington HL, Houts R, Keefe SE, McDonald K, Ward A, Poulton R, Moffitt T, Persistent cannabis users show neuropsychological decline from childhood to midlife.
Proceeding s of the National Academy of Sciences published online before print August 27, 2012, doi: 10.1073/pnas1206820109

Personality:

Because normal chemical messaging is impaired, users have fixed opinions and answers to questions. They find it difficult to find words or solve problems, can't take criticism or plan their days. They have no daily or weekly routines. At same time are lonely, miserable and feel misunderstood (Lundqvist 1995). Development slows, they remain childish and dependent (Tunving 1987) and are twice as likely to drop out of education (Lynskey 2003). Social situations are avoided (Buckner 2011). Cannabis is 'the drug for life's future losers' (Patton 2007).

Lundqvist T Cognitive Dysfunctions in Chronic Cannabis Users Observed during Treatment: An Integrative Approach. Dissertation Stockholm: Almqvist & Wiksell International; 1995.
Tunving K, Psychiatric Aspects of Cannabis Use in Adolescents and Young Adults
Pediatrition 1987; 14: 83-91.
Lynskey M, Coffey C, Degenhardt L, Carlin J Patton G A longitudinal study of the effects of adolescent cannabis use on high school completion Addiction 2003; 98: 685-92.
Buckner JD, Heimbrg RG, Schmidt NB, Social anxiety and marijuana-related problems: the role of social avoidance. Addict. Behav. 2011 Jan-Feb; 36(1-2): 129-32 Epub 2010 Aug 25.
Patton G, Coffey C, Lynskey M, Reid S, Hemphill S, Carlin JB, Hall W, Trajectories of adolescent alcohol and cannabis use into young adulthood Addiction 2007:102(4): 607-615.

MENTAL ILLNESS:

The first paper to link cannabis with psychosis was published in 1845 by Moreau de la Tour, a French psychiatrist.

Jacques-Joseph Moreau (de Tours), Du Hachisch et de l'aliénation mentale, Éditions Fortin, Masson et Cie, Paris, 1845.

Psychosis:

Anyone using cannabis can experience a psychotic episode if they take enough of it on one occasion. They don't have to be regular users. 'THC can induce a transient acute psychotic reaction in psychiatrically well individuals' (Morrison et al 2009). Skunk users are nearly 7 times more likely to experience psychosis than hash users. (Di Forti et al 2009). There is an increase in the release of dopamine ('pleasure' neurotransmitter). People suffering from psychosis/schizophrenia have an excess of dopamine in their brains. On 8th October 2006, Professor Sir Robin Murray (London's Institute of Psychiatry) said, "Five years ago, 95% of psychiatrists would have said that cannabis doesn't cause psychosis. Now, I would estimate that 95% say it does. It's a quiet epidemic".

Morrison PD, Zois V, McKeown DA, Lee TD, Holt DW, Powell JF Kapur S, Murray RM. The acute effects of synthetic intravenous Delta- THC on psychosis, mood and cognitive functioning. Psychological Medicine doi:10.1017/S0033291709005522. 2009

Di Forti, Morgan C, Dazzan P, Pariante C et al, High –potency cannabis and the risk of psychosis. Brit J of Psychiatry 2009; 195: 488-491

Schizophrenia:

Arguably the most important publication on schizophrenia still remains the large study of Swedish conscripts by Andreasson, Allebeck et al in 1987.

Forty-five thousand conscripts had their drug-taking details taken at entry, aged 18 or 19. The levels of schizophrenia were recorded over 15 years. Those on admission who claim to have taken cannabis on more than 50 occasions were found to be 6 times more likely to be diagnosed with schizophrenia than those who had never consumed the drug. When confounding factors were taken into account, the risk became smaller but remained statistically significant. Although the study attracted some criticisms, Negrette, the doyen in this field judged the connection to be reasonable taking other previous studies into account, while accepting there were some weaknesses.

Andreasson in 1989 and Allebeck in 1993 strengthened their position by further research. They examined the medical records of 112 cannabis-dependent and schizophrenic patients. The findings in all significant respects confirmed the original study.

Scientists are now in general agreement that there probably is a genetic component in the development of schizophrenia. The COMT gene, carried by about 1 in 4 of us (Caspi 2005) may be responsible and more recently AKT1 (Van Winkel 2011) has been investigated.

Overall in many papers on the subject, cannabis users are twice as likely than non-users to develop schizophrenia.

Andreasson S, Allebeck P, Engstrom A, Rydberg U, Cannabis and Schizophrenia: A Longitudinal Study of Swedish Conscripts. Lancet 1987; 2:1483-6.

Allebeck P, Adamsson C, Engstrom A, Cannabis and Schizophrenia: A longitudinal Study of Cases Treated in Stockholm County. Acta Psychiatr Scand 1993; 88:21-4.

Andreasson S, Allebeck P, Rydberg U, Schizophrenia in Users and Non-users of Cannabis. Acta Psychiatr Scand 1989; 79: 505-10.

Caspi A, Moffitt T, Cannon M, McLay J, Murray R, Harrington H, Taylor A, Arsenault L, Williams B, Braithwaite A, **Poulton** R, Craig I, Moderation of the Effect of Adolescent-Onset Cannabis Use on Adult

-Psychosis by a Functional Polymorphism in the COMT Gene. Longitudinal Evidence of a Gene X Environment Interaction. Biol. Psychiatry 2005: 57: 1117-1127.
Van Winkel R, van Beveren NJ, Simons C, Kahn S, Linszen DH, van Os J, et al, AKT1 Moderation of Cannabis-induced Cognitive Alterations in Psychotic Disorder Neuropsychopharmacology 2011, July 20th doi: 10.1038/npp.2011.141 (Epub).

Psychological and physical addiction:

Both take place. One in 10 users will become addicted. In teenagers it's about 1 in 6.

THC replaces the neurotransmitter anandamide (Sanskrit word for 'bliss') in the brain so targets the same receptor sites. Production of anandamide starts to slow down as THC replaces it. When the consumption of THC is stopped, the receptor sites are left unfilled. Withdrawal symptoms occur till the brain recommences its production of anandamide. Cannabis dependence is much more similar to than different from other types of substance dependence, even with regard to withdrawal (Budney 2006).

Almost all addictive drugs stimulate a part of the brain, the mesolymbic dopamine system which is the Central nervous System's Reward Pathway. Cannabis receptors are found here. When stimulated, these receptors begin the cycle of reward which can lead people on to take more. This circuit is shared with animals. (Koob GF 1992).

As a result of these findings, cannabis dependence (but not yet "withdrawal conditions following cannabis use" due to continuing disagreement among researchers) was included as a diagnostic unit in the DSM IV (Diagnostic and Statistical Manual of Mental Disorders 1994) and ICD-10, WHO 1992.

A North American population study of 20,000 people reported that, of the 4.4% who abused cannabis, roughly 60% were dependent on it. That is about 2.6% of the population (Hall et al 1994) And in a letter to The Lancet in 1998 Hall and Solowij wrote that, of those who ever start using cannabis, 10% will become daily users and 20 to 30% will use it weekly.

Jan Ramstrom who wrote "Adverse Health Consequences of cannabis Use", A Survey of Scientific Studies published up to and including the autumn of 2003 said, "…there is now general agreement on the issue of cannabis and dependence including the importance of withdrawal symptoms". 'Cannabis use disorder' which included withdrawal symptoms appeared in the new DSM5 in 2013.

Experimental animals had brain changes similar to those resulting from opiate, alcohol and cocaine withdrawal (De Fonseca et al 1997).

Weekly use of cannabis marks the threshold for an increased risk of later cannabis dependency with selection of cannabis in preference to alcohol possibly indicating an early addiction process. 30% of teenagers smoking more than one a week became addicted by their early twenties, those between 14 and 17 were 20 times more likely. Those starting between 14 and 15 progressed to the most harmful use (Coffey 2003).

An article in The Ottawa Citizen on 24/11/06 reported that Psychiatrist Kathy Szirtes, speaking at a "Dazed and Confused" forum for teenagers in Rideau High School, said that

adults may take 2 years to become addicted to marijuana while children can take only about 6 months as their brains are still not properly developed. The risk-taking part of the brain develops before the inhibitory part so children are more likely to take a risk (Chambers 2003).

Dr Romeo Ashruf, a Dutch addiction specialist and Director of the Parnassia Clinic in The Hague, told Network 2's Bijous Theis TV programme on March 20th 2006 that Dutch children as young as 12 were addicted to cannabis. The powerful home-grown nederwiet they are using is up to 20 times stronger in its THC content than imported varieties. Referrals used to be for young people between 16 and 21, but are now for 14 to 19 year olds. He warned parents of the difference in strength of the drug today.

Vandrey et al compared withdrawal symptoms from cannabis and tobacco in a paper in January 2008. They concluded that, "Overall withdrawal severity associated with cannabis alone and tobacco alone was of a similar magnitude.

Budney AJ, Hughes JR, Moore BA, Vandrey R Review of the validity and significance of cannabis withdrawal syndrome American J of Psychiatry Nov. 2004; 161(11);1967-77.
Budney AJ, Hughes JR The Cannabis Withdrawal Syndrome Curr. Opin. Psychiatry 2006; 19:233-238.
Budney AJ Are specific dependence criteria necessary for different substances: how can research on cannabis inform this issue? Addiction 2006; 101 (suppl. 1): 125-133.
Budney AJ, Vandrey RG, Hughes JR, Moore BA, Bahrenburg B Oral delta-9-tetrahydrocannabinol suppresses cannabis withdrawal symptoms Drug and Alcohol Dependence 2006; in press Available online at www.sciencedirect.com
Koob GF Drugs of Abuse: anatomy, pharmacology and function of reward pathways.
Trends Pharm. Sci. 1992; 13: 177-184.
Hall W, Solowij N, Lemon J The Health and Psychological Consequences of Cannabis Use Canberra: Australian Government Publishing Services1994; pages 136-9
Hall W, Solowij N Adverse Effects of Cannabis Lancet 1998; 352: 1611-1616.
De Fonseca R, Carrera MRA, Navarro M, et al Activation of corticotrophin-releasing factor in the limbic system during cannabinoid withdrawal. Science 1997; 276: 2050-2054.
Coffey C, Carlin J, Lynskey M, Ning Li, Patton GC Adolescent Precursors of Cannabis Dependence: Findings from the Victorian Adolescent Health Cohort Study Br. J. Psychiatry 2003; 182: 330-336.
Chambers RA, Taylor JR, Potenza MN Developmental Neurocircuitry of Motivation in Adolescence: A Critical Period of Addiction Vulnerability Am. J. Psychiatry 2003; 160:1041-1052.
Vandrey RG, Budney AJ, Hughes JR, Liguori A, A within-subject comparison of withdrawal symptoms during abstinence from cannabis, tobacco, and both substances. Drug and Alcohol Dependence 2008; 92: 48-54.

Depression and suicides:

In Andreasson and Allbeck's study of 45,000 Swedish conscripts (1987,) exploring relationships between cannabis, schizophrenia and suicide, they concluded that the cannabis indirectly increases the risk of suicide as a result of its ability to precipitate, exacerbate and cause depression and psychosis. In other words, the increasing frequency of suicides in large-scale users was thought to reflect the increased frequency of depression in cannabis abusers.

Data from The US National longitudinal Alcohol Epidemiologic Survey indicated a diagnosis of cannabis use or dependency in the last year was associated with a 6.4 fold increased chance of receiving a diagnosis for major depression in that time (Grant 1995).
A review was conducted in 2004 by Rey and others. Their results were very similar. "There is growing evidence that early and regular marijuana use is associated with later increases in

depression, suicidal behaviour and psychotic illness, and may bring forward the onset of schizophrenia. Most of the recent data reject the view that marijuana is used to self-medicate psychotic or depressive symptoms".

Depression is thought to be caused by cannabis reducing serotonin ('happy' neurotransmitter) levels (Gobbi 2009). This can lead to violent suicides, users are 20 times more likely to jump to their deaths than non-users. (1995 Fugelstad et al)

Andreasson S, Allebeck P, Engstrom A, Rydberg U, Cannabis and Schizophrenia: A Longitudinal Study of Swedish Conscripts. Lancet 1987; 2:1483-6.
Grant BF Comorbidity between DSM-IV drug use disorders and major depression: results of a national survey of adults J of Substance Abuse 1995; 7: 481-97.
Rey J et al Is the party over? Cannabis and juvenile psychiatric disorder: The past 10 years
J of The Academy of Child and Adolescent Psychiatry 2004; 43: 1194-1205.
Gobbi G et al, Cannabis damages young brains more than originally thought Dec. 5, 2009, Neurobiology of Disease, online id=634359
Fugelstad A Gerhardsson de Verdier M Rajs J Cannabis-related deaths Stockholm Cannabis Conference; 1995.

VIOLENCE and AGGRESSION:

Arsenault in 2002 discovered that alcohol dependent individuals were almost twice, marijuana-dependents almost 4 times, and those suffering from schizophrenia spectrum disorder, two and a half times more likely than controls to be violent. A more recent investigation among 5,500 Dutch adolescents between 12 and 16, found that criminality and aggression increased with increasing use of cannabis (Monshouwer 2006). Violence is thought to be associated with the psychosis and/or withdrawal.

Arsenault L Cannon M Poulton R Murray R Caspi A Moffitt TE Cannabis use in adolescence and risk for adult psychosis: Longitudinal prospective study British Medical Journal 2002; 325: 1212-3.
Monshouwer K Van Dorsselaer S Verdurmen J et al Cannabis use and mental health in secondary school children: Findings from a Dutch survey. British Journal of Psychiatry 2006; 188: 148-53

A series of surveys by PRIDE (Parent Resources and Information on Drug Education USA) and ONDCP (Office of National Drug Control Policies) in 2006 added more evidence of the link between cannabis use and violence.

Of those students who reported carrying a gun to school during the 2005/6 school year, 63.9% had also used marijuana, 39.9% cocaine and 36.8% crystal meth in the past year. (PRIDE Surveys (2006) Questionnaire report for grades 6-12: 2006 National Summary 184).

Of those students who reported hurting others with a weapon at school, 68.4% had used marijuana, 48.3% cocaine and 44.1% crystal meth. in the past year. (PRIDE surveys 2006 etc 197).
Of those students who reported threatening someone with a knife, gun or club, or threatening to hit, slap or kick someone in the school year 2005/6, 27% had used marijuana, 7.8% cocaine and 6.2% crystal meth in the past year (PRIDE surveys (2006) etc 194).

During the school year 2005/6, 39.6% of those in trouble with the police used marijuana, 12.2% cocaine and 9% crystal meth in the past year (PRIDE surveys (2006) etc 195).

CARDIAC SYSTEM:

Blood pressure rises – heart attacks and strokes have been documented.

The risk of onset of myocardial infarction in rose by almost 5 times in the hour following the smoking of a joint. (Mittleman 2001).

Three teenagers, 15,16 and 17, who "binge smoked" cannabis suffered strokes, two died and one was left paralysed (Geller et al 2004). The risk for strokes is doubled in cannabis users, mostly male (84%) and tobacco smokers 88%). (Barber 2013).

All reported cases of presumed cannabis related cerebral ischaemic events in the medical literature, as well as pertinent human and animal experimental studies on the cardiovascular and cerebrovascular effects of cannabis were reviewed (Moussouttas 2004). His conclusion was "Cannabis use seems to have been causally related to several instances of cerebral ischaemia and infarction".

Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE, 2001 Triggering Myocardial Infarction by Marijuana Circulation:103 (23): 2805-9.
Geller T, Loftis L, Brink D, 2004 Cerebellar Infarction in Adolescent Males Associated with Acute Marijuana Use Pediatrics; 113: 365-70
Barber A, Smoking Pot May Raise Stroke Risk in Young Adults
Presentation February 2013 to The American Stroke Association annual meeting in Honolulu..
Moussouttas M, Jan 2004 Cannabis Use and Cerebrovascular Disease Neurologist 10(1): 47-53.

CANCERS:

Cancers of the lungs, head, neck, bladder and testes have been reported. Other lung diseases such as emphysema and bronchitis can occur.

Cannabis smoke contains more of some of the same carcinogens present in tobacco smoke (Marijuana and Health report).

A comparison of the carcinogenic effects of cannabis versus tobacco was carried out in New Zealand by Aldington January 2008. They found that the lung cancer risk of one marijuana joint a day equals that of a daily packet of cigarettes. For every one joint/day smoked for a year the risk factor rose 8%. This association was similar to the 7% risk seen for a pack/day for a year of tobacco smoking.

Cancers of the head, neck and throat have been reported in people with an average age of 26. They only occur in tobacco smokers with an average age over 60 (Donald 1993, Zhang 1999).
In patients who smoked tobacco and cannabis the risk was 36 times that of non-smokers.

An association has been found with testicular cancer. Current marijuana use was linked to an increase in the disease of 70% (Daling 2009). Bladder cancer, again only common in tobacco smokers over 60, has occurred in younger men between 44 and 60. A history of cannabis use was found in 88.5% of them.

In adults from 20 to 59 current marijuana use was defined as 100+ lifetime use and at least one day of use in the past month. Self-reported respiratory symptoms included chronic bronchitis, frequent phlegm and wheezing, shortness of breath, pneumonia and chest sounds in the absence of a cold (Moore 2004).

A connection between cannabis smoking and emphysema was described in a paper by Beshay in October 2007. Marijuana smokers face rapid lung destruction, approximately 20 years earlier than tobacco smokers. Bullous lung disease (bullae) is a condition where air trapped in the lungs causes an obstruction to breathing and eventual destruction of the lungs (Hii 2008).

Smoking marijuana and tobacco increases the risk of COPD (Chronic Obstructive Pulmonary Disease). People over 40 who used both tobacco and marijuana were almost 3 times more likely to suffer from COPD. The use of marijuana alone was not linked to this increase in risk. It appears that the marijuana may act as a kind of "primer" in the airways, augmenting the effects of tobacco (Tan WC 2009).

Marijuana and Health: Peterson RC, NIDA Res. Monogr. 1980;31:1-53.

Aldington S et al, Cannabis use and risk of lung cancer: a case-control study European Respiratory Journal 2008; 31: 280-6.

Donald PJ Marijuana and upper aero digestive tract malignancy in young patients in Nahas GG Latour C (eds) Cannabis: Physiology, Epidemiology, Detection. Ann Arbor CRC Press 165-183 1993.

Zhang ZF Morgenstern H Spitz MR Tashkin DP Yu GP Marshall JR Hsu TC Schantz SP Marijuana use and increased risk of squamous cell carcinoma of the head and neck Cancer Epidemiol. Biomarkers Prev. 8: 1071-1078 1999.

Daling JR, Doody DR, Sun X, Britton L,et al, Association of marijuana use and the incidence of testicular germ cell tumors Cancer: Early View, published online 9 Feb 2009. DOI: 10.1002/cncr24159

Moore BA, Augustson EM, Moser RP, Budney AJ Respiratory Effects of Marijuana and Tobacco Use in a US Sample J Gen Intern Med 2004; 20: 33-37.

Hii SW, Tam JDC, Thompson BR, Naughton M, Bullous lung disease due to marijuana Respirology Jan 2008; 13 (1): 122-7.

Tan WC, Lo C, Jong A, Xing L, FitzGerald MJ Vollmer WM, Buist SA, Sin DD, Marijuana and Chronic obstructive lung disease: a population-based study.CMAJ 2009; 180(8). doi: 10.1503/cmaj.081040.

THC AFFECTS FORMATION of DNA:

It causes early apoptosis (programmed cell death) of new cells being made in an adult body. Sperm numbers are reduced. This can cause impotence and infertility. White blood cells are fewer and some abnormal, lowering our ability to fight disease. Babies born to using mothers are smaller and have cognitive impairments (Nahas 1991).

Immune system:

Cabral wrote a review of the literature in 1999 in Marijuana and Medicine (Nahas and Latour eds). "Marijuana has been shown to decrease host resistance to bacterial, protozoan and viral infections in experimental animal models and in vitro systems. Recent immuno-epidemiological studies suggest that marijuana may also influence the outcome of viral infections in humans……Delta-9-THC alters the functioning of an array of immune cells including lymphocytes, natural killer cells and macrophages, thereby affecting their capacity to exert anti-microbial activities.

In a Columbian study in 1999 Dobson found a control group smoking a single marijuana cigarette every other day for a year had a white blood cell count 39% below the normal.

Pacifici and others in 2003 found cannabis smokers had fewer natural immune-enhancing killer cells and lymphocytes and higher levels of a protein that may promote tumour growth called interleukin-10. These changes can dampen the immune system's responses to infection, increasing susceptibility to infection and promoting tumour growth.

Apoptosis is the key mechanism programmed by the genetic code which regulates the life and death of a cell. It is the "programmed cell death" of all mammalian cells. Apoptosis relates to the destruction of the DNA formation by the cell itself. THC induces early apoptosis of the cells. Because of the long-term storage of THC in body fat, the "death signals" from the THC remain in the body and act on the cells for weeks. All new cells, white blood cells, sperm and foetal cells being made in an adult body can be affected (Nahas 1999) .

THC suppresses the immune system by massively expanding the number of myeloid-derived suppressor cells (MDSC) both in vivo and in vitro. These cells in the immune system have only recently been discovered. These cells have been known to increase in cancer patients so they may suppress the immune system against cancer chemotherapy, actually promoting cancer growth . The lead author, Dr Prakash Nagarkatti concluded, 'Marijuana cannabinoids present us with a double-edged sword. On one hand due to their immuno-suppressive nature, they can cause increased susceptibility to cancer and infections. However, further research of these compounds could provide opportunities to treat a large number of clinical disorders where suppressing the immune system is actually beneficial'. (Hegde 2010).

Nahas GG, Osserman EF Altered serum immunoglobulin concentration in chronic marijuana smokers Advances in Experimental Medicine and Biology 1991; 288: 25-32.
Dobson J "Marijuana can cause great harm" Washington Times 23rd February 1999.
Pacifici R, Zuccaro P, Pichini S et al Modulation of the Immune System in Cannabis Users JAMA 2003; 289:1929-31.
Nahas GG, Sutin KM, Harvey DJ, Agurell S, eds Marijuana and Medicine 1999 Humana Press Totowa, NJ.
Hegde VL, Nagarkatti M, Nagarkatti PS, Cannabinoid receptor activation leads to massive mobilization of myeloid-derived suppressor cells with potent immunosuppressive qualities European Journal of Immunology Vol 40 (12); 3358-3371 December 2010

Reproductive System:

Early apoptosis of sperm and developing foetal cells caused by THC takes place. Birth defects, impaired learning and memory, miscarriage, ADHD, neuroblastoma, delinquency and impulsivity have all been reported.

THC damages the formation of DNA in the dividing cells of testes and has been shown to impair the development of sperm cells in man. Marijuana or THC produces an early apoptosis of these fast-dividing cells (Nahas 2002). Fewer sperm are produced and infertility has been reported (Burkman 2003).

The risk of miscarriage or ectopic pregnancy in women smoking cannabis in the early stages of pregnancy was highlighted in research by Dey and others in 2006. THC by mimicking anandamide disrupts the correct signalling process. The embryos of mice treated with THC had more cell abnormalities than the controls and the embryos failed to travel to the uterus.

At the age of 10, over 500 children from a longitudinal study were tested for problem solving, learning, memory, mental flexibility, psychomotor speed, attention and impulsivity. Prenatal marijuana use had a deleterious effect on learning and memory as well as impulsivity (Richardson 2002).

Marijuana use increases the symptoms of ADHD in first grade children (6 year-olds). These children are more likely to show signs of this condition if their mothers smoked 6 or more marijuana cigarettes /week. (Fried 1992)

The offspring of heavier marijuana users were significantly more likely to report delinquent behaviour at age 14 (Day 2011), and prenatal exposure to marijuana with other factors is a significant predictor of marijuana use at 14 (Day 2006). Prenatal use is also associated with an increased risk of neuroblastoma (childhood cancer) in the offspring (Bluhm 2006).

The new high-potency marijuana can interfere with early brain development in developing foetuses.
'Some new high-potency strains, including some medicinal cannabis blends , contain up to 20 times more THC than did 'traditional marijuana from decades past'. Harmful effects can begin as early as 2 weeks from conception. Exposure to today's marijuana in early pregnancy is associated with anencephaly, a devastating birth defect in which infants are born with large parts of the brain or
skull missing. Early pre-natal use was also tied up with ADHD. learning disabilities, memory problems in toddlers and 10 year olds as well as depression, aggression and anxiety in the teens (Psychoyos 2012).

Birth defects from marijuana-using mothers were found to be associated with the CNS, cardiovascular system, oral clefts, limbs and the gastrointestinal system (Forrester and Merz 2007).

Nahas GG, Frick HC, Lattimer JK, Latour C, Harvey D, Pharmakinetics of THC in brain and testes, male gametotoxicity and premature apoptosis of spermatozoa. Hum Psychopharmacol. 2002 Mar; 17(2): 103-113.
Burkman L et al Sperm from Marijuana Smokers Move too Fast too Early, Impairing fertility, UB Research Shows. Annual Meeting Amer Soc of Reprod Med October 13 2003 San Antonio.
Dey S et al (Vanderbilt University Medical centre, Nashville) Journal of Clinical Investigation Aug. 2006.
Richardson GA, Ryan C, Willford J, Day NL, Goldscmidt L, Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. Neurotoxicol Teratol. 2002 May-June 24(3): 309-20**.**
Fried PA, Watkinson B, A Follow-up Study of Attentional Behaviour in Children Exposed Pre-natally to Marijuana, Cigarettes and Alcohol. Neurotoxicology and Teratology 1992; 14: 299-311
Day NL, Goldschmidt, Lidush, Thomas, Carrie Prenatal marijuana exposure contributes to the prediction of marijuana use at age 14. Addiction Sept 2006; 101(9): 1313-22.
Day NL, Leech SL, Goldschmidt L, The effects of prenatal marijuana exposure on delinquent behaviours are mediated by measures of neurocognitive functioning. Neurotoxicol Teratol. 2011 Jan-Feb; 33(1): 129-36.
Bluhm EC, Pollock BH, Olshan AF, Maternal use of recreational drugs and neuroblastoma in offspring: a report from the Children's Oncology Group (United States). Cancer Causes Control 2006 Jun: 17(5); 663-9.
Psychoyos D, Vinod YK, (2012) Marijuana, Spice 'herbal high', and early neural development: implications for rescheduling and legalization Drug Test Analysis. Doi:10.1002/dta.1390 August 2012
Forrester MB, Merz RD, Risk of Selected Birth Defects with Prenatal Illicit Drug Use, Hawaii, 1986-2002. Journal of Toxicology and Environmental Health Part A, Vol 70(1) Dec 2007:7-18.

BRAIN SCANS:

Brain scans have shown reduced volume in several areas of the brain, which may/may not be permanent.

Adolescent brain development particularly in the hippocampus was investigated. Cannabis users showed significantly smaller volumes of the right and left hippocampus compared to controls. (2011 Feb Ashtari).

A lower volume in the right hippocampus in chronic cannabis users was corroborated. Higher THC and lower CBD was associated with this volume reduction indicating neurotoxic effects of THC and neuroprotective effects of CBD. This confirms existing pre-clinical and clinical results. As a possible mechanism the influence of cannabinoids on hippocampal neurogenesis is suggested. (2011 Demirakca)

Long-term cannabis use in healthy individuals is associated with smaller cerebellar white-matter volume similar to that observed in schizophrenia. Reduced volumes were even more pronounced in patients with schizophrenia who use cannabis. Cannabis use may alter the course of brain maturational processes associated with schizophrenia' (Solowij 2011).

Imaging scans show that chronic daily use of marijuana can have a detrimental effect on the brain. There is a decrease in the number of receptors involved in a variety of important mental and bodily functions, including pleasure, pain tolerance, movement coordination, memory, appetite and concentration. CB1 receptors had decreased by around 20% compared to those of the healthy controls who had limited lifetime exposure to cannabis. After a month of abstinence, 14 were re-scanned and the number of receptors were found to have notably increased, suggesting the effects may be reversible. (2011 Jussi Hirvonen)

Cannabis use impacts on brain thalamic volumes in people at familial risk of schizophrenia. MRI scans were obtained at point of entry to the study and approximately 2 years later. It was concluded that there was a significant volume loss bilaterally in the thalamus, more highly significant on the
right. These losses remained significant when individuals using other drugs were removed from the analysis (Welch 2011).

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DRIVING:

Driving is affected for at least 24 hours and increases the accident risk. Combining alcohol and cannabis is 16 times more dangerous. AND an overdose of alcohol may kill but people are often sick. THC inhibits the vomit reflex.

Using more modern techniques for blood analysis an ever-stronger link between cannabis consumption before or during driving and an increased risk of accidents than previously thought was found. Drivers under the influence were 3 to 7 times more likely to be the cause of accidents in which they were involved. (Ramaekers et 2004).

Nearly 11,000 fatal car crashes between 2001 and 2003 were investigated. Nearly 7,000 drivers were held to be responsible for the accident. The controls were around 3000 of the other drivers. Taking into account the age of the vehicle and age of driver, the researchers concluded that cannabis caused a significant number of the fatalities. 7% tested positive for cannabis and 21.4% for alcohol. Cannabis was deemed directly responsible for 2.5% and alcohol 29% of the crashes. A combination of cannabis and alcohol was held to be 16 times more risky than either drug alone. (Laumon 2005).

Drivers who had taken 20 milligrams of THC - a very low dose (A single one-gram cigarette today can contain anything up to 200 milligrams) . showed a significant deterioration in driving ability, especially keeping the car steady in the middle of a lane and a constant distance from the verge. Comparing the 20mg cannabis dose to a blood alcohol level of 1g/litre of blood (just over the legal limit) in identical studies, the results were very close as regards the deterioration in each variable. (Robbe 1994).

The ability to drive safely is inhibited for more than 24 hours after a joint. In a well-publicised study using a dose of 20 milligrams THC, airline pilots in a double-blind experiment on simulators, it was found that the performance was worse in all aspects of flying, even up to and beyond 24 hours after consumption. The pilots were totally unaware of a problem (Leirer 1991).
Someone smoking a joint today should not be driving/flying tomorrow.

Medical marijuana has a great deal to answer for!

A study was carried out into traffic deaths in California following marijuana use. It was found that the largest increase in fatalities in fatal crashes where the driver tested positive for marijuana occurred over the 5 years following the establishment of the medical marijuana programme in January 2004. There were 1240 fatalities under these circumstances for the 5 years compared to 631

fatalities for the 5 years before, an increase of almost 100%. He suggested that the TC2010 (Regulate, Control and Tax Cannabis Act) initiative might triple the number of marijuana-related deaths on California's highways (Crancer 2010).

An analysis of the 2003 Monitoring the Future and Census Bureau data in the USA showed the following results: Out of nearly 4 million high school seniors in America, it was estimated that approximately one in six i.e. 600,000 drove under the influence of marijuana, nearly the

same as for alcohol, 640,000. An estimated 38,000 reported they had crashed while under its influence in 2001, 46,000 while affected by alcohol.

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GATEWAY DRUG?

Evidence from longitudinal studies from birth and experiments on animals in Sweden point in this direction.

30,000 French adolescents showed occasional users 21 and daily users 124 times more likely to progress to other drugs (Mayet 2012).

There appears to be a series of graded steps that is followed. There were four: 1.Beer and wine 2.Cigarettes and spirits 3. Marijuana 4. Other illegal drugs (Kandel, 1989).

The younger they started, the further they progressed and the more intense the abuse at any age the greater the risk of progression to the next stage. Of those who had used cannabis more than 1000 times, 90% moved on to other drugs. Between 100 and 1000 it was 79%, dropping to 51% between 10 and 100 times. Even 1 to 9 times usage saw 16% follow this path. Of non-users, only 6% eventually used drugs other than cannabis. (Kandel, 1986).

Kleber (1995) said that 60% of young Americans using marijuana before the age of 15 will use cocaine later in life, and those between 12 and 17 who use cannabis are 85 times more likely to use cocaine than non-smokers of the same age.

The Christchurch Longitudinal Study concluded, "The use of cannabis in late adolescence and early adulthood emerged as the strongest risk factor for later involvement in other illicit drug use" (Fergusson 2008).

Chronic periodic use of cannabis can interfere with the development of rat brains. Rats trained to self-administer heroin by pushing a lever and exposed to THC, took more heroin than those not previously exposed to it. They were more sensitive to lower concentrations of heroin and took more in response to stress. Her conclusion reads: The current findings support the gateway hypothesis demonstrating that adolescence cannabis exposure has an enduring impact on hedonic processing resulting in enhanced opiate intake, possibly as a consequence of alterations in limbic opioid neuronal populations". (Yasmin Hurd 2006).

Over 29,000 adolescent French teenagers were studied. All possible pathways were modelled from initial abstinence to cannabis initiation, daily cannabis use and OID (other illicit drugs) initiation.

The model was adjusted for tobacco and alcohol use. The risk for OID initiation was 21 times more with experimenters, 124 times higher among daily users than non-users. Tobacco and alcohol were associated with a greater risk of moving on to cannabis (Mayet 2012)

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MEDICAL CANNABIS is a scam!

The clamour for medical cannabis goes back a long way and has much more to do with self-interest than any empathy with people who are ill. It is emotional blackmail and unfortunately too many people are being hoodwinked.

In 1979, Keith Stroup, an American lawyer and founder of NORML (National Organisation for Reform of Marijuana Laws) said at Emory University, "We will use the medical marijuana argument as a red herring on the road to full legalisation". His successor, Richie Cowan, at a 1993 conference celebrating the 50th anniversary of the discovery of LSD said, "Medical marijuana is our strongest suit. It is our point of leverage which will move us towards the legalisation of marijuana for personal use". This is how it all started.

To be licensed as medicines, substances have to be single pure chemicals, so that their effects are predictable and controllable. Pure heroin and cocaine are in this category. Cannabis contains around 400 chemicals, rising to 2000 when smoked. Some are carcinogenic and the effects of others are unknown. Single substances would have to be extracted, purified and undergo clinical testing on animals and humans. This will take years and is correct procedure.

Synthetic THC (tetrahydrocannabinol – psychoactive - gives the 'high') has been licensed as a medicine to counteract the nausea from chemotherapy and stimulate appetite in AIDS patients for nearly 30 years as Nabilone in the UK, Marinol and Dronabinol in the USA. It is unpopular with doctors due to its side-effects. The warning on Marinol states: THC causes mood changes, loss of memory, psychosis, impairment of coordination and perception, and complicates pregnancy.

Sativex, a mixture of THC and CBD (cannabidiol), purified extracts of the cannabis plant, has undergone trials in the UK by GW Pharmaceuticals. It was licensed for use in Canada in 2005 and in the UK in June 2010. However its effectiveness is being questioned and some Health Authorities (e.g. Midlands) are refusing to sanction its provision for this reason and because of cost. CBD alone is being investigated for its medical properties.

Bedrocan (which CLEAR is promoting) is a branded form of herbal cannabis and NOT a purified extract. Bedrocan and Bediol are two of the four varieties of medicinal cannabis available from the Dutch Government's official producer. The THC level in Bedrocan is a constant 19% and CBD 1%.

Penicillin is present in the Penicillium mould common on stale bread. No-one would want to eat mouldy bread to get their penicillin. Or for that matter, chew willow bark for aspirin.

Advocating the use of cannabis to get pain relief or reduce the pressure in the eye caused by glaucoma would require taking cannabis every 3-4 hours. This would render them incapable of driving or indeed doing anything productive. And a large British study of multiple sclerosis found that cannabis failed to slow its progression in patients (MRC funded study May 2013). 'There is no scientific study establishing that marijuana is effective as a medicine' said Robert Bonner, former administrator of the DEA (Drug Enforcement Agency) in The United States.

Almost all marijuana cardholders claim they need it for various kinds of pain, but pain is easy to fake and almost impossible to disprove. In Oregon and Colorado, 94 percent of cardholders get their pot for pain. In

Arizona, it's 90 percent. Serious illnesses barely register. States with medical marijuana laws have always had much higher rates of teenage marijuana use but now the effect is nationwide. Since 2008, teenage use has increased 40 percent, and heavy use (at least 20 times a month) is up 80 percent. (Dr Ed Gogek, addiction psychiatrist, NY Times 12/11/2012).

The USA Monitoring The Future Report in 2013 found that 6.5% of current high school seniors are using marijuana daily compared to just 2.3% in 1993 – a 300% rise in 20 years. THC persists for weeks in the fatty brain cells so that is 6.5% of future adult Americans who will never achieve their full potential. The normal chemical signalling between the brain cells is impaired.

In the UK from 2012 to 2013, 13,581 young people presented to specialist services with cannabis as their primary substance (68% of all young people receiving help during the year), up from 13,200 in 2011 to 2012 (Public Health England December 2013).

The percentage of USA 12th grade students who perceive a great risk of harm, physical or mental, from regular marijuana use has dropped from nearly 80% in 1991 to 40% in 2013 (Cesar Fox 2013). Children with their immature brains think 'They wouldn't have legalised it if it was so harmful' and 'It must be safe, it's a medicine'.

From 1st January 2005 to December 31st 2011, at a hospital for children in Colorado where medical marijuana was permitted in 2009, a total of 1378 patients younger than 12 years were evaluated for unintentional ingestion: 790 patients before September 30, 2009, and 588 patients after October 1, 2009.

The results showed that the proportion of ingestion visits in patients younger than 12 years (age range, 8 months to 12 years) that were related to marijuana exposure increased after September 30, 2009, from 0 of 790 to 14 of 588. Nine patients had lethargy, 1 had ataxia, and 1 had respiratory insufficiency. Eight patients were admitted, 2 to the intensive care unit. Eight of the 14 cases involved medical marijuana, and 7 of these exposures were from food products.

When I gave evidence to the HASC, I said that skunk, average 16.2% THC, now 80% of the UK market, was a vastly different drug from the old herbal cannabis of the 60s and 70s with around 1-2% THC (unavailable now) – a fact completely ignored by FRANK, wrongly telling people that skunk is about twice as strong as old herbal. Hash (resin, the other 20%) has average 6% THC. CBD, thought to be antipsychotic, was present in equal amounts to THC and helped to counteract its effects in the old cannabis. There is only 0.1% in today's skunk.

Hash and skunk can cause psychosis which can make a person violent and aggressive even homicidal as levels of brain dopamine rise, damage young developing brains, lower IQ permanently, cause depression which may lead to suicides, badly affect the immune, cardiac and reproductive systems, can act as a gateway drug to other drugs, and are responsible for various cancers. Drivers on cannabis double their chance of an accident. If they have also drunk alcohol, the risk goes up by 16 times. In Washington USA, incidents of impaired driving rose from -4.6% in 2011-12 to +50.8% in 2012-13 after legalisation. Psychological and/or physical dependence will occur in about 9-10% of users, 1 in 6 in the case of teenagers. Personalities change – they have fixed answers to questions, can't find words and can't plan their day or reason things out.

It is madness to think that children can be protected from medical marijuana. Age limits for tobacco and alcohol have failed miserably. Youngsters have always managed to get cannabis - medical marijuana would simply make it easier. As adults, we have a duty of care to protect all children against any kind of harm.

MARIJUANA IS NOT MEDICINE!

Mary Brett, former Teacher of Biology and Head of Health Education for 30 years at Dr Challoner's Grammar School (boys) Amersham, Bucks, member of WFAD (World Federation Against Drugs), former Vice President of EURAD (Europe Against Drugs) and chair of CanSS (Cannabis Skunk Sense, www.cannabisskunksense.co.uk